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**Editorial**

# Editorial Health Loses more than it Gains from Devolution

**Dr. Mohsin Masud Jan**
Editor

The initial euphoria marking devolution has receded, clearing the way for an analysis of the losses and gains accruing from a decision that was generally hailed in the interest of provincial autonomy.

One year on, it has become evident that the devolution of the Ministry of Health has fragmented health. What did devolution do to health? To begin with, it made Pakistan the only federal country in the world without a federal health institution. Despite its many weaknesses, the pre-18th Amendment Ministry of Health played an important role in numerous areas that should have been retained at the federal level, as practiced in most federating countries. Rather than establishing a re-cast federal structure for health to serve key national functions, all departments that were previously functioning under the umbrella of the Ministry of Health are now lying helter skelter under various ministries, divisions and departments.

The task of national planning and coordination (with provinces and international development partners) has been assigned to the Planning and Development Division. The Economic Affairs Division is handling dealings and agreements with other countries and international organizations in the fields of health, drug, and medical facilities abroad, as well as scholarships and training courses in health from international agencies such as WHO and Unicef.

Responsibilities related to international aspects of medical facilities and public health; international health regulations; port health; and health and medical facilities abroad have been assigned to the National Regulations and Services Division, which is also handling national associations in medical and allied fields such as the Red Crescent Society and TB Association. Institutions such as Pakistan Medical and Dental Council, Pakistan Nursing Council, College of Physicians and Surgeons, National Council for Tibb, Pharmacy Council of Pakistan, Drug Regulatory Agency of Pakistan, and Directorate of Central Health Establishment-Karachi have all been placed under the National Regulations and Services Division.

Similarly, the Directorate of Malaria Control has been placed under the Inter-Provincial Coordination Division while the National Health Information Resource Centre has been merged with the National Institute of Health and the Tobacco Control Cell with the Health Services Academy. Vital health statistics has been placed under the Federal Bureau of Statistics.

While some medical institutions have been devolved, the Cabinet Division has assumed administrative control of others. Medical and health services for federal government employees, as well as the administrative control of some of national institutes, have been placed under the Capital Administration and Development Division. The States and Frontier Region Division has been tasked with coordinating medical arrangements and health delivery systems for Afghan refugees.

Other health domains that have been devolved include several vertical health programmes, lunacy and mental deficiency, and prevention of the extension from one province to another, of infectious and contagious diseases. Legislation pertaining to drugs and medicines are a joint responsibility of the drug regulatory agency and the National Regulations and Services Division. Moving on to medical, nursing, dental, pharmaceutical, paramedical and allied subjects, education norms have been devolved except to the extent of federal areas. However, educational facilities for backward areas and for foreign nationals, with some exceptions fall under the IPC Division.

It is pertinent to recall that in May 2011, Heartfile published a report titled '18th Amendment: retaining national roles in devolution.' The report offered valuable and timely insight about national roles in health, offering strong justifications for retaining this national role. It identified four national subjects in health namely, health information, inclusive of research in health; health regulation; international commitments; and national health policy, with respect to federal mandates in health, overarching norms, norms of care, inter-sectoral action, trade in health, health technology and disaster response. "It is also a national responsibility to ensure policy coordination, and support provinces with weak capacity," it pointed out.

The report pointed out: "despite extensive changes by the 18th Amendment, the Constitution still provides space for national functions and a federal role in health." On the matter of the abolition of the Ministry of Health, it stated: "the proposition of abolishing the Ministry of Health is not a matter defined in the 18th Amendment but interpretation of the same Amendment. The Constitution did not at any time-before or after the 18th Amendment-include health per se, as a specific legislative subject. A federal institutional structure to serve national health responsibilities and within that

context, reform of the Ministry of Health to make it compatible with devolution is an imperative."

The report recommended the establishment of a Health Division as the preferred option. It proposed that unlike the Ministry of Health, which was never structured properly for national functions, and as a consequence, never had the full range of capacities, the new federal structure should have adequate capacity.

In the report, Dr. Sania also published an analysis which looked at the five options with respect to the way forward-i) status quo, i.e., the Ministry of Health stays as it is; ii) abolishing the Ministry of Health and giving its functions to other federal entities; iii) creation of a Health Commission; iv) retaining the Ministry of Health as such, but scaling back is role; or v) recasting the Ministry and scaling it down as a Health Division. A summary evaluation of each option was given using nine evaluation criteria. Unfortunately, the cut-and-chop formula that scored the lowest was selected by the government as the preferred option. Before the ill-effects of this fragmentation reach a point of no return, it is time steps are instituted to rectify the post-devolution chaos in health.

Original Article

# Association of Hepatitis (B, C & D) Viral Infection to Gallstones in Cirrhosis of Liver

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## ABSTRACT

**Objective:** To observe the association between hepatitis viral (B, C & D) infection to gallstones in liver cirrhosis.
**Study Design:** A cross-sectional and hospital based study.
**Place and Duration of Study:** This study was carried out at the Hepatology Clinic of CMC, Larkana during January 2011 to December 2011.
**Materials and Methods:** 913 patients of cirrhosis of liver presenting at Hepatology Clinic of CMC, Larkana during January 2011 to December 2011 were enrolled for study. After informed written consent, blood samples were drawn for HBsAg, anti – HCV antibodies, and anti-HDV Antibodies by ELISA. Ultrasound of all cases was performed to detect gallstones and study the related radiological features. The data was transferred and analyze using SPSS version 17. Means of numeric response variables and categorical response variables were compared by chi-square test and odd ratios calculated when and where applicable. P value less than 0.05 was taken as statistically significant.
**Results:** HBsAg, Anti-HCV Ab and Anti-HDV Ab were documented in 272 (42.2%), 253 (39.3%) and 178 (27.6%) patients respectively. HCV co infection with HBV and HDV was documented in 56 (8.7%) and 44 (6.8%). Gallstones were detected in 269 (29.5%) cirrhotic patients, of these 136 (14.9%) were multiple. Statistically significant association was observe between gallstones and HBsAg seropositivity with odd of 2.17 (95% CI: 1.62 – 2.90) and p value less than 0.001. There was no statistically significant association between Anti-HCV Ab and Anti-HDV Ab seropositivity with gallstones in cirrhosis of liver.
**Conclusion:** HBV infection is documented more frequently in cirrhosis with gallstone. Female were more likely to be infected. HBV infection may be one of the risk factor for development of gallstones in cirrhosis of liver.
**Key Words:** HBsAg, HDV, HCV, Association, Gallstones.

## INTRODUCTION

Worldwide 7% male and 15% females between the ages of 18- 65 years develop gallstones (GS), with overall prevalence of 11%.[1] In Pakistan, 10 – 15% normal healthy population harbours GS, as compared to 23.3 to 31% patients of liver cirrhosis.[2,3,4] The well established risk factors for development of GS are age, sex, obesity, drugs and pregnancy. Recent studies have documented that, liver cirrhosis is also a substantial risk factor for development of gallstones, especially in male.[5,6,7] Gallstones (GS) in cirrhosis are usually asymptomatic and surgery is rarely required but, when surgery is required, these patients carry a higher risk of morbidity than the general population undergoing cholecystectomy.[8]

The pathogenesis of GS in liver cirrhosis may be multifactorial.[9,10] This may be due to high level of estrogen impairing the emptying seen in cirrhosis.[11] Chronic hemolysis secondary to hypersplenism and hyperestrogenism leading to changes in the proportion of biliary lipids, reduction in hepatic synthesis and transport of bile salts and unconjugated bilirubin leading to an impaired binding and polymerization of calcium ions, could in part explain the higher GS frequency in cirrhosis. Gall bladder dysmotility and abnormal contraction due gallbladder wall thickness may encourage GS formation in cirrhosis.[12,13,14]

Another possible explanation of increased GS frequency is persisting infection with viral hepatitis especially HCV. Stroffolini T et al., reported that gallstones were seen in 23.3% anti-HCV positive and 12.4% HBsAg positive patients.[15]HCV can successfully infect gall bladder epithelial cell, it may potentially impair or alter gall bladder mucosal function and contribute to the development of GS.[16] HCV binds to lipoproteins and induce fatty changes of liver. Bile duct damage and hepatic bile duct damage and hepatic steatosis have been cited as histological features of chronic HCV infection both HCV antigens and HCV have been detected in biliary and gallbladder epithelium in patients with chronic HCV infection that correlates with biliary damage and gall stone formation.[17,18,19,20]

Therefore we intend to observe the frequency and association of GS with chronic viral hepatitis in cirrhotic patients. This study will not only inform us regarding the magnitude of disease in cirrhotic patients, but also enable us to understand the association with viral hepatitis.

## MATERIALS AND METHODS

**Design:** A cross-sectional and hospital based study was designed.
**Duration:** The study duration was one year. Started in January 2011 till December 2011.

**Setting:** The cases were enrolled from the weekly hepatology clinic and wards of Medicine Department, Chandka Medical College (C.M.C), Larkana at Shaheed Mohtarma Benazir Bhutto Medical University.

**Sampling Technique:** Purposive sampling.

**Inclusion Criteria:**

- All known diagnosed cases of cirrhosis of liver presenting to hepatology clinic and wards of medicine.
- Of either gender.

**Exclusion Criteria:**

- Patients younger than 15 years and older than 75 years.
- Patients receiving antiviral injectable or oral therapy for hepatitis B, C or D.
- Patients suffering from congenital or familial biliary or hepatic disorders.
- Uses of oral contraceptives,
- Drugs like ceftriaxone, octeriotide, somatostatin and clofibrate.
- History of multiple pregnancies.
- Obesity.
- Suffering from chronic hemolytic disorders.
- Diabetes mellitus.

**Data Collection:** Informed written consent was taken from patients meeting our selection criteria. Detailed clinical examination was conducted to document ascites, hepatic encephalopathy and spleenic status. Spleen was labeled was labeled to be enlarged if it was clinically palpable or pecussable. Blood samples were drawn and sent to central laboratory C.M.C Larkana for detection of viral serology and biochemical indices as HBsAg, Hepatitis C Virus antibodies (Anti-HCV Ab) and Hepatitis D Virus antibodies (anti-HDV Ab) on 3rd generation ELISA, serum bilirubin, serum albumin and international normalized ratio (INR). LFTs were performed by Slectra – E Merck (Germany) auto-analyzing machine.

Abdominal ultrasound (US) of all selected patients were done for gallstones, spleen size, liver parechymal change, portal vein (PV) size, common bile duct (CBD) diameter and gall bladder wall thickness. Ultrasonological examination was done by a senior radiologist with more than 10 years experience, at the Radiology Department C.M.C Teaching Hospital. Toshiba SSA-70 U/S machine was used to carry out U/S examination. A separate Performa was filled for each case entered into the study to record the data of these investigations and demography. All investigations were performed at the laboratory of CMC teaching hospital.

**Data Analysis:** The collected data was transferred to and analyzed using SPSS version 17. Numeric response variables as age, portal vein diameter, common bile duct diameter and gall bladder wall thickness and categorical response variables such as age (15 – 24 years, 25 – 34 years, 35 – 44 years, 45 – 54 years, 55 – 64 years, 65 – 74 years), gender (male, female), portal vein diameter (normal < 12 mm, dilated > 12mm), common bile duct diameter (CBDD < 4 mms, CBDD > 4 mms), gall bladder wall thickness (GBWT < 6cms, GBWT > 6 cms), gall stones (none, solitary, multiple), splenomegaly (none, mild, moderate, massive) ascites (present, absent) and CTP classes (A, B, C) were compared in gall stones positive and negative cases by Chi-square test. Odd ratios (OR) and 95% Confidence Interval (CI) were calculated to assess the association of variables and viral hepatitis with presence of gallstones in cirrhotic patients. Probability value (p-value) of less than 0.05 (<0.05) was considered to be statistically significant.

# RESULTS

A total of 913 cases of liver cirrhosis were enrolled in our study during the specified period with mean age of 43.92 ± 16.24 years. Majority (n = 646, 70.8%) were male. HBsAg, Anti-HCV Ab and Anti-HDV Ab were documented in 272 (42.2%), 253 (39.3%) and 178 (27.6%) patients respectively. Co-infection of HCV with HDV and HBV with HCV was documented in 44 (6.8%) and 56 (8.7%) as shown in table 1. Gallstones were detected in 269 (29.5%) cirrhotic patients, of these 136 (14.9%) were multiple. Gall bladder wall was thickened in 286 (31.3%) patients of liver cirrhosis. (Table 2)

**Table No. 1: Baseline Characteristics of 913 CLD Patients**

| Characteristics | Number | Percentage |
|---|---|---|
| **AGE** | | |
| Mean ± SD | 43.92 ± 16.24 years | |
| Range (Max – Min) | 59 (74 – 15) | |
| **GENDER** | | |
| Male | 646 | 70.8% |
| Female | 267 | 29.2% |
| **AGE CATEGORIES** | | |
| 15 – 24 years | 121 | 13.3% |
| 25 – 34 years | 116 | 12.7% |
| 35 – 44 years | 250 | 27.4% |
| 45 – 54 years | 139 | 15.2% |
| 55 – 64 years | 153 | 16.8% |
| 65 – 74 years | 134 | 14.7% |
| **CHILD TURCOT PUGH (CTP) CLASS** | | |
| CTP CLASS A | 242 | 26.5% |
| CTP CLASS B | 287 | 31.4% |
| CTP CLASS C | 384 | 42.1 % |
| **VIRAL HEPATITIS SEROLOGY** | | |
| HBV | 272 | 42.2% |
| HCV | 253 | 39.3% |
| HDV | 178 | 27.6% |
| HBV & HCV | 56 | 8.7% |
| HCV & HDV | 44 | 6.8% |

**Table No. 2: Radiological Features of 913 CLD Patients**

| Characteristics | Number | Percentage |
|---|---|---|
| **SPLEENOMEGALY** | | |
| Mild | 533 | 58.4% |
| Moderate | 189 | 20.7% |
| Massive | 78 | 8.5% |
| None | 113 | 12.4% |
| **ASCITIES** | | |
| Present | 700 | 76.7% |
| Absent | 213 | 23.3% |
| **GALLSTONES** | | |
| Absent | 644 | 70.5% |
| Present | 269 | 29.5% |
| Solitary | 133 | 14.6% |
| **PORTAL VEIN DIAMETER** | | |
| Mean ± SD | 13.91+2.52mm | |
| Normal | 236 | 25.8% |
| Dilated | 677 | 74.2% |
| **GALL BLADDER WALL THICKNESS (GBWT)** | | |
| Mean ± SD | 5.45+2.11mm | |
| GBWT > 6 mm | 286 | 31.3% |
| GBWT ≤ 6 mm | 627 | 68.7% |
| **COMMON BILE DUCT DIAMETER (CBDD)** | | |
| Mean ± SD | 4.18+0.72 | |
| CBDD > 4 mm | 291 | 31.9% |
| CBDD ≤ 4 mm | 622 | 68.1% |

Patients having gallstones were older than those having no gallstones, with mean age of 49.92 ± 17.35 years as compared to 41.42 ± 15.08 years. Female were more likely to have gallstones with p value < 0.002. Gallstones were more frequently detected in patients aging 65 – 74 years (p < 0.001) with odds of 3.43 (95% CI: 2.35 – 4.99). Patients with gallstones were more likely to have advanced liver disease and were more likely to be in CTP class C (p < 0.001) with odds of 5.17 (95% CI: 3.79 – 7.04) as mentioned in table 3. Patients with gallstones had statistically significant thickened gall bladder wall (p < 0.001) with odds of 4.48 (95% CI: 3.30 – 6.08). (Table 4)

Statistically significant association was observe between gallstones and HBsAg seropositivity with odd of 2.17 (95% CI: 1.62 – 2.90) and p value less than 0.001. The association was also statistically significant for HBV co-infection with HDV and HCV. There was no statistically significant association between Anti-HCV Ab and Anti-HDV Ab co-infection with Anti-HCV Ab seropositivity with gallstones in cirrhosis of liver as tabulated in table 5.

# DISCUSSION

Gallstones (GS) is a common problem and is commonly attributed to "4F" (Female, Forty, Fertile, and Fatty). Our study bring light to an other "F", that is Fibrosis (liver fibrosis / cirrhosis). Our study documented that high percent of patients of liver cirrhosism had gallstones. GS were more frequently seen with aging and detoriating hepatic function. Besides, females were more likely to have stones than males. When we evaluated the serology of patients, it was noted that no statistically significant association was documented between GS and HCV. But the association was significant for HBV, whether it was present in isolation or with HCV and HDV.

**Table No. 3: Comparison of Baseline Characteristics of CLD Patients with and without Gall Stones**

| CHARACTER | GALLSTONES (N = 269) | NO GALLSTONES (N = 644) | P value* | ODD RATIOS OR (95%CI) |
|---|---|---|---|---|
| **AGE** | | | | |
| Mean ± SD | 49.92 ± 17.35 | 41.42 ± 15.08 | < 0.001** | NA |
| **GENDER** | | | | |
| MALE | 171 (63.6%) | 475 (73.8%) | < 0.002** | 0.62 (0.45 – 0.84) |
| FEMALE | 98 (36.4%) | 169 (26.2%) | | |
| **AGE CATEGORIES** | | | | |
| 15 – 24 years | 31 (11.5%) | 90 (14.0%) | < 0.319 | 0.80 (0.51 – 1.23) |
| 25 – 34 years | 18 (6.70%) | 98 (15.2%) | < 0.001** | 0.40 (0.23 – 0.67) |
| 35 – 44 years | 62 (23.0%) | 188 (29.2%) | < 0.058 | 0.72 (0.52 – 1.01) |
| 45 – 54 years | 35 (13.0%) | 104 (16.1%) | < 0.229 | 0.77 (0.51 – 1.17) |
| 55 – 64 years | 51 (19.0%) | 102 (15.8%) | < 0.250 | 1.24 (0.85 – 1.80) |
| 65 – 74 years | 72 (26.8%) | 62 (9.60%) | < 0.001** | 3.43 (2.35 – 4.99)+ |
| **CHILD TURCOT PUGH (CTP) CLASS** | | | | |
| CTP CLASS A | 28 (10.4%) | 214 (33.2%) | < 0.001** | 1.38 (1.28 – 1.48)+ |
| CTP CLASS B | 54 (20.1%) | 233 (36.2%) | < 0.001** | 1.23 (1.14 – 1.33)+ |
| CTP CLASS C | 187 (69.5%) | 197 (30.6%) | < 0.001** | 5.17 (3.79 – 7.04)+ |

*Chi – square test (2 - sided significance). ** Statistically Significant p values (p < 0.05).
+ Statistically significant high odd ratios. NA (Not Applicable)

**Table No. 4: Radiological Comparison of CLD Patients with and without Gallstones**

| CHARACTER | GALLSTONES (N = 269) | NO GALLSTONES (N = 644) | P value* | ODD RATIOS OR (95%CI) |
|---|---|---|---|---|
| **SPLEENOMEGALY** | | | | |
| YES | 218 (81.0%) | 582 (90.4%) | < 0.001** | 1.32 (1.11 – 1.57) |
| NO | 51 (19.0%) | 62 (9.60%) | | |
| **ASCITES** | | | | |
| PRESENT | 221 (82.2%) | 479 (74.4%) | < 0.011** | 1.58 (1.10 – 2.27)+ |
| ABSENT | 48 (17.8%) | 165 (25.6%) | | |
| **GALLSTONES** | | | | |
| SOLITARY | 133 (49.4%) | 0 (0.00%) | < 0.001** | 5.73 (4.92 – 6.68)+ |
| MULTIPLE | 136 (50.6%) | 0 (0.00%) | < 0.001** | 5.84 (5.00 – 6.82)+ |
| **PORTAL VEIN** | | | | |
| Mean ± SD | 14.33 ± 2.79 mm | 13.73 ± 2.38 mm | < 0.519 | NA |
| NORMAL | 67 (24.9%) | 169 (26.2%) | < 0.674 | 0.93 (0.67 – 1.29) |
| DILATED | 202 (75.1%) | 475 (73.8%) | | |
| **GALL BLADDER WALL THICKNESS (GBWT)** | | | | |
| Mean ± SD | 6.87 ± 2.00 mm | 4.86 ± 1.85 mm | < 0.001** | NA |
| GBWT > 6 mm | 148 (55.0%) | 138 (21.4%) | < 0.001** | 4.48 (3.30 – 6.08)+ |
| GBWT ≤ 6 mm | 121 (45.0%) | 506 (78.6%) | | |
| **COMMON BILE DUCT DIAMETER (CBDD)** | | | | |
| Mean ± SD | 4.16 ± 0.63 mm | 4.19 ± 0.75 mm | < 0.856 | NA |
| CBDD > 4 mm | 81 (30.1%) | 210 (32.6%) | < 0.460 | 0.89 (0.65 – 1.21) |
| CBDD ≤ 4 mm | 188 (69.9%) | 434 (67.4%) | | |

*Chi – square test (2 - sided significance). ** Statistically Significant p values (p < 0.05).
+ Statistically significant high odd ratios. NA (Not Applicable)

**Table No. 5: Association of Viral Hepatitis (B, C & D) Infection with Gallstone in 913 Patients of CLD**

| VIRUS | GALLSTONE | NO GALLSTONE | P VALUE* | ODD RATIOS |
|---|---|---|---|---|
| HBV | 165 (61.3%) | 272 (42.2%) | <0.001** | 2.17 (1.62 – 2.90) |
| HCV | 77 (28.6%) | 178 (27.6%) | < 0.762 | 1.05 (0.76 – 1.44) |
| HDV | 143 (53.2%) | 253 (39.3%) | <0.001** | 1.75 (1.31 – 2.33)+ |
| HBV& HCV | 42 (15.6%) | 56 (8.70%) | <0.002** | 1.94 (1.26 – 2.98)+ |
| HCV & HDV | 27 (10.0%) | 44 (6.80%) | <0.099 | 1.52 (0.92 – 2.51) |

*Chi – square test (2 - sided significance). ** Statistically Significant p values (p < 0.05).
+ Statistically significant high odd ratios

GS in liver cirrhosis occur due to multiple adverse factors. In non cirrhotic fertile females, increase secretion of cholesterol in bile under the influence of estrogen, percipitate GS formation. In liver cirrhosis, there is decreased clearance of estrogen due to hepatic insufficiency, which may produce a state of hyperestrogenemia and pecipitate GS formation.[21] Another, possible explanation can be increased gall bladder wall thickness induced decreased contractility of gall bladder. This may be due to hypoalbuminemia secondary to hepatic insufficiency, resulting in decreased oncotic pressure and increased venous hydrostatic pressure. These factors lead to edematous, thickened and non contractile gallbladder, that promote nucleation of GS.[22]

Another possible explanation can be, subclinical autonomic neuropathy resulting in gallblaber dysmotility, as described by Chawla and his colleages.[23] When gallbladder contraction in response to fatty meals is assessed by ultrasonograpy, there is poor contraction in cirrhotic patients. This response (contractility) further detoriates with worsening liver function. [24,25]

Conte D etal., (Italy, 1999), studied the relation between cirrhosis and gallstones. GS were documented in 29.5%. Declining hepatic function and increasing age were strongly associated with GS development. But, there was no role documented for gender and underlying cause of cirrhosis in GS formation. Coelho JCU et al., (Brazil, 2010), documented GS in 24% of patients undergoing transplantation. GS were present independent of age and sex. [26, 13]

# CONCLUSIONS

Based on our study and international literature, it can be concluded that,

⇒ Liver cirrhosis is a strong risk factor for development of gall bladder stones. Though the pathogenesis is multifactorial, but GS increases with detoriating liver function.

⇒ We documented strong relation of GS with aging and female gender, but this matter is internationally controversial.

⇒ HBV seropositivity in isolation or co infection with HCV or HDV is strongly related to GS development in cirrhosis.

### Recommendations

- ❖ Since there is no curative therapy available for HBV eradication, so role of nucleoside / nucleotide inhibitors should be evaluated in context to suppressing HBV proliferation and decreasing the risk of GS formation.
- ❖ Large scale multicentre and randamized controlled trials are need of time to reinforce or refuse the findings of our study.

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**Original Article**

# Treatment Outcome of Enteric Fever in Children at Tertairy Care Hospital Sukkur Pakistan

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## ABSTRACT

**Background:** Enteric fever (Typhoid fever) is widely recognized as a major public health problem in developing countries.

**Objective:** To evaluate the treatment outcome of enteric fever in children

**Study Design:** Retrospective descriptive study.

**Place and Duration of Study:** This study was conducted at the Paediatric department, Ghulam Muhammad Mahar Medical College Hospital Sukkur from January 2009 to December 2011.

**Patients and Methods:** This was a retrospective study, included all patients of enteric fever, of both sex and age ranged from 6m to 13 years. All enteric patients were confirmed by serological test Typhidot IgM or IgM and IgG positive .The data was collected from case record for demography and treatment out come.

**Results:** A total of 360 patients were diagnosed to have enteric fever during this period. Mean age of presentation was 6.47 years and 166 (46.12%) patients were <5 years whereas 194 (53.88%) were > 5 years of age. Male:Female ratio was 2:1. Serological test typhidot IgM was positive in 290 (80.5%) and both (IgM + IgG) were positive in 70 (19 45%) of cases. Raised ALT was seen in 90(25%) of cases. Complications were seen in 52 (14.4%) of cases, hepatitis 10 (2.77%), hepatic abscess 3 (0.83%) intestinal hemorrhage 8 (2.22%), peritonitis 4 (1.11%) intestinal perforation 4 ( 1.11%), cholecystitis 6 (1.66%), paralytic ileus 3 (0.83%) enteric encephalopathy 3 (0.83%), meningitis1(0.27%) osteomyelitis 3 ( 0.83%), septic arthritis 2 (0.55%) pancytopenia 3 (0.83%), pneumonia 1 (0.27%) and renal abscess 1(0.27%). Two patients expired (0.55%), one was enteric encephalopathy and other intestinal perforation with peritonitis.

**Conclusion:** Enteric fever remains a major cause of morbidity and mortality in our part of country. Major complications found in our cases were hepatitis, hepatic abscess, intestinal hemorrhage, intestinal perforation, peritonitis, cholecystitis, enteric encephalopathy, meningitis, osteomyelitis, septic arthritis.

**Key Words:** Enteric fever, complications, children.

## INTRODUCTION

Enteric fever (Typhoid fever) is widely recognized as a major public health problem in developing countries. It is a severe systemic infection caused by Salminella typhi. The disease is endemic in the Indian sub-continent, South-East Asia, Africa, the Middle –East, South and Central America, where provision of pure water supplies and sewage control are inadequate[1]. World wide incidence of enteric fever is estimated that more than 21.7 million cases and more than 200,000 deaths occur annually, the vast majority in Asia[2] The incidence may vary considerably in the developing world, with estimated rates ranging from 100 to 1,000 cases/100,000 population[2].Ochiai LR et al, in their review of disease burden due to enteric fever from five Asian countries, reported a higher incidence of enteric fever from India, Indonesia and Pakistan[3]. Enteric fever represents the 4th most common cause of death in Pakistan[4]. The disease may occur in all ages, with the highest incidence found particularly in children[5] Young age was seen in a study from Bangladesh, that the 57% of Salmonella typhi isolates were in children less than 5years of age and 27% less than 2 years[6] Various organs have been involved in the course of enteric fever resulting in a wide array of presentation[2] Enteric fever is associated with significant morbidity and mortality due to emerging multidrug-resistant strains of salmonella and delay in diagnosis[7].In a local study of 1100 hospitalized children, the mortality rate of 1.6% was found to be related to young age and multidrug-resistant infection[7]. Complications occur in 10-15% of patients and gastrointestinal bleeding (10%), intestinal perforation (1-3%) and neuropsychiatric manifestations (2-40%) are the most important ones reported[8].

The extraintestinal complication of enteric fever reported prevalence 3-35% central nervous system, 1-5%, cardiovascular system,1-6% pulmonary,1-26% hepatobiliary system, less than 1% bone and joint and genitourinary system respectively[9]. Death due to enteric fever ranges from 12.1% to 19.4% of cases reported from Nigeria[10]. Despite appropriate therapy, 2-4% of infected children may experience relapse after initial clinical response to treatment[2].We conducted retrospective study to evaluate treatment outcome of our treated patients in tertiary care hospital, caring for

large number of sick children from rural areas of Sukkur and surroundings.

# PATIENTS AND METHODS

**Place and duration of study:** Paediatric department of Ghulam Muhammad Mahar Medical College Hospital Sukkur Pakistan, from January 2009 to December 2011. This was a retrospective study, included all patients of enteric fever, of both sex and age ranged from 6 months to 13years. All enteric patients were confirmed by serological test Typhidot IgM, or both IgM and IgG positive antibodies. Blood culture was not done Data was collected from case records for demography, laboratory parameters and treatment outcome. All patients underwent investigations such as hemogram, liver and renal function tests. Additional investigation like X-Ray chest and erect posture abdomen, ultrasound abdomen, CSF, MP, serum electrolytes, blood sugar, were done where it was indicated.

All patients initially were treated with Cetriaxone .The clinical course was closely monitored and looked for complications of enteric fever. Persistence of fever for more than 7 days after antibiotics treatment was taken as a sign to start second line antibiotics. Patients who developed surgical complication treated by paediatric surgeon and all others were conservatively managed with all possible supportive care.

# RESULTS

A total of 360 patients were diagnosed to have enteric fever during this period. Mean age of presentation was 6.47 years and 166 (46.12%) patients were < 5 years whereas 194 (53.88%) were > 5 years of age shown in table 1. M:F ratio was 2:1. Serological test Typhidot IgM was positive in 290 (80.5%) and both (IgM +IgG) were positive in 70 (19.45%) of cases. Majority of children were treated with Ceftriaxone 316 (87.77%) for 10-14 days and only 26 (7.23%) of the children received Cefotaxime and 18 (5%) received Ciprofloxacin. Raised ALT was found in 90 (25%) of cases and anemia in 278 (77.23%), and thrombocytopenia in 78 (21.66%) of cases. Complications were seen in 52 (14.4%) of cases, hepatitis 10 (2.77%), hepatic abscess 3 (0.83%), cholecystitis 6 (1.66%), intestinal hemorrhage 8 (2.22%), peritonitis 4 (1.11%), intestinal perforation 4 (1.11%), paralytic ileus 3 (0.83%), enteric encephalopathy 3 (0.83%), meningitis 1 (0.27%), osteomyelitis 3 (0.83%), septic arthritis 2 (0.55%), pancytopenia 3 (0.83%), pneumonia 1 (0.27%), and renal abscess 1(0.27%) as shown in table 2. Relapse of enteric fever was found in 5 (1.38%) of cases after 3 weeks of treatment. Two patients expired (0.55%), one was enteric encephalopathy and other intestinal perforation with peritonitis.

