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Editorial

Original Articles

Editorial A Link Between Caffeinated Beverages and Gout

Dr. Azhar Masud Bhatti
Addl. Director Health Services, EPI Punjab, Lahore
&
Editor in Chief

According to preliminary research, gout may be precipitated by excessive intake of caffeine.

"We found that overall, as the number of servings of caffeinated beverages increased, so too did the chance of having recurrent gout attacks," says Tuhina Neogi, MD, PhD, associate professor of medicine at Boston University School of Medicine. For example, drinking four servings of caffeinated beverages in the previous 24 hours was associated with an 80% increased risk of recurrent gout attacks, compared with having no caffeinated drinks.

Drinking more than six servings of caffeinated beverages in the previous day was associated with a 3.3-fold higher risk of a flare-up, the study of 663 gout patients suggests. When habitual and occasional caffeine drinkers were looked at separately, the link was only observed in people with gout who typically drink less than two caffeinated beverages a day, Neogi tells WebMD, "As little as three servings a day could do it for these people," she says.

"In contrast, in people with gout who usually have two or more caffeinated beverages a day, increasing caffeine intake doesn't appear to raise the risk of gout attacks," Neogi says. The study does not prove cause and effect, just that there appears to be an association between higher caffeine intake in the past 24 hours and an increased risk of gout attacks. People with gout who drink a lot of revved-up beverages may share some other characteristic that makes them more prone to flare-ups, researchers say.

The findings were presented at the American College of Rheumatology's annual meeting. Gout occurs when two much uric acid, a normal byproduct of DNA metabolism, builds up in the body. This leads to crystal formation. The crystals deposit in the joints, causing painful swelling. Previous research has shown that, over the long term, caffeine intake is associated with lower levels of uric acid in the body and a lower risk of developing gout among people who do not have the arthritic condition, Neogi says.

The chemical structure of caffeine is very similar to that of a mediation called allopurinol, which is commonly used to lower uric acid levels in people with gout, she says. Although effective at controlling gout in the long term, allopurinol can precipitate a flare-up among patients taking it for the first time, she says. "Given the potential conflicting effects of caffeine on gout attack risk, we evaluated whether caffeinated beverage intake was associated with the risk for recurrent flare-ups," Neogi says.

The researchers turned to the internet to recruit 633 participants who had experienced a gout attack within the past year. Medical records were used to confirm their gout diagnosis. Participants were asked to log on after having their next attack and answer an extensive questionnaire about medication, foods, and drinks they had consumed in the 24 hours prior to the attack.

Three months after being free of flare-ups, they were asked to answer the same questions. The researchers asked about all types of caffeinated beverages, including coffee, tea, soft drinks, and high energy drinks such as Red Bull as well as non-caffeinated beverages.

Participants were predominantly white (80%), male (78%), and college educated (58&). The link between increased intake of caffeinated beverages in the prior 24 hours and a higher risk for recurrent gout attacks was present even after accounting for other fluid intake. In contrast, non-caffeinated coffee, tea, soda and juices were not associated with an increased risk of gout attacks, Neogi says. The researchers did not ask participants about the amount of sugar in their beverages. Therefore, the findings cannot be compared to that of another study presented at the meeting showing that women who drink one or more servings of sugary soda a day may be increasing their risk for developing gout, she adds.

Using the internet to recruit patients for a study is not ideal, as it results in a self-selected sample that is interested in the topic, says John S. Sunday, MD, PhD, a gout expert at Duke University Medical Center in Durham, N.C. Also, the group as a whole would be expected to be better educated and of higher socioeconomic status than people drawn from the general population, he notes. That said, "It is a way to accumulate a large number of patients in a short period of time. It is good for generating hypotheses" that can then be tested in more rigorous clinical trials, Sundy tells WebMD. Neogi defends the use of the internet for studies like this, pointing out that it allows each person's caffeine intake prior to an attack to be compared to her intake when she is attack-free.

Original Article

Effect of Uric Acid on Vitamin C and E in Induced Hyperuricemic Model

1. Shiza Batool 2. Hasan Ali 3. Khalid Mustafa 4. Moazzam Ali

1. Asstt. Prof. of Biochemistry, AFM&DC, Faisalabad 2. Assoc. Prof. of Biochemistry, BUM&DC, Karachi
3. Assoc. Prof. of Pharmacology, BUM&DC, Karachi 4. Prof. of Anatomy, ZMU, Karachi

ABSTRACT

Objective: To measure the level of uric acids and find out the effect of uric acid on vit C and E in induced hyperuricemic model.

Study Design: comparative study

Place and Duration of Study: This study was conducted at Baqai Medical University, Karachi from June 2010 to January 2011.

Materials and Methods: Forty male albino rats with an average weight of 180±2g were selected. The rats were grouped. The animals were fed on stardards diet and given tap water ad libitum until treatment. The protrocols for experiment was according to institute of laboratory animal resources on life sciences,US National research council,1996 and institutional animal ethical committee(IAEC) of baqai medical university, Karachi. Albino rats were divided into four groups. Group A(10) – control given only standard diet, group B(10) fed on 60%fructose with standard diet , group C(10) fed on fructose, standard diet and intraperitonially oxonic acid 250mg/kg and group D (10) only on injection intraperotonially oxonic acid 250mg/kg. At the end of study 10 ml of blood was drawn from heart of rats. Then blood was estimated for vitamin C, E and uric acids done by kit methods randox-manual /Rx monza UA230/UA 233.

Results: The concentration of vitamin C and E were significantly lowered as compared to uric acid concentration in the group B,C and D.

Conclusion: Decrease level of vit C and E increase the level uric acids were observed. Therefore, it may be suggested that increase intake of vitamin C may be helpful in lowering uric acid concentration**.**

Key Words: Uric Acid, Vitamin C, Vitamin E, Fructose, Al Bino Rats, Induced Hyperuricemia

INTRODUCTION

Free radical can be defined as any molecular species capable of independent existence that contains an unpaired electron in an atomic orbital [1].They are capable of triggering chain reactions which can damage the different cell constituents.

In order to check free radicals formation to avoid oxidative stress, body has different anti- oxidant defence systems. An antioxidant can be defined as: "any substance that when present in low concentrations compared to that of an oxidisable substrate, significantly delays or inhibits the oxidation of that substrate. The physiological role of antioxidants, as this definition suggests, is to prevent damage to cellular components arising as a consequence of chemical reactions involving free radicals.[2] Uric acid now is not considered as merely a metabolic waste. It has been proposed that increase in life span observed in human evolution to some extent might be due to protective action of uric acid [3]**.** Increase uric acid levels have been found in oxidative stress and ischemia which might be compensatory mechanism of protection against free radicals .[4] Ascorbate is a good free radical scavenger due to its chemical properties[5] .In our body Vitamin C is required as electron donor for 8 enzymes which act as monoxygenase or dioxygenase.Three of these enzymes are required for the hydroxylation of lysine and proline in collagen molecule,synthesis of carnitine, norepinephrine synthesis from dopamine and tyrosine metabolism[6].

Ascorbate can reduce lipid peroxidation. Protein also undergo oxidation by different means. [7] DNA are affected indirectly by protein or lipid oxidation or directly by oxidation of DNA[8].The most important mechanisms of DNA damage, however, are believed to involve direct attack of oxidants on individual nucleotides in DNA.[9]. Ascorbate might be able to diminish DNA damage by reducing radical species directly, decreasing formation of reactive species such as lipid hydroperoxides or preventing radical attack on proteins that repair DNA and also can prevent nitrosamine formation so subsequent formation of some reactive nitrogen species is prevented.[6]

The biochemical studies on the mechanism of vitamin E antioxidant potential were initiated by Tappel.[10] Its antioxidant interactions has been demonstrated in vitro long ago but the evidence in humans is now also being established by certain studies.[11].There have been evidence found by scientist in animal studies that multi molecular weight antioxidant systems especially vitamin C and selenium are necessary for the function of Vitamin E[12]

Vitamin E may act as a fat-soluble antioxidant that stops the production of reactive oxygen species formed

when fat undergoes oxidation.[13] In membranes tocopherols react with lipid peroxyl radicals to yield a relatively stable lipid peroxidation and the tocopheroxy radical to interrupt the radical chain reaction. For this reason, vitamin E is the major lipid-soluble antioxidant against lipid peroxidation in plasma and red blood cells .[14] In this way integrity of long-chain polyunsaturated fatty acids which function as important signaling molecules have been maintained. This peroxyl radical scavenger activity of Vitamin E has been described in various studies by scientists.[15]The antioxidant potential of vitamin can be attributed to redox potential of its chromane ring.[16]Vitamin E deficiency in humans may manifest as peripheral neuropathy[17]which is similar to that observed in patients with Friedreich ataxia. Therefore , a specific function vitamin E that might be proposed is in its protection of long chain fatty acids because its deficiency is found to be associated with deficiency of this vitamin.[18]Secondly it is important for preserving membrane qualities such as fluidity, lipid domains., etc.[19] But in addition to this there are certain studies which are in favour that there is no significant antioxidant potential of Vitamin E.[20]

Uric acid now is not considered as merely a metabolic waste. It has been proposed that increase in life span observed in human evolution to some extent might be due to protective action of uric acid.[21]Uric acid along with albumin and ascorbic acid account for more than 85% of total antioxidant activity.[22]Total radical trapping activity (TRAP) includes uric acid as major contributor as it accounts for 38-47% in comparison to vitamin C and vitamin E which account for 13-17% and 2-8% respectively.[23]It has been found at contribute as much as two-thirds of all free radical scavenging activity in plasma therefore it serve as the most abundant aqueous antioxidant in humans .It does so by preventing lipid peroxidation and quenching hydroxyl, superoxide and peroxynitrite radicals.[24] Increase uric acid levels have been found in oxidative stress and ischemia which might be compensatory mechanism of protection against free radicals[25,24]Uric acid cause inactivation of Nitric oxide and peroxynitrite radicals.[26].Along with dopamine ,uric acid also help in repair of oxidative free radical induced damage of DNA in certain brain cells.[27]Another important function of urate is found in its ability to form chelating agents with transition metals ions like iron and copper ,thus scavenging them. This protects ascorbic acid from oxidation by these metals and interesting feature is that uric acid is itself does not get oxidized.[28]

We carried out an animal study to see the effect of uric acid on vitamin C and E in an induced hyperuricemia with 60% fructose. Since there was no previous assumed biologic rationale to support a potential effect of Vit E on serum uric acid.