**Table No.1: Age, Sex and Typhidot antibodies positive.**

| Age | %age | Male | Female | Typhidot IgM | Typhidot IgM +IgG |
|---|---|---|---|---|---|
| 6m to 12m No;20 | 5.56% | 12 | 8 | 10 | 10 |
| 1y to 2y No: 56 | 15.56% | 39 | 17 | 36 | 20 |
| 2y to 5y No 90 | 25% | 60 | 30 | 56 | 34 |
| 6y to 10y No:144 | 40% | 94 | 50 | 121 | 23 |
| 11y to 13y No:50 | 13.88% | 35 | 15 | 47 | 03 |

**Table No.2: Complications of enteric fever in 52 (14.4%) of children**

| Complication | Number of patients | Percentage |
|---|---|---|
| Hepatitis | 10 | 2.77% |
| Hepatic abscess | 03 | 0.83% |
| Cholecystitis | 06 | 1.66% |
| Intestinal hemorrhage | 08 | 2.22% |
| Peritonitis | 04 | 1.11% |
| Intestinal perforation | 04 | 1.11% |
| Paralytic ileus | 03 | 0.83% |
| Enteric encephalopathy | 03 | 0.83% |
| Meningitis | 01 | 0.27% |
| Osteomyelitis | 03 | 0.83% |
| Septic arthritis | 02 | 0.55% |
| Pancytopenia | 03 | 0.83% |
| Pneumonia | 01 | 0.27% |
| Renal abscess | 01 | 0.27% |
| Death of patients | 02 | 0.55% |

# DISCUSSION

Enteric fever still remains a major endemic public health problem in Pakistan especially in areas where healthcare facilities being limited and peoples are illiterate, living in unhygienic surroundings, drinking raw-water from canals and especially in rural areas or kachiabadies. Enteric fever accounts for significant cause of morbidity in children, in developing countries. In our study 46.12% of patients were under 5 years, similar to the reported by Shah I, et al[11] from India. Most of 53.88% our cases were old than 5 years as reported in most of studies[12, 13, 14] in children. Also in our patients males were 66.66% more common affected as compared to females, similar to the reported from India by Shah I et al [11, 13] whereas Abdel Wahab et al [15] found equal distribution between the boys and girls. Typhidot IgM was positive in 290 (80.5%) of cases similar to the results of locally reported by Hayat AS et al[16].Majority of children were treated with Ceftriaxone 316 (87.77% , similar to the reported by Ganesh R et al from India[12].Raised serum ALT was found in 90 (25%) cases in our cases which is lower when compared to

earlier studies by Ganesh R et al[12] where hepatic dysfunction was seen in 57% of cases, and 60% of cases[17].In majority 278 (77.23%) of our children anemia was seen and only (21.66%) of cases thrombocytopenia was seen, while Shah I et al[11] from India reported in his series 87.9% anemia and 33.33% thrombocytopenia.

Complications of enteric fever were seen in 52 (14.4%) of patients, similar to previously reported in other studies [2,8,11]whereas complications seen by others in over 30% of the patients[18,19,20].

Hepatitis was the most common complication seen in our children 10 (2.77%) which is very low than reported by Ahmed A et al[10] from Nigeria 31 (12.2%) of patients. Hepatic abscess was seen in 3 (0.83%) of children, similar to previously reported by Chaudhary R et al[21] in his series of enteric cases. Cholecystitis was seen in 6 (1.66%) children in our study as reported by others [2,9,22].The second most common complication was seen intestinal hemorrhage in 8 (2.22%) children, which is less than reported in other study from India 10% gastrointestinal bleeding[8], but very low results are also reported <1%[2]. Perforation and peritonitis was seen in 4 (1.11%) our children respectively, similar to the other studies[2,8,] but unlike to the Nigerian study where intestinal perforation was seen 17.8%-to 29% of enteric patients[10].Enteric encephalopathy and psychosis were seen in 3 (0.83%) in our children which is very low than (3-35%) reported in other studies[8,9,10] . Paralytic ileus was seen in 3 (0.83%) in our patients as reported by Malik AS et al from Malaysia[18]. Common complication of enteric fever has been reported by Malik AS et al[18] as bone marrow suppression, we had seen pancytopenia in our 3(0.835). Osteomyelitis was seen in 3 (0.83%) children in our study, similar to the reported by Huang BD[8].

The other less common complication seen in our children were septic arthritis 2 (0.55%), meningitis, pneumonia and renal abscess 1(0.27%) in each respectively as reported in many other studies[2,7,8,12]. Relapse of enteric fever was seen in 5 (1.38%) of cases within 2-3 weeks after treatment, similar relapse of enteric fever was seen in 4 (1%) by Ganesh R et al from India[12],unlike to our results high relapse was seen in 6 (19.4%) patients in Nigeria by Ahmed A et al[10].

Mortality was minimal in our study as has been reported by others studies[11,22].Only two patients expired in our study 2 (0.55%), one was enteric encephalopathy and an other intestinal perforation with peritonitis. Higher mortality was reported from Nigeria by Ahmed A et al[10] that 12.1% to19.4%. The high mortality was associated with the presence of jaundice, anemia or malnutrition[23].

# CONCLUSION

Enteric fever remains a major cause of morbidity and mortality in our part of country. Major complications seen in our children were hepatitis, hepatic abscess, cholecystitis, intestinal hemorrhage, intestinal perforation, peritonitis, enteric encephalopathy, meningitis osteomyelitis, septic arthritis, pancytopenia and renal abscess. Relapse rate was seen1.38% patients.

## Recommendations:

1. Enteric fever should be suspected in young children and infants with fevers of unknown origins in our settings.
2. The preventive strategies for enteric fever include safe water, hygiene and appropriate vaccination strategies.
3. Mass immunization programs using Vi and Ty21a vaccines for more than 2 years of children.
4. Early diagnosis (Typhidot IgM) and referral to prevent complications is essential.
5. Third generation cephalosporins is associated with higher cure rates and can be used empirical in absence of culture and sensitivity facilities.

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**Original Article**

# Relationship Between Histone Modification and Seizures in Rat Brain

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## ABSTRACT

**Objective:** To see the Effect of prigesterone on GABA transporter-1 & Glutamate transporter-2 expression in the cerebral cortex of developing rats after recurrent seizures.

**Study Design:** Quasi Experimental study.

**Place and Duration of Study:** This study was carried out in Experimental laboratory at Pediatrics Department, Xiangya 2nd Hospital, Central South University Changsha Hunan P.R China, from September 2011 to April 2011.

**Materials and Methods:** This experiment included 90 PN-7d the SD rats, Flurothyl to cause convulsions in group and progesterone in the intervention group, one died, died of status epilepticus, a mortality rate of 2.2% in each group were randomly selected eight test SD rats (72) for the analysis of experimental results. Flurothyl induced seizures stopped after the group of SD rats had no spontaneous seizures is the emergence of limb movement disorder and abnormal reactions.

**Results:** The cerebral cortex GAT-1 immunohistochemistry AOD changes in the control group, PN-13d (ARS-1d), the PN-15d (ARS-3d) and PN-19d Service (ARS-7d), the convulsions rats cerebral cortex GAT-1 immunohistochemistry AOD expression than the control group was significantly higher ($P<0.01$); progesterone in the intervention group, the GAT-1 immunohistochemistry AOD than the convulsions were significantly lower ($P<0.01$) difference between the groups is not significant. The cerebral cortex GAT-1 protein expression was significantly higher and progesterone in the intervention group ($P<0.01$); progesterone at each time point after the intervention of the GAT-1 expression levels than the control group was significantly increased statistically significant ($P <0.01$). Changes of expression of the GLT-1 protein in the rat cerebral cortex in the control group, the PN-13d, PN-15d and PN 19d cerebral cortex of the GLT-1 protein expression was no significant difference ($F = 1.852$, $P= 0.182$).

**Conclusion:** In conclusion , Progesterone through its participation in regulation of neonatal recurrent seizures caused by an imbalance in the brain cerebral cortex, GAT-1, GLT-1 expresion, the maintance of the central nervous system excitation-inhibition of the balance of the system, which play an anticonvulsant effect.

**Key Words:** Histone modification**,** Seizures, Traumatic Brain injury, Sodium Valporate

## INTRODUCTION

Seizure is an uncontrolled electrical activity in the brain, which may produce a physical convulsion, minor physical signs, thought disturbances, or a combination of symptoms. The type of symptoms and seizures depend on where the abnormal electrical activity takes place in the brain, what its cause is, and such factors as the patient's age and general state of health.

The annual incidence for all types of seizures is 1.2 per 1,000 and, for recurrent seizures, is 0.54 per 1,000. Isolated seizures may occur in up to 10% of the general population. Approximately 10–20% of all patients have intractable epilepsy, a disorder characterized by recurrent seizures, is the second most common neurological disorder, affecting more than 50 million people worldwide.[1] Population studies show that seizure incidence is highest in the first month of life,[2] The incidence is highest among young children and the elderly. High-risk groups include persons with a previous history of brain injury or lesions.

Seizure disorders and their classification date back to the earliest medical literature accounts in history. In 1964, the Commission on Classification and Terminology of the International League Against Epilepsy (ILAE) devised the first official classification of seizures, which was revised again in 1981. This classification is accepted worldwide and is based on electroencephalographic (EEG) studies. Based on this system, seizures can be classified as either focal or generalized. Each of these categories can also be further subdivided. A focal (partial) seizure and a generalized seizure. Simple partial seizures can be caused by congenital abnormalities (abnormalities present at birth), tumor growths, head trauma, stroke, and

infections in the brain or nearby structures. Generalized tonic-clonic seizures are associated with drug and alcohol abuse, and low levels of blood glucose (blood sugar) and sodium [3].

## MATERIALS AND METHODS

This experiment included 90 PN-7d the SD rats, Flurothyl to cause convulsions in group and progesterone in the intervention group, one died, died of status epilepticus, a mortality rate of 2.2% in each group were randomly selected eight test SD rats (72) for the analysis of experimental results. Flurothyl induced seizures stopped after the group of SD rats had no spontaneous seizures is the emergence of limb movement disorder and abnormal reactions.

## RESULTS

The cerebral cortex GAT-1 immunohistochemistry AOD changes in the control group, mainly distributed in the cell membranes of rat cerebral cortical neurons in the PN-13d, the PN-15d and PN 19d, the control group between the GAT-1 immunohistochemistry AOD values were significant differences (F= 0.218, *P*=0.806). PN-13d (ARS-1d), the PN-15d (ARS-3d) and PN-19d Service (ARS-7d), the convulsions rats cerebral cortex GAT-1 immunohistochemistry AOD expression than the control group was significantly higher (*P*<0.01); progesterone in the intervention group, the GAT-1 immunohistochemistry AOD than the convulsions were significantly lower (*P*<0.01) difference between the groups is not significant (Table 1,Figure 1)

Table No.1: The Cerebral Cortex GAT-1 immunohistochemistry AOD changes ( $\bar{x} \pm s$ ) (n = 8)

| | ARS-1d | ARS-3d | ARS-7d |
|---|---|---|---|
| Control group | 1733±85 | 1763±99 | 1751±86 |
| Seizure group | 2038±76[a] | 2055±92[a] | 2067±105[a] |
| Progesterone intervention group | 1854±84[a,b] | 1869±103[a,b] | 1853±94[a,b] |
| F-value | 28.260 | 18.278 | 22.953 |
| *P*-value | <0.001 | <0.001 | <0.001 |

a *P* <0.05 vs. the control group,; b *P* <0.05 vs. the seizure group

The cerebral cortex GAT-1 protein expression was observed in control group, the PN-13d, PN-15d and PN-19d rat cerebral cortex GAT-1 expression was significant difference; seizure group rats of ARS-1d (PN-13d), ARS-3d (PN-15d ) and ARS-7d (PN-19d), the GAT-1 protein expression was significantly higher and progesterone in the intervention group (*P*<0.01); progesterone at each time point after the intervention of the GAT-1 expression levels than the control group was significantly increased statistically significant (*P* <0.01). (Table 2, Figure 2).

Table No.2: The Cerebral Cortex GAT-1 protein expression ( $\bar{x} \pm s$ ) (n = 8)

| | ARS-1d | ARS-3d | ARS-7d |
|---|---|---|---|
| Control group | 0.344±0.006 | 0.340±0.010 | 0.346±0.010 |
| Seizure group | 0.553±0.014[a] | 0.569±0.010[a] | 0.567±0.010[a] |
| Progesterone intervention group | 0.466±0.012[a,b] | 0.439±0.01[a,b] | 0.464±0.016[a,b] |
| F-value | 679.102 | 1038.766 | 492.971 |
| *P*-value | <0.001 | <0.001 | <0.001 |

a *P* <0.05 vs. the control group,; b *P* <0.05 vs. the seizure group

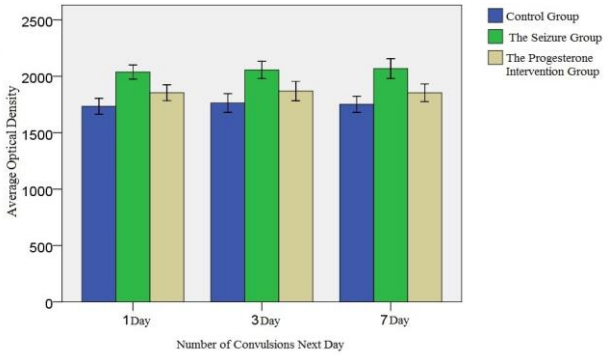


Figure No.1: the cerebral cortex GLT-1 immunohistochemistry AOD changes (n = 8)

## DISCUSSION

Traumatic brain injury is a serious and complex injury that occurs in approximately 1.4 million people each year in the United States. [4] TBI is associated with a broad spectrum of symptoms and disabilities, including a risk factor for developing neurodegenerative disorders, such as Alzheimer's disease. [5-7]. The inflammatory cascade is characterized by proinflammatory cytokines [9, 10] which can exacerbate other pathologies. Although the role of inflammation in experimental TBI is well established, no truly efficacious and approved anti-nflammatory therapies are currently available for the treatment of traumatic brain injury. Under normal conditions microglia are in a resting state, characterized by a small cell body with fine, ramified processes and low expression of surface antigens. CNS injury triggers rapid changes in the morphology and function of microglia. Hypertrophic microglia with thickened and slightly shorter processes are in a reactive state which suggests a largely passive response to injury. In contrast, activated microglia and phagocytic microglia (or macrophages) have a more aggressive role which,

depending upon the circumstances; can produce deleterious effects to the CNS through secretion of various inflammatory molecules. [14, 15] Residential microglia activation and infiltration of macrophages from the peripheral blood is well known to contribute to post-injury inflammation after TBI. [16,17] Such secondary injuries often occur following the initial TBI insult and contribute to further brain pathology and neurological impairment. [18,19] Changes in epigenetic gene expression influence normal neuroplasticity, learning, and memory [20], the signaling events mediating such changes are unknown. Epigenetics has been defined as "the study of the processes that mediate metastable and somatically heritable states of gene expression without altering the DNA sequence". [24]

After post injury survival, rats were perfused with 4% paraformaldehyde and sections of the mid-dorsal hippocampus were stained with hematoxylin and eosin (H&E) for neuronal density or reacted with antibodies for immunohistochemistry. Immunohistochemical staining was performed by an avidin–biotin–peroxidase method (ABC) using an acetyl–histone H3 (lys 9) antibody (40 µg/ml, New England Biolabs), a histone H3 antibody (100 µg/ml, Upstate Biotechnology), and a dimethyl (lys 9 and lys 4) histone H3 antibody (20 µg/ml, Upstate Biotechnology). Regional relative optical density was used for statistical analysis (one-way ANOVA analysis followed by a Bonferroni post hoc analysis). Antibody specificity was examined in naive rats using Western blot analyses (1 µg/ml of each antibody). The ipsilateral hippocampal CA3 and CA1 sectors are selectively vulnerable to TBI [25], in their study, they have confirmed that acute seizure, in this case ECS, increases H4 acetylation selectively at the BDNF P2 promoter. Interestingly, such chromatin remodeling appears to shift toward the P3 and P4 promoters under chronic ECS conditions. It is noteworthy that whereas only BDNF P4 mRNA levels were significantly increased 24 hr after chronic ECS, H3 acetylation was induced at both the P4 and P3 promoters. This increase at P3, in the absence of increased BDNF P3 mRNA levels, could be explained by the fact that the P3 and P4 promoters are only 0.8 kb apart in the primary BDNF transcript [30], thus permitting some of the histone enrichments at P4 to also be detected at the P3 promoter. H3 acetylation at Lys9 and Lys14, similar to H4 acetylation, is found in transcriptionally active promoters [31]. Here, they similarly showed that acute ECS treatment increases H3 phosphoacetylation; however, this change was delayed compared with the induction of H4 acetylation and c-fos mRNA levels. Chromatin remodeling is normally described as a dynamic process induced by transient histone modifications. However, they observed several chromatin modifications that were changed in chronic ECS conditions and persisted 24 hr after the last seizure. Thus, it is likely that adaptations in chromatin structure exert not only short-term, transient effects, but also longer-term effects on gene activity. Specifically, the down regulation of H4 acetylation at the c-fos and CREB promoters, and the up regulation of H3 acetylation at the BDNF P3 and P4 promoters, provide proximal mechanisms by which chronic ECS might alter the expression of these three genes in the hippocampus. Such changes may well play an important role in modulating neuroplasticity in the adult brain. Indeed, the sustained activation of BDNF expression after chronic ECS, which we hypothesize may be mediated in part via H3 acetylation at the P3 and P4 promoters, could contribute to the antidepressant effects of ECS [21]. May be mediated in part via reduced H4 acetylation at the promoter of the gene. Histone acetyltransferases (HATs; enzymes that increase histone acetylation), or proteins that regulate these enzymes. It is generally believed that HDACs and HATs are controlled mainly at the level of their recruitment to target promoters, but some evidence suggests that at least CREB-binding protein, a type of HAT, may be regulated directly through Ca2+ signaling. [22]

Valproic acid (VPA) is a widely used preventive treatment for seizures and bipolar disorder [8], Using a rodent model of TBI, we examined if post-injury VPA administration is neuroprotective, and improves motor and cognitive outcomes. Our preclinical findings show that post-injury systemic administration of VPA: 1) reduced cortical contusion volume, 2) improved blood-brain barrier integrity (BBB), 3) reduced hippocampal MAP2 disruptions, and 4) improved motor and cognitive function. Valproate [2-propylpentanoic acid] (VPA) is a simple branched- chain fatty acid with well established efficacy for seizures. [33] It is also commonly prescribed for bipolar disorder, acute mania and migraines. [34] The therapeutic concentration of valproate is 40–100 mg/ml, and it has a serum half-life of 8–17 hours in adults. This therapeutic concentration is achieved by a loading dose followed by maintenance doses. In rodents, an i.p. dose gives rise to a peak serum post injection concentration that rapidly decreases post-infusion. [35]. Consistent with this, Shein et al., have shown that acute treatment of mice following TBI with the HDAC inhibitor ITF2357 reduces contusion volume and improves motor function. [36] Further, Lyeth and colleagues have shown that DMA-PB (a novel HDAC inhibitor) attenuates the TBI-associated decrease in histone acetylation and reduces microglia-mediated inflammation. [32] However, post-injury treatment with SAHA did not improve motor or cognitive function, suggesting that the HDAC-inhibiting activity of VPA is not sufficient to improve behavioral outcome following TBI. we have recently reported that post-injury treatment with sodium butyrate, a non-selective HDAC inhibitor, also failed to improve cognitive function when administered acutely following TBI. [12] We

have previously shown that the activation of ERK following TBI is neuroprotective, and its inhibition exacerbates TBI-associated motor and cognitive deficits. [11] Although our western blots did not reveal any significant increase in ERK phosphorylation in response to VPA injection, its activation at an earlier/later time point than that examined here (45 min post-injection) cannot be ruled out. Lastly, while not specifically examined in the current study, valproate has also been shown to enhance GABAergic neurotransmission. Previous studies have shown that administra- tion of a GABA agonist acutely following injury can be used to reduce hyperactivity and improve neurological outcome. [27, 28] Consistent with these benefits, food restriction has been shown to be associated with a recovery of spatial memory following global ischemia. [23], one potential limitation of valproate therapy to improve cognitive function is that it appears to only be effective post- injury. Further experiments will be required to establish the exact time window, the best routes of administration, and if this improvement can be observed following different injury magnitudes. [26]

While GluR-mediated excitation is enhanced in the immature brain, receptors and the synthetic enzyme (glutamic acid decarboxylase) for the major inhibitory neurotransmitter γ-aminobutyric acid (GABA) do not achieve maximal expression levels until the fourth postnatal week in rats. Furthermore, whereas GABA is inhibitory and hyperpolarizing in the mature brain, this neurotransmitter can be excitatory and depolarizing in the immature brain. GABA release can activate GABAA receptors (GABAARS), which are ligand-gated chloride channels. Studies have demonstrated that the NKCC1 inhibitor bumetanide can block seizures in a rodent model of neonatal seizures, and this agent might have potential in the clinic as an antiepileptogenic therapy. [13]

# CONCLUSION

Our review concludes that the importance of better understanding the role of these enzymes and associated proteins and the signaling pathways that regulate them, not only in activity-dependent transcription but also in models relevant for chronic adaptation in the brain is required. Even though many researches were done regarding histone modification in seizures in experimental animals especially in rats ,the results are encouraging but still research are not enough to implement in humans. Thus still further researches on mammals and human itself is required then only its positive implementation can be done in human beings.

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Original Article

# When to Operate an Abdominal Gunshot Wounds

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## ABSTRACT

**Background:** Violence has become part and parcel of the daily routine of living, the prospective study of 86 patients, sustaining abdominal gunshot wounds was designed to evaluate the pattern, presentation and treatment outcome.

**Study Design:** Descriptive Study.

**Place of Study**: This study was conducted at the department of Surgery, Ghulam Muhammad Mahar Medical College Sukkur from January 2011 to January 2012.

**Materials and Methods:** Patients presenting with abdominal firearm wounds at accident and emergency department were included in this study, clinically all were evaluated, resuscitated and their findings were recorded on proforma. Patients with signs of acute abdomen (peritonitis)/shock underwent midline emergency laparotomy, others having minimal or equivocal abdominal signs were selected for observation (non-operative management) group.

**Results:** Total number of patients included was 86, all were males, they belonged to age varying from 15-70 years , 54 (62.8%) were below the 40 years of age , in 44 ( 51.1% ) cases instrument of attack used by assailant was pistol/shotgun , 45(52.3%) cases were victims of armed robbery , in 75(87.2%) entrance wounds were present in anterior abdominal wall where as in 11(12.1%) were present posteriorly , 67(77.9%) underwent emergency laparotomy and 19(22%) were observed initially. Two patients belonging to observation group showed failure, needed delayed laparotomy and both had positive laparotomy.

**Conclusion:** Gunshot wounds of abdomen can be safely managed non-operatively, in the absence of abdominal tenderness haemodynamic instability or inevaluable factors as head injury and heavy intoxication. Success of non operative management depends upon continuous monitoring and frequent clinical examination.

**Key Words**: Abdominal Gunshot, laparotomy, haematemesis. hemicolectomy.

## INTRODUCTION

Gunshot injuries are major problem worldwide from medical and economical perspectives[1], and are associated with profound morbidity and significant mortality[2]. In many Africans and developing countries the reason behind firearm injuries are communal clashes, sectarian religious crisis, armed robbery, hunting, political violence, student strife and suicidal attempts.[3,4,5]

After World War I, laparotomy remained standard for penetrating abdominal injuries[6], till 1960 when Shafton[7] demonstrated that patient with penetrating abdominal wounds could be accurately identified and selectively managed non-operatively.

In 1974 Nance et al[8] found that selective observation of abdominal gun shot wounds could be safe and effective, with decreasing morbidity and hospital stay without additional mortality. Subsequently Muckart et al[9] and Demetriades[10] et al, concluded that selective, non operative management could be safely carried out without rise in morbidity and mortality, and decrease in the number of negative laparotomies. Keeping this in mind this study was designed to evaluate the patients, who deserve emergency laparotomy and who do not.

## MATERIALS AND METHODS

This descriptive study was carried out prospectively in surgical department of Ghulam Mohammad Mahar Medical College Hospital Sukkur, from Jan 2011 to Jan 2012. Patients included were of any sex belonging to age group above 15 years, with abdominal firearm wounds.

Anatomical abdominal land marks were, anterior abdomen (Area between xiphoid and costal margins superiorly, pubic symphysis, inguinal ligament inferiorly and mid axillary line posteriorly), back area (confined between tips of scapula superiorly, mid axillary lines laterally and gluteal folds inferiorly).

Patients with gunshot wounds within these surface markings, or patients with entrance wounds outside these land marks, but clinical features of abdominal injuries or radiological evidence of missile in abdomen were included in the study too. The patients having unevaluable trauma due to intoxication and head injuries were excluded from the study. All patients under went primary and secondary survey according to ATLS guide lines. After brief clinical history and examination, entry & exit wounds with their location were noted; the type of weapon used and reason for the attack was recorded.

I/V line established, Foley's catheter retained and nasogastric intubation was done. Haemodynamically unstable patients were promptly resuscitated, and immediately shifted to operation theatre .Surgery within 4hours of arrival at accident & emergency department was considered to be operative management. Shock ( BP <90 mmHg and pulse >100b/min), generalized peritonitis, leakage of intestinal contents through the wound, bleeding per rectum, haematemesis and frank blood in urine were all indications for exploration of abdomen. Tangential through and through abdominal gun shot wounds were not considered absolute indication for laparotomy, patients having tenderness localized to wound with no evidence of cardiovascular instability were regularly assessed two hourly, and were labeled conservative management group, surgery in such cases after four hours was considered as observation (non operation management) failure .The cut of point of four hours was selected, as is used in audit filter in trauma registers for delayed operative management according to North American National trauma Database.

Pre operative chest radiograph, abdominal ultrasound and x-rays, and urine examination were carried in haemodynamically stable patients; IVP were ordered in selective patients. Radiological features suggestive of pneumoperitoneum, presence of missile intra abdominally with presence of physical signs were candidates for surgery. Each patient was kept on third generation cephalosporin. During surgery visceral injuries were recorded and dealt accordingly.

# RESULTS

Eighty Six patients of abdominal gun shot wounds were included in study from Jan 2011 to Jan 2012,all were males, belonged to age group from 15-70 years Table-I

Sixty seven (77.9%) presented with clinical picture of peritonitis)/ state of shock, all under went emergency laparotomy, 19 (22%) had minimal or equivocal abdominal findings and were kept in initial observation (non-operative management) group.

Time interval from incidence to arrival at emergency department varied from ½ hour to 6 hours with mean of 3 hours. Wounding weapon used by assailant could be identified in 44 patients where as in rest of cases remained unidentified Table-II. Reason for firearm abdominal wounds are shown in Table-III. In 75(87.2%) patients entry wounds were present in anterior abdominal wall, and in 11(12.7%) cases posteriorly (thorax, trunk and gluteal region). Entry wound was single in 63 cases (73%) where as in 23 (26.7%) entry wounds were more than one. Clinical features with which patienents presented are shown in Table-IV.

**Laparotomy group n=67:** Patients belonging to this group were 67(77.9 %) they presented with hypotension (B.P less than 90) or clinical picture of frank peritonitis, all underwent laparotomy immediately, within 4 hours. Organ system injuries were 129, these are shown in Table-V, commonly involved system was GIT, predominantly affected was small intestine in the form of perforations or tangential lacerations .Majority needed simple repair ,others ,segmental resection and end to end single layer sero sub mucosal anastomosis , colonic injuries were dealt with simple repair , right hemicolectomy, segmental resection anastomosis with protective diversion or exteriorization of affected segment according to the situation .

Liver was the second , commonly involved organ by fire arm injuries 17(24.26%) cases , superficial and deep lacerations were present in ten cases , through and through in four and three were associated with complex injuries involving hepatic & portal vessels, and were dealt with resectional debridement, deep stitches with selective vascular ligation sponge stone and packing. Cholecystectomy was performed in 02 cases of gall bladder injuries. Stomach, diaphragm, and urinary bladder injuries were repaired simply. Rectal injuries were treated by repair and covering colostomy. Spleenectomy was done in most of the cases where as splenorrhaphy in few. Nephrectomy was performed in major trauma of kidney.Two patients had pancreatic injury one was treated by distal pancreatectomy other did not require any surgical procedure .three patients sustaining inferior vena caval injuries were repaired ,but died immediately post operatively due to irreversible shock .Vast majority of patients suffered two or more injuries and mortality rate was proportional to number of organs involved ,twelve patients(13.9% ) in the immediate laparotomy group expired ,03 inferior vena caval injury,02 with liver injuries ,06 from associated colonic injuries and one from transfusion induced coagulopathy .Hospital stay ranged from 05-120 days (median 15 days ) .Postoperative complications were wound infection (20.9% ), anastomotic leak (4.5% ) ,intra abdominal abscess (5.8%),septicemia (12.7%) ,pneumonia (8.1%) ,burst abdomen (8.1%) ,these were treated accordingly .

**Initially observed group n=19:** Nineteen patients (22%) presented with equivocal or minimal abdominal findings, they were kept in non operative management (observational) group. Eleven cases had entry and exit wounds, 04, were with tangential anterior abdominal wounds, and 04 had only entry wounds. Radiological examination did not reveal findings suggestive of pneumoperitoneum or multiple significant air and fluid levels. Ultra sound findings were not significant. All of them were haemodynamically stable, so were observed closely, two cases resulted into failure by developing fever, progressive diffuse abdominal tenderness and tachycardia, so underwent delayed exploratory laparotomy after 04 hours. Both cases had two

perforations in small gut, which were primarily repaired. None of the patient belonging to this group died.

**Table No.1: Age distribution of abdominal gunshot wounds N=86**

| Age of the patients in years | Number of patients |
|---|---|
| 15-20 | 5 |
| 21-30 | 31 |
| 31-40 | 18 |
| 41-50 | 15 |
| 51-60 | 13 |
| 61-70 | 4 |
| Total | 86 |

**Table No.2: Weapons Used in n=44 patients**

| Weapon used | No of patients | %age |
|---|---|---|
| Pistol | 17 | 38.6% |
| Hand gun | 10 | 22.7% |
| Revolver | 3 | 6.8% |
| Shot gun | 12 | 27.2% |
| Rifle | 2 | 4.5% |

**Table No.3: Causes of gunshot abdominal injuries N=86 cases.**

| | | |
|---|---|---|
| Armed robbery attack | 45 | 52.3% |
| Accidental | 2 | 2.33% |
| Shot by unknown | 5 | 5.81% |
| Communal strife | 10 | 11.62% |
| Property dispute | 11 | 12.7% |
| Celebration ceremony | 4 | 4.6% |
| Sectarian | 7 | 8.1% |
| Family dispute | 2 | 2.3% |

**Table No.4: Clinical features of abdominal gunshot injuries. n=86**

| Symptoms | N | % | Signs | N | % |
|---|---|---|---|---|---|
| Abdominal pain | 86 | 100 | Peritonitis | 67 | 77.9 |
| Distension | 19 | 22 | Shock | 17 | 19.7 |
| Vomiting | 25 | 29.6 | Paraplegia | 1 | 1.16 |
| Haematemesis | 5 | 5.8 | Evisceration | 6 | 6.9 |
| Haematuria | 5 | 5.8 | Haemothorax | 2 | 2.3 |
| Rectal bleeding | 6 | 6.9 | | | |

**Table No.5: Type of Organ Injured n=69**

| | Organ Injured | N | % |
|---|---|---|---|
| 1 | Small bowel | 41 | 59.4 |
| 2 | Colon | 25 | 36.2 |
| 3 | Liver | 17 | 24.6 |
| 4 | Stomach | 11 | 15.9 |
| 5 | Urinary bladder | 5 | 7.2 |
| 6 | Spleen | 6 | 8.6 |
| 7 | Kidney | 4 | 5.7 |
| 8 | Rectum | 6 | 8.6 |
| 9 | Gall bladder | 2 | 2.8 |
| 10 | Pancreas | 2 | 2.8 |
| 11 | Major vessel | 3 | 4.3 |
| 12 | Retroperitoneal haematoma | 7 | 10.1 |

# DISCUSSION

Violence has become part and parcel of daily routine living and is extremely difficult to obtain true magnitude of problem[11].The escalation of trauma and inter personal violence in many countries is referred as neglected epidemic[12], that has resulted in approximately 50% of murders committed with fire arms. In this study all patients were male, as in the study of Onuba[13], majority 54(62.8%) were below the age of 40 years, and weapons used were identified in 44(51.1%) cases , locally made pistols/ shot guns were the weapons of attack in majority of cases. In 45 (52.3%) cases reason for violence was armed robbery attack that coincides with the study of Chiana Kwana et al[14]. Pistols/ shotguns used were loaded with locally made pellets which resulted in multiple entry and exit wounds mainly. Time between incidence and arrival at accident and emergency department ranged from ½ hour to 6 hours average delay in this study was 03 hours, in contrast with other studies which was 50 minutes[15]. The prolong delay in arrival and getting medical treatment might had impact upon many number of severely injured patients, those possibly might have expired during transportation, it could have also be detrimental effect in patients with non fatal injuries as blood loss and faecal contamination of peritoneal cavity gets prolonged, that may be a contributing factor for post operative septicemia and mortality in cases of colonic injuries. Primary repair in colonic injuries was done only in carefully selected patients, otherwise colostomy was of choice for colorectal trauma has got place in our setup as is adopted by others[16,17,18] Post operative Complications were higher than in the study of Mohammed Iqbal[19]. In this series 67(77.9%) cases presented with clinical picture that deserved emergency laparotomy , similar figure is mentioned by Inchien in literature , that ranges from 69-78% . A. salim &G. C. Velmahos believe that a carefully performed physical examination is the cornerstone of the management of abdominal gunshot wounds[20]. S.Nabeel Zafar et al[21], has observed successful non operative management in 22.2% of abdominal gunshot wounds, in our series we have managed 19.7% cases successfully conservatively. Commonly injured systems were gastro intestinal tract, and biliary tract because these occupy wide area of the abdominal cavity. In vast majority of cases surgical intervention was done within 04 hours on the basis of clinical examination , some delay in surgery on the basis of equivocal physical signs did not prove detrimental , can be postponed safely until clinical findings of injury become evident. This policy of selective non operative management has been re appraised by Muckart et al. The proponents of mandatory exploration often under estimate the importance of negative laparotomy; some has reported significant morbidity and even mortality[22]. The present

selective conservatism policy adopted is based exclusively on physical examination as was adopted by Inchlen, that is based upon careful initial examination and frequent serial examinations, failure was noted in 02 patients who were being treated under this policy, showed failure and underwent laparotomy for peritonitis and fever without any complication.