MATERIALS AND METHODS

Locally bred forty (40) male Albino rats with an average weight of 180±20g were purchased. The rats were grouped and housed in environmentally controlled room(ambient temperature 24±2°C and relative humidity of 55±5%) in the animal house and acclimatized for 07 days**.** The animals were fed standard diet and given tap water ad libitum until treatment. The protocols for experimentation was approved and performed in strict accordance with the Guide for the care and use of laboratory animals (Institute of Laboratory Animal Resources on Life Sciences, US National Research Council, 1996) and the Institutional Animal Ethical Committee (IAEC) of Baqai Medical University, Karachi. Pakistan. The cage size was 8"X18"X10" to keep a group of 05 animals in the cage to prevent from cannibalism.

Sodium Tungstate 10%, 2/3N sulphuric acid,10% sodium bicarbonate,LiCO3, 40%Formaline,Acetic acid, Fructose, Oxonic acid. Spectrosol grade reagents and acids from B.D.H, Poole, UK, were employed. All purified enzymes, coenzymes, substrates, standards and buffers will be purchased from Sigma Chemicals Company, USA. All other chemicals were of analytical grade and was procured from SRL and Qualigens, USA.

All animals housed in standard conditions were initially fed standard diet and allowed adaptation of one (01) week.Albino rats were divided in four(04) groups; A,B,C & D.

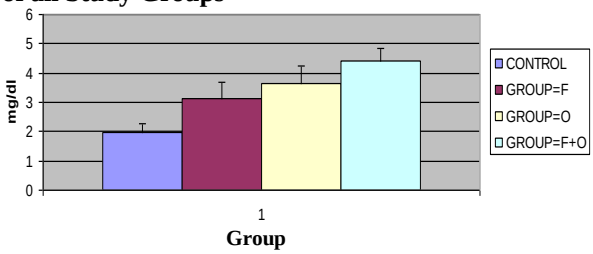
Group A:Ten (10) male albino rats as Control were kept as control and were fed standard diet and water ad libitum for 10 weeks. Group B: Ten (10) male albino rats were fed 60% fructose mixed in standard diet and water ad libitum for 10 weeks. Group C:Ten (10) male albino rats were fed 60% fructose mixed in standard diet and water ad libitum for 10 weeks. They were also injected intraperitonealy oxonic acid 250mg/kg every third day for 10 weeks.Group D:Ten (10) male albino rats were injected intraperitonealy oxonic acid 250mg/kg every third day for 10 weeks. They were fed standard diet and water ad libitum for 10 weeks.Body weights were measured at the commencement and at the end of study. The amount of diet was measured before giving and then subtracted from the amount of food left over daily. At the end of study, rats were dissected in a nearby room separate from experiment area. Approximately 10 mls of blood was drawn from heart using disposable syringe. 8 mls of blood was transferred in heparanized tube, mixed and centrifuged to separate plasma and divided in two epindorf cups for estimation ofvit C ,E and uric acid done by kit methods by randox-manual /Rx monza UA230/UA 233.

RESULTS

Graph 1 shows the comparison of mean plasma uric acid levels of Control with rest of the groups. Mean plasma level of uric acid of Control is found to be 1.97 mg/dl(±0.09) .Group B(fructose) showed mean plasma uric acid of 3.15 mg/dl(±0.17) .This reflects that uric acid was raised to 37% in rats which were exposed to diet comprising 60% Fructose than control. On comparing both groups i.e Control with Group B highly significant statistical correlation (P <0.001) was observed.

The mean plasma uric acid levels of Group C (oxonic acid) was 3.63 mg/dl(±0.22)which is 45% higher than Control. The probability calculated was highly significant (P<0.001) when both groups were evaluated. While comparing Group D (Fructose +Oxonic acid) with Control, highly significant correlation was observed(P<0.001).It was due to high mean plasma serum uric acid level of Group D which was 4.41mg/dl(±0.14) .The combination of fructose with uricase inhibitor ,Oxonic acid raises uric acid to 55% from control and this level is highest of all these groups.

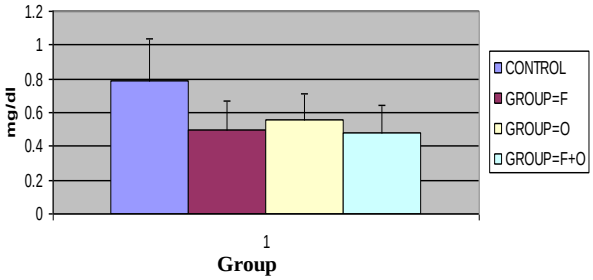
Bar Graph 1: Comparison of Serum Uric Acid levels of all Study Groups



Serum Uric Acid

Groups	Control	Group=F	Group=O	Group=F+O
M.V	1.97	3.15	3.63	4.43
S.D	0.3	**0.55**	**0.63**	**0.43**

Bar Graph 2: Comparison of Serum Vitamin E levels of all Study Groups



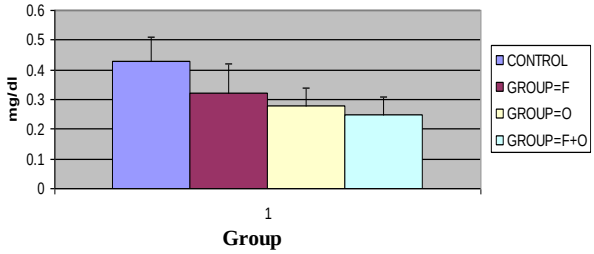
Vitamin E

Groups	Control	Group=F	Group=O	Group=F+O
M.V	0.79	0.5	0.56	0.48
S.D	0.25	**0.17**	**0.15**	**0.16**

Graph 2 shows the comparison of mean plasma vitamin E levels of Control with rest of the groups. Mean plasma vitamin E level of Control was found to be 0.79mg/dl(±0.08) .Group B(Fructose) showed mean plasma vitamin E of 0.5mg/dl(±0.05) reflecting 58% lower vitamin E levels in rats which were exposed to diet comprising 60% Fructose. On comparing both groups i.e Control with Group F significant statistical correlation (P<0.01) was observed. The mean plasma vitamin E levels of Group C (oxonic acid) was 0.56mg/dl(±0.05)which are although lower but somewhat closer to Control. Therefore non-significant (P>0.01) correlation was observed on comparison of both group .While comparing Group D (Fructose +Oxonic acid) with Control, significant correlation was observed(P<0.01).It was due to the fact Group D had considerable low mean plasma vitamin E levels of 0.5 8 mg/dl(±0.06) which are 64% less than rats of group control.

Graph 3 shows the comparison of mean plasma vitamin C levels of Control with rest of the groups. Mean plasma vitamin C level of Control was found to be 0.43mg/dl(±0.03) .Group B (Fructose) showed mean plasma vitamin C of 0.32mg/dl(±0.03) reflecting 34% lower vitamin C levels in rats which were exposed to diet comprising 60% Fructose. On comparing both groups i.e. Control with Group B significant statistical correlation (P<0.01) was observed.The mean plasma vitamin C levels of Group C (oxonic acid) was 0.28mg/dl(±0.02)which which are 53% lower than Control. Therefore highly significant (P<0.001) correlation was observed on comparison of both group .While comparing Group D (Fructose +Oxonic acid) with Control,highly significant correlation was observed(P<0.001).It was due to the fact Group D had considerable low mean plasma vitamin C levels of 0.25 mg/dl(±0.02) which are 72% less than rats of group control.

Bar Graph 3: Comparison of Serum Vitamin C levels of all Study Groups



Vitamin C

Groups	Control	Group=F	Group=O	Group=F+O
M.V	0.43	0.32	0.28	0.25
S.D	0.08	**0.1**	**0.058**	**0.06**

DISCUSSION:

Uric acid has long been described as metabolic waste of purine metabolism with strong relation to number of pathologies involving many organs of body. On the other hand scientific research has also revealed its role as an antioxidant making its pathological status

ambiguous. In present study we elaborated that antioxidant status by incorporating vit C and E as antioxidants and evaluating their relationship with uric acid.

One of the important features of this study was the method by which hyperuricemia have been induced in animal model. Group B (Fructose) was given fructose, group C (fructose +Oxonic acid) was treated with "oxonic acid" and group D (Oxonic acid). The principle hyperuricemic factor in this study was fructose as it is extensively used in beverages and food .Its a rather controversial factor as number of studies both animals and human, are in the favour that fructose can induce hyperuricemia [29] but many studies have opposed this hypothesis[30] and even mixed response has been shown.[31]Present investigation tried to verify this theory. Very few studies have used this combined model of fructose plus oxonic acid. In order to make conditions similar to human, uricase inhibitor oxonic acid was incorporated to abolish the effect of this enzyme in rats . Also these different regimens were used to establish the extent of hyperuricemia caused by fructose.

It was noted that serum levels of ascorbate in all four groups, were found to be decreased in all three hyperuricemic models in comparison with control. Especially the lowest levels were observed in the both groups which were treated with 60% fructose only group B (Fructose) and 60% fructose and 2% oxonic acid group C (Fructose+Oxonic acid) respectively .The levels of ascorbate dropped to 34% and 72% of the levels of Control group. These findings are in harmony with MM Hamalainen and KK Makinen (1982)[33] which have demonstrated that dietary carbohydrates including fructose exhibit selective effects on ascorbic acid metabolism in liver. This might be due to influence on UDP-glucuronic acid pathway or glucuronate-xylose cycle both of which are responsible for producing ascorbic acid in liver.banhegyi et.,al. [33] have also shown the similar findings that fructose has inhibiting effect on ascorbic acid synthesis in animals .Randamized trials have demonstrated the inverse relation between serum levels of urate and ascorbate by using supplements of vitamin C.[34]The proposed underlying mechanisms involved kidneys showing that vitamin C can increase glomerular filtration and/or compete with urate for reabsorption as both depend upon anion exchange transport at proximal tubules.[35] The possible means by which ascorbate favour urate filtration at glomeruli may be due to antioxidant effect which reduces the microvascular ischemia in glomeruli leading to increase blood flow at the site. It has been demonstrated in one study that 500 mg/d vitamin C supplementation for 8 wk reduced uric acid levels by 0.5 mg/dl.[36] While citing this literature about vitamin C it could be taking into mind that present study was only measuring the levels of vitamin c in response to fructose and oxonic acid , the instrumental to the uric acid increase. This was in accordance with the study done in johns hopkin university.[37] Therefore, it can be speculated that the decreased levels of ascorbate may be due to increased levels of uric acid. In fact there is evidence that urate alone when preventing oxidation of lipids, may itself become proxidant. This might be prevented by adding ascorbate to oxidizing LDL.[38]This may lead to utilization of ascorbate. On the contrary, there are number of studies demonstrating ability of uric acid in supplementing antioxidant property of ascorbate by preventing oxidation of ascorbate by forming stable compounds with transition metals such as iron and copper[28]

The levels of vitamin C were found to be lower than normal in all four groups. This might be due to the reason that ascorbate is strong reducing agent and may even get oxidized by when exposed to atmosphere and as we have used the method to estimate ascorbate levels based on virtue of its property of reduction it might be the possible factor in relevant decrease in levels.

In ongoing study, the levels of α tocopherol were found to be decreased in all groups when compared with the control and lowest levels of 0.4 mg/dl observed in the group of highest urate levels that is group D .In comparison to rats of group Control,tocopherols of the hyperuricemic rats of rest of study group is observed to be fallen to 58% and 64% respectively. These findings are in agreement with Marco Bagnati et, al.,[39] who have pointed out in their experimental study the interrelationship between urate and tocopherol by demonstrating that in some selected circumstances, uric acid even at physiological pH is capable of stimulating oxidation of LDL . The synergistic action described in this research by uric acid is that it may reduced tocopheroxyl radical back to its parent compound .This is made possible by the fact that α-tocopherol is present at the LDL water interfaced as proposed by number of studies, therefore it is in access to water soluble uric acid. However it was also revealed in an experimental study that irrespective of the levels of endogenous tocopherol, uric acid may still enhance LDL oxidation by reducing copper so vitamin E is rather consumed in the process. However, some studies including Ruggiero C, et al.[40] demonstrated that no correlation exists between the urate and tocopherols.

CONCLUSION

Increased level of vit C and E decreases the level uric acid. Therefore, it may be suggested that increase intake of vitamin C may be helpful in lowering uric acid concentration especially in gout patient. It is further suggested that future trials are needed to determine the role and relationship of vitamin E and C with uric acid concentration in human.

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Original Article

Comparison of Different Modalities of Treatment of Hypertrophic Scars and Keloids

1. Quddus-ur-Rehman 2. Usman Latif 3. Anwar Saood Saqib 4. Asim Elahi

1. Asstt. Prof. of Anatomy, AFM&DC, Faisalabad 2. Assoc. Prof. of Anatomy, Sharif MC, Lahore 3. Head of Forensic Medicine, AFM&DC, Faisalabad 4. Demonstrator, AFM&DC, Faisalabad

ABSTRACT

Introduction: Hypertrophic scars and keloids are extreme overgrowth of scar tissue.

Aims and objectives: To improve the cosmesis and symptomatology, to compare the results of different treatment modalities and to find out the most workable treatment option.

Study design: Prospective randomized clinical trial.

Place and Duration of Study: This study was conducted at the Allied Hospital, Faisalabad from April 2009 to September 2011.

Materials and Methods: In this study 72 patients were studied. Most of them were treated on outdoor basis while others in wards. Detailed history and physical examination were carried out and applied different treatment options and followed them up.

Results: In our study of patients of hypertrophic scars and keloids, 29 were males and 43 were females. There was 20 % recurrence rate in intralesional injections of steroid, 25 % in silicone gel sheeting, 25 % in surgery and postoperative intralesional injection, 50 % in case of surgery and postoperative irradiation and 20 % in surgery alone. In case of intralesional injections of triamcinolone acetonide 62.5% patients had excellent results. In both silicone gel sheeting and surgery with steroid injections 50% had excellent results. In 2 patients in whom we combined surgery with radiotherapy 1 patient improved while the other got recurrence. After surgical excision of hypertrophic scars 40% patients had excellent results.

Conclusion: Intralesional injections of triamcinolone acetonide had good results. In early lesions silicone gel sheeting was useful option while recurrent scars can be treated by combined modalities of treatment.

Key words: Hypertrophic Scars, Keloids, Intralesional injection, Silicone gel sheeting, Postoperative radiation

INTRODUCTION

Scar is the natural result of any wound; it closes the wound and imparts strength to it. As it matures, aesthetic appearance is attained though not completely. The patient's contribution to scar formation is far more important than that of the surgeon.[1]The contour deformity of scars exists either as positives that is scar overgrowth for example, hypertrophic scars and keloids or negatives that is creases, pits or atrophies. It is generally easier to improve negative deformities as compared to positive deformities related to scars.[2]

Hypertrophic scars and keloids are extreme overgrowth of scar tissue that result from an abnormal connective tissue response to trauma, inflammation, surgery, burns and occasionally seem to occur spontaneously. Keloids grow beyond the confines of original wound. The hypertrophic scars remain confined to the boundaries of original wound. These lesions are raised above the surface to a variable extent and may regress with the passage of time.[3, 4]

MATERIALS AND METHODS

We included 72 patients in our study, 29 males and 43 females with hypertrophic scars and keloids who came to outpatient department of Allied Hospital, Faisalabad from April 2009 to September 2011. The duration of study was 2 years and 5 months. We randomized the patients according to response adaptive randomization and applied different options of treatments in different patients and followed them up for improvement of their lesions and complications, if any, of our procedures.

Inclusion criteria: All those patients who came to outpatient department of Allied Hospital, Faisalabad with Hypertrophic scars and keloids were included in our study.

Exclusion criteria: All those patients unwilling for treatment were excluded from our study.

We treated most of our patients on outdoor basis by intralesional injections of steroid and occlusive silicone gel sheeting. We also admitted our patients in surgical wards for surgical and other treatments. We evaluated the patients on the basis of histories and physical examinations.

Preoperative investigations like hemoglobin, TLC, DLC, blood sugar and blood urea were performed for indoor patients. Five groups of patients were formed for the undermentioned modalities of treatments according to outcome adaptive randomization.

1. Intralesional injections of triamcinolone acetonide (Kenacort A).
2. Treatment by application of silicone gel sheeting.
3. Combination of surgery and application of steroid injections.
4. Surgery followed by radiotherapy.

5. Surgery alone.

We used insulin syringe with fixed needle to give intralesional injections of kenacort-A. The dosage range varied from 40 mg to 120 mg for these patients. We repeated these injections after 1 and 3 months intervals. Silicone gel sheeting was applied on 12 patients for 24 hours a day. It is washable and can be reused after washing. Application of dressing was recommended for six months in early lesions.

In 9 patients after surgical excision of keloids, postoperative intrawound injection of triamcinolone acetonide was given. In two patients we excised the keloids and applied superficial X-ray irradiation to the wounds. The radiation was given in fractionated doses to a total of 1600-1800 rads in 6 days at 300-400 rads /day. The beam was focused directly at the site of the lesion.

In 5 patients with hypertrophic scars we did excision and covered the raw area with split thickness skin graft. All of the patients were advised to pay regular visits to outdoor for follow up at one, three and six months intervals.

RESULTS

In our study, age of the patients varied from 10-55 years. Out of 72 patients 29 (40.27%) were males and 43 (59.72%) were females. 33 patients presented with keloids, 11 (33.33%) males and 22 (66.66%) females. 39 patients presented with hypertrophic scars and out of these, 18 (46.15%) were males and 21 (53.84%) were females. (Table No. 1)

Table No.1: Age and sex distribution

Range of Age (years)	No. of patients	Sex Distri-bution	No. of patients with keloids	No. of pts with hyper-trophic scars	Total No. of patients
1-10	2	Males	11 (33.33%)	18 (46.15%)	29 (40.27%)
11– 20	14				
21 - 30	21				
31 - 40	19	Females	22 (66.66%)	21 (53.84%)	43 (59.72%)
41 - 50	13				
51 - 60	3				
Total	72	Total	33	39	72

We also noted the sites of the lesions in these patients. Out of 72 patients, 16 (22.22%) had lesions on head and neck area, 15 (20.83%) on anterior trunk, 10 (13.88%) on shoulders and 14 (19.44%) on posterior trunk. 4 patients (5.55%) got lesions on arms, 6 (8.33%) on forearms and hands, 5 (6.94%) on thighs, and 2 patients (2.77%) had lesions on legs and feet. The size of the lesions ranged from 1cm x 1cm to 15cm x 7cm in these 72 patients.

Out of 72 patients, 21 (29.16%) had hyperpigmented, 15 (20.83%) had hypopigmented, 24 (33.33%) had white and 12 (16.66%) had pink to red lesions. Out of these, 35 (48.61%) patients had mildly elevated (1mm to 2mm), 30 (41.66%) had moderately elevated (3mm to 4mm) and 7 (9.72%) patients had severely elevated (4mm to 5mm) lesions. 25 (34.72%) patients had tenderness of their lesions and 47 (65.27%) had non tender lesions. 4 (5.55%) out of 72 patients had neck contracture associated with hypertrophic scars resulting in functional problems. The functional impairment ranged from mild to severe. 2 out of 4 patients had mild restriction of neck movements, 1 patient had moderate restriction of neck movements and 1 patient had severely restricted movements of the neck. 21 (29.16%) out of 72 patients had psychological upsets because of these lesions. (Table No.2)

We divided cosmetic impairment in these patients into mild, moderate and severe types. Out of 72 patients, 40 (55.55%) had mild, 11 (15.27%) had moderate and 21 (29.16%) patients had severe cosmetic problems.

We admitted 16 patients in the wards for surgery and other treatments and treated 56 patients on outdoor basis. We applied 5 different options of treatments according to our management plan. We injected kenacort-A intralesionally in 44 (61.11%) patients on outdoor basis. We applied silicone gel sheeting on 12 (16.66%) patients. We performed surgery and gave postoperative intralesional injections of kenacort-A in 9 (12.5%) patients. In 2 (2.77%) patients, we applied postoperative radiation therapy after excising their lesions. In 5 (6.94%) patients with hypertrophic scars we performed surgery without the addition of any other treatment.

In 44 patients who were treated by intralesional injections of steroid, we noticed hypopigmentation in 2 (5%) patients. There was recurrence of the lesions in 8 (20%) patients. Out of 44 patients only 40 patients came back for follow up while 4 patients did not return after application of first dose of Kenacort-A. We observed recurrence in 3 (25%) patients out of 12 patients in whom we applied silicone gel sheeting. 2 (16.66%) patients developed itching at the site of the lesions and one (8.33%) patient got superficial ulceration. We observed recurrence in 2 (25%) out of 9 patients in whom we combined surgery with steroid therapy. Hypopigmentation was observed in 1(12.50%) patient. 2 (22.22%) patients developed infection postoperatively. 1 patient did not turn up for follow up after first month interval. In 2 patients we applied superficial X-ray irradiation after surgery and recurrence was observed in 1(50%) patient. We performed surgery and split thickness skin grafting in 5 patients with hypertrophic scars. 2 (40%) patients developed infection at the recipient site. 1 (20%) patient got hematoma formation. 2 (40%) patients had displacement of grafts. 1 (20%) patient developed infection at the donor site. Recurrence was seen in 1 (20%) patient after this type of treatment. We did follow up of all these patients whom we treated on outdoor basis or in the surgical wards at intervals of one, three and six months.