## CONCLUSION

Gunshot wounds of abdomen can be safely managed non-operatively, in the absence of abdominal tenderness haemodynamic instability or inevaluable factors as head injury and heavy intoxication. Laparotomy is not mandatory for all cases.

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**Original Article**

# Pattern of Homicide in Muzaffarabad (AJK)

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## ABSTRACT

**Background:** Homicide is the highest level of aggression found in all cultures and ages and is one of the oldest crimes in the human history. The pattern of Homicide has changed with the passage of time except for the motives which almost remain the same that is the lust for woman, money and land.

**Objective:** The objective of this study is to determine the pattern of homicide in Muzaffarabad AJK.

**Study Design:** Prospective study.

**Place and Duration of Study:** This study was conducted at combined Military Hospital (CMH) Muzaffarabad (AJK) during the period of 1st Jan 2010 to 31st December 2011.

**Material & Methods:-** Thirty cases of homicide presented for autopsy was selected on basis of police inquest and autopsy findings. These causes were examined regarding age, Sex, type of weapon used, part of body involved along with seasonal variations.

**Results:-**The Homicide rate in Muzaffarabad during the years 2010 and 2011 is 2.748/100,000 per year Males are the primary targets with 30% between 30-39 years of age. The most common weapons used for this offence are the Blunt weapons.

**Conclusion:-**The Homicide rate is high with the use of Blunt weapons followed by firearms.

**Key words:**-Autopsy, Homicide, Blunt Weapons, Fire Arms.

## INTRODUCTION

Homicide is the death of one human being as the result of conduct of another[1].The first homicide on earth was done by the son of Adam(Qabeel). He used a stone to kill his brother (Habeel) which is classified as blunt weapon. To commit murder two elements "Mens-rea" which means pre-planning or afore thought or intention and "Actus-reus" which means actual execution should work together to constitute a crime[2].

Homicide is generally considered the most serious of all crimes with obviously the most serious consequences for the victim[3].In majority of cases the end point of arguments between acquaintances, domestic violence, drug addiction, robberies and terrorism is the homicide[4].

Persons are not only killed but also are injured in violence and suffered from Physical, mental , sexual and reproductive health problems that results in massive burden on national economics [5].The incidence of homicide is also increasing with change in the pattern because of changing life style and easy availability of various type of weapons.

Studies on the pattern and rate of homicide are well documented in developed countries since long, but now in Pakistan data is also appearing in different medical journals [6,7,8,9,10].

However no data for Muzaffarabad Azad Jammu and Kashmir has yet been reported.

There are different Inquest Systems in the world. In our country, there is police/magistrate inquest system the bodies are sent to authorized medical officer in authorized centers for postmortem examination when the Investigating officer is not satisfied with cause of death.

The various patterns of Homicide include assault by Blunt weapons, Sharp weapons, Firearms, Strangulation, Smothering, hanging, drowning, and burn etc.[11]

This study was conducted to know the various parameters of Homicidal deaths.

## MATERIALS AND METHODS

The study was conducted at CMH Muzaffarabad for the period of two years from 1-1-2010 to 31-12-2011.The study included all cases which was labeled as homicide on basis of autopsy and police inquest. These cases were examined regarding age, sex, type of weapon used, part of the body involved, along with seasonal variations.

## RESULTS

During the period of study a total number of thirty Homicidal deaths were reported out of total seventy five autopsies thus being 40% of all deaths reported for autopsy.

In Homicidal Cases twenty five were Male and five were Female; thus having a ratio of 5:1.

The victims which are more prone to Homicide belong to 30-39 years (30 %) followed by 40-49 years (26.66%).The sex and age distribution are summarized in table 1& 2.

The most Common weapon used for offence is the blunt weapon (40%) followed by Firearms (26.66%) which are summarized in table 3.

The most Common part of the body involved is the head (46.6%) followed by chest (33.33%) which is summarized in table 4.

**Table No.1: Sex distribution of Homicide victims**

| Sex | Number of victims |
|---|---|
| Male | 25(83.33%) |
| Female | 05(16.66%) |

**Table No.2: Age distribution of Homicide victims**

| Age Group in years | Number of victims |
|---|---|
| 0-9 | Nil |
| 10-19 | 02(6.66%) |
| 20-29 | 02(6.66%) |
| 30-39 | 09(30%) |
| 40-49 | 08(26.66%) |
| 50-59 | 06(20%) |
| 60-69 | 02(6.66%) |
| More then 70 | 01(3.33%) |

**Table No.3: Type of Weapon**

| Type of Weapon | No of cases |
|---|---|
| Blunt | 12(40%) |
| Firearm | 08(26.66%) |
| Asphyxia<br>. Drowning - 3<br>. Throttling - 2<br>. Strangulation - 1<br>. Hanging - Nil<br>. Smoltz - Nil | 06(20%) |
| Sharp | 04(13.33%) |
| Burn | Nil |

**Table No.4: Part of the body involved**

| | |
|---|---|
| Head | 14(46.6%) |
| Chest | 10(33.33%) |
| Neck | 03(10%) |
| Abdomen | 03(10%) |
| Upper limb | Nil |
| Lower limb | Nil |

# DISCUSSION

During the period under study (1-1-2010 to 31-12-2011) thirty deaths were labeled as Homicide out of the total seventy Five autopsies. This comes out to be the 40% of the total. This is lower percentage than reported in other cities of Pakistan.

The total number of 4,68,000 homicides results in a global average homicide rate of 6.9 per 100,000 population per year [12].

Homicidal rates vary greatly in different parts of the world being low in places like Austria (0.56 per 100,000 populations per year) and Norway (0.68 per 100,000 populations per year) and high in countries like Honduras (86 per 100,000 populations per year) republic in Central America[13].

Muzaffarabad having a population of 5,45,817 during the study period, the rate of Homicide comes out to 2.748 per/100,000 population per year.

This is higher as compared to Austria and Norway but lower as compared to Honduras, Russia etc. The reason of this low incidence may be the low level of urbanization and industrialization.

Globally men make up 82% of all victims of homicide suggesting that the most typical homicide pattern is a case of men killing men while women represents a smaller share of homicide victims only as they are the predominant target of intimate partner/ Family related violence[14].

In our study the Male to Female ratio is 5:1. It is lower than reported in Abbottabad (6.8:1),Bahawalpur (6.82:1),Peshawar (6.22:1) and is higher than that in Faisalabad (3.47:1).

This is because of aggressive nature of male than females. And this is male dominant society and they handle most of the disputes of family and society. Similar observations were made by Alan Fox [(15)],but in study conducted by Kominatoy[(16)] male to Female ratio of the victims was 1:1.

Our study indicated that 56.66% of all homicides occurred in the age groups between 30-49years of age with (30%) in third Decade of life. Other studies in Pakistan show the lower occurrence of homicide in the same age group and the highest occurrence with 28-40% in the age braket of 20-29 years.

While the studies in USA indicate the highest rate in earlier age(10-25y) this is because the individual starts its independent life at an earlier age [(17,18).]In one of the studies done in India most of the victims of sharp force were between 21 and 40 years and those of blunt force between 31 and 40 years. The problems faced by this age group are the land disputes and other serious family issues.[19]

In our present studies, blunt weapons were the major weapons of offence (40%) followed by firearms(26.6%) that is not consistent with other studies in Pakistan where the major weapons of the offence are firearms. This may because of less urbanization.

The part of the body involved in case of blunt weapons are Head (46.6%) and chest (33.33%) in case of firearms and sharp weapons.one of studies shows that thorax was the commonest site to be involved in sharp force in contrast to head in blunt force.The majority of the blunt force victims had lesions in only one region in contrast to involvement of 2-4 regions in sharp force. The majority of the victims were killed by acquaintances in bluntforce, Knife and wooden/iron rods were the weapons of choice in their respective categories.[20]

We have also noted that there is no influence of season on crime rate.

# CONCLUSION

Most of the victims belong to age group of 30-39years.The problems faced by this age group are the land disputes and other serious family issues which should be addressed by referring the parties to the appropriate agency for counseling.

There should be strict enforcement of law on possession of dangerous weapons.

Prevention of violence in our society does not rest only on the law enforcement agencies. Religious scholars must also assist in preventing the primary violence. We must follow the injunction of Islam which clearly condemn these crimes in the following words in the Holy Quran

"Whoever kills another person is as if he killed the whole humanity".

In another verse the Qur'an says.

"Do not let your hatred of a people incite you to aggression".

Homicides due to blunt-force injury still pose a significant challenge for the forensic experts who must obtain a complete and accurate history of the fatal incident, interpret patterns of injury and other findings at autopsy, and correlate all of the findings to make an accurate ruling of the cause and manner of death.

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Original Article

# Prevalence of Methicillin Resistant Staphylococcus Epidermidis in Biomaterial Related Infections

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## ABSTRACT

**Objective:** To determine the prevalence spectrum of methicillin resistant Staphylococcus epidermidis in biomaterial infections.

**Study Design:** Experimental and Observational Study.

**Place and Duration of Study:** This study was conducted in the department of Microbiology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, during the period of January 2010 to Dec. 2010.

**Materials and Methods:** A total of 300 subjects of all ages and sex were included. Swab from cannulae tips, catheters tips, old cannulae infected wounds, injection abscess were collected from Jinnah Postgraduate Medical Centre, National Institute of Child Health and Civil Hospital, Karachi and processed according to standard laboratory methods.

**Results:** A total 103 methicillin resistant Staphylococcus epidermidis, causing biomaterial related infection, isolated from 300 patients were analyzed. Bacterial pathogens were commonly isolated from patients of all ages who developed biomaterial related infections.

**Conclusion:** Patients suffering from infections related with biomaterial should be monitored for MRSE at regular intervals.

**Key Words**: Staphylococcus epidermidis, cannulla, catheter tip.

## INTRODUCTION

Staphylococcus epidermidis is a gram positive coagulase negative cocci that is part of our normal flora (Nilsson et al., 1998)[1]. It is one of the most significant bacteria in context of hospitalized infection (Nomura et al., 2010). Catheter infections along with catheter induced UTI's lead to serious inflammation and pus secretions (Nilsson et al., 1998)[1].

Staphylococcus epidermidis is one of the five most common organisms that cause nosocomial infections due to the increase in usage of biomaterials in the clinical environment (Mack et al., 2007).[2]

Resistance to methicillin in staphylococci is known to be associated with the presence of mec A gene, which codes for a penicillin binding protein with low affinity for β-lactam antibiotics (Miragia et al., 2007).[3]

Staphylococcal infection in hospitalized patients has been a major concern for well over a century (Ekrami et al. 2010).[4] They expressed methicillin resistance which involves all beta lactam antibiotics and leads to a significant limitation in therapeutic options.

Infections caused by Staphylococcus epidermidis are persistent and relapsing which further complicates treatment of biomaterial infections (O'gara, 2001)[5]. Between 35 and 66% of clinically important coagulase negative staphylococci are resistant to methicillin (Keramidas et al., 2003).[6]

The infection by methicillin resistant coagulase negative staphylococci, such as Staphylococcus epidermidis tends to show a higher level of prevalence (60-70%) (Buonavoglia et al. 2010).[7]

The inherent capacity of this organism to cause infection derives primarily from its ability to form mucoid biofilms on inert synthetic surfaces of indwelling medical devices. At biochemical level extracellular polysaccharide adhesion play an essential role in initial bacterial adherence and intercellular adhesion (O'gara, 2001).[5]

Intravenous access lines and needles connectors have been demonstrated to be a risk factor for blood stream infection (Chaieb et al., 2005).[8]

It is clear that Staphylococcus epidermidis is an important cause of bacteremia and has been correlated with the increase in the use of prosthetic and indwelling devices and the growing number of immune-compromised patients in hospitals (Jeong, 2002).[9]

The number of multiple resistant strains including methicillin resistant coagulase negative staphylococci has increased (Jain, 2004).[10]

Methicillin resistant Staphylococcus epidermidis was proven to be an infection associated with hospitalization. The routes of transmission are through to be patient-to-patient and patient-to-medical professional-to-patient (Nomura et al., 2010).[11]

# MATERIALS AND METHODS

**Study site:** The study was performed in Microbiology Department of BMSI, JPMC, Karachi from January 2010 to December 2010.

**Enrollment:** 300 patients of all ages were selected from medicine, surgery and paediatric Departments. Samples were collected from cannulae tips, catheter tips, cannulae infected wounds, operated wound infection with the help of sterile swab. Swabs were inoculated into peptone water that was used as transport medium. Specimen were streaked on blood agar and MacConkey's agar plates and incubatged overnight at 37°C aerobically. Phenotypic characteristics of the colonies were used for presumptive identification of Staphylococcus epidermidis. Staphylococcus epidermidis identification was confirmed by gram staining, catalase test and coagulase test and inoculation on Mannitol salt agar. The isolates were gram positive cocci with catalase positive, coagulase negative with no fermentation on mannitol salt agar.

Final identification was made by Kirby-Bauer disc diffusion method as recommended by the National Committee for Clinical Laboratory Standards Institute (2005). The bacterial colonies introduced after following the procedure as described by McFarland. The following antibiotic disks (Oxoid-UK) were used; Oxacillin (1µg), Novobiocin (5µg), Methicillin (10µg). The isolates were inoculated on Mueller Hinton agar and incubated at 37°C for 24 hours to assess the susceptibility of the isolates to methicillin. The isolates were taken as methicillin resistant if the zone of inhibition was <10mm for oxacillin, < 9 mm and for novobiocin > 16mm.

# RESULTS

A total of 300 clinically suspected cases of biomaterial related infections attending OPDs or indoor patients in surgical department, medicine department and Paediatrics Department from JPMC, NICH, LGH and CHK were included in this study and yielded 103 (34.3%) methicillin resistant Staphylococcus epidermidis.

Table 1 shows out of 300 cases 103 (34.3%) methicillin resistant Staphylococcus epidemidis were isolated.

**Table No.1: Occurrence ofMRSE in patients**

| No. of patients | Positive for MRSE | Percentage |
|---|---|---|
| 300 | 103 | 34.3% |

Table 2 shows hospital wise distribution with MRSE. 100 samples from JPMC with 38 (38%) positive, 100 samples from CHK with 37 (37%) positive and 100 samples from NICH with 28 (28%) positive cases respectively.

**Table No.2: Distribution of MRSE positive specimens according to hospital**

| Hospital | No. of patients | Positive for MRSE | Percentage |
|---|---|---|---|
| JPMC | 100 | 38 | 38% |
| CHK | 100 | 37 | 37% |
| NICH | 100 | 28 | 28% |

Table 3 shows age wise distribution of patients with MRSE. 28 out of 100 (28%) cases were found in 0-12 years age group, 12 out of 25 (48%) in 12-18 years age group, 23 out of 48 (47.9%) in 18-30 years, 15 out of 41 (36.5%) in 30-40 years of age, 12 out of 43 (27.9%), 6 out of 21 (28.5%) in 50-60 years of age, 5 out of 11 (45.4%) in 60-70 years, 2 out of 8 (25%) in 70-80 years of age and finally 1 out of 3 (33.3%) in 80-90 years of age respectively.

**Table No.3: Distribution of patients with MRSE in different age groups**

| Age group (Years) | No of patients | Positive for MRSE | Percentage |
|---|---|---|---|
| 0-12 | 100 | 28 | 28.0% |
| 12-18 | 25 | 12 | 48.0% |
| 18-30 | 48 | 23 | 47.9% |
| 30-40 | 41 | 15 | 36.5% |
| 40-50 | 43 | 12 | 27.9% |
| 50-60 | 21 | 06 | 28.9% |
| 60-70 | 11 | 05 | 45.4% |
| 70-80 | 08 | 02 | 25.0% |
| 80-90 | 03 | 01 | 33.3% |

Table 4 shows distribution of MRSE according to gender. Of the 300 specimens, 132 (44%) were female showing 48 (36.3%) positive for MRSE while 84 (63.6%) were negative for MRSE. 168 (56%) specimens were taken from male patients out of which 55 (32.7%) were positive for MRSE and 115 (68.4%) were negative for MRSE.

**Table No.4: Distribution of MRSE on the basis of gender**

| Gender | No of patients | Positive for MRSE | Negative for MRSE |
|---|---|---|---|
| Female | 132 (44%) | 48 (36.3%) | 84 (63.6%) |
| Male | 168 (56%) | 55 (32.7%) | 115 (68.4%) |

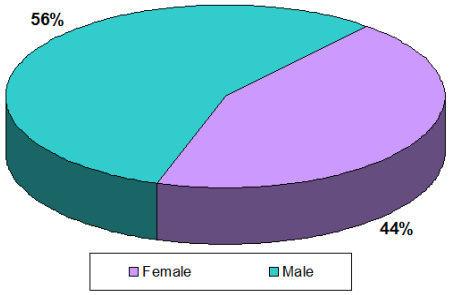


**Figure: Distribution of MRSE on the basis of gender**

Table 5 shows the results of MRSE isolated on the basis of department. 50 specimens were taken from medicine department showing 18 (36%) positivity for MRSE and 32 (64%) were not positive for MRSE. 200 specimens were collected from department surgery showing 76 (38%) positive for MRSE and 124 (62%) negative for MRSE. 50 specimens were collected from Paediatric department showing 14 (28%) positive for MRSE and 36 (72%) negative for MRSE.

**Table No.5: Distribution of MRSE according to department**

| Department | No of patients | Positive for MRSE | Negative for MRSE |
|---|---|---|---|
| Medicine | 50 | 18 (36%) | 32 (64%) |
| Surgery | 200 | 75 (38%) | 124 (62%) |
| Paediatrics | 50 | 14 (28%) | 36 (72%) |

Table 6 shows the results of MRSE isolated on the basis of the sample type. 167 samples were from operated wound infections showing 60 (35.9%) positive for MRSE, 63 samples were taken from cannulae wound infections out of which 21 (33.3%) were positive for MRSE. 47 samples were taken from Injection abscess out of which 17 (36.1%) were positive for MRSE. 23 samples were collected from tips of cannulae catheters showing 5 (21.7%) positive for MRSE.

**Table No.6: Distribution of MRSE according to sample type**

| Sample site | Number of patients | Positive for MRSE |
|---|---|---|
| Operated wound infections | 167 | 60 (35.9%) |
| Cannulae wounds infection | 63 | 21 (33.3%) |
| Infection abscess | 47 | 17 (63.1%) |
| Catheter tips and cannula tips | 23 | 05 (21.7%) |
| **Total:** | **300** | **103** |

# DISCUSSION

Methicillin resistant Staphylococcus epidermidis are the common cause of infections associated with the use of catheters, cannulae, sutures, injection needles in both indoor and outdoor hospital patients. The present study was conducted to determine the prevalence of biomaterial related infections due to methicillin resistant Staphylococcus epidermidis.

The purpose of this study was to assess the frequency of MRSE in infections associated with biomaterial culture and biochemical tests were performed for isolation of MRSE. In this study out of a total 300 cases MRSE were isolated among 103 (34.3%).

This study supports the finding that most common etiological agent of biomaterial related infection is methicillin resistant Staphylococcus epidermidis. Yameen et al. (2010)[12] stated that the prevalence rate of methicillin resistant Staphylococcus epidermidis in hospitalized patients were 29.78%.

Chaieb et al. (2005)[8] mentioned that Staphylococcus epidermidis is responsible for 33.5% of nosocomial blood stream infections. Intravenous access lines and needles connectors have been demonstrated to be a risk factor for blood stream infection. In a study done by Chaieb et al. (Tunisia) in 2007, a high frequency of Staphylococcus epidermidis (72%) isolated from biomaterials. A significant study of neonatal infections was conducted in Naples by Villari et al. (2000)[14]. Results found indicated that Staphylococcus epidermidis was the pathogen leading to blood stream infections (39.8%). Surface infections (29.8%) and meningitis (58.3%) also related to the use of biomaterials. In accordance to study conducted by Manikandan et al. in 2005[13] the prevalence of Staphylococcus epidermidis (57.1%) in hospitalized patients and is resistant to methicillin and oxacillin. In another study conducted by Mohanty et al. (2007)[15] the prevalence of Staphylococcus epidermidis in surgical patients is 34.5%.

In accordance to another study conducted in surgical wards of JPMC the prevalence of Staphylococcus epidermidis was 46.8% (Budvi, 2007).

Keramidas et al. (2003)[6] mentioned the prevalence of methicillin resistant Staphylococcus epidermidis between 35 to 66%. In another study by Buonavoglia et al. (2010),[7] Staphylococcus epidermidis shows a higher level of prevalence (60-70%) demonstrating the ability of staphylococci to spread from hospital environment to community.

# CONCLUSION

Methicillin resistant Staphylococcus epidermidis tends to show a higher level of prevalence. These most susceptible to infection are intravenous users, new borns, elderly, and those using catheters as artificial appliances. Infections caused by MRSE are often persistent and relapsing, and it have the ability to spread from hospital environment to community and to colonize health individual.

The alarming increase in prevalence of MRSE suggested to fully assess its importance, it may be essential to determine its species, prevention, and treatment as no particular pattern can be predicted in any problematic situation.

Patients suffering from infections related with biomaterial should be monitored for MRSE at regular intervals.

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Original Article

# Clinical Presentation and Evaluation of Histopathological Patterns of Hospital-based Frequency of Thyroidectomic Biopsies

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## ABSTRACT

**Objective:** The aim of this study is to evaluate the clinical presentation of different histopathological pattern of hospital-based surgical thyroidectomic specimens.

**Study Design:** Multicentre, Prospective Study.

**Place and Duration of Study**: This study was conducted at the department of Pathology, Isra University Hyderabad; Liaquat University of Medical and Health Sciences, Jamshoro; Memon Hospital, Hyderabad and Al-Tibri Medical College & Hospital, Isra University Karachi Campus from July 2009 to December 2011.

**Materials and Methods:** In the present 358 thyroidectomic specimens were collected from four different hospitals of Sindh. Specimen of thyroid tissue was taken after the end of thyroidectomy. The tissues were fixed in buffered neutral formalin and after processing embedded in paraffin to form tissue blocks. A 5µm thick sections were cut by microtome and the sections were then stained with Hematoxylin and Eosin (H &E) strain. Special stain like PAS were also used for confiring specific diagnosis. The histopathalogical examination was then carried out for any morphological changes.

**Results:** The results showed that hospital-based frequency of throidectomy specimens was found to be 4.1%, indicating that the thyroid diseases are common in plain areas of Sindh. Multinodular goiter was the most common histopathological pattern in 202 cases and usually presents as asymptomatic lump in the neck. Thyroid neoplasms were found to be the second most common disease in 94 cases specially the follicular adenoma and papillary carcinoma. The mean±SD age of the patients in 358 thyroidectomy specimen was 32.65±10.66 years. The persons having age ranges between 10 to 70 years were considered. The youngest patient included in our study was 10 years old female with colloid adenoma. The female to male ratio was 2.5:1.

**Conclusion:** Thyroid diseases are common in plain areas. Multinodular goiter is the most prevalent thyroid disease. Follicular adenoma and papillary carcinoma are the most frequent thyroid neoplasms. It is therefore concluded that multinodular goiter and thyroid neoplasm are the most common pattern in thyroid diseases in these areas.

**Key Words:** Histopathological pattern, Thyroidectomy, Biopsies, Hospital-based frequency.

## INTRODUCTION

Goiter or enlarged thyroid gland is one of the major health concerns and common disorder of the endocrine system. It occurs in about 3-5% of the population world wide.[1] A female preponderance is seen for thyroid diseases especially in the adolescent females for non-neoplastic and neoplastic diseases.[2] Enlargement of thyroid gland or goiter may present as diffuse, solitary or multinodular swelling, which requires total, subtotal thyroidectomy or lobectomy depending on the clinical diagnosis.[3] Thyroid diseases have also propensity for different geographic locations that is because of different amount of iodine intake in the diet. [4]

In Pakistan goiter has critically high prevalence in iodine deficient Northern areas of the country in the lap of Himalayas[5.] Disorder resulting from iodine deficiencies are not only common in mountainous areas but are also reported in plain areas such as Karachi, Lahore and Islamabad with an alarming prevalence.[6] In a study conducted at Lahore, about one fourth of the pregnant women screened were reported as moderately iodine deficient.[7] WHO Global database on iodine deficiency reported in Pakistan is struggling with severe iodine deficiency, and due to this reason about 128 million population are at risk of iodine deficiency.[8]

## MATERIALS AND METHODS

The material used for this study consisted of thyroidectomic specimens that were collected from the department of Pathology, Isra University Hyderabad, Liaquat University of Medical & Health Sciences, Jamshoro, Memon Hospital, Hyderabad and Al-Tibri Medical College, Karachi during the period of July 2009 to June 2011. The thyroidectomic specimens were selected regardless of age, gender and social classes. The thyroid tissues were taken out and preserved in 10% formalin before microscopic examination. The tissues were then fixed in normal saline for 24-48 hours and processed through a series of ethyl alcohol of ascending strength (70, 80 and 95%) for period of 1 hr, twice in absolute alcohol (for 1 hr) and twice in xylene (for 1 hr) in order to render the tissue elements transparent. The tissues were then infiltrated with

molten paraplast at 58 ºC twice (1 hr on each occasion). The transparent tissues after clearing all elements were embedded in a solid mass of paraplast. The blocks were labeled, allowed to cool and the metal blocks were removed. The solid mass was then trimmed free of excess paraplast, leaving some free margins around the embedded tissues.

Five microns thick longitudinal sections were cut with a rotary microtome. The sections were mounted on thoroughly cleaned gelatinized slides and were placed on hot plates at 37ºC for 24 hrs for proper fixation. The slides were then stained by Hematoxylin and Eosin (H & E) stain according to prescribed staining method (Bancroft and Stevens, 1990). Several slides were prepared accordingly for microscopic examination. In addition relevant special stain like PAS was also used for specific diagnosis of the diseases and histopathological changes in the tissues.

Statistical analysis was done by using SPSS version 16 with P-value of <0.05 as significant.

# RESULTS

A total of 8725 histological samples were received from three different institutes included in this study during July 2009 to June 2011. Out of these, thyroidectomic specimens constituted 358 cases, making thyroid specimens 4.1% of the total samples examined.

The mean±SD age of the patients in 358 thyroidectomic specimen was 32.65±10.66 years. The age ranged between 10 to 70 years. The youngest patient in our series was 10 years old female with colloid adenoma and the female to male ratio was 2.5:1.

The results showed lump in the neck as the most common clinical presentation observed in 60% of the cases followed by increase in the size of a long standing goiter in 22% and solitary thyroid nodule in 12% of cases. Hoarseness, dysphagia and shortness of breath were seen in 5.8% of the cases and lymph node involvement was noted in 0.3% (one) case of papillary carcinoma.

**Table No. 1: Histopathological pattern of thyroid diseases**

| Patterns of thyroid disease | Frequency | Percent |
|---|---|---|
| Multinodular Goiters | 202 | 56.4 |
| Benign Tumors | 66 | 18.4 |
| Thyroiditis | 33 | 9.2 |
| Diffuse Goiters | 29 | 8.1 |
| Malignant Tumors | 28 | 7.8 |
| Total | 358 | 100 |

Histopathological examination revealed multinodular (adenomatous) goiter as the most common thyroid lesion seen in 202 (56.4%) cases followed by benign tumors in 66 (18.4%) cases. Thyroiditis constituted 33 (9.2%) cases where as diffuse goiter was seen in 29 (8.1%) of the cases and thyroid carcinoma in 28 (7.8%) cases (Table 01).

Benign tumors of thyroid gland constituted a total of 66 (18.4%) cases; out of which follicular adenoma was the most common lesion seen in 51 (77.3%) cases followed by colloid adenoma 8 (12.1%) cases, Hurthle cell adenoma 5 (7.6%) cases and papillary adenoma 2 (3%) cases (Table 02).

**Table No. 2: Distribution of Benign thyroid tumors of thyroid**

| Type | No. of cases | Percentage |
|---|---|---|
| Follicular Adenoma | 51 | 77.3 |
| Colloid Adenoma | 8 | 12.1 |
| Hurthle cell Adenoma | 5 | 7.6 |
| Papillary Adenoma | 2 | 3 |
| **Total** | **66** | **100** |

Malignant tumors constituted 28 (7.8%) of the cases in this study. Papillary carcinoma was the commonest malignant thyroid lesion with total of 67.9% (19 cases), followed by 14.3% (4 cases) of follicular carcinoma, 10.7% (3 cases) of anaplastic carcinoma and 7.1% (2) cases of medullary carcinoma (Table 03).

**Table No. 3: Distribution of Malignant thyroid tumors of thyroid**

| Type | No. of cases | Percentage |
|---|---|---|
| Papillary Carcinoma | 19 | 67.9 |
| Follicular Carcinoma | 4 | 14.3 |
| Anaplastic Carcinoma | 3 | 10.7 |
| Medullary Carcinoma | 2 | 7.1 |
| **Total** | **28** | **100** |

# DISCUSSION

Thyroid diseases are of great concern because most of them are amenable to medical or surgical management. Nodular thyroid diseases, which include both solitary nodules of the thyroid and multinodular thyroid gland, are fairly common entities. [9,10] According to WHO 4-7% of world population is suffering from clinically apparent goiter. Developing countries show the highest incidence, where the disease is attributed to iodine deficiency.[5]

This study was conducted in four different institutes. Two of these represent the only teaching hospitals laboratories of the Hyderabad city, third one is a well reputable hospital laboratory in the same city where as fourth one is also a teaching hospital based at Karachi. The hospital-based incidence in our series could be crudely projected to population-based incidence, giving the population-based incidence of thyroid diseases in the plain areas of Sindh.