Table No.2: Types, colour, thickness of the lesions and their associated problems

Indoor/ outdoor patients	No. of pts	Types of lesions	No. of patients	Colour of the lesions	No. of pts	Thickness /elevation	No. of pts	Tender-ness	No. of pts	Associated problems	No. of pts	Cosmetic impair-ment	No. of pts
Indoor patients	16	HTS	39 (54.1%)	Hyperpig-mented	21	Mild 1 mm to 2 mm	35	Tender	25	Neck contracture	4	Mild	40
								a. Mild	12	with	2		
				Hypopig-mented	15	Moderate 3 mm to 4 mm	30	b.Moderate	10	functional	1	Moderate	11
								c. Severe	3	impairment	1		
Outdoor patients	56	Keloids	33 (45.8%)	White	24	Severe 4 mm to 5 mm	7			a.Mild b.Moderate c.Severe			
				Pink to red	12							Severe	21
								Non tender	47	Psychological upsets	21		
Total	72	Total	72	Total	72	Total patients	72	Total	72	Any other	Nil	Total	72

The patients in whom we applied intralesional injections of steroid, 40 out of 44 patients came back at one, three and six months intervals for follow up. In cases of surgery and postoperative intrawound steroid injections, one patient did not return at 3 and 6 months intervals. We divided our results into excellent, good, satisfactory and poor categories at 6 months interval for our final outcome.

In case of intralesional injections of triamcinolone acetonide 25 (62.5%) out of 40 patients had, excellent results. 6 (15%) patients had good results. 1 (2.5%) patient had satisfactory and 8 (20%) patients had poor outcome.

Table No.3: Final outcome

Sr. No	Treatment options	Results	No. of pts	Percentage
1	Intralesional Triamcinolone Acetonide Injection	Excellent Good Satisfactory Poor	25 6 1 8	62.53% 15% 2.5% 20%
2	Silicone gel sheeting	Excellent Good Satisfactory Poor	6 2 1 3	50% 16.6% 8.33% 25%
3	Combination Of surgery with steroid injections	Excellent Good Satisfactory Poor	4 1 1 2	50% 12.5% 12.5% 25%
4	Combination of surgery with radiotherapy	Excellent Good Satisfactory Poor	NIL 1 NIL 1	NIL 50% NIL% 50%
5	Surgery alone	Excellent Good Satisfactory Poor	2 2 NIL 1	40% 40% NIL% 20%

In silicone gel sheeting out of 12 patients 6 (50%) had excellent, 2 (16.6%) good, 1 (8.33%) satisfactory and 3 patients had (25%) poor results. In those patients in whom we combined surgery with steroid injections, 4 (50%) patients had excellent results, 1 (12.5%) patient had good results, 1 (12.5%) patient had satisfactory and 2 (25%) patients had poor outcome.In 2 patients in whom we combined surgery with radiotherapy 1 patient improved while the other patient got recurrence. After surgical excision of hypertrophic scars in 5 patients, 2 (40%) patients had excellent, 2 (40%) good, and 1 (20%) patient had poor results. (Table No.3)

DISCUSSION

Different treatments had been tried in different patients to achieve best cosmetic results. Mustoe TA, Cooter RD, Gold M, et al evaluated the use of intralesional trimacinolone acetonide and came to the conclusion that 64% of the lesions became completely flat and 72% of the patients became symptom free after the use of triamcinolone acetonide intralesionally.[5]In our study 62% of the patients treated by intralesional injections of steroid had excellent results that is they have appreciable improvement in their symptoms and flattening of their scars. It is comparable to above study and other studies conducted around the world.

Response rates have been highly variable with intralesional injection of triamcinlone acetonide with figures ranging from 50% to 100%, and a recurrence rate of 9% to 50%.[6] injections may be used alone or combined with other therapies, of which the combination with cryotherapy or surgery are the most widely used modalities in clinical practice.[7] There is 20% recurrence rate in intralesional injections of steroid in our study and response rate is 62%.The above mentioned study has fairly comparable results to our study.

Muneuchi G et al studied the long term outcome of treatment of triamcinolone acetonide in Asian patients. Improvement in subjective symptoms was seen in 82% patients while in objective symptoms, fair or better results were seen in 63%, and good or better results in 39% patients.[8]When combined with excision, postoperative intralesional TAC injections resulted in a recurrence rate of 0-100 percent, with 50 percent reported as the most common recurrence rate. [9, 10]As can be seen in our study 62 % of the patients had excellent results while 15 % of the patients showed good results with intralesional injection of steroid. In case of combination of surgery and postoperative intralesional injection of steroid recurrence was

observed in 25% of the patients in our study. These results are comparable to above mentioned study.

These studies indicate that intralesional injections of steroid in hypertrophic scars and keloids give good results after their repeated use in terms of symptomatic improvements, scar colour, texture and scar height. In many other studies people used intrawound injections of steroid during and after surgery.[11, 12]

Recurrence rates of keloids after excision, in contrast, range between 45% and 100 %.[13]Given this high recurrence rate, surgical intervention without adjuvant therapy, such as post-excisional corticosteroid injections or radiations, should be considered with caution. Excision may frequently result in a longer scar than the original keloid and recurrence in this new area of trauma may lead to an even larger keloid.[14]

In an open-label pilot study, Lacarrubba et al (2008) made assessment of the effectiveness and tolerability of a silicone gel in the treatment of hypertrophic scars. A topical self-drying silicone gel was applied two times a day on 8 hypertrophic scars. Six months later, all lesions revealed evident clinical and/or ultrasound improvement, with a mean scar thickness reduction of 37 % (range of 20 % to 54 %). The authors concluded that although larger controlled trials are needed, these findings might point to the fact that the self-drying silicone gel may represent a safe and effective treatment for hypertrophic scars.[15, 16]

Gold used an open labeled approach to see the effect of silicone gel sheets on hypertrophic scars and keloids secondary to surgical procedure and trauma. He concluded that moderate improvement was seen regarding scar colour and thickness in all those patients who underwent the trial.[17]Evidence supports silicone sheeting, pressure dressings, and corticosteroid injections as first-line treatments[16].In our study patients treated by silicone gel sheeting showed excellent results in 50 % of the patients and good results in 17 % of the patients and recurrence rate of 25%. These results are comparable to above mentioned studies.

Different studies using surgery followed by radiotherapy have been performed in different parts of the world. Veen RE et al came to the conclusion that HDR (high-dose-rate) brachytherapy after keloidectomy is quite effective provided that the total HDR (high-dose-rate) dose is sufficient. They used radiation at the dose of 3 × 6 Gy.[18] In a study conducted by Garg MK et al the salvage treatment consisted of excision of the keloid and wound closure followed by HDRB high dose rate brachytherapy (15 Gy in three fractions given on three consecutive business days beginning the day of surgery). At the time of last follow up, 88% (15/17) of the keloids were without any evidence of recurrence.[19]In our study there is 50 % recurrence rate and 50 % patients showed good results. Though it is different from above mentioned study but the results are fairly good. The difference in results may be because of different geographical situation, recurrent and intractable keloids we treated by this method and non availability of sophisticated equipment for X-ray irradiation in our set up.

Ideally surgical excision of keloid should be avoided as far as possible, because the failure rate is significantly high. Surgical excision of hypertrophic scars may be efficacious in selected cases but requires meticulous adherence to the surgical principles and adjunctive measures like radiation, intralesional interferon or topical imiquimod.[20]In our study 40 % of the patients showed excellent results and there is 20 % recurrence in case of surgery followed by application of split thickness skin grafts in hypertrophic scars patients.

CONCLUSIONS

After observing the final results we reached the conclusion that intralesional injections of triamcinolone acetonide had good results. In early lesions silicone gel sheeting was useful option while recurrent scars can be treated by combined modalities of treatment.

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Address for Corresponding Author;
Dr. Quddus-ur-Rehman
Associate Professor of Anatomy
Aziz Fatimah Medical and Dental College, Faisalabad.
Email:drquddus_2003@hotmail.com
Ph #: 03336517421

Original Article

Accuracy of Estimated Fetal Weight by Clinical Assessment and Ultrasonography

1. Tabassum Naheed Kauser 2. Sania Tanveer Khattak

1. SMO, Deptt. of Obs. & Gynae. Lady Reading Hospital, Peshawar 2 Asstt. Prof. of Obstet and Gynae, Saidu Medical College, Swat

ABSTRACT

Objective: To compare accuracy of estimating fetal weight of term fetus by clinical assessment and Ultrasonography.

Study Design: Comparative Clinical Trial Study.

Place and Duration of Study: This study was conducted in obstetrics and gynecology unit of Hayat Abad Medical Complex.

Materials and Methods: - This study was carried out on 300 subjects, with full term; normal pregnancy. Patients had fetal weight estimation by two approaches

1) Clinical assessment done by Leopold's maneuvers and symphysio fundal height in centi-meters and
2) Sonographic measurement by using Toshiba capacee with curvilinear transducer of 3.5 MHz.

Birth weight at delivery was used on gold standard.

The accuracy of these two methods of estimating fetal weight was compared using student t test, and $\varkappa^2$ P> .05 was considered significant.

Result: Out of 300 cases, 292 cases were compared both. Ultrasonically and by clinical assessment .while 8 babies could not be picked up of ultrasonically because of fetal weight more than 4.0 KG , out of 292 cases (218) 72.7% were assessed. Correctly by clinical assessment while (224) 74.7% were assessed .correctly by ultrasonography.

Conclusion: - Clinical assessment is equally accurate as ultrasonography in normal term birth weight estimation.

Key Words: Fetal Weight, Ultrasonography, Clinical Assessment, Biparietal diameter, abdominal circumference.

INTRODUCTION

Accurate estimated fetal weight is of paramount importance in the management of labour and delivery. Ultrasonic methods of evaluating the fetus are now employed widely for many reasons.

The two main methods for predicating birth weight in current obstetrics practice are

1) Clinical techniques based on abdominal palpation of fetal parts and fundal size.
2) Sonographic measurements of selected fetal parts, which are then inserted into the regression equations to derive the EFW.

The former is composed of fundal height, size of fetal head and body amniotic fluid volume. Clinical and ultrasound estimation of fetal weight have recently been used in many centers. The advantages of clinical estimation are easy and quick without any instruments. However there is no standard method. The experience of clinician is very important .By ultrasound estimation, the anomaly scan can be performed at the same time but ultrasonography is costly and a well trained Ultrasonographer is needed. Several investigators have suggested that palpating the uterus to estimate fetal weight is in accurate .it generally is accepted that the objectivity and reproductivity of sonographic measurement yield more accurate estimates than clinical assessment of birth weight, but only a few studies have compared both methods[1] (Colman et al, 2006).

Several formulas that use, multiple ultrasonic, parameters, are used to estimate fetal weight .The most widely used formula in that of [2]Shepard et al ,1982 in which estimated fetal weight is derived from BPD and Ac.This equation predicts fetal weight with an accuracy of 15% to 20%.[3,4] Hadlock et al(1985), Warsof et al(1977) also have introduced equations to estimate fetal weight using combinations of BPD (Biparietal diameter) Ac (Abdominal circumference) and FL(Femur length) it may be in accurate if there is dolicocephalic or braclycephalic head.