Thyroid specimens in our series were 4.1% of the total 8725 histological samples examined. This finding is comparable with reported prevalence of thyroid

diseases by other authors; [9,11,1] however in iodine deficient areas of the world overall prevalence of goiter is reported upto 22.8%.[12]

The mean age in the present series 32.65 years (SD±10.66) was in accordance with the study conducted in Lahore.[13] The peak incidence in 3rd decade of life reported in 132 (36.9%) of the cases, was found consistent[11]. In the present study female predominance incidence was seen in all thyroid diseases constituting of 255 (71.2%) cases out of 358 thyroidectomic specimen and 103 (28.8%) cases in males. The female to male (F: M) ratio was found to be 2.5:1 which is in accordance with the findings reported by other workers[5,9]. However higher female to male ratio of 5.5:1, 4.5:1, 6:1 and 6:1 respectively was also found in some cases.[1,11,14,15]

The most common indication for thyroidectomy in this study was lump in the neck (60%) of the cases followed by increase in the size of a long standing goiter in 22% of cases, which is consistent with the results of the study carried out in Karachi and Nigeria.[10,16]

The histopathology findings were grouped into five major patterns: Multinodular goiter, diffuse goiter, thyroiditis, benign tumors and malignant tumors. Strict histopathological diagnostic criteria were attempted for the above grouping. Multinodular goiter was considered as thyroid tissue with colloid or multinodular growth pattern and with absence of features of malignancy. The thyroiditis included lymphocytic thyroiditis, Hashimoto's disease, granulomatous thyroiditis and Riedel's thyroiditis.

This study also showed that most prevalent histopathological pattern of the thyroid diseases in the series was multinodular goiter 202 (56.4%) followed by thyroid neoplasm 94 (26.2%) cases. These findings were consistent with study conducted in Malaysia[14] showing multinodular goiter (64.8%) as the commonest entity followed by neoplastic lesion (28.1%). The thyroid adenoma was seen in 66 (18.4%) cases and thyroid carcinoma in 28 (7.8%) cases. The same frequency 14(15.5%) in case of follicular adenoma was also reported[9]. However, a higher number of malignant lesion 26 (24%) were seen in his study. Thyroiditis constituted 33 (9.2%) cases where as diffuse goiter was seen 29 (8.1%) of the cases in our series. These results are in agreement with studies done in Bahrain[9] and Karachi[5]; however in Ethiopia and Nigeria a relatively lower frequency 2.1% and 1.8% of thyroiditis was reported.[12,15]

Multinodular goiter was the most common nonneoplastic thyroid disease with a frequency of 202 (76.5%) and a comparatively high frequency 97.2% was reported.[17] Diffuse goiter was 2nd common nonneoplastic disease (11%), followed by autoimmune thyroiditis (9.4%) i.e., lymphocytic thyroididtis (4.9%), hashimoto's thyroiditis (4.5%), reidel's thyroiditis (2.3%) and granulomatous thyroiditis (0.8%)]. These findings are in accordance with study done in Bahrain[9] i.e., diffuse goiter was 2nd common nonneoplastic disease (8%) and autoimmune thyroiditis affecting (7%) of the cases. However, a lower frequency of diffuse goiter 2% and 3.18% and autoimmune thyroiditis 5.6% and 3.92% respectively was reported,[18,19] which is in contrast to the findings in the present study.

The information in the present study may be considered as a baseline data of thyroid diseases in plain areas of Sindh and a more multicentric prospective study should be carried out on a large scale to investigate the national patterns of thyroid diseases in Pakistan, that will also help in outlining the plans for early detection, diagnosis and planning uniform intervention policy for the thyroid diseases.

# CONCLUSION

This study was done to detect the various histopathological patterns in thyroidectomic specimen, and to correlate theses histopathological findings with clinical presentation. Identification of thyroid diseases can be effectively done by proper diagnostic tools, including ultrasonography, reliable FNAC for the preoperative assessment of patients plays a vital role in the diagnosis of thyroid nodules and permits the number of surgical operations to be reduced. Marked variations in the relative frequency of thyroid diseases in different parts of the country are recognized.

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Original Article

# Comparison of Adynmic External Fixator with Dynamic External Fixator in the Management of the Comminuted Fractures of Distal Radius in the Patients Between 40-65 Years Age

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## ABSTRACT

**Objective**: To compare the treatment outcome of comminuted intra-articular fractures distal radius with adynamic external fixator and dynamic external fixator in patients of 40-65 years of age.

**Study Design:** Experimental Study.

**Place and Duration of Study:** This study was carried out in the Department of Orthopaedic, Nishtar Hospital, Multan from Jan 2010 to December 2011.

**Materials and Methods**:- This experimental study was carried out in the Department of Orthopaedic, Nishtar Hospital, Multan. A total of 60 patients in both groups were included in the study.

**Results**: Out of the 60 patients, 43 (71.7%) were male and 17 (28.3%) were female with the right hand 35 (58.3%) and left hand 25 (41.7%).

**Conclusion**: It is concluded that dynamic external fixator is a better method of treatment for the comminuted fractures of the distal radius than adynamic external fixator because it allows early motion of tendons, muscles and adjacent joints and later, of the wrist itself while reduction and especially radial length were maintained in bridging external fixation.

**Key Words**: Distal Radius, Comminuted fracture, Dynamic external fixator.

## INTRODUCTION

The distal radius fracture is the most common skeletal injury that affects women, particularly between 50-60 years, 3 times more frequently than men[1]. This is usually caused by fall on outstretched hand though sports and road traffic accidents also sometimes result in such fractures.

Fracture distal radius was used to be managed conservatively. Now the differentiated management has led to a change from a purely conservative treatment method to a more varied treatment methods for fractures distal radius[2]. Fracture of the distal radius traditionally had been managed by closed reduction and forearm plaster[3]. It had been treated as trivial injury with the resulting 40% poor outcome because of redisplacement of fractures in the cast. Many methods designed to prevent redisplacement have been developed including open reduction and internal fixation and kirschner wire fixation[4]. The external fixator is an essential part of differentiated treatment method with reference to the several types of distal radius fractures in older patients[5]. New dynamic external fixator has been evolved to further enhance the good prognosis.

The seeming contradictions in literature serve to illustrate that individual outcomes are not entirely predictable because of different functional demands, expectations and pain tolerance for each patient[6]. There is no consensus regarding the description of the condition, the appropriate treatment or even the anticipated outcome[7]. It is generally accepted that restoration of anatomy, in particular to joint congruence, is essential to ensure a satisfactory functional result[8,9].

## MATERIALS AND METHODS

This experimental study was carried out in the Department of Orthopaedic, Nishtar Hospital, Multan from January 2010 to December 2011. A total of 60 patients were included in the study. These patients were divided in two groups (group-A was treated by adynamic external fixator and group-B with dynamic external fixator) under anaesthesia.

## RESULTS

The age of the patients was between 40-65 years. In group-A average age was 47.71 $\pm$ 5.55 years in males and 49.89 $\pm$ 3.33 years in females. In groups-B average age was 49.68 + 5.45 years in males and 50.38 $\pm$ 4.58 in females. Most of the injuries occurred due to the trauma i.e. fall on the outstretched hands in road accidents or fall from height like tree. In present study 52.1% of patients sustained injuries in various automobile accidents, 29.4% due to falls from height (tree. Roof, stairs and well), 18.4% from domestic falls.

Involvement of right wrist was shown in 35 (58.3%) and left wrist in 25 (41.7%).

With the application of Frykman's classification, 13 (21.7%) fractures were of type-III, 9 (15%) of type-IV, 25 (41.7%) of type-V and 13 (21.7% of type-VI.

In group-A average radial length on post injury film was 4.3 mm, which was brought to 9 mm on post reduction films. In group-B average length in pre-reduction film was 4 mm, which was brought to 9.2 mm in post reduction films (Table-1).

In group-A, 12 (40%) patients had excellent , 14 (46.7%) patients had good and 4 (13.3%) patients had fair anatomical end results. In group-B, 12 (40%) patients had excellent, 15 (50%) good and 3 (10%) patients had fair anatomical end results (Table-2).

In group-A, 10 (33.3%) patients had excellent, 12 (40%) had good, 5 (16.7%) patients had fair and 3 (10%) patients had poor functional end results. Whereas in group-B 11 (36.7%) patients had excellent, 15 (50%) had good, 3 (10%) had fair and 1 (3.3%) patient had poor functional end results (Table-3).

Pin tract infection developed in 4 (13.3%) patients in group-A and 2 (6.7%) in group-B as shown in table-4.

**Table No.1: Average radiological measurements in both groups**

| | Average pre-reduction | Post-reduction | Final |
|---|---|---|---|
| **GROUP-A** Radial angle | 8.6° | 18.5° | 17° |
| Dorsal angle | + 18° | 2.4° | 2.2° |
| Radial length | 4.2 mm | 9 mm | 8 mm |
| **GROUP-B** Radial angle | 8.2° | 19° | 17.2° |
| Dorsal angle | 18.4° | 3.6° | 2.4° |
| Radial length | 4 mm | 9.2 mm | 8.4 mm |

**Table No.2: Anatomical end results in both groups**

| Group | Excellent | Good | Fair |
|---|---|---|---|
| A | 12 (40%) | 14 (46.7%) | 4 (13.3%) |
| B | 12 (40%) | 15 (50%) | 3 (10%) |

**Table No.3: Functional end results in both groups**

| Group | Excellent | Good | Fair | Poor |
|---|---|---|---|---|
| A | 10 (33.3%) | 14 (40%) | 5 (16.7%) | 3 (10%) |
| B | 11 (36.7%) | 15 (50%) | 3 (10%) | 1(3.3%) |

**Table No.4: Complications of distal radius fracture management**

| Complication | Group-A | Group-B |
|---|---|---|
| Pin tract infection | 4 | 2 |
| Stiff wrist | 1 | 0 |
| Re-displacement | 0 | 1 |
| Radial nerve superficial branch | 1 | 0 |
| Implant failure | 0 | 1 |
| Total | 6 (20%) | 4 (13.3%) |

# DISCUSSION

Distal radius fracture is not a trivial injury as used to be wrongly considered earlier. It needs a distinguished treatment depending upon the different types of injuries: intra/extra articular, simple/compound and stable/unstable. There is consensus that the goals of distal radius fracture treatment should be to allow early functional recovery of the upper extremity and to improve the long term function of the wrist.

Sex and age distribution in various series is different. In our study patients were included between 40-65 years of age. In older age groups the results are comparable with other studies mentioned in the literature because bone mineral density of distal forearm decreases with age. In group-A average age of 47.71 $\pm$ 5.55 years was among the males and 49.89 $\pm$ 3.33 was among the females. In group-B the average age of 49.68 $\pm$ 5.45 years in the males and 50.38 $\pm$ 3.58 was among the females.

Some series showed male predominance while others showed female predominance. In females the incidence rises at 40 to 60 years of age due to post menopausal osteoporosis. In our study, 43 (71.7%) patients were male and 17 (28.3%) were female. Male to female ratio is 2.53:1, while in another study, male to female ratio was 1.5:1[10]. It might be due to our different socio-economic setup in which male is the dominant and active member of our society and female has to go outside to earn livelihood for his family, so exposed to more chances of the trauma.

It is observed that right hand is affected in almost all series because it is the dominant hand. It is reported that 55% right radius involvement in a study[11]. In another study is reported 52% involvement of right wrist[12]. In our society where the use of right hand in routine manual activities, is religious obligation, therefore, in our study, the fracture of the right distal radius was found to be 58.3% in prevalence.

External fixator is valuable for unstable, comminuted distal radius fractures because it neutralizes compressive forces generated across the fracture by long extrinsic flexor and extensor muscle. By applying the principles of ligamentotaxis it reduces the comminuted fragments, resotres the articular congruity to acceptable anatomical level and maintains the reduction till union is achieved in good anatomical position. While dynamic external fixator allows early start of movement at the wrist joint within the period of external fixation.

Besides the high rate of better functional outcome, there had been few complications like pain, pint tract infection, implant failure, radial nerve superficial branch paraesthesis and wrist stiffness in our study. In both groups, symptoms of pain reduced with time. Pain was due to multiple reasons e.g. excessive distraction, pin insertion site irritation and sensory disturbance in the thumb. In one orthofix case, on second postoperative day, 1 patient reported back with complains of severe pain. On examination, he had free movement at proximal ball joint due to mechanical

failure of the device. He had lost reduction as well. So the patient was re-maipulated under anaesthesia and a new orthofix frame was mounted on the same pins previously applied.

In our study, pint traction infection occurred in 6 (10%) patients which were about the same as observed in other studies. In a study it is also noted almost the same percentage of pin tract infection in his study[13]. Fortunately in our study the in tract infection was superficial and was treated by short course of antibiotic therapy and blood sugar control in diabetic patients. No joint infection or oteomyelitis occurred in any patient.

Range of movement, recorded at different stages of evaluation showed better results in dynamic external fixator groups[14]. Independently there was no significantly difference in outcome among male and female patients[15].

In our study few patients had their ulnar styloid fractured at the time of injury but is did not have any adverse effect on the final outcome therefore these fractures were not particularly mentioned. This is comparable with the literature. In a study it is noted that fracture of ulnar styloid process, a frequent injury in concominance with fracture of the distal end of the radius. He observed to have no impact upon long term wrist function. In other series associated fractures of scaphoid had also been discussed with fracture distal radius but we have excluded such patients from the study.

# CONCLUSION

It is concluded from the study that the best anatomical and functional results can be obtained with dynamic external fixator in comparison to adynamic external fixator.

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Original Article

# The Use of Alpha-Blockers & Hyoscine N-butyl Bromide (HBB) for the Treatment of Nephrolithiasis is most Effective Treatment for lower Uretric Stones

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## ABSTRACT

**Background:** Medical expulsion therapy has been shown to be a useful adjunct to observation in the management of ureteral stones. Alpha-1-adrenergic receptor antagonists have been studied in this role.
**Study Design:** Experimental Study.
**Place and Duration of Study:** This study was conducted Urology at GMMMC Hospital Sukkur from January 2008 to December 2010.
**Materials and Methods:** In this study 480 patients were selected, with stones located in the distal tract of the ureter with stone diameters of 5 to 10mm were enrolled in the present study and were randomized into 4 equal groups. Group 1 received hyoscine N-butyl bromide (HBB), Group 2 received alfuzosin, Group 3 received doxazosin and Group 4 received terazosin. The subjects were prescribed diclofenac injection (75 mg) intramuscularly on demand for pain relief and were followed-up after two weeks with x-rays of the kidneys, ureters, bladder and urinary ultrasonography every week. The number of pain episodes, analgesic dosage and the number of days of spontaneous passage of the calculi through the ureter were also recorded.
**Results**: The average stone size for groups 1, 2, 3 and 4 was comparable (6.13, 5.83, 5.59 and 5.48 mm respectively). Stone expulsion was observed in 11%, 52.9%, 62%, and 46% in groups 1, 2, 3 and 4 respectively. The average time to expulsion was 10.55 ± 6.21 days in group 1, 7.38 ± 5.55 days in group 2, 7.85 ± 5.11 days in group 3 and 7.45 ± 5.32 days in group 4. Alpha blockers were found to be superior to HBB ($p < 0.05$).
**Conclusion:** Medical treatment of distal ureteral calculi with alfuzosin, doxazosin and terazosin resulted in a significantly increased stone-expulsion rate and decreased expulsion time when compared with HBB. HBB seems to have a negative effect on stone-expulsion rate.
**Key Words:** Alpha-Blockers, Hyoscine, N-butyl Bromide (HBB), Nephrolithiasis, Tamsulosin

## INTRODUCTION

Medical expulsion therapy has been shown to be a useful adjunct to observation in the management of ureteral stones. Alpha-1-adrenergic receptor antagonists have been studied in this role. Alpha-1 receptors are located in the human ureter, especially the distal ureter. Alpha-blockers have been demonstrated to increase expulsion rates of distal ureteral stones, decrease time to expulsion, and decrease need for analgesia during stone passage. Alpha-blockers promote stone passage in patients receiving shock wave lithotripsy, and may be able to relieve ureteral stent-related symptoms. In the appropriate clinical scenario, the use of α-blockers is recommended in the conservative management of distal ureteral stones.

Anti-spasmodic agents, such as hyoscine -N-butylbromide, are often prescribed by general practitioners or by emergency services as soon as renal colic is diagnosed. HBB may help provide analgesia by inducing smooth muscle relaxation, which decreases ureteral spasm. For this reason, anti-spasmodic agents are still recommended in the treatment of renal colic, usually as adjuvant therapy to NSAIDS and/or opioids[5]. Tamsulosin has been the most commonly studied alpha-1 blocker in the treatment of ureteral stones with increased spontaneous stone expulsion; however, the efficacy of other alpha-blockers has not been well studied, although many are less costly and more available than tamsulosin. Studies that have assessed anti-spasmodic agents primarily focused on the effect of pain management in renal colic treatment. For this reason, a prospective randomized study was planned to compare the effectiveness of three different types of non-specific alfa1-adrenoreceptor antagonists and HBB for relieving ureteral colic and facilitating the spontaneous expulsion of distal ureteral stones.

## MATERIALS AND METHODS

A total of 480 adult patients who were admitted to the Urology ward at GMMMC hospital Sukkur, with complaints of renal colic were prospectively evaluated between January 2008 and December 2010. The study was approved by the local Ethics Committee. Patients

who had radio-opaque stones located in the distal tract of the ureter with stone diameters of 5 to 10 mm were included in the study.

Exclusion criteria were as follows: presence of urinary tract infection, diabetes mellitus, pregnancy, renal insufficiency (serum creatinine greater than 1.8 mg/dL), a solitary kidney, radiolucent stones, multiple stones, a previous history of distal ureter surgery, severe hydronephrosis, current alpha-blocker use or allergic reaction to the study medication.

All patients were evaluated with x-rays of the kidneys, ureters, and bladder as well as ultrasonography of the urinary system. Stone size was recorded for each patient. The treatment was fully explained to patients before obtaining informed consent.

Patients were randomly divided into four groups. Each group initially included 120 patients. Group 1 received HBB (30 mg oral tablet three times a day); Group 2 received alfuzosin (10 mg daily); Group 3 received doxazosin (4mg daily) and Group 4 received terazosin (5 mg daily). Alpha-blocker drugs were administered before going to bed in the evening. The patients receiving terazosin and doxazosin were started on their therapeutic doses upon entering the study rather than being titrated to that dose. All patients were instructed to drink at least 3 L of fuids daily. The patients were prescribed a diclofenac injection (75 mg) intramuscularly on demand for pain relief. The subjects were advised to flter their urine, and those who had passed their stones were asked to stop taking the medication. The patients were followed-up weekly for up to two weeks with x-rays of the kidney, ureter and bladder region, and urinary ultrasonography and urine analysis were performed to exclude infection. Subjects recorded daily pain using a visual analog pain score (linear 11-point scale from 0, no discomfort, to 10, the most severe pain ever experienced), and they maintained a pain medicine diary that recorded the number of doses of diclofenac medication consumed per day. The date and time of stone passage were recorded. The criteria for treatment discontinuation and the need for hospitalization and/or endoscopic treatment were intolerable pain, fever and/or the development of new severe hydronephrosis or worsening of already present hydronephrosis, or lack of success of stone expulsion after two weeks.Two endpoints were chosen to determine the effect of alpha-blockers and HBB on the treatment of ureter stones, stone expulsion rate and pain score reduction.Statistical analyses were performed with ANOVA and Pearson's chi-square test using the parameters of stone size, expulsion rate, time to expulsion, amount of analgesic compound and number of pain episodes. A value of $P < 0.05$ was statistically significant.

# RESULTS

There were no statistically significant differences between the groups with respect to age, sex, stone size, baseline degree of hydronephrosis present and previous stone passage history (Table-1).

**Table No.1: Patients Characteristics:**

| | | HBB | Alfuzosin | Doxazosin | Terazosin | p Value |
|---|---|---|---|---|---|---|
| Mean age | | 45+/-10 | 45+/-5 | 30+/-6 | 36+/-3 | 0.283 |
| Male-female% | | 68%-25% | 55%-42% | 39%-50% | 69%-30% | 0.065 |
| Stone size(mm) | | 7.13+/-1.11 | 6.83+/-1.76 | 6.59+/-1 | 6.48+/-1.72 | 0.626 |
| Hydronephrosis | 0 | 72% | 45% | 49% | 42% | 0.477 |
| | 1 | 6% | 31% | 30% | 28% | |
| | 2 | 16% | 15% | 14% | 25% | |
| Previous stone passage | yes | 32% | 25% | 16% | 34% | 0.715 |
| | no | 64% | 72% | 70% | 63% | |

**Table No.2: follow-up Results of the Group:**

| | | Hbb | Alfuzosin | Doxazosin | Terazosin | p Value |
|---|---|---|---|---|---|---|
| Stone expulsion rate% | | 29% | 71% | 76% | 68.10% | 0.05 |
| Mean day to expulsions | | 10.55 +/- 6.21 | 7.38 +/- 5.55 | 7.85 +/- 5.11 | 7.45 +/- 5.32 | 0.05 |
| Decrease pain score (VAS) | BL | 7.50 +/- 2.4 | 7.94 +/- 2.1 | 7.64 +/- 2.8 | 7.44 +/- 2.3 | |
| | F | 3.98 +/- 2.5 | 4.3+/- 2.4 | 3.9 +/- 2.3 | 3.9 +/- 2.6 | 0.567 |
| Diclofenac requirment (n) | | 5 +/- 1 | 7.36 +/- 1.2 | 6 +/- 2 | 5.36 +/- 2 | 0.567 |

(BL= baseline, F=follow-up, VAS= visual analogue scale

stone expulsion was observed in 35 of 118 patients in group 1 (29%), 85 of 119 patients in group 2 (71%), 89 of 117 patients in group 3 (76%), and 79 of 116 patients in group 4 (68.1%). In groups 2, 3 and 4, the rate of the spontaneous passage of the calculi was found to be higher compared with that in group 1 ($P < 0.05$) (Table-2). There was no difference detected between the alpha-blocker groups with respect to the rate of the spontaneous passage of the stones. Average time to expulsion was $10.55 \pm 6.21$ days in group 1, $7.38 \pm 5.55$

days in group 2, 7.85 ± 5.11 days in group 3 and 7.45 ± 5.32 days in group 4. Time to expulsion was recorded significantly less often in groups 2, 3 and 4 than in group 1 ($P < 0.05$). However, no significant difference was noted between groups 2, 3 and 4 ($p = 0.756$). Decreases in baseline pain were noted in 53%, 55.6%, 51% and 52% with the use of HBB, alfuzosin, doxazosin and terazosin, respectively. When comparing the improvement in the baseline pain score, there were no significant differences between the groups ($p = 0.567$). Similarly, the mean number of diclofenac administrations was observed to be similar in the groups ($p = 0.567$) (Table-2).

Of the 480 patients, 10 were removed from the study due to urinary tract infection, patient request for intervention and lack of compliance in 5, 2 and 3 patients, respectively. Requiring to stop the medication due to the adverse events was not recorded in the groups.

# DISCUSSION

The availability of minimally invasive treatment alternatives and the high success of extracorporeal shockwave lithotripsy (ESWL), emergency ESWL and ureteroscopic extractions have greatly changed the way in which stone treatment is approached[6]. However, urologists are often doubtful about the best form of therapy and should consider the possibility of spontaneous passage of stones or the use of medical therapy. With the introduction of MET, the clinical treatment of ureteral stones has undergone a major evolution. Treatment regimens involving alpha adrenergic drugs are aimed at promoting ureteral smooth muscle relaxation. Alpha-1-adrenergic receptor antagonists have some degree of selectivity for the detrusor muscles and distal ureter and have thus been investigated for their potential to promote stone expulsion and decrease pain[7,8]. Because there is no need to titrate the dose, tamsulosin has been the most commonly studied alpha-blocker in the treatment of ureteral stones[9-11]. Alpha-blockers are still an off-label treatment for ureteral stones. We aimed to evaluate the effectiveness of the other three alpha-blockers, which are less expensive and more available than tamsulosin. Ureteral stones are most prevalent in patients between the ages of 40 and 45[12], and with respect to cardiovascular stability, this population is relatively more stable than patients diagnosed with benign prostatic hyperplasia (BPH). Dose titration with doxazosin and terazosin, which is recommended in the management of BPH, may not be required for this particular population. In this study, patients receiving terazosin and doxazosin were started on their therapeutic doses upon inclusion into the study rather than being titrated to that dose.HBB acts by inhibiting cholinergic transmission in the abdominal-pelvic parasympathetic ganglia, thus relieving spasm in the smooth muscles of the gastrointestinal, biliary, and urinary tract[13]. In Turkey HBB is the most prescribed agent for the symptomatic treatment of renal colic. To our knowledge, the present study is the first to compare the effectiveness of HBB and nonselective alpha-1 blockers in the treatment of ureteral stones.In complete obstruction, the signs of kidney injury appear within three to four weeks[14]. For this reason, clinicians may wait up to four weeks to see if the stones will pass spontaneously, provided that the patient is comfortable. Studies with MET showed that 80-90% of stone expulsion occurs within 15 days[15].

In the current study, intervention was suggested after a two week follow-up. It was determined that the stone expulsion rate for three different alpha-adrenergic blockers was significantly higher when compared to the HBB group (alfuzosin, 71%; doxazosin, 76%; terazosin, 68.1%; HBB, 29%%). In addition, alpha-blockers were better than HBB with respect to the time to the spontaneous passage of the stones (7.5 days versus 10.55 days). The pain medicine requirement also decreased significantly with alpha-blockers; however, this difference was not significant when compared with HBB. Yilmaz et al. compared the efficacy of three different alpha-adrenergic blockers[16]. The stone expulsion rates of tamsulosin, terazosin, and doxazosin were found to be 79.31%, 78.57%, and 75.86%, respectively. The mean time to passage was significantly lower in the groups receiving alpha-1 blockers compared with the control group. In the present study, the stone-expulsion rates were found to be 62% and 45.1% in the doxazosin and terazosin group, respectively. A meta-analysis of 11 clinical trials that enrolled a total of more than 900 patients suggested that alpha-blockers increase the rate of spontaneous stone passage by 44%[17]. Tamsulosin has been the most commonly studied alpha-1 blocker in the treatment of ureteral stones. Direct comparison of alfuzosin and tamsulosin in the management of lower ureteral calculi has shown that both drugs increase the stone-expulsion rate (82.3% vs. 70.5%), decrease expulsion time (12.3 versus 14.5) and reduce the need for analgesics[18]. Ukhal et al. found that the rate for the spontaneous passage of distal ureteral stones with doxazosin was 71.1% and demonstrated that the drug decreases the frequency of renal colic[19].

In the present study, the expulsion-rate of stones using alpha-blockers was slightly lower than the literature findings. Our explanations are as follows: 1) Steroids or anti-edema agents have generally been included in medical treatment for their anti-in?ammatory action, presumably to reduce local edema; however, in our study, no steroids were used. 2) A factor that might

have affected stone-expulsion rate other than stone size might have been the duration of colic and the degree of impaction and obstruction by the stone, which was not addressed in the current study. 3) Stone sizes < 5 mm were also included in previous reports. 4) The duration of MET was longer in previous reports. In our study, stone sizes < 5 mm were excluded, and the duration of MET was two weeks.Anti-spasmodic agents such as HBB may theoretically help provide analgesia by inducing smooth muscle relaxation, which decreases ureteral spasm. For this reason, anti-spasmodic agents are still recommended in the treatment of renal colic, but with inconsistent clinical benefit[20]. Most studies administering anti-spasmodic agents focused only on the control of analgesic symptoms for renal colic due to ureteral stone. The current study was performed to assess and compare the expulsive effects of orally administered HBB and alpha-blockers. Dabella et al. evaluated the expulsive effects of orally administered phloroglucinol, tamsulosin and nifedipine for distal ureteral stone[3]. The expulsion rate was found to be higher for tamsulosin, followed by nifedipine and phloroglucinol; the expulsion rates were 97.1% and 77.1%, 64.3%, respectively. Surprisingly, the expulsion rate in the HBB group was found to be 11% in the current study. The relatively larger stone size and the lack of corticosteroid administration may explain the lower expulsion rate. Pain relief of 53% was noted on the visual analog scale with the use of HBB, which was similar to that of the alpha-blockers. The efficacy of HBB can only be due to a reduction in ureteral hypermotility, as no direct analgesic property of the compound has been documented at the dose used. We speculate that the lower stone-expulsion rate in HBB may be due to its anti-spasmodic effect, resulting in the diminished ureteral activity necessary for stone expulsion. With regard to the two end points of the current trial, alpha-blockers proved to be superior to HBB. Treatment to relieve the pain associated with ureteral colic was found to be similar for all groups.

# CONCLUSION

Alpha-1 blockers, regardless of the type, were found to be effective in the treatment of distal ureteral stone in terms of stone expulsion and pain control. HBB was found to be effective at controlling pain; however, the effect of stone expulsion was lower than that of alpha-blockers. HBB seems to have a negative effect on stone expulsion. The major limitation of the current study was the small sample size. Further studies may be needed to evaluate the effect of anti-spasmodic agents and non-tamsulosin alpha-blockers in the treatment of ureteral stones.

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Original Article

# A Break up of Autopsies Conducted at District Head Quarter Hospital Kasur

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## ABSTRACT

**Background:** This is the first time study to find out the cause and manner of death through medico-legal autopsies in a small district comprising municipal boundaries and rural setup (District Kasur) and comparing it with urban studies conducted by the Forensic Medicine Departments of various medical colleges. This study is also aimed to assess the criminal behavior in this segment of society.

**Study Design:** Observational Study.

**Place and Duration of Study:** This study was conducted at District Head Quarter Hospital Kasur from 2008 to 2010.

**Materials and Methods:** This study was carried out on 451 medico legal autopsies performed at District Head Quarter Hospital Kasur. The findings were extracted from autopsy reports, chemical examiner reports, relevant hospital record and police documents. The cases were examined for various characteristics like cause and manner of death, age and sex of victim and condition of body at the time of autopsy.

**Results:** The results revealed that homicide was the most common manner (82.26%) among unnatural deaths and males became three times more victims than females. The most vulnerable age group in unnatural deaths were from 15 to 45 years (77.39%). In 44.12% cases firearm is the weapon responsible for death. Regarding condition of body at autopsy, 364 (80.71%) bodies were in fresh condition.

**Conclusions & Recommendations:** Medico legal autopsy rate reflects the incidence of crime & criminal behavior of that segment of society. Compared with more civilized societies the crime incidence in our society is very high. In order to control it, we need to change the behavior of society through improvement in literacy rate, socioeconomic status and law & order situation. In order to improve the quality of medico-legal reporting there is need to strengthen the expertise in forensic medicine both at urban and rural level.

**Key Words:** Autopsis, un-natural death, crime & criminal behaviour

## INTRODUCTION

The term autopsy derived from the ancient Greek autopsia, "to see for oneself" is made up of 2 words autos _ "oneself" and opsis _ "eye".[1] It is a highly specialized surgical procedure that consists of a thorough examination of a corpse to determine the cause and manner of death and to evaluate any disease or injury that may be present. The other synonyms used for this procedure are postmortem examination, necropsy, autopsia cadaverum and obduction.