In an effort to increase the accuracy of ultrasonic estimation of fetal weight,[3] Hadlock et al (1985) advocate the use of HC, AC and FL measurements in combination. They have shown that the prediction of fetal weight has a standard deviation of $\pm$ 15(2 standard deviation).

However the accuracy in predication of fetal weight decrease in small fetuses (less than 1500gm) and the error approaches $\pm$ 20%.

MATERIALS AND METHODS

This study was conducted in obstetrics and gynecology unit of Hayat Abad Medical Complex. The cases were included on the basis of strict inclusion criteria . In all cases ultrasound estimated fetal weight and clinical assessment for fetal weight was obtained on the day of patients admission for labour related reasons , and delivered within 48-72 hours .Additionally cases were excluded in which fetal head was embedded in the

pelvis because of the well documented reduced accuracy of biparietal diameter measurement made on such heads .Individual ultrasound estimated fetal weight were calculated by the formula of Hadlock. All clinical assessment was made by Leopold's maneuvers and measuring symphsio fundal height in (cm) by senior trained medical officers. Imaging studies were carried out by using Toshiba Capacee with a 3.5 Mhz Curvilinear probe.

300 cases were included in this study and it was convenience sampling (not probability).

The inclusion criteria was all term patients with period of gestation 37th to 41weeks singleton pregnancies who delivered alive fetus , with intact membranes at time of ultrasongraphic estimation and clinical assessment , exclusion criteria were all high risk pregnancies, Intrauterine growth retardation , multiple pregnancies and all those who were unsure of dates.

RESULT

This study included 300 cases who met the inclusion criteria as all term patients with period of gestation 37th to 41 weeks singleton pregnancies who delivered alive fetus with intact membrane at time of ultrasonographic estimation and clinical assessment 24.3% of patients were primi para, 52.6 % patients were multi Para and 23.0 % of patients were grand multi Para.

Table No.1:Clinical and ultrasonographic estimation of fetal weight.

Author	Method	Accuracy
Watson[7]	Clinical examination	7.7 % mean error
Loeffler[10]	Clinical examination	Within 1 pound in 80 % of estimate
Shepard[11]	Ultrasound (BPD, AC)	Within 10% in 51 % of estimation
Hadlock[6]	Ultrasound HC, AC , FL)	7.5 error =1s
Warsof	Ultrasound (AC, FL)	10.9% mean error

Table No.:2 Percentage of normal term birth weight

Weight /gm	n	% age
≤ 2500	32	10.6
≤ 3000	63	21
≤ 3500	106	35.3
≤ 4000	94	31.3
≤ 4500	5	1.6

Majority of patients 69.0 % belonged to middle class and only 3.3% belonged to high class . 21.3 % of patients had 37 weeks period of gestation 23.0 % had 38weeks, 18% had 39weeks, 23.0 % had 40weeks and only 14.3 % of patients had 41 weeks period of gestation.

Regarding mode of delivery 76.0 % has spontaneous vaginal delivery 10.3% had instrumental delivery , 13.7 % had caesarean delivery , 11% of babies were born with poor APGAR score at birth , 9% of babies had satisfactory.APGAR score while majority of babies 80 % were born with good APGAR score.

Table No.3: Accuracy of birth weight estimation by clinical assessment and ultrasonographic assessment

	By clinical assessment		By ultrasonographic assessment	
Degree of accuracy	n = 300			
Accurate estimation	218	72.7%	224	74.7%
Over estimation	45	15.0%	45	15.0 %
Under estimation	37	12.3 %	23	07.7%

In these babies 56.7 % were males and 43.3 % were female.

The actual birth weights of babies were between 2300gm uptil 4500gm.

The degree of accuracy of estimation of fetal weight by clinical assessment and ultrasonographic assessment are. Shown in table-3

Eight cases were not estimated ultrasonographically because the ultrasound machine was not calibrated for it.

Mean weight by clinical assessment is 3271.91gm while mean weight by ultrasound estimation is 3258.21gm.

On the basis of sample data, we conclude that there is no significant difference between both techniques (P value 0.206>0.05).

The advantage of using ultrasound for EFW has been questioned .Bawm et al(2002) concluded that ultrasound offered no advantage over clinical estimates of fetal weight at term, An EFW should be recorded in the assessment of all patients who are at term and again when they are in labour, with full awareness of the limitation of the methods for making such estimation[5].

DISCUSSION

Accurate estimation of fetal weight is of paramount importance in the management of labour and delivery .During the last decade, EFW has been incorporated into the standard routine ante partum evaluation of high risk pregnancies and deliveries .

The accuracy of predicting birth weight by a variety of different formulas incorporating different ultrasonic measurement has been studied extensively. However, no particular formula or biometric measurement has superior quality.

The basic characteristic of 300 women included in our study were parity of women, socio economic status, period of gestation although all the three above

characteristic does not directly affect the weight of baby, but socioeconomic status, a well as the parity of women effect weight of baby . In this study 69.0% of patients belonged to poor socioeconomic class, as a consequence about 8.3% of babies weight less than 2500gm although term babies.

According to William's obstetrics (2001), the principal determinants of fetal growth rate in pregnancy are related in large part to factors influenced by the socioeconomic status of mother, such as diet, smoking or substances abuse.

In general the greater the socioeconomic deprivation, the slower the rate of fetal growth rate in pregnancy.

In this study none of the patients were smoker or addict, Term infants, however frequently weight less than 3200 gm and some time as little as 2250gm or even less, In this study 5.3% of fetus although term weighted <2500gm as in table-2 although mothers were sure of their dates, but no record of serial ultrasound or other diagnostic procedures were available to lable them as IUGR, but by ponderal index[6] (Reece EA and Hobbins JC, 1995) they were not IUGR, 10.6% of small for gestational age ,infants identified by birth weight percentiles are not growth retarded by their ponderal index.

$$\text{Ponderal index} = \frac{\text{Birth weigh (gm)} \times 100}{\text{Crown heal length (c.m)}^3}.$$

Regarding POG, this study included term pregnancies (37-41weeks) but during the second half of pregnancy the fetal weight increases in a linear manner with time until about 37weeks of gestation and then the rate slows hence after 37weeks of gestation, POG does not have marked effect on fetal weight[7] (William, 2001)

The fetal basic characteristics included mode of delivery, sex of the baby, APGAR score of baby at birth and actual weight of baby.

In this study majority of babies (76.0%) were born by spontaneous vaginal delivery and majority of babies 81.0% were born with good APGAR score. Since most of deliveries were normal with male babies 56.7% and female 43.3%, the boys weigh about 100gm heavier than girls (William, 2001) but in this study this factor is not considered.

In a study conducted by Suneet et al(1998) at the department of obstetrics and Gynecology, Medical college of Geargia, Augusta in which patients in early labour had fetal weight estimation by two approaches[8].

1) Clinical evaluation and palpation followed by.
2) Sonographic menesuration of fetal diparietal diameter, abdominal circumference and femur length applied to Hadlock's formula.

The accuracy of these two methods of estimating fetal weight was composed using t test, welcoxon test and $\varkappa^2$ test P<.05 was considered significant[8] (Suneet et al 1998), it was found that sonographic EFW was more accurate then clinical EFW in preterm but not in term or post term pregnancies, similarly in our study with p.value 0.206 and P> 0.05 considered significantly, it was calculated that there was no significant difference between both techniques for term fetuses as in table-3

In the study of Shamley K T and Landon MB 1994[5] 70-79% of birth weight predication were within 10% of actual birth weight and 79—91% were within 400gm by ultarsonography[9]. For clinical estimation of weight 66% were within 10% of actual birth weight and 77% within 400gm

The formula with greatest accuracy and clinical use was Hadlock equation using four parameter of BPD, HC and AC (Hadlock et al ,1985). [3]

Log 10 EFW =1.3596+0.00064(HC) =0.024(AC) + 0.174(FL) +0.0061(BPD) (AC) - 0.00386(AC) (FL).

Hence in our study, the equation to determines fetal weight was that of Hadlock et al (1985)[3] in which ultrasonic prediction of fetal weight gave 74.7% accuracy (table-3) .

In our study as in table 5, shows degree of accuracy by clinical assessment as 72.7% with under estimation 15.0% and our estimation 7.7%, the results being comparable with the study conducted by Shermon et al (1998) [10], conducted at the department of obstetrics and Gynecology, Asraf 2010 – Harafeh Medical center Zeriyin , Israel as in this study in the middle range of birth weight (2500 - 4000gm) [11].

The clinical estimation had no systemic error, the accuracy was 69% and the ultrasonic method under estimated the actual weight by 9.2% while accuracy was 72% .In the high birth weight group (greater than 4000gm) both methods under estimated systematically the actual birth weight, but mean errors were not significantly different.

In a study conducted by Watson et al (1998) the fetal weight was calculated by the formula of Shepard and coworkers[12].

In this all estimations were made with in 48hrs of delivery.

The mean error in clinically estimated weight was 277gm while that in the ultrasound calculated weight was 286gm.

In a study conducted by Noumi G et al (2005) even when performed during labour by residents ,which consisted of achieving clinical followed by sonographic EFW by the admitting resident during active phase of labour .The results of this study showed that clinical EFW was correct (within ±10%) in 72% of cases and sonographic EFW was correct in 74% of the cases[13]. However the sensitivity of predicting birth weight of 4 k.g or more was only 50% both clinical and sonographic EFW with 95% and 97% specificity respectively.

In our study more than 4000gm of fetuses could not be compared ultrasonically because the ultrasound machine in our unit was not calibrated for fetuses with

weight greater than 4000gm there were 8 such cases weighted more than 4000gm . Hence they were estimated only clinically although total number of cases were 300, 292 cases were compared both ultrasonically and by clinical estimation. This problem has also been quoted by Shamley and Landon (1994) in his study as their sensitivity of 62% confirms Had lock observation about limited ability of sonographic equation to identify the macrosomic fetuses[9] .Conversely specificity for predicting birth weight under 3800 gm was good.

In a study done by Ashrafganjoog et al 2010 the sensitivity values of predicting birth weight for ultrasound, clinical and maternal EFW were 17.6%, 11.8% and 6.3% with specificity of 93.5% , 99.6% and 98.0% respectively, the conclusion drawn in above mentioned study were that EFW by ultrasound offers no advantage over clinical assessment when performed during pregnancy or labour.

CONCLUSION

Our data indicate that clinical examination may be as accurate as ultrasound determination in estimating the weight of term fetuses, both methods have as approximate of 25 % error. It is not surprising that clinical estimation is no different from ultrasound estimation for average sized fetus. In term fetuses of <3000 gm and >4000, Ultrasound estimation was not superior to clinical estimation.