About 3000BC, the ancient Egyptians were one of the first civilizations to practice the removal and examination of the internal organs of the humans in the religious practice of mummification[1]. Autopsies that opened the body to determine the cause of death are attested in the early 3rd millennium BC. [2] There are three main types of autopsies, i.e., medico legal or forensic autopsy to find the cause and manner of death and to facilitate identity of deceased in unknown cases; clinical or pathological autopsy to diagnose a particular disease or for research purpose; and anatomical or academic autopsy performed by students of anatomy for study purpose only. In legal medicine, deaths are placed in one of five manners: (1) Natural, (2) homicide, (3) suicide, (4) accidental, and (5) undetermined. In 2004 in England and Wales, there were 514,000 deaths, out of which 225,500 were referred to coroner & out of these referrals 115,800 (22.5%) resulted in autopsy.[3] Medico legal autopsies also give important statistical data related to legal incidents in the cities and regions where the autopsies are conducted.[4]

Medico legal autopsy is performed when death is believed to result from an unnatural cause or in cases of sudden death. These examination are performed under a legal authority and do not require the consent of the relatives of the deceased .Conduction of medico legal autopsy is a statutory duty of the authorized medical officer being designated by the provincial government.[5] In many cases there are circumstances in which it is possible to state whether the fatal injury or poison is homicidal, suicidal or accidental but in other cases it will need collaboration of many other facts and details to give opinion about causative weapon and manner of death (scene of crime, statements of witnesses).[6] Homicide refers to the act of one human killing the other human which can be criminal as well as non

criminal. The criminality is determined by the state of the mind of the perpetrator and statutes defining the crime. Murder and manslaughter are criminal homicides. Non criminal homicides can take place in circumstances like automatism, self defense, insanity & immaturity. As homicidal cases comprise a major portion of medico legal autopsies, therefore they get special importance in general criminal profile of the society.[7] The Geneva Declaration on Armed Violence and Development states that there were approximately 49,000 intentional homicides in 2004 & the global rate for this year was 7.6 intentional homicides per100,000 inhabitants.[8] The latest data reveals that in 2010 Honduras topped the world with homicide rate 78 per 100,000 inhabitants[9] and Austria remained lowest with rate of 0.56 persons per 100,000 inhabitants.[10] The latest available data about Pakistan for the year 2008 shows a rate of 6.8 homicides per 100,000 inhabitants.[11] Data about some of the individual cities of Pakistan is available in medical journals.[12-16]

The WHO estimates that suicide is the 10th leading cause of death worldwide with about a million people dying by suicide annually.[17] Worldwide suicide rates have increased by 60% in developing countries. A disproportionate amount of suicides in the world occur in Asia, which is estimated to account for up to 60% of all suicides. According to WHO, China, India and Japan may account for 40% of all world suicides.[18] The human costs of both suicide and homicide are severe and they are creating public health and legal issues in any country.[19] The No. of accidental deaths ,including those for motor vehicle accidents is also increasing all over the world. According to centers for Disease Control and Prevention in US in 2008 the No of deaths taking place from all unintentional injury deaths was 123,706 with a rate of 41.0 deaths per100, 000 population and ranking 5. Of this motor vehicle traffic deaths were 42,031 at a rate of 13.9 per 100,000 populations.

Unnatural deaths have remarkable impact on the society at large and the victim's families in particular. For every person who dies as a result of violence, many more are injured and suffer from a range of physical, social and mental health problems. This places a massive burden on the country.[20] According to Kasur Police, the crime statistics show a decline in number of homicidal deaths, During the years 2007, 2008, 2009 and 2010 respectively the attempted murders were 274,263,236 & 219 with approximate population more than 3 millions.[30]

# MATERIALS AND METHODS

This study was undertaken on the cases autopsied at District Head Quarters Hospital Kasur for a period of 3 years, i.e, from 1st January 2008 to 31st December 2010. These cases were examined regarding manner of death, age and sex of the victim, cause of death & condition of the body at the time of autopsy. The Findings were extracted from autopsy reports, chemical examiner / bacteriologist to Government of Punjab reports, relevant hospital record and police documents. The cases were examined for various characteristics like cause and manner of death, age and sex of victim and condition of body at the time of autopsy.

# RESULTS

A total of 451 autopsies were conducted during study period. Out of this 371(82.26%) were homicides, 9(1.99%) were suicides, and 25(5.54%) were accidental. 18(3.99%) cases remained undetermined whereas 22(4.88%) were found to die from natural causes (Table 1). The sex and age distribution are given respectively in Table 2 and Table 3. The distribution of causes of death is given in Table 4.

The condition of body was determined by the post mortem changes affecting the body. 'Fresh' describes the condition in which exterior of the body is intact and the maximum time interval between death and post mortem is within 48 hours. 'Early putrefaction changes' describes a condition in which decomposing skin change have taken place but the corpse is still identifiable in terms of facial recognition, age assessment sex identification and both external injuries and visceral damage. The probable duration between death and post mortem examination in this type was 2-5 days, depending upon the weather conditions. In the 'late putrefaction changes' the body has undergone advance changes. It is not recognizable. The age can be assessed by anatomical parameters & sex may be identified from internal sexual organs. This kind of presentation is found in cases where more than 5 days have elapsed. In the skeletonized condition bodies were presented in the form of just bones. In skeleton form bodies were brought both buried as well as not buried. This condition could result in days to years depending the burial status .They were further sent to Anatomist Govt. of Punjab for his opinion. (Table 5, Fig. 1)

**Table No.1: Distribution of manner of death (n=451)**

| Manner of death | 2008 | %age | 2009 | %age | 2010 | %age | Total cases in 3 yrs | %age |
|---|---|---|---|---|---|---|---|---|
| Homicidal | 129 | 82.69 | 121 | 79.60 | 121 | 84.61 | 371 | 82.26 |
| Suicidal | 5 | 3.20 | 2 | 1.32 | 2 | 1.40 | 9 | 2.00 |
| Accidental | 7 | 4.49 | 16 | 10.53 | 8 | 5.60 | 31 | 6.87 |
| unascertained | 6 | 3.85 | 4 | 2.63 | 8 | 5.59 | 18 | 3.99 |
| Natural | 9 | 5.77 | 9 | 5.92 | 4 | 2.80 | 22 | 4.88 |
| Total | 156 | 100.00 | 152 | 100.00 | 143 | 100.00 | 451 | 100.00 |

**Table No.2: Sex Distribution (n=451)**

| Sex | 2008 | %age | 2009 | %age | 2010 | %age | Total cases in 3 yrs | % age |
|---|---|---|---|---|---|---|---|---|
| Male | 120 | 76.92 | 117 | 76.97 | 109 | 76.22 | 246 | 76.72 |
| Female | 35 | 22.44 | 35 | 23.03 | 34 | 23.78 | 104 | 23.06 |
| Undetermined Sex | 1 | 0.64 | - | - | - | - | 1 | 0.22 |
| Total | 156 | 100.00 | 152 | 100.00 | 143 | 100.00 | 451 | 100.00 |

**Table No.3: Age Distribution (n=451)**

| Age group (in years) | No. of cases | %age |
|---|---|---|
| 0<15 | 30 | 6.65 |
| 16-30 | 206 | 45.68 |
| 31-45 | 143 | 31.71 |
| 45-60 | 48 | 10.64 |
| 61 - Onward | 19 | 4.21 |
| stillbirths | 4 | 0.89 |
| Aborted material | 1 | 0.22 |
| Total | 451 | 100.00 |

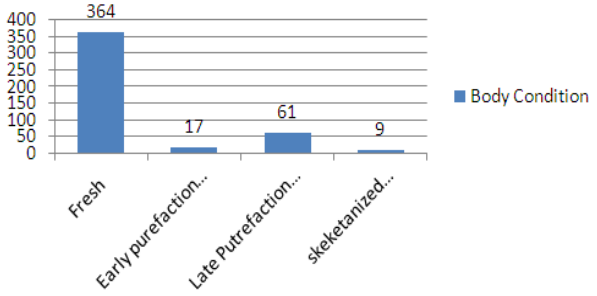


**Figure No. 1: Distribution of condition of body at the time of autopsy**

**Table No.4: Distribution of causes of death (n=451)**

| Weapon or mean of death | 2008 | %age | 2009 | %age | 2010 | %age | Total cases in 3 yrs | % age |
|---|---|---|---|---|---|---|---|---|
| Firearm | 60 | 38.46 | 72 | 47.37 | 67 | 46.85 | 199 | 44.12 |
| Asphyxia | 38 | 24.36 | 20 | 13.16 | 28 | 19.58 | 86 | 19.07 |
| Blunt | 10 | 6.41 | 15 | 9.87 | 10 | 6.99 | 35 | 7.76 |
| Sharp | 21 | 13.46 | 10 | 6.57 | 11 | 7.69 | 42 | 9.31 |
| Poisoning | 3 | 1.92 | 2 | 1.32 | 4 | 0.70 | 9 | 2.00 |
| Chronic Addiction leading to Starvation | 5 | 3.21 | 4 | 2.63 | 3 | 2.10 | 12 | 2.66 |
| Road Traffic Accidents | 6 | 3.85 | 11 | 7.24 | 8 | 5.59 | 25 | 5.54 |
| Diseases | 3 | 1.92 | 2 | 1.32 | 0 | 0 | 5 | 1.11 |
| Drowning | 2 | 1.28 | 6 | 3.95 | 1 | 0.70 | 9 | 2.00 |
| Burns | 1 | 0.64 | 2 | 1.32 | 1 | 0.70 | 4 | 0.89 |
| Electrocution | 0 | 0.00 | 0 | 0.00 | 1 | 0.70 | 1 | 0.22 |
| stillbirth | 1 | 0.64 | 2 | 1.32 | 1 | 0.89 | 4 | 0.89 |
| Unascertained | 6 | 3.85 | 6 | 3.95 | 8 | 5.59 | 20 | 4.43 |
| Total | 156 | 100.00 | 152 | 100.00 | 143 | 100.00 | 451 | 100.00 |

**Table 5: Condition of body at the time of autopsy (n=451)**

| Condition of body | Year 2008 | Year 2009 | Year 2010 | Total | % age |
|---|---|---|---|---|---|
| Fresh | 119 | 125 | 120 | 364 | 80.71 |
| Early putrefaction changes | 6 | 6 | 5 | 17 | 3.77 |
| Late putrefaction changes | 26 | 18 | 17 | 61 | 13.53 |
| Skeletonized | 5 | 3 | 1 | 9 | 1.99 |
| Total | 156 | 152 | 143 | 451 | 100.00 |

# DISCUSSION

Violence is generally increasing all over the world though its expression has changed in the last two decades. The use of bomb blasts and explosives has increased a lot in the recent years which has resulted in mass causalities instead of single cases. The number of autopsies due to other causes of deaths has generally fallen. This is evident both from the number of autopsies conducted during the three consecutive years under study and district Kasur police report already quoted above. During the three years under study there have been 371 homicidal deaths.

The aggregate suicidal rate for the three years of study remained 2.00%. It is less than that in a study conducted in Lahore, i.e., 3.42% in 2006-2008.[21] A comparable study in Lahore showed 0.62%[22] in 1996(one year study). But lower than that in D.I. Khan[23] which in 2004 was 2.00% (one year study).[23] It is substantially lower than western countries and our

neighbor India where it is 19.50%.[24] The studies conducted in London showed that the strongest risk factor for suicide is mental disorder especially depression.

The accidental death incidence in our study is 6.8% which is close to 7.42%[21] but lower than 11% in 1996.[25] In 2002, in the world, the road traffic injuries were the 11th leading cause of death. This rate is lowest in the high income countries and highest in East Mediterranean (26.4) and African countries (28.3)[21]. In our society most of the suicidal and accidental cases are disposed off without autopsy so the figures determined are approximations. At least if we consider the number of daily road traffic accidents reported in the media this number looks to be ridiculous. Therefore to know the correct statistics and make them useful for future planning, the autopsy of every accidental and suicidal death must be made mandatory.

The unascertained incidence in this 3year study is 3.99% which is half to that of Lahore in1996 8% (one year study)[25] but higher than (0.8%) during 2007-08 of D.I.Khan (two year study)[15]and 1.42% of Peshawar during 2004 (one year study).[26] The natural death incidence rate in this study was 4.88%. It included those cases in which the death occurred due to starvation and malnutrition secondary to chronic addiction. There were 12 such cases (2.66%).

As regards sex in our study of 451 deaths, 346 (76.72%) were males and 104 (23.06%) were females. In one case of aborted material sex remained undetermined. Age distribution reveals that major chunk of the victims falls in the age group of 15-30 years, that is 206 (45.68%) and 30-45 years 143 (31.71%). Though no age group is immune from violence, 19(4.21%) cases were above 60 years. The unnatural death of adolescents and young adults in any society has many socioeconomic repercussions for the bereaved families and the country at large. The male to female ratio is 3.33:1 which is roughly half to that of 6.22:1[27] in Peshawar in2006 but almost similar to those of other studies of 3.47:1 in 2004 in Faisalabad[13] and 3:1 of Lahore.[28] The obvious reason for more males involved in unnatural deaths is their more involvement in outdoor activities and more public interaction which sometimes can lead to conflicts and murders. In some parts of Pakistan and world violence against women in the form of honor killings is common .But such cases are infrequent in this study period because the literacy rate and socioeconomic conditions in this region are quite satisfactory.

An analysis of causes of deaths shows that firearms injuries constitute a major portion both annually during the three years [60(38.46%), 72( 47.37%) and 67( 46.85%)] as well as collectively 199 (44.12%). It is followed by asphyxia 86 (19.07%), sharp edged weapons 42 (9.31%), blunt means 35(7.76%), road traffic accidents 25(5.54), drowning 9(2.00%), burns 4(0.89%), diseases 5(1.11%). In 12(2.66%)cases in which the death occurred due to starvation and malnutrition secondary to chronic addiction. Of sharp edged cases half, i.e., 21 were due to cut throat and in one case torso without head was produced for post mortem examination. In cases of blunt weapons or blunt means, out of total 35 cases & 24(68.57%) were due to trauma to head resulting in brain damage.

This district was lucky enough in the sense that it remained safe from terroristic activities of bomb explosives whereas it was 2.12% in Peshawar[27] and as high as 32.96% in D.I. Khan.[29] Bomb explosions take a heavy toll of deaths every year in terror stricken areas of Pakistan, Afghanistan, and Iraq etc.

At the time of autopsy 364(80.71%) bodies were in fresh condition whereas 61(13.53%) were in condition of late putrefaction. Most of cases in the latter condition were recovered from canals and crop fields as unknown bodies. An exhaustive process is required to trace the origin of such bodies. It needs the full cooperation and coordination of many institutions like NADRA, police, intelligence, medical and forensic sciences experts.

# CONCLUSION

Medico legal autopsy rate reflects the incidence of crime & criminal behavior of that segment of society. Compared with more civilized societies the crime incidence in our society is very high. In order to control it, we need to change the behavior of society through improvement in literacy rate, socioeconomic status and law & order situation. In order to improve the quality of medico-legal reporting there is need to strengthen the expertise in forensic medicine both at urban and rural level.

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Original Article

# Knowledge and Practices of Mothers regarding acute Respiratory Infection in Children under 5 Years of age in Urban Slums of Multan

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## ABSTRACT

**Background:** Acute Respiratory Infection (ARI) is the leading cause of morbidity and mortality in children under 5 years of age in developing countries. The knowledge of mothers regarding ARI is inadequate which leads to delayed care seeking and other factors contributing to high mortality

**Objective:** To determine the Knowledge and Practices of mothers regarding Acute Respiratory Infection.

**Study Design:** Cross-sectional descriptive study.

**Place and Duration of Study:** Urban slums of Multan, from April 2010 to March 2011.

**Material and Methods:** A semi-structured questionnaire proforma was used to interview 500 mothers selected by stratified random sampling technique from urban slums of Multan. SPSS software was used to analyze the data.

**Results:** Mother's description of the causes of ARI in children was mostly exposures to "Thand" (cold), after bathing, sour and cold foods. Mothers also had inadequate knowledge of severity of symptoms of ARI including pneumonia. About 44% showed prompt care seeking response within 24 hours of ARI and rest (55.8%) showed delayed response to health care seeking. Thirty three percent mothers preferred private doctors to get treatment, 27.2 % favored to go to the public sector, and the rest did home remedy i.e. Tea, Honey, Vicks rub and Warm wrapping. The reasonable majority of mothers (58%) did self medication in their children suffering from ARI.

**Conclusion:** Mothers living in urban slums in Multan have insufficient knowledge and inappropriate health care seeking practices regarding management of ARI in their children.

**Key Words:** Acute Respiratory Infections, Mothers, Knowledge, Practices, Urban slums, Home Remedies, Multan.

## INTRODUCTION

Acute respiratory infections are the major causes of morbidity and mortality in children throughout the world. 1 The majority of the diseases are mild and self-limiting but some are life threatening and serious.[2,3] Moreover, ARI is one of the major groups of diseases of infants and children responsible for deaths worldwide. 4 It is a global health problem as it is estimated that yearly there are 2000 million episodes of ARI, of which one out of fifty are cases of Pneumonia, and among Pneumonia, 10% to 20% die.4 Each year 12.9 million children die, 28% of deaths are caused by ARI.4 Acute respiratory infection rank number one health problem to look for medical advice. Each child in the first 5 years of life approximately suffers from 2-8 episodes of ARI yearly.6 In developing countries, children are more vulnerable to get acute respiratory infections, which carry an elevated mortality rate, and ARI is the second most important cause of the deaths in children under 5 years of age.[7,8] Various risk factors for acquiring respiratory infections in developing countries, such as poverty, limited family income, low mother's education level, low birth weight, and starvation, have been described.1 ARI is the major cause of morbidity and mortality in Peru principally in children under five. 9 About 11-20 million (7-13%) of the children need hospitalization and two millions die each year due to ARI.10 In Pakistan ARI is the major killer disease under 5 years of age. Four million children die every year from acute respiratory infections, 11 and responsible for 20-30 percent of all child deaths under 5 years in Pakistan12

The fundamental reason to carry out this study was to assess the knowledge and practices of mothers regarding Acute Respiratory Infections in children under 5 years of age. The morbidity and mortality in children under five could only be reduced by developing proper knowledge and practices of mothers regarding ARI which is major killer disease

## MATERIALS AND METHODS

It was an interview based cross sectional descriptive study of urban slums of Multan.

**Inclusion criteria:** The study was restricted to the mothers who had at least one child under five years of age having the symptoms of ARI at the time of interview or had suffered from ARI during the preceding two months.

**Exclusion criteria:** The mothers who had not even one child under five years of age or having the child but not suffering from ARI at the time of interview or had not suffered from ARI during the preceding two months.

The area map of urban slums with house numbers and street numbers were available in Director Health Services Office, which was used to draw a sample of 500 mothers from five slums, randomly selected out of total 17 urban slums of Multan. Stratified Random Sampling Technique was used to carry out the study, based on proportionate sampling i.e. 20% from each urban slums of Multan. Five hundred mothers were interviewed who met the inclusion criteria from the following five urban slums of Multan.

1 Basti Kumharan Bosan Road, Multan. (No. of households 490)
2 Koocha Subhan Singh. (No. of households 474)
3 Kachi abadi shamsabad & mahallah nawazabad. (No. of households 379)
4 Barket Pura near Kabooter mandi. . (No. of households 378)
5 Dewan da Bagh. (No. of households 790)

**Method of Data Collection:** A semi-structured interview proforma was used to collect the data about knowledge and practices of mothers regarding acute respiratory tract infection in children under 5 years of age. A total of 500 mothers were interviewed after getting consent from them. The sampling frame was used for data collection in each slum; first household and street was selected by the simple random method. Suppose it was household two of the street, so systematically every alternate household i.e. 2, 4, 6, 8 and so on were chosen to fill the proforma till approximately 20% from each urban slum..

**Data Analysis:** Analysis used in this study was descriptive. Continuous variable like respondent age was expressed as mean ± 2SD. Variables like education of mothers, occupation, disease symptoms etc. were expressed as a frequency and proportion. All data collected was entered in SPSS program version-16 and data was analyzed accordingly.

# RESULTS

Mean Age of mothers = 28.68, 2SD = ± 6.148

In our study majority of mothers did not have the proper knowledge regarding the causes of ARI. Exposure to cold, intake of sour or cold food and after bathing was the mother's favorite causes of ARI.

n= (500)

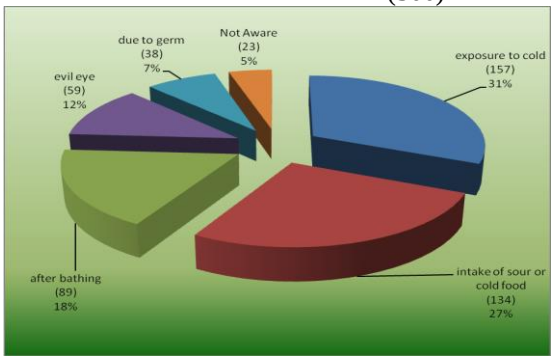


**Figure No.1: Mother's Knowledge Regarding Causes of ARI**

The majority of mothers identified and narrated symptoms of ARI in their local language. The children were having multiple symptoms of ARI in an episode, so mothers narrated multiple answers to the same question and there was overlap in their response. The most common symptoms were coughing runny nose and sore throat.

**Table No.1: Local Terminologies used by Mothers Regarding Symptoms of ARI n = 500**

| Local Terminologies | Frequency | % age |
|---|---|---|
| Naak band (blocked nose) | 172 | 42.57% |
| Naak bahna (runny nose ) | 274 | 67.82% |
| Galla Kharab (sore throat ) | 264 | 65.34% |
| pasli chalna (indrawing of chest ) | 66 | 16.33% |
| khana kam kar diya (stopped taking feed) | 42 | 10.39% |
| Khansi (cough) | 326 | 80.69% |
| chhati per bodge (noisy breathing) | 146 | 36.13% |
| Sans Taiz (fast breathing ) | 196 | 48.51% |
| NOTE *multiple answers to the same question. | | |

**Mother's Knowledge of "No Pneumonia" symptoms as dangerous or not dangerous**

Almost 48% mothers had wrong knowledge of No Pneumonia as "dangerous" and remaining 52% mothers had correct knowledge of symptoms of No Pneumonia as "not dangerous".

**Mother's Knowledge of Pneumonia Symptoms as Dangerous or Not Dangerous**

One half of the mothers (50%) had wrong knowledge of Pneumonia as "dangerous". And another half of the mothers (50 %) had correct knowledge of symptoms of Pneumonia as "not dangerous". Fast breathing was considered as dangerous symptom.

**Mother's Knowledge of "Severe Pneumonia" symptoms as dangerous or not dangerous**

About two third of mothers had correct knowledge of symptoms of severe Pneumonia as "dangerous", while about one third of mothers had wrong knowledge of symptoms of severe Pneumonia as "not dangerous"

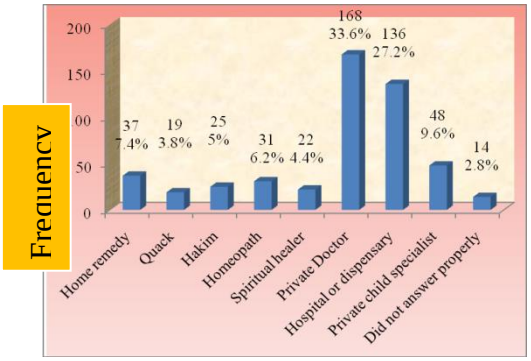


**Figure 2: Mother's Health Care Seeking Practices n = (500)**

Less than half of mothers (42%) responded promptly at the beginning of acute respiratory infection within 24 hours and rest more than fifty percent did not respond promptly.

**Table No.2: Mother's Health Care Seeking Behaviour either Prompt or Delayed n = (500)**

| When Necessary to get Treatment from Qualified Doctor (promptly or delayed) | Frequency | Percentage |
|---|---|---|
| Promptly at the beginning of the disease | 221 | 44.2% |
| Delayed , when the illness is severe | 146 | 29.2% |
| Delayed, after trying some other medication | 87 | 17.4% |
| Delayed, let the flue settle first | 18 | 3.6% |
| Delayed, never to get treatment | 28 | 5.6% |
| Total | 500 | 100% |

**Practices of Mothers:** The emerging pattern on care seeking practices of mothers has been studied. It was found that large percentage of mothers (33.6%) consulted private doctors and 27.2% went to govt. hospitals or dispensaries to get treatment for their children suffering from ARI. A very little percentage (7.4%) of mothers did exclusive home remedy and rest went to homeopath doctors, hakims, spiritual healer and quacks for seeking health care of their children suffering from ARI.

Various modalities and totkaas (myths) were used by mothers either alone or in combination to treat the ARI children. In the current study, mother's believed that home remedies could cure ARI within a few days, and believed that tea, honey, Vicks rub and deep warm wrapping were few major modalities to treat the children suffering from ARI.

**Table 3: Mother's Home Remedy Practices**

**n = (500)**

| Home Remedy | Frequency | Percentage |
|---|---|---|
| **Practices** | | |
| Tea | 82 | 16.4% |
| Malish with oil | 50 | 10% |
| Soup | 26 | 5.2% |
| Soanf / Ajwain water | 17 | 3.4% |
| Urq | 25 | 5% |
| Honey | 80 | 16% |
| Brandy | 23 | 4.6% |
| Joshanda | 47 | 9.4% |
| Deep Warm (Wrapping) | 74 | 14.8% |
| Vicks Rub | 76 | 15.2% |
| Total | 500 | 100% |

Almost 58% mothers did self medication in their children suffering from ARI and the rest of the mothers responded in negation to do self medication in their children of ARI.

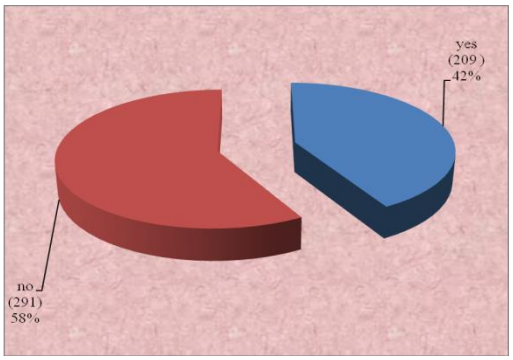


**Figure 3: Mother's Self Medication Practices**

# DISCUSSION

In our study mothers narrated symptoms of ARI in their own local Multani (Saraiki) language. It was beneficial to understand local vocabulary and traditional terms used by mothers about ARI symptoms. Some of the other previous studies also used different vernacular terms to explain symptoms of ARI pertinent to their own regional languages. [13] The study at Multan[14], vernacular terms like Pasli chalna, chhati per bohj, saans taiz, and chhati per balgham were local terms used by the mothers for ARI symptoms. Almost similar vernacular terms were used in the present study. This was due to the fact that both the studies conducted in the same Saraiki population of Multan. In a study in Western Uganda there was no term for rapid breathing. [15] This was in contrast with what was found in the present study. In our study the knowledge about severe pneumonia was same as reported in Mexican study[16] and in the study done in 2008, which found that Knowledge of severe Pneumonia as dangerous was 60% which supported our study.[17] Knowledge awareness was much higher than the level of awareness noted in a study conducted in Bolivia,[18]Athumani Juma study[19] and USAID report[20] in 2005 concerning fatal symptom knowledge in severe Pneumonia, almost all the mothers (96.1%) were aware of one or more fatal

symptoms of severe Pneumonia. This awareness was much higher than our study. Which was, possibly, due to better health education and implementation of IMNCI campaign that might lead to increased mother's acquaintance about ARI.

The study done in Iraqi mothers showed that a high percentage of mother's knowledge regarding symptoms of ARI as dangerous that paid attention for seeking medical advice were fever and cough, while a small percentage of mothers considered chest indrawing convulsion, drinking difficulties, sleep disturbance as a dangerous symptom of ARI. This may indicate that Iraqi mothers were not different from mothers of our population who had considered fever and cough as an important symptom that needed medical attention and this might be due to the defect in implication of the IMNCI campaign by the ministry of health regarding dangerous symptoms.[21]

The result of the present study showed correlation with the study done in the Mexican population, [16] and a study done at Multan. [14] in which firstly very small numbers (6%) of mothers incriminated germs as the cause of ARI, secondly the idea of cold (Thand) was so strong that the breast feeding mothers feeling cold (Thand) thought that this cold would transfer to the breast feeding children. The belief of supernatural influences causing ARI was also there in our study; this was supported by the study done by Mrs. Sarojamma[22] which showed that most of the mothers had a traditional belief of supernatural influence as to the cause of ARI. .

The current study showed emerging pattern on care seeking practices of mothers which was a similar pattern to the studies done in Uganda[23] which showed that mother's prompt response to seek health care in their children suffering from ARI was less as compared to delayed response due to any reason. This similar pattern might be due to the similar socio- economical condition of the mothers living in developing countries. While a high percentage of promptly behaving mothers to seek health care were recorded from studies in Kenya and Nigeria.[24] This could be again due to differences to get access to health care facilities, educational backgrounds.

Home remedy practices include not only identification of symptoms of Pneumonia but also the administration of safe home remedies, taking care of feeding and fluid requirement of the child. [25] In a study of New Delhi, [26] it was found that Honey and ginger were the two most popular home remedies, which did not show correlation with the present study in which, honey and tea were the two most popular home remedies used by the mothers for ARI in children. This could be due to the geographical and cultural differences.

The present study showed correlation with the study done by Awad, [27] which showed that 55% households used self medication. Lack of consultancy practices in mothers for rational drug use in children suffering from ARI might be the major reason for this increased frequency of self medication,

**Conclusion:**

The majority of mothers of under 5 years children had poor knowledge of causes of ARI, they did not differentiate between simple and dangerous symptoms of ARI. There was a lack of knowledge of medically significant terms such as fast breathing and chest in drawing (Pasli Chalna). They also had inappropriate care seeking practices. There is the need to develop effective messages which could be delivered to the mothers to increase their understanding and to improve their practices. Our study offers sensible insights regarding baseline knowledge and practices of mothers regarding ARI in their children.

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Original Article

# Frequency and Pattern of Medico Legal Cases Reported at Sandeman Civil Hospital Quetta Balochistan- One Year Study

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## ABSTRACT

**Introduction:** Medicolegal cases are an integral part of medical practice that is frequently encountered by Medical Officers working in casualty department and dealing with Police/Court cases. To prevent the problem of increasing violence and criminal assault result in personal injury or death deserves a detailed examination.

**Objective:** To present the profile of medicolegal cases reported in the Sandeman Civil Hospital Quetta, a teaching hospital of Bolan Medical College Quetta, a tertiary care health delivery and medicolegal center for the entire city as well as its suburbs, with in the period of one year that is 2009. To highlight the vulnerable gender, age, cause (motive) and type of weapons used with seasonal frequency to assess the trend of the incidences and frequency of crime committed in different area of Quetta Balochistan with comparison to other parts of the country.

**Study Design:** Retrospective study

**Place and Duration of Study:** This study was conducted in medicolegal section of Sandeman Civil Hospital Quetta, from 1st January to 31st December, 2009.

**Materials and Methods:** 9915 medicolegal cases admitted in medicolegal registers/record by medicolegal officers were included. Cases found non-medicolegal excluded. The variable considered were gender, age, weapon or cause of injury, inhabitant and seasonal variations in medicolegal cases. Findings were expressed in numbers and percentages.

**Results:** Out of these 9915 medicolegal cases males were 8636 (87.1%) and females 1279 (12.9%).Maximum (33.46%) victims were age group of 20 – 29 years followed by 26.13% victims in age group of 30 – 39 years. Among this sample, the most common type of injury was Assault caused by blunt and hard object 5665 (57.13%) followed by Road traffic accidents 1945(19.61%), firearms 558 (05.62%), Urban inhabitant victims were 6143 (61.96%) and rural 3772 (38.04%). Most of cases occurred in summer than in winter.

**Conclusion:** Majority of victims were young adult males, urban inhabitants, blunt and hard weapons were commonly employed in this region for assault cases. More trauma care centers with necessary facilities are suggested in remote areas so the burden on main hospital can be decreased and life of trauma patients could be saved. Proper counseling for developing positive attitude and controlling the aggression in youth have to be promoted.

**Key words:** Medicolegal case, pattern, Quetta.

## INTRODUCTION

Medicolegal cases include all the eventualities where medical aspects of law, be it for criminal or civil purposes or legal aspects of medical practices are utilized for comprehension, interpretation and following for both professionals belonging to legal as well medical fraternities. Utilizing this knowledge by doctors and lawyers, serve the masses in their own directions and spheres.

General perception about the medicolegal cases is all those happenings where criminal force has been applied against the person whether sexual or physical, intentionally, inadvertently or accidently.

The quantum of medicolegal cases represent the magnitude of behavior and attitude in interpersonal conduct, respect for fellow human being, law of land, tolerance of a community and over all status of peace and harmony in a given society/country.

The data about the incidences and patterns of medicolegal cases belonging to various parts of the country is documented in the medical literature; ironically, Quetta has not shared its contribution in such a crucial statistics. Quetta is the capital of Balochistan, a blend of rural and urban culture, abode a pluristic society having followers of different traditions, displaying multiracial, multi religious, multi linguistic, multi tribal spectrum.

According to our knowledge till date there has been no such study ever conducted in Balochistan. Therefore realizing the need to establish baseline data on pattern of medicolegal cases, this present study was conducted in Sandeman civil hospital Quetta.

## MATERIALS AND METHODS

The cases which were brought to medicolegal examination and certification to medicolegal section

from 1st January to 31st December, 2009 in Sandeman Civil Hospital Quetta were included in the study.

Data regarding the medicolegal cases of assault, accident, poisoning and intoxication is incorporated in a especially designed proforma and results are tabulated, information regarding gender, age and inhabitant whether belong to rural or urban, cause of injury, weapon used for hurting the victim and time and season of sustaining wounds is incorporated for this study.

The total numbers of victims registered in the medicolegal section of the hospital were 10,395. On scrutiny, 480 cases were found non-medicolegal having nonviolence and showed no signs of injury on their body, probably these cases were of verbal altercation of parties or gestures or threats displayed by offenders. These cases were excluded from this study. The remaining numbers 9915 under study.

All findings were compiled by proforma for study. Findings of medicolegal examination, hospital record, police inquest, history and circumstances of each case were scrutinized and necessary data were used for analysis.

# RESULTS

In this study 9915 medicolegal cases were reported in medicolegal department during the period of one year (Jan 1st 2009, to Dec 31st, 2009). On average, 826 cases per month attended Sandeman Civil Hospital Quetta. Victims were predominantly males 8636 (87.1%) males and 1279 (12.9%) female. Males: females was being 6.75:1 (Table -1).

**Table No.1: Gender Distribution of Total Cases**

| Sex | No. of cases | Percentage |
|---|---|---|
| Male | 8636 | 87.1% |
| Female | 1279 | 12.9% |
| Total | 9915 | 100 |

**Table No.2: Age and gender distribution of total cases**

| Age group (Yr) | Male | | Female | | Total | |
|---|---|---|---|---|---|---|
| | No. | % age | No. | % age | No. | %age |
| 0-9 | 365 | 4.23% | 72 | 5.63% | 437 | 4.41% |
| 10-19 | 1898 | 21.98% | 306 | 23.92% | 2204 | 22.23% |
| 20-29 | 2886 | 33.42% | 432 | 33.77% | 3318 | 33.46% |
| 30-39 | 2320 | 26.86% | 271 | 21.19% | 2591 | 26.13% |
| 40-49 | 644 | 7.46% | 81 | 6.33% | 725 | 7.31% |
| 50-59 | 355 | 4.11% | 63 | 4.93% | 418 | 4.22% |
| 60-69 | 118 | 1.36% | 36 | 2.82% | 154 | 1.55% |
| >70 | 50 | 0.58% | 18 | 1.41% | 68 | 0.69% |
| Total | 8636 | (100%) | 1279 | (100%) | 9915 | 100% |

Maximum 3318 (33.46%) victims were age group of 20 – 29 years followed by 2591 (26.13%) victims in age group of 30 – 39 years though (59.59) victims of age group of 21-39 years.. (Table–2)

**Assault/Violence: n= 7083 (71.44%):** Of the total reported cases, maximum number of cases were of assault by blunt and hard object 5665 (57.13%), Firearms account 558(05.62%) Sharp force (4.06%), bomb blasts 269 (02.71%), and domestic violence (00.35%).

**Accidents: n=2418 (24.39%):** Road traffic accidents account 1945(19.61%), fall 151(01.52%), electric shock 41(00.41%) coalmining accidents 113 (01.14%), railway accidents 51(00.51%), natural (Sui) gas poisoning 47(00.47%), burn 36(0.36%), drowning 3(0.03%).

**Poisoning and intoxication: n=414(4.17%):** Among these, cases of poisoning and drugs (03.77%) and alcohol ingestion 40 (00.40%).

All medicolegal cases reported in Medicolegal section during the study year (2009) are listed in Table 3.

**Table No.3: Mechanism /Cause of injury seen in medicolegal cases**

| Medicolegal cases | No. of patients | %age |
|---|---|---|
| Blunt assault injury | 5665 | 57.13% |
| Road Traffic accidents | 1945 | 19.61% |
| Firearm injury | 558 | 05.62% |
| Sharp force injury | 556 | 05.60% |
| Domestic violence | 35 | 00.35% |
| Falls | 151 | 01.52% |
| Machinery injury | 26 | 00.26% |
| Bomb blast injury | 269 | 02.71% |
| Electrocution | 41 | 00.41% |
| Natural (Sui) gas poisoning | 47 | 00.47% |
| Drowning | 03 | 00.03% |
| Burn | 36 | 00.36% |
| Coal mining accidents | 113 | 01.13% |
| Poisoning | 374 | 03.77% |
| Alcohol poisoning | 40 | 00.40% |
| Railway accidents | 51 | 00.51% |
| Others | 05 | 00.05% |
| Total | 9915 | 100 |

About inhabitants, victims belonged to the urban area of Quetta city were 6143(61.96%) where as cases belonged to rural areas of the Quetta and other areas of province adjacent to Quetta were 3772 (38.04%).

**Table No.4: Urban/Rural distribution of cases**

| Area | No. of cases | Percentage |
|---|---|---|
| Urban | 6143 | 61.96% |
| Rural | 3772 | 38.04% |
| Total | 9915 | 100 |

Most of cases 5123 (51.23%) have reported the medicolegal section during daylight times (6:00 a.m to 6:00 p.m) where after sunset to sun rise 4792 (48.33%) victims attended the section.

**Table No.5: Time of reporting/arrival**

| Time | No. of cases | Percentage |
|---|---|---|
| 6:00 am to 6:00 pm | 5123 | 51.67%age |
| 6:00 pm to 6:00 am | 4792 | 48.33%age |
| Total | 9915 | 100 |

Season wise cases were categorized and observed that during winter (November to April) number of cases were 3143 where as 6772 cases were brought during summer (May to October) with peak in month of September.

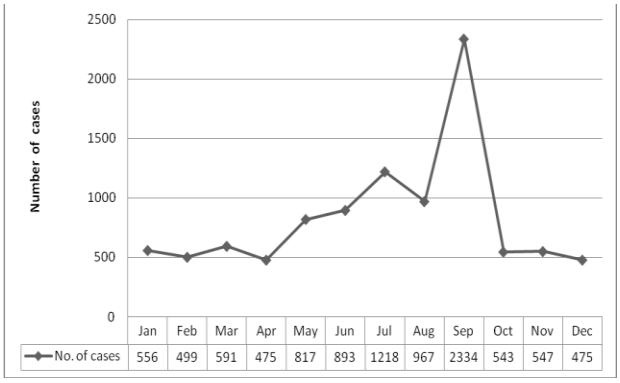


**Figure No.1: Monthwise variation in Medicolegal cases**

# DISCUSSION

In all government hospitals medical officer working, in the casualty department of, rural health centers, Tehsil/District Headquarter Hospitals, teaching Hospitals and Forensic Medicine Department of a Government Medical College are required to do medicolegal work of the concerned police stations. As a general rule in accident and emergency department, the injured person has been managed to safe his/her life and medical officer on duty may be asked to examine the injured/victim and completes the medicolegal task as well. The details of physical examination must be entered in medicolegal register and in death cases in postmortem autopsy register. The report submitted to police/court must be concise, clear and legible. All the injuries/wounds with the characteristics of tissues involved in wound must be recorded in detail. Authorized Medical Officer must use all the tools required to clear the nature of injury[1,2,3].

In Pakistan the medicolegal investigation for any forensic case are primarily ordered and decided by the medicolegal officer[4].They are required to write medico-legal certificate or report and send it to assist the law. They could be required to stand as expert witness in courts of law, thus medico legal injuries are of forensic significance as medico-legal reports on injuries could help authorities and courts of law to arrive at logical conclusions[5,6].

Sandeman Civil Hospital is located in the centre of Quetta city. It is a teaching hospital of Bolan Medical College and provides tertiary care health delivery and medicolegal service. The medicolegal work is supervised by Police Surgeon, a senior doctor of health department Balochistan and casualty medical officer/medicolegal officer do medicolegal examinations in police/court cases.

During the period of the study a total of 9915 medicolegal cases were registered for certification in medicolegal section of casualty Department of Sandeman Civil Hospital Quetta. Result shows Males comprised (87.1%) and females (12.9%) of the total 9915 cases. The Male: Female ratio being 6.75:1. The male predominance in our study is in line with various authors from Pakistan[7,8,9,10,11,] and worldwide[12,13,14,15] .

The reason may be we are living a male dominated society. Males are more involved in outdoor activities and women remain in house and are dependent on men. In a traditional society like Balochistan females are generally spared in quarrels but they are facing lot of problems in family honor values (Karo Kari).

In present study most commonly affected 3318 (33.46%) victims were in age group of 20 – 29 years followed by (26.13%) victims in age group of 30 – 39 years though (59.59) victims of age group of 21-39 years.

This was in accordance with Mirza HM et al [16] reported 59.3% victims of age 20-39 yrs. Hassan Q et al [17] reported 58.4% victims of age 20-39 yrs. Chaudhry TH et al [6] reported 58% of victims of age group 21-40 yrs. Bhullar DS and Aggarwal KK [2] reported 58.5% victims of age group 21-30 yrs. Oberoi SS et al[18] reported 55% victims of age 20-39 yrs. K Ali et al [19] reported 38.63% in age group 21-30 yrs. Humayun M et al [20] reported majority of victims were between 16-45 yrs of age.

The high incidence of cases in above age group may be explained by the fact that they are active phase of life and more of required to death outer world to pursuit work, travel, education, sports and social activities.

Most of assaults were caused by hitting blunt and hard objects had the maximum number of cases (33.42%).

Sharp force weapon used in (6.60%) cases, Blunt weapons are some of the most easily available weapon and used in fighting where the intention is to inflict harm not to kill. Sharp weapons still stand as a very frequent cause of medico-legal deaths. The present study found firearm was used in (6.64%) cases and Bomb blasts victims were (02.71%). Probably this shows individuals prejudice, tolerance, obedience to law and criminal bents of minds. Assault and homicide by firearm and bomb attack show extreme violence and cause of fatalities in our society.

It was found in our study that the most common mode of accident was road traffic accident 1945 (19.61%), followed by fall 151(1.51%), coal mining accident injury in workers (01.13%), natural (sui) gas poisoning (0.47%).Road Traffic Accidents are a large problem everywhere in the world. The high number of injuries attributed to RTAs caused by recklessness and negligence of the driver, complete disregard of traffic laws, over speeding, overloading, often driving under the influence of drugs, underage driving and poor conditions of roads and vehicles.

Poisoning has been fifth in rank of medicolegal cases and that too predominantly organophorous poisoning. A previous study on deliberate self harm also noted this point[21]. In Balochistan majority of the rural people are dependent on agriculture, vegetable and fruit farming. There is probability of easy availability and individuals accessibility of agriculture poisons. Such cases are preventable by use safer methods of pest control and counseling them personally.

The present study also found that the majority of cases were belonged to urban area 61.96% as compared to rural 48.33%.It has been by present study that the offence of medicolegal nature could occur at any moment in time but highest number of incidences 6772 (68.3%) were reported during summer from May to October. The high number of medicolegal cases in summer could be due to early loss of temperament in hot season, larger daytime and increased people's activity.

The majority of patients 6143 (61.96%) were brought in casualty between 06:00 am to 06:00 pm as compared by 06:00 pm to 06:00 am. In daytime hours people come in contact more with each other and traffic density in urban streets may be main reason. As for time of choice for violence or criminal acts happening is concerned, our study like other studies points to summer and daytime hour preference. This may be due to the habitat, tolerance, their needs and their local day to day activities.

# CONCLUSION

At this point it is needed that more studies are supposed to be conducted to further research and produce validate data in forensic and medicolegal issues in Balochistan. A proper surveillance system should be in place to monitor all the types of injuries as most of the victims belong to highest productive age group.

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Original Article

# Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency in Neonates Presenting with Jaundice at Tertiary Care Hospital Sukkur

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## ABSTRACT

**Background:** Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most important disease of the hexose monophosphate pathway. G6PD is an X-linked recessive enzymopathy that is a well-known cause of hyperbilirubinemia that may be severe enough to cause kernicterus, or death in neonates. Early detection of this enzymopathy and close surveillance of the affected newborns may be important in reducing the risk of severe hyperbilirubinemia. This emphasizes the necessity of neonatal screening of G6PD deficiency.

**Objective:** To detect the frequency of glucose-6-phosphate dehydrogenase (G6PD) deficiency in neonates presenting with Jaundice.

**Study design:** Retrospective study.

**Place and duration of Study:** This study was conducted at Paediatric department of Ghulam Muhammad Mahar Medical College Hospital (GMMMCH), Sukkur from March 2011 to June 2012.

**Materials and Methods:** This retrospective study was conducted in paediatric department of GMMMCH, Sukkur from March 2011 to June 2012. Two hundred forty cases of neonatal Jaundice of both sexes admitted to hospital were enrolled in the study. Detailed history and clinical examination was recorded. All the neonates were subjected to be estimation of serum bilirubin (Total, Direct and Indirect) and G6PD qualitative detection.

**Results:** Out of 240 icteric neonates, 192 (80%) were males and 48 (20%) were females. Twenty nine (12.1%) neonates were found to be G6PD deficient. The age of presentation of G6PD deficient neonates was between 2nd to 4th day of life. In G6PD deficient patients, male to female ratio was 8.7:1. Serum total bilirubin level of 10-40 mg/dl was found in these G6PD deficient neonates.

**Conclusion:** G6PD deficiency is quite high in neonates presenting with Jaundice. The diagnosis is simple and if left undetected may cause serious consequences in situations of oxidant stress.

**Key Words:** Neonates, Jaundice, G6PD deficiency.

## INTRODUCTION

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an X-linked inherited disorder. A total of 400 million persons are affected by this disorder worldwide most commonly affects people of African, Asian, and Middle-Eastern origin [1-8]. G6PD deficiency is one of the commonest enzyme deficiencies in humans [9, 10]. Homozygotes and heterozygotes can be symptomatic, although the disease typically is more severe in persons who are homozygous for the deficiency[11-13]. G6PD catalyzes the first step in the pentose monophosphate pathway, to produce nicotinamide adenine dinucleotide phosphate hydroxide (NADPH) [3, 10]. NADPH protects cells from oxidative damage. Precipitants of cellular damage include; infection, drugs, and ingestion of fava beans[1, 2]. Red blood cells are at greater risk of damage as these cells lack the cellular organelles such as mitochondria that produce NADPH[2, 3 and 11]. Oxidant damage of hemoglobin leads to the precipitation of hemoglobin, which may be morphologically recognized as Heinz bodies[2].

Infants with G6PD deficiency may have significant hyperbilirubinemia and may require phototherapy or exchange transfusion to prevent kernicterus. Hemolysis is not the main determinant of neonatal jaundice in G6PD-deficient babies[14].

Infants with the severe variant of glucose-6-phosphate dehudrogenase (G6PD) deficiency may develop hyperbilirubinaemia sufficiently severe to cause kernicterus and death, acute haemolysis on exposure to oxidant stress, congenital non-spherocytic haemolytic anaemia and, rarely, increased susceptibility to bacterial infection. In spite of these potential problems, G6PD deficiency is often not included among screening programmes for inherited disorders[15].

G6PD deficient newborns are more prone to develop neonatal jaundice which is, on its own, no more severe than jaundice from other causes[16, 17]. In cases of oxidant stress due to various drugs, bees stings or Fava beans the patient may develop life threatening acute haemolytic crises[18].

It was observed by some of the authors that the frequency of G6PD deficiency is more in icteric patients than in nonicterics. Therefore we evaluated G6PD deficiency in infants presenting with jaundice.

# MATERIALS AND METHODS

**Study Design:** It was hospital based retrospective study.
**Study Duration:** From March 2011 to June 2012
**Study Location:** Paediatric department of Ghulam Muhammad Mahar Medical College Hospital

**Inclusion Criteria:** Total of 240 cases of jaundiced neonates, aging 1st day of life to 30 days were included in the study.

**Exclusion Criteria:** Premature Jaundiced neonates, those with neonatal sepsis and neonates with direct hyperbilirubinemia were excluded from the study.

**Assays:** After taking detailed history and clinical examination, all the jaundiced neonates were subjected to the estimation of bilirubin (Total, Direct and Indirect) and G6PD qualitative test. The test was performed by using the BinaxNow G6PD test provided by Binax/Inverness medical USA.
The BinaxNow G6PD test is an in vitro enzyme chromatographic test for the qualitative detection of G6PD enzyme activity in human venous whole blood. The BinaxNow G6PD test is a visual screening test used for differentiating normal from deficient G6PD activity levels in whole blood.

**Principle of BinaxNow G6PD test:** The BinaxNow G6PD test device consists of a lateral flow test strip comprised of a white sample pad and a reaction pad, which is located at the top of the strip. The reaction pad contains the reagents necessary for the G6PD enzymatic reaction and the subsequent reduction of a nitro blue tetrazolium dye into its concomitant blue formazan product. The resulting color change on the strip indicates enough G6PD activity is present to presume the sample is not deficient. For a deficient sample, there is no color change in the top half of the reaction pad.

# RESULTS

The total number of patients who were jaundiced and having G6PD test performed were 240. There were 192 (80%) male and 48 (20%) female. Out of these 240 icteric neonates 29 (12.1%) were G6PD deficient. In G6PD deficient patients male to female ratio was 8.7:1 (Table 1)

**Table No. 1: Frequency of G6PD deficiency**

| Group | Number | %age | Male | Female | M:F ratio |
|---|---|---|---|---|---|
| Total Patients | 240 | 100% | 192 | 48 | 4:1 |
| G6PD Normal | 211 | 87.9% | 166 | 45 | 3.7:1 |
| G6PD Deficient | 29 | 12.1% | 26 | 03 | 8.7:1 |

Majority of neonates having G6PD deficiency presented with jaundice between 2-4 days of life (Table 2).

**Table No. 2: Age of presentation in G6PD neonates (n=29)**

| Age at presentation | Number of cases | %age |
|---|---|---|
| Up to 24 hours | 02 | 6.9% |
| 2nd day to 4th day of age | 22 | 75.9% |
| After 4th day of life | 05 | 17.2% |
| Total | 29 | 100% |

Serum total bilirubin range from 10mg/dl to 40mg/dl in these G6PD deficient neonates. Out of 29 G6PD deficient neonates, only 3 (10%) developed severe hyper bilirubinemia (serum total bilirubin level of > 20 mg/dl) (Table 3)

**Table No.3: Serum Bilirubin total in G6PD deficient babies (n=29)**

| Grade | S. Bilirubin total | No. of patients | %age |
|---|---|---|---|
| Mild to moderate | <20 mg/dl | 26 | 90% |
| Severe | >20 mg/dl | 3 | 10% |

# DISCUSSION

The frequency of G6PD deficiency in this study was 12.1%. This figure correlates with other local studies like Khan et al[19] in 2002 reported G6PD deficiency in 13% at Peshawar, Imran et al[20] reported as 12%, Parveen et al[21] as 12.1% and Khattak et al[22] observed G6PD deficiency in 12% patients.
The results are, however, in contrast with other local studies, like Alvi et al[23] in 2006 observed 10% at Lahore, Rehman H et al[24] showed 8.2% and Rashid et al[25] in 2005 as 6%.
This is also a relatively high occurrence rate as compared to studies from India[26] (7.5%), Saudi Arabia[7] (2%) and Tehran[27] (2.1%). On the other hand, this frequency of G6PD deficiency in the jaundiced neonates is quite lower than the frequency reported from Thailand[28] (25.5%), China[29] (18.42%) and Nigeria[30] (38%). These variations may be due to demographic difference in the genetic make-up of societies. Socio-cultural differences, frequency of carrier individuals, sample size, method used for G6PD enzyme estimation and detection rate.
Majority of neonates with G6PD deficiency in one study presented with neonatal jaundice between 2nd and 4th day of life. This is supported by other similar studies conducted locally and internationally[30-32].
In our study in G6PD deficient patients, male to female ratio was 8.7:1. According to Khattak et al[22] (2006) the male to female ratio was 7:1 and another study by Khan et al[19] showed male to female ratio as 7.6:1. Majority (90%) of neonates with G6PD deficiency in our study

showed serum total bilirubin level below 20 mg/dl, Khan et al[19] also reported mean serum bilirubin levels as 18.7 mg/dl in G6PD deficient neonates.

# CONCLUSION

As obvious from this study as well as other studies quoted, G6PD deficiency is quite high in neonates presenting with jaundice.

**Limitations:** The limitations of this study include, neonates were screened in a single centre and the study population was not large enough to draw a firm conclusion regarding the incidence in the community. However, this study gives an indication that G6PD deficiency represents a health problem in the Sukkur region and provides evidence for feasibility and justification for universal newborn screening in this area.

**Recommendations:** Early detection of G6PD deficiency should be done through mass screening programmes. It can avoid the incidence of permanent brain damage resulting from hyperbilirubineuria with subsequent kernicterus and death. The mass screening for G6PD would be invaluable in identifying babies at the time of their birth. This can easily be achieved by saving cord blood and performing the test on the sample without causing extra discomfort to infant. The identification of deficient babies would aid the health workers to counsel parents in avoiding exposure of their babies and themselves (if lactating) to oxidizing agents, to watch for jaundice and to bring jaundiced infant to hospital at their earliest. The mothers can also be advised to check for G6PD levels in other children.

For the screening program to be effective doctors, nurses, lady health workers and dais should be trained and home deliveries should be monitored.

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Original Article

# Frequency of Low Birth Weight in Primigravida reported at PUMHS Hospital Nawabshah

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## ABSTRACT

**Objective:** To determine the frequency of low birth weight in primigravida reported at PMC Hospital Nawabshah.
**Study Design:** Descriptive case series study.
**Place and Duration of Study:** Departments of Gynaecology & Obstetrics and paeds medicine, at Peoples University of Medical & Health Sciences Nawabshah, from Jan 2011 to the Dec 2011.
**Materials and Methods:** This study consisted of 319 pregnant women at 16 weeks of gestational age with singleton pregnancy reporting to the Antenatal Clinic, Obstetrics and Gynaecology Department were selected. Weight was measured by using weight machine throughout antenatal checkups. Weight and height was measured by same person rechecked. Their pregnancies were followed to assess the low birth weight. The neonatologist evaluated the babies. All primigravida women in the reproductive age group between >18 to <35 years with singleton pregnancy, normal fetal lie, and Height 5 feet or more were included. Exclusion criteria were patients associated with uterine anomalies (like uterine polyp, uterine septae, submucosal fibroid), smoking, short stature, other medical disorder like diabetes, hypertension, thyroid disorders, epilepsy and asthma. Results were prepared with help of tables and graphs. Data was analyzed through SPSS software.
**Results:** 319 patients included in this study. There was a wide variation in age was noted. The youngest patient was 18 years old and the oldest patient was 35 years old. The mean age was 21.21 + 4.22 years and peak age group for presentation of primigravida in our study is 26 to 30 years. Clinical asses the fetal weight and observed 42(13.16%) cases were <2.5kg weight while remaining 277(86.83%) cases were 2.5 to 4 kg weight.
**Conclusion:** In conclusion, we observed in our study that low body weight of primigravida mother is associated with low birth weight babies.
**Key Words**: Low birth weight, Low body mass index, Primigravida .

## INTRODUCTION

Intrauterine growth and development is one of the most vulnerable process in the human life cycle[1]. Low birth weight (LBW) is a known problem of reproductive health and general health status of population worldwide[2]. It continues to still a major public health problem throughout world. The prevalence of low birth weight according to WHO estimation about 25 million low birth weight babies are born per year, approximately 95% of them is reported in developing countries[3].

Maternal circumstances is the most important factor of birth weight and factors that prevent normal circulation across the placenta cause poor nutrient and oxygen supply to the fetus and leads restricting growth[4]. Different factors vary from one area to another, depending upon geographic, socioeconomic and cultural factors. Underweight primigravida women have a greater frequency of preterm birth (32-37 weeks) and preterm labour [5]. In primigravida women with low body mass index there is reduction in birth weight [6].

This study was done to find out the frequency low birth weight in primigravida women delivering singleton babies at term.

## MATERIALS AND METHODS

This study was conducted at the department of Obs & Gynae and peads medicine of Peoples University of Medical & Health Sciences, Nawabshah, from Jan 2011 to the Dec 2011. Descriptive case series study, 319 pregnant women at 16 weeks of gestational age with singleton pregnancy reporting to the Antenatal Clinic, Obstetrics and Gynaecology Department were selected. Weight was measured by using weight machine throughout antenatal checkups. Weight and height was measured by same person rechecked. Their pregnancies were followed to assess the low birth weight. The neonatologist evaluated the babies. All primigravida women in the reproductive age group between >18 to ≤35 years with singleton pregnancy, normal fetal lie, and Height 5 feet or more were included. Exclusion criteria were patients associated with uterine anomalies (like uterine polyp, uterine septae, submucosal fibroid), smoking, short stature, other medical disorder like

diabetes, hypertension, thyroid disorders, epilepsy and asthma.

# RESULTS

There was a wide variation in age was noted. The youngest patient was 18 years old and the oldest patient was 35 years old. The mean age was 21.21 ± 4.22 years and peak age group for presentation of primigravida in our study is 26 to 30 years (Chart No.1).

In this study clinical asses the fetal weight and observed 42(13.16%) cases were <2.5kg weight while remaining 277(86.83%) cases were 2.5 to 4 kg weight. (Chart No.2).

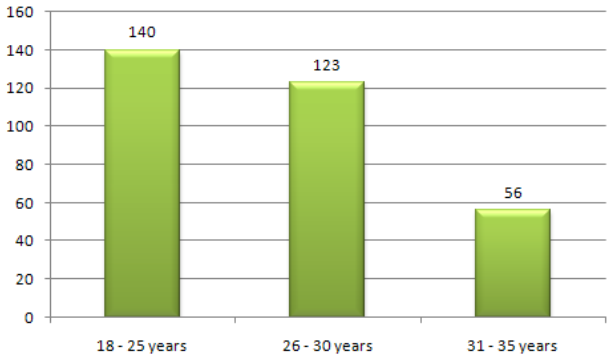


**Chart No.1: Age Distribution**

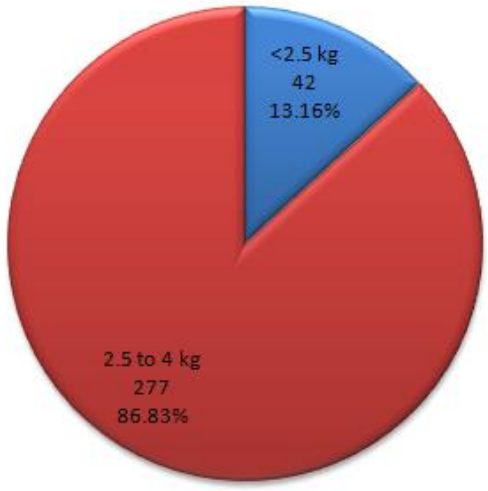


**Chart No.2: Distribution of cases by fetal weight**

# DISCUSSION

Motherly diet is an important determinant of outcomes of pregnancy malnutrition during pregnancy and its consequences maximally affect the health and long term outcomes of the population. Low birth weight related with maternal malnutrition as a risk factor in primigravida [7].

Factors associated with low birth weight and their presence in an individual woman indicates an increased possibility, or risk, of bearing a low birth weight infant. The relationship of maternal underweight with obstetrics performance are less clear. Some studies reported [8,9] increased incidences of preterm delivery, low birth weight and increased perinatal loss in these women, an other study [10] have reported a protective effects of maternal underweight on certain pregnancy complications and interventions.

In Pakistan mostly rural area women have lower socioeconomic status, maternal education, maternal occupation farm labourer and having heavy physical activity during antenatal period were significantly associated with low birth weight in primigravida. **R**ural women from lower socio-economic status are more susceptible to poor diet and more likely to undertake physically demanding work during pregnancy. Uneducated mothers from rural area are not utilizing or inadequately utilizing antenatal care services.

In our study maternal age was 18 years old and the oldest patient was 35 years old. The mean age was 21.21 ± 4.22 years and peak age group for presentation of primigravida in our study is 26 to 30 years. Some international authors Krammer[5], Hirve and Ganatra[11] , Deshmukh et al[12] also reported significant relationship between socioeconomic status and birth weight of baby. The frequency of illiterate and primary education was more in 35.5% cases as compared to control group 24.5%. Hirve and Ganatra[12] reported adjusted odds ratio for delivering LBW decreases significantly with increasing education status of the mother. In rural area women are regularly continue strenuous physical work in reproductive period due to lower socioeconomic status. In this study clinical asses the fetal weight and observed 42 (13.16%) cases were <2.5kg weight while remaining 277 (86.83%) cases were 2.5 to 4 kg weight, while in the study of Urooj U reported out of 114 patients (with BMI<19), 15 (13.1%) patients presented with preterm labour and 12 (10.5%) patients gave birth to fetus with weight <2.5kg[13]. Another prospective study conducted by Watson-Jones et al in antenatal clinics in Mwanza, a prevalence of as low as 8% LBW and 12% preterm birth has been reported[14].

# CONCLUSION

In conclusion, we observed in our study that low body weight of primigravida mother is associated with low birth weight babies. Provide nutritional education and food supplements to the rural area women for antenatal period of pregnant mothers is an established to improve pregnancy outcome.

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Original Article

# Incidence of Benign Ovarian Tumors in Rural Areas: A 10 Years Study in a Tertiary Care Hospital Nawabshah

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## ABSTRACT

**Objective:** To determine the frequency of benign ovarian tumors attending the tertiary care hospital Nawabshah.
**Study Design:** Descriptive cross-sectional study.
**Place and Duration of Study:** This study was carried out in Department of Gynaecology & Obstetrics, at Peoples University Hospital Nawabshah, from Jan 2011 to the Dec 2011.
**Materials and Methods:** This study consisted of 419 patients of benign ovarian tumours admitted through the outpatient department, as well as from casualty department of Peoples University Hospital Nawabshah.
Detailed history of duration of complain and clinical examination of the patient was done. All patients underwent for base line and specific investigations especially ultrasonography and biopsy sampling for assessment of histopathological examination. All patients in the reproductive age group between 15 to 60 years with any one or more presenting complains of ovarian tumors like abdominal mass, bloating, discomfort, pain or pelvic swelling were included. Exclusion criteria were patients more than 60 years of age , previous history of ovarian tumor and non-consenting women. Results were prepared with help of tables and graphs. Data was analyzed through SPSS software No.16.
**Results:** 419 patients included in this study . There was wide variation of age ranging from a minimum of 10 years to 60 years. The mean age was 31.68 $\pm$ 5.45 years. In this study incidence of ovarian neoplasm slowly increase per year. Clinical examination of patients revealed that pain in abdomen was the commonest presenting symptom 396(94.5%) followed by mass per abdomen seen in 297(70.88%), bloating in 146(34.88%) and abdominal swelling in 167(39.85%). Histopathology findings revealed was serous cystadenocarcinoma in 182(43.4%) cases, mucinous cystadenoma 116 (27.7%) cases, mature teratoma 98(23.4%) cases, thecoma 16(3.8%) cases, fibroma in 05(1.2%) cases and brenner tumor 02 (0.5%) cases.
**Conclusion:** In conclusion our study revealed that histopathologically most common type is serous cystadenoma followed by mucinous cystadenoma. The peak incidence of benign tumors was seen in the 3rd and 4th decades of the life.
**Key Words:** Ovarian Tumor, Benign, Rural Area, Different Age Group.