One advantage of ultrasound in this setting, however, may be in eliminating a significant variation between observers.

In the term fetus, the estimation of fetal weight with Leopold's maneuvers is still useful clinically.

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Address for Corresponding Author:
Dr. Tabassum Naheed Kauser.
SMO, Deptt. of Obs. & Gynae.
Lady Reading Hospital, Peshawar.

Original Article

Pattern and Outcome of Admissions to Neonatal Unit of Tertiary Care Hospital Nawabshah

1. Ali Akbar Siyal 2. Ali Raza Brohi 3. Arbab Ali Junejo

1. Assoc. Prof. of Pediatric Medicine, PUMHS Women, Nawabshah 2. Assoc. Prof. of Pediatric Surgery, PUMHS Women, Nawabshah 3. Assoc. Prof. of Pediatric Medicine, PUMHSWomen , Nawabshah

ABSTRACT

Objectives: To determine the number, disease pattern and outcome of admitted patients in neonatal unit of tertiary care hospital Nawabshah.

Study Design: Retrospective, Descriptive study.

Place and Duration of Study: This study was conducted at NICU pediatrics ward People's Medical College Hospital, People's University of Medical & Health Sciences for women, Nawabshah, Sindh from 1st January 2010 to 31st December 2010.

Materials and Methods: Data was retrieved from file record regarding sex, gestational age (term and preterm), reason for admission and outcome (discharge, expired).

Result: 2584 neonates were admitted during study period, among them 1776 (68.73 %) were males and 808 (31 .27%) were females, majority of patient 1657(64.12%) were admitted during first 24 hours with the clinical diagnosis of birth asphyxia, 489 (15.85%) having neonatal sepsis,312 (10.67%) because of prematurity, 117 (8.63s%) admissions were due to neonatal jaundice and 19 (0.73%) having various conditions like hydrocephalus associated with meningomyelocele, prune belly syndrome, down syndrome, Icthyosis, HDN and TORCH infection.

Conclusion: Birth asphyxia, Pre-maturity, neonatal infection, neonatal jaundice were the main causes of neonatal admissions. Regular antenatal visits and timely referral to tertiary care hospitals will hopefully result in better outcome.

Key Words: Pattern, Admissions, Neonates, Outcome

INTRODUCTION

Neonatal period (0 to 28 days of life) is the most sensitive period of life because of various problems / diseases which a neonate faces. According to "state of the world's newborn Pakistan" around 270000 neonatal deaths occur annually in this country and neonatal mortality rate is 42/1000 live births in year 2009 [1]. Globally about 3 million newborns are dying within first week of life [2].

Majority of newborn babies do not develop any serious problem or difficulties and require only minimal care, which can be provided by the mother if properly guided by a health worker/care provider.

In most of the cases neonatal morbidity in our country is preventable.[3] Pre-maturity accounts for majority of high risk newborns as they face a large number of problems.[4.] The prognosis of these premature babies depends upon their underlying condition & its severity, management and their outcome. For this purpose neonatal audit is carried out in Pakistan from time to time in order to create an awareness regarding the pre-term babies and other neonatal problems which they are facing & their management in a proper way.[5-7.] To decrease the neonatal morbidity and mortality such audits are very much needed to be done, especially in developing countries like Pakistan, so as to minimize the high infant and neonatal mortality and eventually decreasing under 5 mortality rate (MDG 4).

In our country about 70-80% of the births take place at home and that also contributes to poor newborn problem based care[8]. In Pakistan the rate of low birth weight babies contribute to 25% of all births[9,22,23] and that also contributes to over all morbidity and mortality. So this study is also done to look at the disease pattern and common causes of neonatal admissions so that we can take preventive measures to improve the outcome of neonates.

MATERIALS AND METHODS

This retrospective descriptive study was conducted at NICU Paediatric ward PMCH Nawabshah, the data included sex, gestational age (term and preterm), and outcome (expired, discharged) was recorded from the files of all admitted patients in NICU during our stud period. The patients who left against medical advice (LAMA) were not included.

Diagnosis was mainly clinical or based on WHO definition for pre-maturity (live born neonates delivered before 37 weeks from 1st day of last menstrual period (LMP) & low birth weight (LBW) with birth weight of less than 2.5kg. Neonatal Jaundice (NNJ) was diagnosed by clinically as well as by assessing serum bilirubin level. Sepsis & meningitis were diagnosed on clinical grounds along with positive blood Culture & CSF examination. Birth asphyxia was mainly clinical diagnosis on the basis of sarnet-staging. HDN (hemorrhagic disease of

newborn) was diagnosed on clinical ground along with an increase in prothomobin time.

RESULTS

During our study period, total 2584 neonates were admitted, among them 1776 (68.73 %) were males and 808 (31.27%) were females (fig 1), majority of patients 1657 (64.12%) were admitted during first 72 hours of life with the clinical diagnosis of birth asphyxia, out of these patients with birth asphyxia 1052(40.71%) were received within first 24 hours of life.

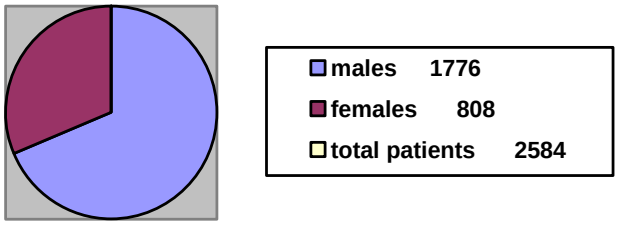

Figure No. 1: Ratio of Males: Female Patients

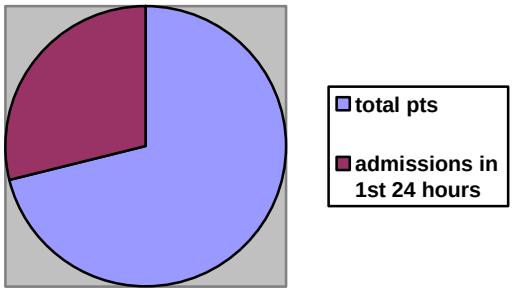

Figure No. 2: Total Admissions in NICU: Admissions in First 24 Hour of Life

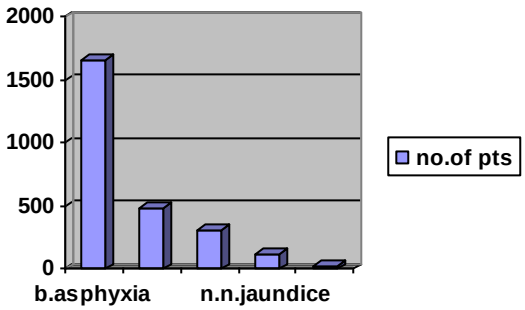

Figure No.3 Number of Patients Admitted in NICU

Second major reason for admission was neonatal sepsis in which 489 (18.9%) neonates were admitted, third major cause of admission in which 312 (12.07%) newborns were admitted was prematurity, fourth major cause for which 117 (4.53%) neonates seek admission was neonatal jaundice and 19 (0.735%) were admitted because of various conditions like hydrocephalus associated with meningomyelocele, prune belly syndrome, down syndrome, Icthyosis and TORCH infection.

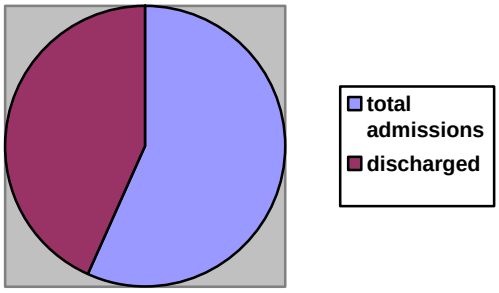

Figure No. 4: Total Admissions: Discharged Patients

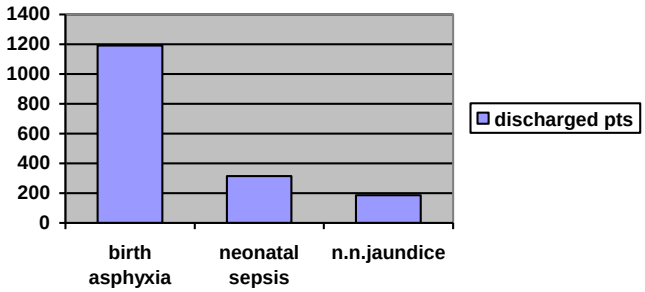

Figure No. 5: Number 0f Discharged Patients

Out of 2584 admitted patients, 1982 (76.7%) discharged (FIG.03), among these patients 1191 (60.1%) were admitted with diagnosis of birth asphyxia, 314 (15.85%) patients of neonatal sepsis were discharged, 186(9.38%) preterm babies were discharged, 5.05 % babies with neonatal jaundice were discharged.

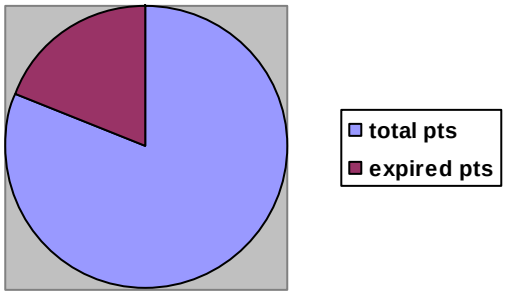

Figure No. 6: Number of Patients Admitted: Expired Patients

Of these admitted patients 602(23.29%) expired during admission (FIG. 05), and amongst these the

top cause was found to be birth asphyxia, in which 466 (18.03%) neonates expired, second major cause of mortality was sepsis in which 175(6.77%) and third cause preterms with various complications, caused 126 (4.87%) and rest of 36(1.39%) patients expired due to various reasons like kernicterus, complication of meningomyelocele and various other causes.

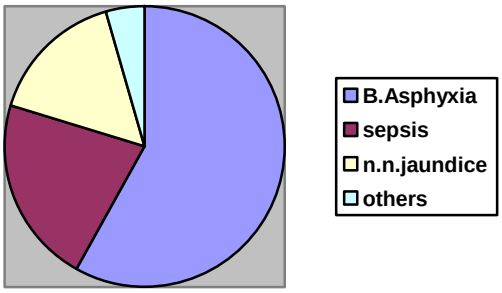

Figure No. 7: Patern of Discharged Patients

DISCUSSION

Of 2584 patients admitted in neonatal unit during our study period, 41.71% of patients were admitted during the 1st 24 hours of life. The other studies conducted at different cities of the country shows that 33.61% were admitted during first 24 hours at Karachi [10] 44.47% from Larkana[7] and 75% from Lahore.[11] These figures shows that most of the neonatal problem occur during the 1st 24 hours of life. Birth asphyxia in particular as 41.7% in our study, It was reported 18.85 from Karachi, [10] 40.66% from Lahore, [12] 31% from Rawalpindi[13]. Birth asphyxia is one of the common causes of morbidity and mortality in neonates and the incidence is 2-9 per 1,000 live births[14]. There is a male predominance in our study also consistent with other studies conducted at different institutions of various cities of Pakistan. In our study the second major cause of seeking admission in nursery was neonatal infection, that caused 489 (18.92%%) and as we know Neonatal infection is one of the main causes of neonatal morbidity and mortality in developing countries[15,16,21], it was found to be 45.21% from Karachi[10]. The number of preterm neonates admitted reported was 312(12.07%) as compared to 26.50% in Khyber[16,23], while 117(4.5%) babies were admitted because of neonatal jaundice, Neonatal jaundice was responsible for the 20%[14] 13.15% from Karachi,[10] 8.33% from Lahore[13]and 3.5% from Larkana.[15] It was reported high (30.71%) from Bangladesh [15,19] the discharge %age in our study was 76.7%,in Khyber 71.54% neonates were discharged home satisfactorily after receiving the necessary treatment[14],48.53% were discharged with satisfactory condition[10] in study from Karachi. The mortality rate was 23.29% at our setup, while it was 14.87% at Peshawar[14,18]. It was reported 25.85% from Karachi[10] 34% from Lahore[13,16] and 38 % from Larkana[7]. The commonest cause of mortality was birth Asphyxia, worst being HIE stage III, in which 18.03% of patients expired, followed by neonatal sepsis, prematurity and others which contributed to 6.77%, 4.87% and 1.39% respectively.

CONCLUSION

Birth asphyxia, Pre-maturity, neonatal infection, neonatal jaundice were the main causes of neonatal admissions in our study. This could be reduced by proper antenatal visits and timely referral to tertiary care hospital and provision of neonatal intensive care facilities are necessary for better outcome.

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Address for Corresponding Author:
Dr. Ali Akbar Siyal
Associate Professor of Pediatric Medicine,
PUMHS Women, Nawabshah

Original Article

Malpractices of Hand Hygiene in Nursing Staff: A Global Threat for Increasing Incidence of Infections

1. Kiran Mehtab 2. Waqas Ahmed 3. Samrah Shafiq 4. Yusra Jamal 5. Anosh Inkesar 6. Mehwish Ikram 7. Saleha Akhtar 8. Madiha Hashmi 9. Maheen Mughal 10. Sabeen Dhanani 11. Sundus Anwer 12. Hassan Ahmed

1. Asstt. Prof. of Community Medicine, Sindh Medical College, DUHS, Karachi
2 to 12. Final Year MBBS Students, Sindh Medical College, DUHS, Karachi

ABSTRACT

Objective: This study assessed the knowledge, practice of standard hand hygiene in nursing staff to identify the causes of not adapting hand hygiene techniques during routine patient care.
Study Design: A cross sectional study.
Place and Duration of Study: This study was carried out in Karachi in various public sector hospitals i.e. Jinnah Postgraduate & Medical Centre, National Institute of Child Health, Civil Hospital Karachi, Sindh Institute of Urology Transplantation, National Institute of Cardiovascular Diseases. The study completed in six months from May to November 2010.
Materials and Methods: A sample of 335 nursing staff was selected, convenient sampling was used, consent was taken. They were asked about their practices of hand hygiene through structured questionnaire at five major public sector hospitals of Karachi. Pakistan.
Results: Out of 335 nursing personnel, 71.9% were unaware that washing hands under running water for 30sec to 1min remove most of the germs. 74.62% knows that hand washing is necessary. Regarding practices, 35.5% use sanitizers while 47.2% use antiseptic, normal soap for washing hands. 67.1% practice hand washing before & after coming in contact with patients. 43.7% took some treatment after needle prick while others (56.3%) didn't feel the necessity to take any treatment, regardless of the risk of Hepatitis, HIV. 36.1% adopted sterile techniques after hand washing. Surveillance was below average (46.6%)..
Conclusion: Hand hygiene knowledge, practices of nursing staff is part & parcel for minimizing infections. Adequate hand washing facilities, positive attitude towards hand hygiene, adherence to practice, strict surveillance system for hand hygiene is essential to combat increasing incidence of infections.
Key Words: Hand Hygiene, malpractice, infections.

INTRODUCTION

Hand hygiene is considered to be the most effective measure to prevent microbial pathogens cross-transmission, healthcare-associated infections and the spread of anti-microbial resistance. The skin on hands is first defense against infection from pathogenic organisms. Hands are the most likely way in which infections or microorganisms spread between people. So washing hands is simply the most effective method of preventing the transmission of infections.

The Centers for Disease Control and Prevention (CDC) and other healthcare-related organizations states that through cleaning hands before and after having contact with patients is one of the most important measures for preventing the spread of infections in healthcare settings.[1]

Hand hygiene is a major component of standard precautions and one of the most effective methods to prevent transmission of pathogens associated with health care. [2] It is considered to be the primary measure to reduce the transmission of nosocomial infections. [3-4] Noncompliance with hand hygiene, however, remains a major problem in public sector care hospitals in Pakistan.

According to World Health Organization (WHO), the five moments must be remembered to wash hands; i.e. before and after patient contact, before performing aseptic procedure, after exposure to body fluids and after contact with patient surroundings.

Health Education is one of the cornerstones for improvement with hand hygiene practices. Health Care Workers education must be promoted at all levels of experience.[7] This study high-lights the lack in practices of standard hand hygiene in nursing staff and their attitude to maintain proper hand hygiene with increasing experience.

MATERIALS AND METHODS

A cross sectional study was carried out in Karachi in various public sector hospitals i.e. Jinnah Post-graduate & Medical Centre (JPMC), National Institute of Child Health (NICH), Civil Hospital Karachi, Sindh Institute of Urology & Transplantation (SIUT) and National Institute of Cardiovascular Diseases (NICVD).

The study completed in six months from 15th May to 25th November 2010. The required permission was obtained from the administrators of various departments prior to study.

Nursing staff & Trainees working in the public sector Hospitals, departments of Medicine & Allied, Surgery & Allied, Gynecology & Obstetrics and Pediatrics were included.

A pilot study was carried out in Jinnah Post-graduate Medical Centre (JPMC) to test the applicability and consistency of the tools.

The sampling technique used is convenient sampling and a sample size of 335 has been taken by keeping a population result of 68.8% with 95% confidence interval (95% Cl) and 5% margin of error, p-value of 0.05 was considered as statistically significance.

The study protocol was approved by Research Supervisor, Community Medicine Department, Sindh Medical College (DUHS), and an informed consent was taken from the subjects who were personally interviewed through a structured questionnaire.

Nursing personnel working in these hospitals were assessed according to the World Health Organization (WHO) protocol based on basic concepts of hand hygiene & its parameters.

Data Analysis*:* The significance of the data was determined by using Statistical Package of Social Sciences software Version 16.0. The results are expressed as frequencies, percentages, cross tabulations, pie charts and bar charts.

RESULTS

Out of 335 individuals, 219 (65.37%) were females and 116 (34.62%) are males including 183 (54.6%) staff nurses & 152 (45.6%) trainees having ages between16 years to 50 years.250 (74.62%) has sufficient knowledge about the benefits of hand washing while the facilities were available only to 115 (34.3%). Regarding knowledge, 240 (71.6%) didn't even know that running water for 30 seconds to 1 minute can wash out most of the micro-organisms from their hands leaving only 95 (28.4%) with this piece of knowledge.

83.3% staff was daily getting exposed to body fluids (blood/urine/CSF/peritoneal fluid). 66% of the staff claimed that it was common practice if they didn't wash hand in heavy rush hours of patients.

Regarding practice, 279 (83.3%) staff was daily getting exposed to body fluids (blood/urine/CSF/peritoneal fluid etc). 221 (66%) of the staff claimed that it was common if they didn't practice hand washing in heavy rush hours of patients

Only 114 (34%) said that they properly practice hand washing in heavy rush of patients. 189 (56.4%) remembered that they had needle prick during their nursing practice at least once & 146 (43.6%) couldn't recall or didn't have needle prick.

Table No. 1: Frequencies of positive & negative results asked to the nursing staff.

S. No.	Questions	Yes%	No %
1	Staff having formal training regarding hand hygiene	71.9%	28.1%
2	Staff practicing hand washing before & after coming in contact with patients	67.1%	32.9%
3	staff using antiseptic or normal soap	47.2%	12.83%
4	Staff using sanitizers for hand washing	35.5%	64.5%
5	Staff practicing sterile techniques after hand washing	36.1%	63.9%
6	Staff using gloves while performing aseptic techniques	92.8%	7.2%
7	Staff practicing hand washing in heavy rush of patients	34%	66%
8	Staff having surveillance	46.6%	53.4%

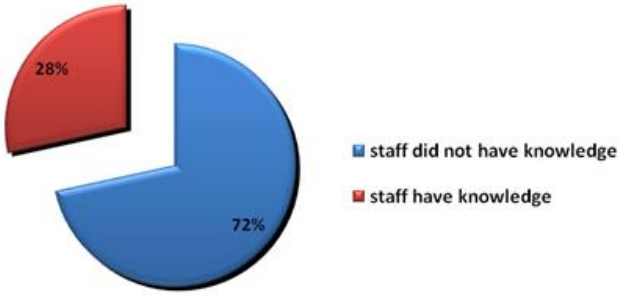

Figure 1.1: Percentage of staff having knowledge of keeping hands under running water for 30 seconds to one minute.

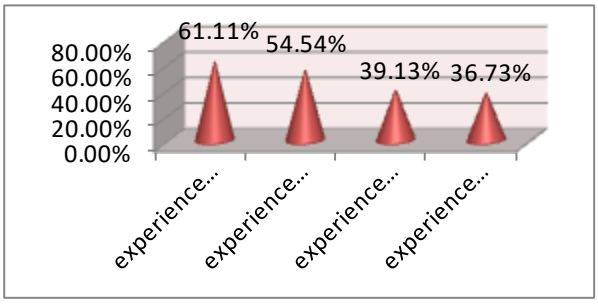

Figure 1.2: Comparison of needle prick treatment among nursing staff with increasing experience.

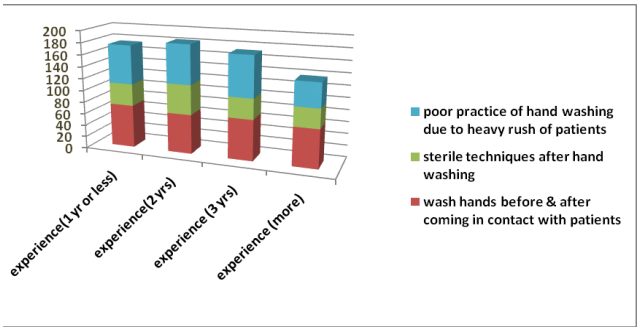

Figure 1.3: Practices of hand washing in heavy rush of patients with increasing experience.