## INTRODUCTION

Ovarian tumors of the genital tract are not a single problem but a complex wide spectrum of tumors involving a different variety of histological tissues like epithelial tissues, connective tissues, specialized hormone secreting cells to germinal and embryonal cells[1]. Ovarian cancer accounts for almost 90% of malignancies in Western world[2] while in Pakistan accurate incidence is not conform due to not proper organized patients data but ovarian cancer is the 4th most common cancer among Pakistani females[3]. In eastern India, the fourth most frequent reported malignancy in females was ovarian [4]. Asian countries and Japan reported incidence of cancer is slowly increasing increased approximately 2 to 6.5 new cases of ovarian malignancy per 100,000 women every year[5].
Mostly ovarian tumors occur in perimenopausal and post menopausal women, rarely in children. The risk for developing ovarian tumors peaks in fifth decade of life[6]. Ovarian tumors in children and teenagers are not frequently encountered in clinical practice. The rarity of the condition, asymptomatic nature in the earlier stage, variation in clinical presentation and lack of knowledge among the girls and parents sometimes makes diagnosis delayed and difficult[7].
This study was conducted to determine the frequency of common types of benign ovarian tumors in different age groups reported at Peoples university Hospital Nawabshah.

## MATERIALS AND METHODS

This study was conducted at the department of Obs & Gynae of Peoples University Hospital Nawabshah, from Jan 2011 to the Dec 2011. Ten years case records retrieved from ward file, who were admitted with the diagnosis of Benign ovarian lesion. Detailed history of duration of complain and clinical examination of the every patient was done. The diagnosis of ovarian tumour is based on especially ultrasonography and biopsy sampling for assessment of histopathological examination. All patients in the reproductive age group between 15 to 60 years with any one or more presenting

complains of ovarian tumors like abdominal mass, bloating, discomfort, pain or pelvic swelling were included. Exclusion criteria were patients more than 60 years of age , previous history of ovarian tumor and non-consenting women.

## RESULTS

This study was conducted on 419 patients in Department of Gynaecology & Obstetrics at Peoples University of Medical Health Science Hospital Nawabshah.

There was wide variation of age ranging from a minimum of 10 years to 60 years. The mean age was 31.68 ± 5.45 years. In this study incidence of ovarian neoplasm slowly increase per year (Chart No.1).

In this study clinical examination of patients revealed that pain in abdomen was the commonest presenting symptom 396(94.5%) followed by mass per abdomen seen in 297(70.88%), bloating in 146(34.88%) and abdominal swelling in 167(39.85%) (Chart No.2).

Histopathology findings revealed was serous cystadenocarcinoma in 182(43.4%) cases, mucinous cystadenoma 116 (27.7%) cases, mature teratoma 98(23.4%) cases, thecoma 16(3.8%) cases, fibroma in 05(1.2%) cases and brenner tumor 02 (0.5%) cases.

There was a wide variation in age was noted. The youngest patient was 10 years old and the oldest patient was 60 years old. The tumors were most common in 20-30 years age group 168(40.1%) and 31-40 years of age group 139(33.2%) cases, followed by 41-50 years of age group 48(11.4%) (Table No.1).

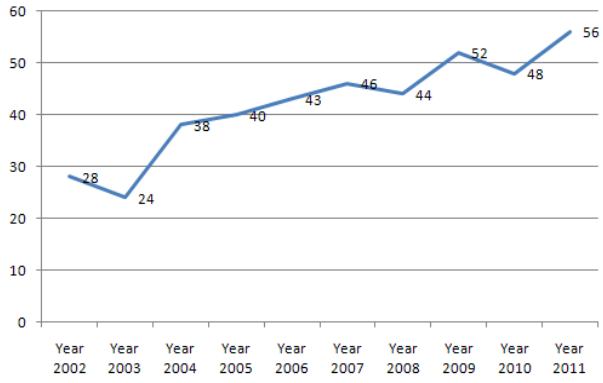


**Chart No.1: Number and incidence of ovarian neoplasm per year**

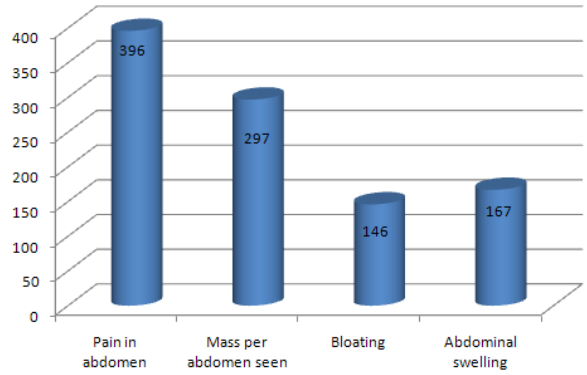


**Chart No.2: Symptoms of Patients**

**Table. No.1: Age wise distribution of histological types of benign ovarian neoplasms**

| Age group | Benign histological types No (%) | | | | | | Total |
|---|---|---|---|---|---|---|---|
| | Mature Teratoma | Serous cystadenoma | Mucinous cystadenoma | Thecoma | Fibroma | Brenner tumor | |
| 10-19 | 12 | 09 | 07 | - | - | - | 28 |
| 21-30 | 28 | 86 | 46 | 02 | 04 | 02 | 168 |
| 31-40 | 34 | 58 | 42 | 04 | 01 | - | 139 |
| 41-50 | 16 | 15 | 10 | 07 | - | | 48 |
| 51-60 | 8 | 14 | 11 | 03 | - | - | 46 |
| **Total no.** | **98(23.4%)** | **182(43.4%)** | **116(27.7%)** | **16(3.8%)** | **05(1.2%)** | **02(0.5%)** | **419(100%)** |

## DISCUSSION

Tumors of the ovary create many problems due to their high complication rate and they are biggest diagnostic challenge in field of gynecological oncology. The benign character of the tumor to remain silent clinically for a long period of time tests the gynecologist. Though many workers have worked extensively in the field of ovarian tumor pathology, the wide variation in facts and figures reflects the confusion prevailing in the area of tumor nomenclatures and different morphological subtypes of tumor.

The ovarian tumors can occur at any age but their peak incidence is in the reproductive age group. The peak incidence of the ovarian tumors in the present study were in the 3rd and 4th decades, 168(40.1%) and 139(33.2%) tumors were seen in these age groups respectively. In an earlier study of Pilli G reported, the peak incidence was in 3rd decade which accounted for 28.72% of total number of cases [8]. Thus the ovarian tumors were more common in the reproductive age group.

The Ovarian tumors manifest with wide variety of clinical manifestation and mass per abdomen is the usual complaint. In our study all patients presented with pain in abdomen was the commonest presenting symptom 396(94.5%) followed by mass per abdomen seen in 297(70.88%), bloating in 146(34.88%) and

abdominal swelling in 167(39.85%). These results were correlated with the study of Pilli G and reported 93.16% of patients had mass per abdomen and 64.90% of cases had pain abdomen associated with mass per abdomen[8]. Another study conducted by Sumaira Yasmin at Peshawar region and reported the clinical symptoms were pain abdomen 48(70.59%), Mass abdomen 10(14.71%), Gastrointestinal disturbances 5(7.35%), menstrual 3(4.41%) and Urinary 2(2.94%)[9] .

Germ cell tumor is the most common tumor of teenage group. They arise from primordial gem cell that becomes malignant and if it remains undifferentiated then lead into Dysgerminoma. It may result in mature and immature teratoma. Among benign tumors, teratomas are the commonest variety as reported by De Silva et al .In our study frequency of different histopathological types of benign ovarian tumour showed that the commonest tumour was serous cystadenocarcinoma in 182(43.4%) followed by mucinous cystadenoma 116 (27.7%) cases, mature teratoma 98(23.4%) cases, thecoma 16(3.8%) cases, fibroma in 05(1.2%) cases and brenner tumor 02 (0.5%) cases. However study reported by Swamy GG ,that epithelial tumors were commonest variety of ovarian tumors followed by germ cell tumors[11] . A group of workers reported that the most common type of ovarian cyst was serous cystadenoma (40.2%) followed by mature cystic teratoma (15.7%)[12].

# CONCLUSION

Serous cystadenoma is the commonest benign tumour. Germ cell tumours were next to epithelial ovarian tumours. The peak incidence of benign tumors was seen in the 3rd and 4th decades of the life. Amongst benign ovarian tumours patients commonly present late and patients frequently present with advanced stages of the disease.

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Original Article

# Brain Abscess in Cyanotic Congenital Heart Disease: A Preventable Complication with Heavy Financial Burden and Poor Outcome

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## ABSTRACT

**Objectives:** To evaluate the financial burden and outcome of the children with brain abscess and underlying congenital cyanotic heart disease. To emphasize the need of early diagnosis and surgery of congenital cyanotic heart disease.

**Study Design:** Cross Sectional Descriptive Study.

**Place and Duration of Study:** This study was conducted at the department of paediatric cardiology The Children's Hospital and The Institute of Child Health, Multan from February 2010 to January 2012.

**Patients and Methods:** All the patients presenting with brain abscess and having underlying congenital heart disease were included in the study. All the patients underwent transthoracic echocardiography and computed tomography (CT) scan of the brain. Data was taken on a written proforma after proper consent.

**Results:** A total of 58 patients with cyanotic congenital heart disease presented with CNS manifestations including headache, fever, focal neurological signs, fits or altered sensorium during the study period. Out of these 24 turned out to have brain abscess. Multiple brain abscesses were found in 7 patients. All the patients were given broad spectrum IV antibiotics. 19 of the patients required surgical intervention. Repeat CT scan was performed in all the patients. Only 5 patients recovered without any neurological sequalae.7 patients expired during hospital stay. All of the remaining 12 patients survived but with some permanent neurological deficit.IV antibiotics, supportive treatment, CT scan, other laboratory investigations and surgery, all have a lot of cost. Around 1500 to 2000 US $, on an average, were spent by the government on one patient during hospital stay.

**Conclusion:** The only way to avoid CNS complications of CCHD is early diagnosis and early surgical treatment. But unfortunately, in this country because of lake of paediatric cardiology services and deficiency of paediatric cardiac surgery centers, corrective surgery of congenital cyanotic heart disease is delayed. It increases the risk of brain abscess formation which in turn leads to excessive financial burden on government resources and also increases the risk of long term neurological sequalae. Establishment of more and more paediatric cardiac surgery centers in this country is urgently required.

**Key Words:** Congenital cyanotic heart disease, Brain abscess.

## INTRODUCTION

Central nervous system (CNS) complications of congenital cyanotic heart disease (CCHD) include cerebral infarction leading to stroke and cerebritis leading to abscess formation. Both have high morbidity and mortality. Cerebral infarction usually occurs in younger kids < 2 years of age, while abscess formation occurs in older children > 2 years of age. A brain abscess is a focal collection of infectious material with in the brain, which can arise as a complication from a variety of causes including infection trauma and surgery [1]. A wide variety of organisms (bacteria, fungi, protozoa, and parasites) can cause abscess formation. Brain abscesses occur relatively infrequently because of the abundant blood supply to the brain and the protection of the brain by the blood – brain barrier [2].

Congenital cyanotic heart diseases (CCHD) are one of the common predisposing factors of brain abscess in our setup. In the patients with congenital cyanotic heart disease with decreased pulmonary blood flow, hypoxia polycythemia and relative iron deficiency anemia take the patient to a greater risk of developing brain abscess. These factors cause hyperviscosity and sludging of RBCs in the micro circulation of brain parenchyma which lead to micro infarctions and encephlomalacia. These infracted areas then serve as a nidus for brain abscess. The hematogenous spread through right to left shunting in these cardiac lesions further increases the risk[3].

## PATIENTS AND METHODS

This is a cross sectional descriptive study conducted at the department of paediatric cardiology The Children's Hospital and The Institute of Child Health, Multan from February 2010 to January 2012. All the patients presenting with brain abscess and having underlying congenital heart disease were included in the study.

**Inclusion criteria:**

- All the patients presenting with brain abscess and having underlying congenital cyanotic heart disease diagnosed on the basis of computed tomography (CT) scan of brain.

Exclusion criteria:

- The patients with brain abscess without underlying congenital heart disease.
- The patients with congenital heart disease with CNS complications other than brain abscess like cereberitis or infarction.

Toshiba Nemio XG machine was used for transthoracic echocardiography of all the patients which were performed by the trained paediatric cardiologist. CT scan brain with contrast was performed of all the patients. Toshiba Aquillion 16 slice CT scan machine was used for this purpose. The data was taken on a written proforma after proper consent.

## RESULTS

A total of 58 patients with cyanotic congenital heart disease presented with CNS manifestations including headache, fever, focal neurological signs, fits or altered sensorium during the study period. CT brain with contrast was performed of all these patients. Out of these 24 turned out to have brain abscess. Multiple brain abscesses were found in 7 patients. All the patients with brain abscess were more than 4 years of age with a range of 4-13 years and a mean of 8.5 $\pm$ 2.1 years. A majority, 17 of the total brain abscess patients had tetrology of Fallot (TOF) as underlying cyanotic congenital heart disease.

**Table No. 1: Types of underlying congenital cyanotic heart disease (CCHD)**

| Congenital cyanotic heart disease | No. of patients n = 24 (%) |
|---|---|
| TOF | 17 (70 %) |
| TGA VSD ,PS | 3 (12.5 %) |
| Tricuspid atresia | 1 (4.2%) |
| Univentricular heart with pulmonary stenosis | 2 (8.3%) |
| Pulmonary atresia with VSD | 1 (4.2%) |

TOF = tetrology of Fallot, TGA = Transpositional of great arteries,
VSD = Ventricular septal defect, PS = Pulmonary stenosis.

**Table No. 2: Types of surgical procedures**

| Surgical Procedure | Number of patients n = 24 (%) |
|---|---|
| Single Burr hole | 11 (45.8%) |
| Twice Burr hole | 05 (20.8%) |
| Thrice Burr hole | 01 (4.2%) |
| Craniotomy | 02 (8.3%) |

All the patients were given empirically broad spectrum IV antibiotics in the form of ceftriaxone, vancomycine and metronidazole. After culture & sensitivity reports and clinical response antibiotics were reviewed.19 of the patients required surgical intervention. Burr hole was performed in 17 of the patients, out of these 5 underwent burr hole aspiration twice and 1 patient thrice. 2 patients required craniotomy and surgical excision of the abscess. Hospital stay ranged from 23 to 42 days with a mean of 34 $\pm$ 3 days. Repeat CT scan was performed in all the patients and few of them required multiple scans to see the response.

**Table No. 3: CT scan exposures**

| Number of patients | Number of CT scans n = 24 (%) |
|---|---|
| 09 | 02 (8.3%) |
| 11 | 03 (12.5 %) |
| 04 | 04 (16.8%) |

Only 5 patients recovered without any neurological sequalae.7 patients expired during hospital stay. All of the remaining 12 patients survived but with some permanent neurological deficit.

**Table No. 4: Outcome of the patients**

| Outcome | Number of patients n = 24 (%) |
|---|---|
| Fully recovered | 05 (22%) |
| Expired | 07 (28%) |
| Neurological deficit | 12 (50%) |

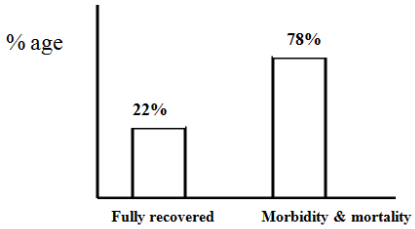


**Figure No. 1: Mortality and Morbidity**

**Table No.5: Neurological Sequalae**

| Neurological deficit | Number of patients n = 24 (%) |
|---|---|
| Fits | 07 (29.1%) |
| Blindness | 01 (4.2 %) |
| Aphasia | 01 (4.2 %) |
| Facial palsy | 02 (8.3%) |
| Hemiplagia (motor deficit) | 03 (12.5%) |

**Table No. 6: Expenses (disposable items)**

| | Pk Rs | US $ |
|---|---|---|
| IV antibiotics | 60,000/- | 705 |
| Supportive treatment | 30,000/- | 352 |
| Lab investigations | 10,000/- | 117 |
| CT scan | 15,000/- | 176 |
| Surgical procedure | 25,000/- | 294 |
| Total | 140,000/- | 1644/- |

IV antibiotics, supportive treatment, CT scan, other laboratory investigations and surgery, all have a lot of cost. Around 1500 to 2000 US $, on an average, were spent by the government on one patient during hospital stay. This calculation is only for the expenses of disposable items. While the financial burden in the

form of hospital stay charges, nursing care and operation theater charges, consultant and other medical personnels charges is much more.

## DISCUSSION

Congenital cyanotic heart disease is an important predisposing factor for brain abscess formation, accounting for 25 to 46%[4.] of cases. The risk of brain abscess complicating CCHD is inconstant but is more common after 2 years of age and increases continuously until the age of 12 years. Instantaneous risk at that time is quoted as 1.75 ± 0.12%. but decreases thereafter[5]. Risk factors predisposing to the development of brain abscess in CCHD include hypoxia and its consequent polycythemia and hyperviscosity. The latter results in sluggish blood flow in cerebral microcirculation that allows micro-thrombi formation and focal encephlomalacia. It also alters blood brain barrier permeability[5]. Shunted blood from the right side escapes the bacterial phagocytes in the lung and contains infectious organisms that seed these sites causing focal cereberitis[6]. One study demonstrated reduced bactericidal and phagocytic functions of leucocytes in children with CCHD[7]. Although it occur in any CCHD, the commonest CCHD associated is tetrology of Fallot[8]. In our study 69%of the children have tetrology of Fallot. Multiple brain abscesses are particularly associated with CCHD. Prusty has reported multiple abscesses in 10 % of 60 cases of brain abscess in patient of CCHD[9]. Whereas, Shehzad at al reported multiple brain abscesses in 36 % cases[10]. In our study, 29 % of the patients had multiple brain abscesses. Surgical intervention is required for abscesses which are larger than 2cm in diameter or situated in critical areas of the brain or causing significant mass effect[11, 12, 13]. It can take the form of needle aspiration through a burr hole, CT guided stereo tactic aspiration or excision of abscess by open craniotomy. Some advocate stereo tactic aspiration as the method of choice, while others favor complete excision of abscess cavity[14]. In our study, 77% of the patients required surgical intervention. Needle aspiration through burr hole was done in 69 %, while excision of abscess cavity by craniotomy was performed in the rest of 8 % children. Fits were the commonest long term sequalae observed in our study. Similar high incidence of seizures disorder sequalae has been reported by Kao et al[2]. This might be related to severe local inflammation or infection resulting in a more severe local cerebral reaction[15]. Overall mortality observed in our series was 29 %. While other local and international studies have reported mortality between 15 to 30 %[8, 16, 17].

As far as financial burden and excessive use of government resources is concerned, mean hospital stay of the patients was 34 ± 3 days along with the expenditure of 1500 to 2000 US $ per patient during the hospital stay. Inspite of this heavy expenditure and excessive use of government resources the patients suffered a lot of agony, high mortality and morbidity, prolonged hospital stay and even those who fully recovered still lived with underlying congenital cyanotic heart disease. While a corrective cardiac surgery procedure for CCHD requires only 5 to 7 days of hospital stay and about the same amount of money as was spent on the management of brain abscess. The mortality and morbidity for these procedures is < 1 % these days. Above all, the patient becomes free from his CCHD and also from its complications. In developed world, the incidence of CNS complications of CCHD has dropped markedly in past 20 years because of early diagnosis and surgery of CCHD. But unfortunately in our set up this incidence is still at the same level because of delay in diagnosis and availability of very few cardiac surgery centers.

## CONCLUSION

Ideally, CCHD patient should be diagnosed early in neonatal or infantile age group and suitable medical and surgical treatment should be provided according to the indication at proper timings. This will help a lot in avoiding these CNS complications of CCHD. But unfortunately in our set up, the diagnosis is made very late because of ignorance and poor patient referral system. Even if the diagnosis is made early still we do not have much facilities for the surgical repair of these CCHD patients. That is why surgery is delayed and the incidence of CNS complications in CCHD patients is much higher than in the developed world. The need of the day is to establish more and more paediatric cardiology and cardiac surgery centers in this country. This will help in off loading burden of these cardiac patients from government health care facilities and also will avoid the lethal CNS complications.

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Original Article

# Ameliorating Role of Pomegranate on Minocycline induced Pigmentation in the Epidermis of Guinae Pig

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## ABSTRACT

**Objective:** To investigate the ameliorating role of pomegranate on minocycline induced pigmentation in the epidermis of guinea pig.

**Study Design:** An experimental observational study.

**Place and Duration of Study:** This study was conducted at the Anatomy Department, BMSI, J PMC, Karachi.

**Materials and Methods:** 30 adult guinea pigs were divided into 3 groups A B and C. In this study, A served as control, B was given Minocycline, while C was given Minocycline with Pomegranate for 8 weeks, after which their skin was processed for histological examination of morphology of melanocytes and pigmentation in Dopa Oxidase stained sections under light microscope.

**Results:** The melanin pigmentation deposition in Minocycline treated group B was distributed densely and extended till stratum corneum as compared to the control group A, while in the Pomegranate treated group C along with Minocycline, the melanin pigmentation was considerably reduced and was observed to be distributed sparsely extended till stratum basale. The morphology and number of melanocytes in both treated groups remain same as compared to control group A

**Conclusion:** Based on the present study it is concluded that pigmentation induced by Minocycline can be reduced and may be prevented by taking pomegranate simultaneously.

**Keywords:** Pomegranate, Minocycline, Epidermal Pigmentation, Melanocytes, Guinea pigs.

## INTRODUCTION

Skin the largest human body organ provides a major interface between the environment and the body and is constantly exposed to an array of chemical and physical environmental pollutants. In addition a large number of dietary contaminants and drugs can manifest their toxicity in skin[1]

Drugs may cause exanthemas, utricaria, hypersensitivity syndromes, cutaneous necrosis and hyperpigmentation of the skin[2]

Numerous common drugs can stimulate human skin pigmentation such as certain antibiotics (sulfonamides and tetracycline's), diuretics, nonsteroidal anti-inflammatory drugs, pain relievers, and some psychoactive medications.[3] These pigmentary changes caused by drugs usually result in a limited degree of morbidity,[2] but unwanted pigmentation can produce a significant Psychological stress.[4] The pathogenesis of these pigmentary disorders can be categorized into several mechanisms out of which one is enhanced melanin production with or without an increase in the number of active melanocytes.[2]

Minocycline, a semi synthetic, broad spectrum antimicrobial tetracycline that was introduced in 1967,[5] to be used in the treatment of acne, [6,7] is extensively being used as an anti-inflammatory, antiapoptotic, antichemotactic, collagenase inhibitory, and immunomodulatory agent.[8,9,10] It also acts as an inhibitor of hydrogen peroxide-induced oxidative stress.[11] A well- documented and cosmetically displeasing side effect is skin pigmentation in its long term therapy.[12,13,14]. Burns et al[15] (2011) had quoted multiple histological and electron microscopic studies that have demonstrated increased melanin, haemosiderin, and either Minocycline or a metabolite in the skin.

Pomegranate is native from the Himalayas.[16] It is used in the traditional medicines of different Asian cultures for the treatment of a variety of ailments.[17] The fruit is a rich source of polyphenol compounds, [18] which are: anthocyanins such as cyaniding, delphinidin and hydrolysable tannins such as ellagic acid, gallic acid accounting for 92% of the antioxidant activity.[19] Its main constituent, ellagic acid, is an antioxidant,[20] cytoprotective agent against oxidative stress induced by alcohol[21] and drug-induced liver injury.[22] It is mostly abundant in berries, walnuts, pecans, pomegranate, cranberries and other plant food in the form of hydrolysable tannins called ellagitanins.[21] Ellagic Acid has been reported to prevent pigmentation caused by sunburn.[23] Also, in a topical application study on guinea pig and human skin, inhibitory effect of ellagic acid on UV –induced pigmentation in the skin was observed.[24,25]

As the most essential enzyme in the melanin biosynthetic pathway is tyrosinase and it is the only enzyme absolutely required for melanin production

which is known to be a metaloenzyme, containing copper at an active site, and ellagic acid suppresses tyrosinase activity.[23] Zho and Goa[26] (2008) also reported the copper chelating role of ellagic acid resulting in decrease proliferation of melanocytes.

In the perception of above mentioned literature and studies, it is clear that although various studies being done to explore the protective effects of pomegranate against pigmentation induced by UV-irradiation. The present experimental study was designed to explore the protective role of pomegranate in Minocycline induced pigmentation of skin.

# MATERIALS AND METHODS

In this experimental study,30 adult male guinea pigs weighing between 400 – 600 grams were taken and divided into 3 groups A, B and C. Group A animals served as control, group B received Minocycline 0.0003mg/G body weight/ day orally, and group C received Minocycline 0.0003mg/G body weight of animal/day orally along with pomegranate 0.4mg/G body weight of animal/day orally for 8 weeks. All the guinea pigs were sacrificed under ether anesthesia in a glass container and one skin fragment of two inches size, from abdomen was taken from each animal. It was fixed in 10% formalin in the pH 7.4 buffer (v/v) plus 0.44 M sucrose for DOPA-OXIDASE TISSUE BLOCK METHOD. A 2 mm thin vertical section was cut from the fragment and paraffin blocks were made, 4 to 5 micron thick sections were obtained were counter stained with Meyer's Haematoxylin and observed under light microscope. The results were considered statistically significant if the P-value was < 0.05.

# RESULTS

In control group A, the shape of DOPA positive melanocytes was observed and found to be ovoid to round in shape with sparsely stained dendrites spread within the keratinocytes of stratum spinosum. The nuclei were ovoid to round in shape while the cytoplasm was pale staining with varying dendritic processes (black brown) scattered between keratinocytes of stratum basale and spinosum. Melanin pigment was deposited in scattered pattern within the stratum basale and graded as "+" (Figure-1 & table-1). The mean number of melanocytes in abdomen was 1.52 ±0.05 (table-2).

**Table No. 1: Distribution and Extension of Melanin Pigment Deposition in Epidermis of Guinea Pig**

| Group | Treatment given | Dose & duration | Distribution and extension of melanin pigment deposition | | |
|---|---|---|---|---|---|
| | | | Sparse* | Moderate** | Dense*** |
| A (n=10) | Control | Laboratory diet ad labitum for 8 weeks | + | | |
| B (n=10) | Minocycline | 0.0003mg/G body weight/day(Orally) for 8 weeks | | | +++ |
| C (n=10) | Minocycline + Pomegranate | 0.0003mg/G body weight/ day + 0.4mg/G body weight/ day(Orally) for 8 weeks | + | | |

*Sparse: melanin pigment deposited in scattered pattern up to stratum basale
** Moderate: melanin pigment deposited in patches up to stratum spinosum
*** Dense: melanin pigment deposited uniformly up to stratum corneum

**Table No.2: Mean number of melanocytes in the abdominal epidermis of various groups in guinea pig**

| Group | Treatment given | Dose & duration | Mean number of melanocytes |
|---|---|---|---|
| A (n=10) | Control | Laboratory diet ad labitum for 8 weeks | 1.52± 0.05* |
| B (n=10) | Minocycline treated | 0.0003mg/G body weight/day(Orally) for 8 weeks | 1.51± 0.01* |
| C (n=10) | Minocycline + Pomegranate | 0.0003mg/G body weight/ day + 0.4mg/G body weight/ day(Orally) for 8 weeks | 1.50± 0.003* |

*P-value >0.05 (Insignificant); **P-value < 0.05 (Significant); ***P-value < 0.01 (Moderately significant); ****P- value < 0.001 (Highly significant)

In group B, the morphology of melanocytes appeared to be similar but the intensity of melanin pigment was dark when compared with the group A animals. Melanin pigment deposition was dense in uniform pattern within all the layers of epidermis i.e. from stratum basale up to stratum corneum and graded as "+++" (Figure-2 & table-1). The mean number of melanocytes in abdomen was 1.51 ± 0.05 which was insignificant (P- value>0.05) compared to control group A animals (table- 2).

In group C, not only the morphology of melanocytes but also the intensity of melanin pigment was appeared to be similar to that in group A animals. Melanin

pigment deposition was sparse in scattered pattern within the stratum basale and graded as "+" (Figure-3 & table-1). The mean number of melanocytes in abdomen was 1.50 ± 0.003 which was insignificant (P-value > 0.05) when compared to the both groups B and A animals (table-2).

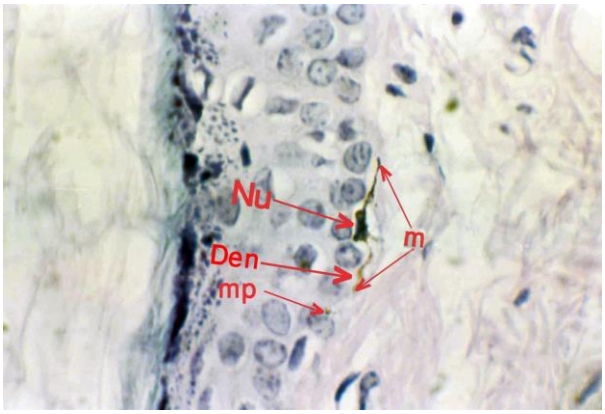


**Figure-1:DOPA-OXIDASE & Mayer's Haematoxylin stained section, from abdominal epidermis of control guinea pig animal, showing the morphology of normal melanocyte(m) with ovoid nucleus(Nu) and brown black pigmented dendrites(Den) scaterred among the adjacent keratinocytes and melanin pigment deposition(mp) sparsely distributed and extended within the stratum basale. Photomicrograph X100.**

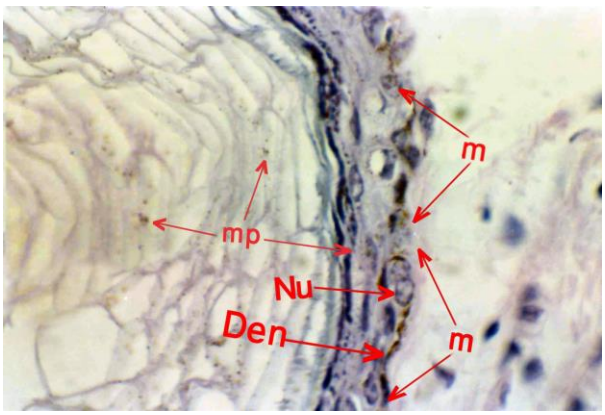


**Figure 2: DOPA-OXIDASE & Mayer's Haematoxylin stained 5 µm thick section, from abdominal epidermis of Minocycline treated guinea pig, showing the morphology of melanocyte (m) with ovoid nucleus (Nu) and brown black pigmented dendrites (Den) scaterred among the adjacent keratinocytes and melanin pigment(mp) deposition is densely distributed and extended up to stratum corneum. Photomicrograph X100**

# DISCUSSION

Human skin exists in a wide range of different colors and gradations, ranging from white to brown to black.[3] Differences in skin color are related to the number, size, shape distribution and degradation of melanin - laden organelles called melanosomes.[15] Thus, melanin synthesis within melanosomes and their distribution to keratinocytes within the epidermal melanin unit determines skin pigmentation, [3] which also protects the skin from the harmful effects of sunlight.[4] Melanin is synthesized in the melanocyte, with tyrosinase playing an important role in the process. As a result of tyrosinase activity, tyrosinase is transformed first into 3, 4-dihydroxyphenylalanine (dopa) and then into dopa quinone, which is converted, after a series of transformations, into melanin. [3,15]

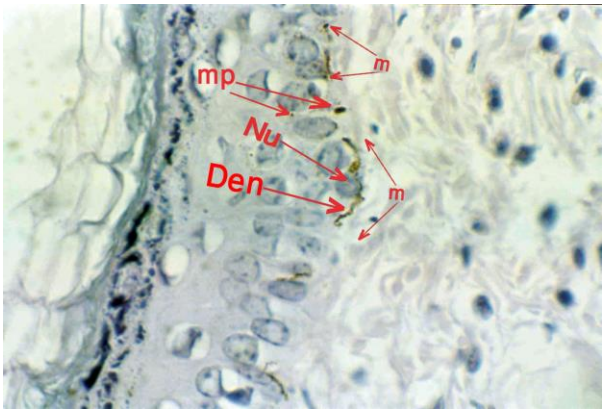


**Figure 3: DOPA-OXIDASE & Mayer's Haematoxylin stained 5 µm thick section, from abdominal epidermis of Minocycline treated guinea pig protected with pomegranate, showing the morphology of normal melanocyte (m) with ovoid nucleus (Nu) and brown black pigmented dendrites (Den) scaterred among the adjacent keratinocytes and melanin pigment(mp) deposition sparsely distributed and extended within the stratum basale. Photomicrograph X100.**

Minocycline, a tetracycline derivative antibiotic, is commonly used to treat infections of various systems such as integumentary, genital and urinary systems.[9] It is also recognized as an effective, well tolerated therapy in rheumatoid arthritis, induces pigmentation. Thus, cutaneous pigmentation is a well recognized complication of Minocycline therapy.[13,14]

Pomegranate (Punica granatum) is used as a medicine for a variety of ailments. It is used in the form of an aqueous decoction for dysentery and diarrhea; [20] The fruit has been developed into dry and liquid forms to provide an alternative convenient source form of ellagic acid.[18] The Ellagic Acid has been proved to be highly effective in suppressing the melanogenesis by reacting with activated melanocytes and without causing any cellular injury.[23]

In Group B, the morphology of melanocytes was similar to the group A animals but melanin deposition was dense and deposited till the stratum corneum due to the inhibition of hydrogen peroxide induced selective destruction of melanocytes by the minocycline that acts as an inhibitor of free radical production and lipid per oxidation capable of attenuating the oxidative stress-induced toxicity.[11] Prasad and Kanwar[10] (2010) explained that 90% of the vitiligo patients showed the progression of the disease was arrested and 22% showed repigmenttation of the diseased lessons due to

direct radical Scavenging activity of minocycline. The increased pigmentation was due to the activation of melanocytes through its surface receptors through α-MSH that is being modulated by Minocycline activated Keratinocytes in vitro.[6] Mouton, Jordan and Schneider[7] in 2004 reported that the pigmentation that started after 4-6 weeks of Minocycline treatment in 36% acne vulgaris patients.

In group C, the morphology of melanocytes and the melanin pigmentation was similar to control group A animals of melanin because of inhibitory effects of Ellagic Acid on the tyrosinase enzyme resulting in decreased pigmentation.[24] Yoshimura et al (2005) demonstrated that the Ellagic Acid rich pomegranate extract inhibited the mushroom tyrosinase activity and exhibited its inhibitory effects in U-V induced pigmentation of skin in rats when given orally by showing the decrease in number of DOPA positive melanocytes quantitatively. Kasai et al (2006)[25] also suggested that Ellagic Acid rich pomegranate extract when given in its lowest dose for 4 weeks shows protective effect on sunburn caused by UV irradiation.

# CONCLUSION

It is concluded that Pomegranate is very potent in providing protection against Minocycline induced pigmentation due to its main constituent, ellagic acid, which directly inhibits melanogenesis. This suggests that the concomitant use of pomegranate with Minocycline can reduce pigmentation in patients on long term Minocycline therapy. The present work is under progress for further extended studies in exploring the role of pomegranate.

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Original Article

# To Study the Effect of Tribulus Terristris on Urinary PH, Uric Acid and Calcium as a Herbal Diuretic Agent

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## ABSTRACT

**Objective:** To study the effect of tribulus terristris on urinary pH, uric acid and calcium as a herbal diuretic agent.
**Study Design:** Descriptive Study.
**Place and Duration of Study:** The study was conducted postgraduate Medical Institute (PGMI) Lahore and duration of study was two weeks.
**Materials and Methods:** Tribulus terristris extract (100 mg/kg body weight) was administered in rabbits. Rabbits are divided into two groups CT and Tt.
**Results:** There were significant alkalinization of urine and significant reduction in urinary uric acid level and insignificant urinary calcium level observed.
**Conclusion:** It is concluded that alkalinization and reduction of urinary uric acid by Tt would be help ful to reduce renal stone formation.
**Key words:** Control=CT, Tribulus terristris = Tt, Urinary pH, Urinary uric acid Urinary, Calcium=Ca++.

## INTRODUCTION

T. terrestris is a tropical plant distributed throughout India and Sri Lanka. The entire plant and particularly, the fruits are extensively used in indigenous medicine. The roots and fruits are useful in improving appetite, urinary output, vesicular calculi and pruritus ani, alleviate burning sensation, reduce inflammation, cough, asthma, and cure renal diseases (kirtikar and Basu 1993).[1] T. terristris is useful in the treatment of urolithiasis, dysurea, impotence or erectile dysfunction and kidney dysfunction, and has also shown antibacterial & antifungal activity and anti-inflammatory Activity (Al Bayati F.A 2008)[2].

Urinary stone formation is a common health problem in Pakistan and all forms of calculi are found in the kidney. Urolithiasis is more prevalent in males than females with the ratio 4:1 (Smith D.R. 1975)[3]. There are multiple factors involved in the stone formation. High intake of oxalate, carbohydrate, fat, purine dairy products protein and sodium chloride increase the incidence of stone formation (Smith D.R. 1975)[3].

Thiazide and several non thiazide diuretics (Abraham P.A. & Smith C.L. 1984)[4] and percutaneous nephrostomy and hemiacidrin (Dretler S.P. & Pfister R.C. 1984)[5] are used to treat urolithiasis. High energy shock waves were used to disintegrate kidney stones. (Chaussy C., Bredel W. & Schmiedt E. 1980)[6]. Laser and pneumatic lithotripcy are safe and effective (Naqvi S.A.A. et al 1994)[7]. Banana stem extract has also been tested in rats (Poonguzhali P.K. & Chegu H. 1994)[8] (Prasad K.V.S.R.G., et al 2007)[9]. Rice bran therapy has been tested to prevent the recurrence of urinary stone diseases. (Ebisuno S. et al 1986)[10] (Ohkawa T. & Morimoto S. 1987)[11].

This animal study was carried out to reveal the effects of indigenous herb Tt extract on urinary pH, Uric acid and calcium.

## MATERIALS AND METHODS

**Experimental animals:** Sixteen rabbits of mixed breed were purchased locally and kept in the animal house of Postgraduate Medical Institute, Lahore for a week for acclimatization before starting the experiment. Twelve hours light and dark cycle was maintained. They were fed on grass, grain seasonal vegetables and water adlibitum Animals were weighed for calculation of dosage of herb.

**Study Duration:** Study duration was two weeks.

**Drug used:** Tribulus terrestris extract (Aqueous).

**Preparation of extract:** Tribulus terrestris was purchased from local market with the help of experts of PCSIR, Lahore. The herb was made free of particulate impurities manually and spread in a stainless steel tray for drying (Sattar 1995)[12]

The extract was prepared by Maceration method (5gm in 100ml water). 100 gram air dried Tribulus terrestris was soaked in 2 liter (2000ml) of distilled water in a flask for 24 hours, shaking frequently during 6 hours and allowed to stand for 18 hours. Than filterate was taken and fiber waste material was discarded. After that concentrated dry powder extract was obtained by evaporating the filtrate at $70C^0$ in a scientific instrument/oven mod Eminex 854 SCHWABACH, Germany Din 12880 Kim Nem Tempt. 220 (Pharmacopoeia Anonymous 1993).[13]

The dry powder extract thus obtained was weighed with electronic balance which came out to be 8.5 gram/100 gram air dried tribulus terrestris and this dry powder of herb was dissolved in 1000ml D/W to get herbal preparation as 100 mg/ml for oral use. Herbal preparation was kept in refrigerator (Winfield A.J and Richards RME 1998)[14].

**Methodology:** Sixteen rabbits of mixed breed were divided into two groups, control (CT) and Tribulus terrestris (Tt).

**Group-I (Ct):** Control groups (No medicine). They were kept under the same condition and handled like drug group animals.

**Group-II (Tt):** They received tribulus terrestris.

**Dose:** 100mg / kg body weight and administered orally twice daily (Said 1996).

**Collection of sample:** For urine collection rabbits were kept in special cages for twenty four hours on day 0, day 7 and day 14 completed on day 1, day 8, day 15.

**Urine:** Twenty four hours urine sample was collected in plastic bottles attached below the cages. The urine samples were taken three times during the study period i.e. on day 1, day 8 and day 15.

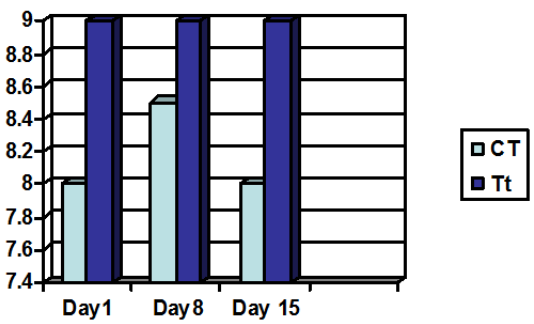
Urinary pH was measured (on day 1 day 8 and day 15) with the help of (Meditest Combi-3A).

# RESULTS

After the administration of 100mg/kg body weight of Tt. for two weeks, the urinary pH was found to be statistically significant P<0.05 throughout the period study. Reduction in urinary uric acid was also found to be statistically significant (P<0.05) on day 1, day 8 and day 15 changes in urinary calcium levels were insignificant.

**Table No.1: Effects of Tt on urine pH**

| Group | Day 1 | Day 8 | Day 15 | Comparison of levels | | |
|---|---|---|---|---|---|---|
| | | | | Day 1-8 | Day 8-15 | Day 1-15 |
| | Mean ± SEM | | | Significance | | |
| Control | 8.00 ± .23 | 8.50 ± .13 | 8.00 ± .00 | .121 | .007 | 1.00 |
| Tribulus terrestris | 9.00 ± .13 | 9.00 ± .00 | 9.00 ± .00 | 1.00 | .000 | 1.00 |




**Graph 1: Effect of Tt on Urine pH**

**Table No.2: Comparison of effects of Tt on Urine pH**

| Group | Comparison of levels | | |
|---|---|---|---|
| | Day 1 | Day 8 | Day 15 |
| | Significance | | |
| Control Vs Tribulus terrestris | .005 | .007 | .000 |

**Table No.3: Effects of Tt on urinary uric acid µmol/lit**

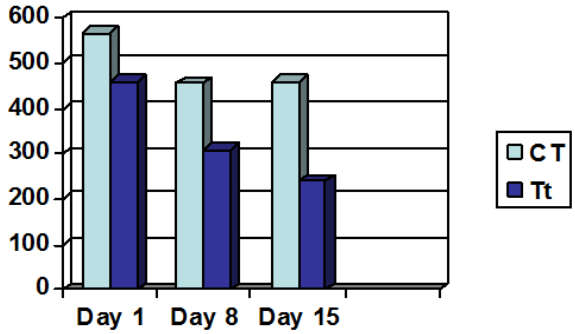
| Group | Day 1 | Day 8 | Day 15 | Comparison of levels | | |
|---|---|---|---|---|---|---|
| | | | | Day 1-8 | Day 8-15 | Day 1-15 |
| | **Mean ± SEM** | | | **Significance** | | |
| Control | 567.00 ± 14.02 | 454.25 ± 11.78 | **458.00** ± 14.04 | .001 | .000 | .000 |
| Tribulus terrestris | 458.00 ± 14.04 | 308.25 ± 11.85 | 239.00 ± 12.31 | .000 | .004 | .000 |

**Table No.4: Comparison of effects of Tt on urinary uric acid**

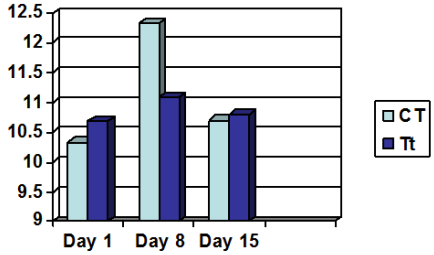
| Group | Day 1 | Day 8 | Day 15 |
|---|---|---|---|
| | Mean ± SEM | | |
| Control Vs Tribulus terrestris | .000 | .000 | .035 |

**Table No.5: Effects of Tt on urinary calcium mg/dl**

| Group | Day 1 | Day 8 | Day 15 | Comparison of levels | | |
|---|---|---|---|---|---|---|
| | | | | Day 1-8 | Day 8-15 | Day 1-15 |
| | Mean ± SEM | | | Significance | | |
| Control | 10.33 ± .24 | 12.33 ± .44 | 10.70 ± .45 | .002 | .060 | .544 |
| Tribulus terrestris | 10.68 ± .63 | 11.08 ± .63 | 10.80 ± .44 | .690 | .729 | .906 |




**Graph 2: Effect of Tt on Urinary uric acid**




**Graph 3: Effect of Tt on Urinary Calcium**

**Table No.6:Comparison of effects of Tt on urinary calcium**

| Group | Day 1 | Day 8 | Day 15 |
|---|---|---|---|
| | Mean ± SEM | | |
| Control Vs Tribulus terrestris | .611 | .243 | .759 |

# DISCUSSION

It produced alkalization of urine and our results are in agreement with satish et al 1996)[15]. Study conducted in University Jaffna reviewed that urinary uric acid decreased after the administration of Tt for one week in normal individuals and diseased patients and results are consistent with our study conducted in PGMI Lahore. The results of our study regarding the urinary calcium are not consistent with vassanthy Arasartnam et al 2010)[16].

Tribulus terristris acts as a herbal diuretic agent and hypovolumic associated effect may causes increased reabsorption of uric acid in nephron (proximal tubal) and further causes reduction of urinary uric acid level in urine (like thiazide diuretics). Urates stones are found in 15-20% patients with hyper uricosuria(Cameron J.S & Simmonds H.A 1987)[17], (Coe F.L. & Raisin L. 1973)[18]. The increased urinary uric acid level is a cause for stone formation and therefore the Tt extract has a positive effect on the reduction of urinary stone formation while reducing uric acid level in urine, the extract also increased the urine volume would help in propeling renal stone and thereby reducing urate stone formation (Ali at el)[19]. Stone former must ensure plenty of fluid/water intake to maintain high urine volume which would keep the solutes well diluted (Christopher Haslett et al 2002)[20].

In our study urinary calcium level result shows statistically no significant reduction or increment therefore our result are inconsistent with Vasanthy Arasartnam et al 2010[16]. At alkaline pH Calcium salts are insoluble and precipitate calcium renal stone formation (Harlan E.I, David GW)[20]. So that it need further investigation. While reduction in urinary calcium decreased renal stone formation. Thiazide diuretics, reduce calcium excretion variable in recurrent stone formers and patients with hypercalciuria (Christopher Haslett et al 2002)[20].

# CONCLUSION

Tribulus Terristris is a herbal diuretic agent. It changes the urinary pH towards alkalinity may decrease the incidence of crystal uria and renal stone formation (Satish el al 1996).

The result of our study shows reduction in urinary uric acid level and has a positive effect on the reduction of urinary stone formation. Because urate stone are formed in 15-20% patient, with hyperuricosuria (Cameron J.S & Simmonds H.A 1987, Coe F.L. & Raisin L. 1973).

There is no significant change in urinary calcium level. It means that Tt as a diuretic agent does not affect much more cation i.e. calcium. It needs further study to evaluate the effects on divalent cations.

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Original Article

# In Vitro Evaluation of Antimicrobial Activity of Calcium Hydroxide with Oily Vehicles in Dental Treatment

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## ABSTRACT

**Objective:** The purpose of this study was to assess the in vitro antimicrobial activity of calcium hydroxide with oily vehicles against aerobes and facultative anaerobic microorganisms commonly isolated from infected root canals.
**Study Design:** Experimental Study.
**Place and Duration of Study:** This study was conducted in the Department of Pharmacology, University of Karachi from April 2009 to March 2011.
**Materials and Methods:** The microbial strains were evaluated against calcium hydroxide pastes prepared with calcium hydroxide powder mixed with oily vehicles. Antimicrobial activity of the vehicles was also evaluated. For such purpose agar diffusion and broth dilution method were used.
**Results**: The results showed that calcium hydroxide mixed with oily vehicles was inhibitory against all the microbial strain tested. Calcium hydroxide pastes eliminated the *Enterococcus faecalis* (the most resistant organism in infected root canals) as well as other microorganisms effectively and the oily vehicles have also inherent antibacterial properties.
**Conclusion:** We concluded from our study that although calcium hydroxide when mixed with oily vehicles can eliminate the endodontic bacteria but such oily vehicles may be irritant to the periapical tissue. Therefore further studies should be done on their role as an intracanal medicine in different combinations with calcium hydroxide.
**Key Words:** Calcium Hydroxide, Oily Vehicles, Root Canal Treatment.

## INTRODUCTION

Calcium hydroxide is used widely in dental treatment throughout the world particularly in root canal treatment, since its introduction in dentistry by Hermann in 1920. However, its mechanisms of cell damage are still not well known. The most accepted explanation for Calcium hydroxide antimicrobial mechanism is its high pH. The release of hydroxyl ions in an aqueous environment causes damage to the bacterial cytoplasmic membrane and disrupts both protein denaturation and DNA of bacterial cells. Calcium hydroxide also absorbs carbon dioxide which is responsible for its antimicrobial activity. It impedes the carbon dioxide supply to $CO_2$-dependent bacteria in the infected canals.[1, 2]

One of the main goals of root canal treatment is to eliminate bacteria and their by-products before obturation. Although dentists try to clean and irrigate the root canal system properly, some bacteria still remain entrapped in the dentinal tubules which causes root canal infection or re-infection.[3] During root canal treatment, apart from the root canals bacteria can also exists in those areas which are inaccessible to mechanical instrumentation and irrigating solutions.[4, 5] It has been shown that, if the canal is not dressed with a disinfectant between two visits, microorganisms will multiply rapidly within days to near the original numbers. To eliminate as many bacteria as possible from the root canals it is necessary to maintain proper mechanical instrumentation, irrigation of the canals with the irrigating solutions which are used to remove or dissolve the organic and inorganic debris.[6, 7, 8]

Calcium hydroxide is considered to possess many of the properties of an ideal root canal dressing, acting as a physical barrier, preventing root canal re-infection and interrupting the nutrient supply to the remaining bacteria. However, for calcium hydroxide to exert its antimicrobial activity, directly or indirectly, an ideal timing is required for effective destruction of microorganisms.[6]Although calcium hydroxide has been used for over 80 years there are still many questions to be answered regarding its inhibitory activity against pathogens.[9]

## MATERIALS AND METHODS

The microbial strains were evaluated against calcium hydroxide pastes prepared with calcium hydroxide powder mixed with oily vehicles by agar diffusion method[10, 11]and broth dilution method.[9]The antimicrobial activity of vehicles was also evaluated by using the above mentioned methods.

**Vehicles:** The vehicles include:

- Camphorated paramonochlorophenol

- Camphorated paramonochlorophenol + glycerine
- Camphorated paramonochlorophenol + polyethyleneglycol

The pastes were prepared on a sterile glass slab with a sterile spatula. The consistencies of the pastes were similar to that of the tooth paste.

**Microbial strains:** The following microbial strains were used in this study, commonly isolated from infected root canals.

**Aerobic strains:**

- Staphylococcus aureus
- Bacillus subtalis
- Streptococcus mutans
- Escherichia coli

**Fungi/ Yeast:**

- Candida albicans

**Facultative anaerobe**

- Enterococcus faecalis

All microorganisms were previously sub cultured in appropriate culture media and under gaseous conditions to confirm purity.

**Agar Diffusion Method:** The agar diffusion method has been widely used to test the antimicrobial activities of endodontic medicaments.[12, 13]

**Preparation of Mueller-Hinton Agar:**

- Suspend 38 g of the medium in one liter of distilled water.
- Heat with frequent agitation and boil to completely dissolve the medium.
- Autoclave at 121°C (15 lbs pressure) for 15 minutes. Cool to room temperature. Pour cold Mueller Hinton agar into sterile petri dishes on a level, horizontal surface to give uniform depth. Allow to solidify at room temperature. Check prepared Mueller Hinton agar to ensure the final pH is 7.3 ± 0.1 at 25°C.

**Inoculation of the test plates:**

- Tubes containing 5 ml of sterile saline were individually inoculated with aerobes and facultative anaerobic strains.
- The suspension was adjusted spectrophoto-metrically to match the turbidity of 0.5 McFarland scale.
- Glass flasks containing 50 ml of BHI agar at $46^0$C were inoculated with 500 microlitre of each microbial suspension, mixed and poured on to 130-mm plates containing a previously set layer of Mueller Hinton (MH) agar.[14,15]

**Formation of the wells in the test plates:**

- Three wells of 6mm were made for six microorganisms each time on Mueller Hinton agar.
- Wells were formed by removing the agar.
- A total of 36 wells were used, compromising 18 wells for the tested pastes and 18 for control groups.

**Addition of calcium hydroxide pastes and controls:**

- Each well was filled with test substance and its control.

**Incubation of the test plates:**

- The plates were kept for 2 hours at room temperature to allow the diffusion of the agents through the agar and then incubated at $37^0$C under appropriate period of time for 24 hours in an incubator. The complete antimicrobial effect was observed after 24 hours on all microbial indicators.[16]

**Measurement of zones of microbial growth inhibition:**

- Zones of inhibition of microbial growth around the well containing the tested substances and controls were measured and recorded after the incubation period.
- The inhibitory zone was considered the shortest distance (mm) from the outer margin to the initial point of the microbial growth. The measurement was done by vernier calliper.

Analysis of variance (ANOVA) was used to determine the differences in susceptibility to intra-canal medication between microbial species after 24 hours and by calculating the p-values using Newman-Keuls test.

**Broth Dilution Method:** In broth dilution method[9], 18 test tubes were prepared for the tested pastes and another18 for the control groups.

**Inoculation of the broth:** The microorganisms were individually inoculated in to tubes containing 5 ml (Brain Heart Infusion) BHI sterile 0.85% saline solution. The suspension was adjusted spectrophotometrically to match the turbidity of 0.5 McFarland scale.

**Addition of calcium hydroxide pastes and controls:**

- Calcium hydroxide pastes and controls were added to the prepared tubes respectively.

**Incubation of the test tubes:**

- The tubes were kept for 2 hours at room temperature to allow the diffusion of the agents through the broth and then incubated at $37^0$C under appropriate period of time for 24 hours in an incubator.
- Antimicrobial activity was visually determined either by growth or no growth of bacteria.

# RESULTS

Table 1 shows the area of zones of microbial inhibition in mm by calcium hydroxide with oily vehicles. Based on the diameters of the zones of microbial growth inhibition, the antimicrobial effects of calcium hydroxide pastes could be ranked from strongest to weakest according to the vehicle: calcium hydroxide + CMCP (34.5mm), calcium hydroxide + CMCP + glycerine (25.5mm), calcium hydroxide + CMCP + polyethyleneglycol (23.833mm). Data analyzed by one-way ANOVA showed that calcium hydroxide combined with vehicles showed no significant effect on tested microorganisms ($p < 0.05$).

Table 2 shows that oily vehicles such as CMCP, CMCP + glycerine and CMCP + polyethyleneglycol showed larger inhibition zones of microbial growth of 31.166mm, 33.166mm and 21.166mm respectively.

Table 3 shows the comparison of calcium hydroxide pastes with oily vehicles against oily vehicles alone. According to Newman-Keuls test the results are not statistically significant when calcium hydroxide mixed with oily vehicles: ($Ca(OH)_2$ + CMCP, $p = 0.53$), ($Ca(OH)_2$ + CMCP + glycerine , $p = 0.11$), ($Ca(OH)_2$ + CMCP + polyethyleneglycol, $p = 0.62$) ($p < 0.05$).

**Table No.1: Zones of microbial growth inhibition (in mm) produced by calcium hydroxide associated with oily vehicles.**

| **Ca (OH) $_2$ + Vehicles** | **Candida albicans** | **Bacillus subtalis** | **Staphlyococcus aureus** | **Enterococcus faecalis** | **Sterptococcus mutans** | **Escherichia coli** | **Mean** |
|---|---|---|---|---|---|---|---|
| CMCP | 30 | 21 | 30 | 41 | 48 | 37 | 34.5 |
| CMCP + Glycerin | 24 | 21 | 24 | 29 | 32 | 23 | 25.5 |
| CMCP + Polyethyleneglycol | 18 | 21 | 22 | 23 | 34 | 25 | 23.833 |

Ca (OH) $_2$: Calcium Hydroxide, CMCP: Camphorated paramonochlorophenol

**Table No. 2: Zones of growth inhibition (in mm) produced by oily vehicles used as control.**

| **Vehicles** | **Candida albicans** | **Bacillus subtalis** | **Staphlyococcus aureus** | **Enterococcus faecalis** | **Sterptococcus mutans** | **Escherichia coli** | **Mean** |
|---|---|---|---|---|---|---|---|
| CMCP | 22 | 22 | 30 | 40 | 40 | 33 | 31.166 |
| CMCP + Glycerin | 30 | 23 | 30 | 40 | 48 | 28 | 33.166 |
| CMCP + Polyethyleneglycol | 18 | 0 | 20 | 29 | 30 | 30 | 21.166 |

CMCP: Camphorated paramonochlorophenol

**Table No.3: Comparison of calcium hydroxide + oily vehicles against oily vehicles alone**

| | CMCP | | | CMCP+G | | | CMCP+P | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean (mm) | St.dev | p | Mean (mm) | St.dev | p | Mean (mm) | St.dev | p |
| Calcium hydroxide + oily vehicles | 34.50 | 9.52 | 0.530 | 25.50 | 4.14 | 0.11 | 23.83 | 5.49 | 0.62 |
| Oily vehicles | 31.17 | 8.11 | | 33.17 | 9.13 | | 21.2 | 11.6 | |

G = glycerin, P = polyethyleneglycol

**Table No.4: Growth inhibition provided by calcium hydroxide associated with oily vehicles.**

| Ca (OH) $_2$ + Vehicles | Candida albicans | Bacillus subtalis | Staphlyococcus aureus | Enterococcus faecalis | Sterptococcus mutans | Escherichia coli |
|---|---|---|---|---|---|---|
| CMCP | N.G | N.G | N.G | N.G | N.G | N.G |
| CMCP + Glycerin | N.G | N.G | N.G | N.G | N.G | N.G |
| CMCP + Polyethyleneglycol | N.G | N.G | N.G | N.G | N.G | N.G |

Ca (OH) $_2$: Calcium Hydroxide, CMCP: Camphorated paramonochlorophenol, N.G: No Growth

**Table No.5: Growth inhibition produced by several vehicles used as control.**

| Vehicles | Candida albicans | Bacillus subtalis | Staphlyococcus aureus | Enterococcus faecalis | Sterptococcus mutans | Escherichia coli |
|---|---|---|---|---|---|---|
| CMCP | N.G | N.G | N.G | N.G | N.G | N.G |
| CMCP + Glycerin | N.G | N.G | N.G | N.G | N.G | N.G |
| CMCP + Polyethyleneglycol | N.G | N.G | N.G | N.G | N.G | N.G |

CMCP: Camphorated paramonochlorophenol, N.G: No Growth

Table 4 shows that when calcium hydroxide mixed with oily vehicles it showed no growth of bacteria and the broth appeared transparent as compared to the broth that was turbid containing bacteria. The above table proves that calcium hydroxide is an excellent antimicrobial agent against all microorganisms tested.

Table 5 shows that when only the oily vehicles were mixed in to the test tubes containing bacteria, it showed

no growth and the broth appeared transparent. Result shows that oily vehicles shows antimicrobial activity against all organisms tested.

# DISCUSSION

Intra-canal medicaments are indicated if there are clinical signs such as exudation, hemorrhage, perforation, root resorption, trauma or incomplete root formation. One of the intra canal medicines is calcium hydroxide and it has to be used with a vehicle. The type of vehicle used to prepare calcium hydroxide pastes produces differences in the velocity of ionic dissociation. Depending on the vehicle used, the medicament can have a different viscosity, which plays an important role.[17] Vehicle also plays a very important role in the overall disinfection process because it determines the velocity of ionic dissociation causing the paste to be solubilized and resorbed at various rates by the periapical tissues and from within the root canal.[17,18]

Calcium hydroxide should be combined with a liquid because the delivery of dry calcium hydroxide powder in narrow curved canal is difficult and a vehicle is required also for the release of hydroxyl ions. When calcium hydroxide is mixed with the vehicle, $Ca^{++}$and $OH^-$ are rapidly released.[17, 18]

Oily vehicles are non-water-soluble substances that promote the lowest solubility and diffusion of the paste within the tissues. Pastes containing this kind of vehicle may remain within the root canal for longer period.[19]

The results of this study shows that when calcium hydroxide was mixed with camphorated paramonochlorophenol gives the largest mean values of growth inhibition against all microorganisms tested followed by camphorated paramonochlorophenol + glycerin and camphorated paramonochlorophenol + polyethyleneglycol respectively.

The antimicrobial activity is also confirmed when camphorated paramonochlorophenol alone was used. This control also destroyed the microorganisms by producing larger zones of microbial inhibition. Camphorated paramonochlorophenol with glycerin and camphorated paramonochlorophenol with polyethyleneglycol also showed larger zones of growth inhibition respectively.

Thus, this study showed that the oily vehicles gave the largest zones of microbial inhibition. However, without sufficient water available, camphorated paramonochlorophenol forms calcium parachlorphenolate thus preventing further hydrolysis as confirmed by Vianna et al.[20] in 2009. For this reason, pastes containing oily vehicles have restricted use and are only employed in those clinical situations that require a very slow ionic dissociation. Camphorated paramonochlorophenol has been shown to become ineffective in the root canal within 24-48 hours. Another fact that does not recommend the use of camphorated paramonochlorophenol as intra-canal medicament is that it does not act as a physicochemical barrier because it is commonly applied on sterile cotton pledgets placed in the pulp chamber or on paper points slightly moistened with this medicament. Such a barrier is important for preventing root canal recontamination due to growth of bacteria that are not removed during biomechanical preparation or to saliva and microorganisms infiltration caused by coronal micro leakage. The antimicrobial effect is delivered through vaporization of the medicament. Thus, the antimicrobial action of the medicament within the dentinal tubules and in the apical portion is therefore dependent on the volatility of the medicament. As the material does not persist for prolonged periods, hence some bacteria may survive and have the opportunity to multiply and persist in the root canal system.[17] Camphorated paramonochlorophenol is also irritant to the periapical tissues as confirmed by Vianna et al.[20] So it is better to use with a safe dental material such as calcium hydroxide as described by Magalhaes et al.[21] in2011.

# CONCLUSION

Present study showed that calcium hydroxide combined with different oily vehicles produced larger zones of growth inhibition. These pastes alone show larger zones of growth inhibition, hence the results are not statistically significant because the oily vehicles themselves show the antimicrobial activity against the tested organisms. These oily vehicles may be irritant to the priapical tissues, therefore further studies should be done on their role as an intra-canal medicine in different combinations with calcium hydroxide.

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