DISCUSSION

Poor hand hygiene is the main source of infections amongst nursing staff as well as in patients. World Health Organization has given reviewed results of different studies done worldwide about hand hygiene which showed that the adherence of health care workers to recommended hand hygiene procedure was unacceptably poor with the overall average of about 40 %.[8] The study showed that 74.62% nursing staff knew about the significance of hand washing but the basic knowledge was lacking. For instance, 71.6% of nursing staff was not aware of the fact that keeping hands under running water for 30 seconds can decontaminate hands to quite an extent. Regarding practice, 67.1 % washed their hands before and after attending the patient. But many of them didn't use sterile technique s after washing hands. Reason behind malpractice were found to be heavy rush of patients in public sector hospital resulting in low staff to patient ratio and also lack of proper surveillance system. Another contributing factor was experience of the nursing staff as it was assessed that as the experience increases, the mal-practices to work properly increases.

Most of the nursing staff had experienced needle prick out of which less than half had taken some treatment. Previously, many studies have been carried-out worldwide regarding hand hygiene amongst nursing staff. In our study it was found that 74.62% nursing staff had sufficient knowledge but only 66% were practicing it. It also showed that 34.3% had facilities available for hand washing. A very similar observational study was done locally at a major public sector hospital in Karachi, and it showed that 68.8% had sufficient knowledge about hand washing but 59% were practicing it, while 16.8% were provided with hand washing facilities.[9]The study also assessed that the positive attitude was significantly higher among younger individuals who were working as trainee and about 67.1% decontaminate their hands before and after coming in contact with patients while compliance for invasive procedures was 92.8%. Another study done in Italy showed that hand hygiene practice was significantly higher among the older personnel and in those with the high level of knowledge and 72.5% decontaminate hands before and after patient contact. High compliance is reported for invasive maneuvers (96.5%). [10] Regarding needle prick, our study revealed that only 43.7% took some treatment after needle prick. While a study done in the US showed that a large proportion of respondents did not take any treatment after needle prick. [11]In this study, 71.6% of the staff did not even know that washing hands under running water for 30 seconds can wash out most of the micro-organisms but a study in Peru showed that mean duration for hand washing following patient contact is 14.5 seconds.[12]According to the study, the surveillance system was found to be 46.6% while a study in Switzerland showed that compliance improved progressively from 48% in 1994 to 66% in 1997 after implementing proper surveillance program, because of same frequency of hand disinfection substantially increased during the study period and overall nosocomial infections decreased from 16.9% in 1994 to 9.9% in 1997. [13] Study revealed 35.5% of staff used sanitizer for hand washing, it was revealed that hand washing increased significantly by the introduction of waterless hand sanitizers from 73% to 83% before and 80% to 90% after patient contact.[14]

CONCLUSION

The study highlights the lack in practice of hand hygiene by nursing staff. The striking reasons found for poor practices were either lack of knowledge, facilities or intense patient flow. The study assessed as the experience increased, the adherence towards hand hygiene decreased, making a strong indication for transmission of microorganisms among the patients, health care personnel. Adequate hand washing facilities, adherence to practice, strict surveillance system for hand hygiene is essential, should be installed in different wards to ensure the compliance of hand hygiene techniques. Nursing staff should be highly aware of the consequences of needle prick; Upgrading knowledge regarding hand hygiene of nursing staff should be a part of routine work.

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Address for Corresponding Author:
Dr. Kiran Mehtab,
Asstt. Prof. of Community Medicine,
SMC, DUHS, Karachi
Email: kiranalisyed@yahoo.com
Cell #: 0333-3188237

Original Article

Role of Polymorphonuclear Leukocyte in Diabetic Foot

1.Saba Fazle Rabbi 2.S.Mohsin Turab 3.Meh Jabeen 4. Shah Nawaz Jamali

1. Assoc. Prof. of Pathology 2. Assoc. Prof. of Pharmacology & Therapeutics 3. Assoc. Prof. of Physiology 4. Asstt. Prof. of Pharmacology & Therapeutics, Hamdard College of Medicine and Dentistry Hamdard University, Karachi.

ABSTRACT

Objective: To study the etiopathogenesis of foot injuries in patients of uncontrolled diabetes mellitus.

Study Design: Retrospective study of tissue samples received from diabetic patients clinically diagnosed as gangrene.

Place and Duration of Study: This study was conducted in the Department of Ophthalmology, JPMC, Karachi from July 2009 to June 2011.

Materials and Methods: 150 cases of uncontrolled diabetes mellitus with wounds of foot were included. 150 cases of known diabetics with peripheral neuropathy and history of loss of sensation were subjected to follow up of 2 years Follow up was done on the cases. As a first step blood sugar was brought under control and broad spectrum antibiotic was given. Wound debriment was done in all cases. The specimens were subjected to H/E and Gram's staining.

Result: In H/E, liquifactive necrosis, polymorphonuclear leukocyte, mononuclear cell infiltrate, few lymphocyte plasma cells & fibroblasts were seen. New blood capillaries were few or absent. Both gram positive and gram negative organisms were isolated. 79% were gram positive and 21% were gram negative.

Conclusion: Hyperglycemia causes relative anoxia in the micro environment of the tissue due to damage of peripheral neurons. Lack of adequate circulation leads to ischemia, which is super added by infection of the subcutaneous tissue. The resultant effect is liquifactive necrosis and complete lysis of tissue. Removal of such putrefied tissue is mandatory to stop further damage to the tissue.

Keywords: Diabetes mellitus, gangrene, staphylococcus aureus.

INTRODUCTION

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia due to relative or absolute deficiency of insulin[1]. A complex called AGE is deposited systemically in different tissues. Uncontrolled hyperglycemia affects the peripheral nerve fibers which hampers the autonomous control of micro-capillaries in the peripheries. The mechanism of vasodilatation in warm environment and vasoconstriction in cold is due to the autonomic control of the peripheral capillaries. In diabetes the small capillaries remain in constant vasoconstriction and the microcirculation is reduced due to non-compliance of capillaries. [2]. The tips of distil phalanges are dependent on simple diffusion of nutrients, glucose and oxygen from viable and competent capillaries which is reduced and area becomes hypoxic. Due to lack of vasodilatation of venular end of the capillaries the transudate starts to accumulate in this area. The toxic waste matter like lactic acid, oxygen derived free radicals slowly starts to damage the tip of the fingers. Hence there is relative hypoxia from the beginning that finally results as ischemia [3]. Peripheral neuropathy also leads to the destruction of sensory neurons especially those of touch and pressure. This desensitization leads to minor foot injury which is missed at the initial phase and most of the time ignored by the patient. Minor cracks also appear in cold and dry climate which are the actual portal of entry for normal commensals.

The PML Polymorph nuclear leukocytes which are the first line of defense against normal commensals are sluggish and have a tendency to stick on the capillary wall. The chemotaxis is slow and they fail to reach site of injury and very few successfully phagocytose the bacteria. The most common bacteria found in diabetic foot are Staphylococcus aureus and Pseudomonas[4,5]. These bacteria thereby gain access to the subcutaneous tissue through the damaged skin. Here they multiply and produce enzymes/ toxins like coagulase/ leukocidin or have antigenic domain on their cell wall like Lipid A[6]. These microbiological chemicals entice polymorphonuclear leukocyte to the site of injury. The number of PML gradually starts to increase and a time comes when PML are the predominant cell observed at the site.[7] The MAO system of PML is designed to kill these bacteria but as their capability to phagocytose is greatly reduced in controlled diabetes the fail to destroy them. Absence of vasodilation ends in ineffective and trapped PML. Hence the inflammation becomes suppurative. This phenomenon is appreciated in histological sections of wound samples collected from diabetic foot [8]. The PML contain lysosomal enzymes like lipases, protinases DNAses which digest viable tissue. The type of necrosis seen in diabetic foot is therefore liquifactive instead of coagulative[9]. This type of necrosis provides platform for further bacterial

multiplication and they quickly replicate and later appear as necrotizing type[10]. The chemokines like VEGF and FGF are not secreted by the inflammatory cells and new capillaries are not formed which further aggravates the situation. Therefore until a lot of collagen, necrotic tissue and heavy bacterial growth and damaged capillaries are not removed, the routine medical management of hyperglycemia alone would be insufficient to treat such cases. It is therefore necessary to debride the wound. This decreases the bacterial load and removes favorable environment for their growth. The dead non-functional capillaries and permanently damaged tissue is removed which encourages nerve vasculiztion. The more this process is delayed the slower is the healing which later may result in amputation of a limb[11].

MATERIALS AND METHODS

Retrospective study carried out department of surgery, Jinnah Post Graduate Medical Centre, Karachi, consisting of 150 cases of known uncontrolled diabetics with diabetic foot injury over a period of 2 years. The contaminated wound samples were subjected to Haematoxyline and Eosine. All cases without foot lesions and all euglycemic patients were excluded from this study.

Table No.1: Percentage of Male and Female in Gram +ve & Gram -ve

Type of Bacteria	Male	Female	Total
Gram positive	81(54%)	38(26%)	119(79%)
Gram negative	20(13%)	11(7%)	31(21%)

Table No.2: Percentage of Male and Female in different microscopic features

Microscopic features	Male	Female	Total
Liquifactive necrosis	101	49	150 (100%)
PML	101	49	150 (100%)
Macrophages	17	03	20 (13%)
Fibroblast	16	06	22 (15%)
Lymphocytes	11	04	15 (10%)
Plasma cells	08	02	10 (7%)
New blood vessels	02	00	02 (1%)

RESULTS

Total number of patients enrolled was 150.Among them we isolated Gram positive cocci in 54% which were males and 26% females and Gram negative bacilli in 13% males and 7% females. It was noted that significant number of cases had Gram positive cocci infection that is 79% shown in table # 1.

With reference to table # 2 in all of 150 cases we observed infiltration with PML and liquifactive necrosis. There was presence of macrophages (13%), lymphocytes (10%), plasma cells (7%) and fibroblasts (15%). Only 1% of patient showed newly formed capillaries.

DISCUSSION

The incidence of gangrene is greater in patients of uncontrolled diabetics[12]. The factors responsible for its development are peripheral neuropathy and micro-vascular disease. There is loss of peripheral sensation and inflammatory process for minor daily injury[13]. This is further aggravated by secondary invasion of the site of injury by normal commensuals specially gram positive bacteria[14]. Complex of AGE is formed due to constant hyperglycemic condition. As there is no enzyme system to affectively neutralize AGE, it gets deposited within the microvasculature throughout the body[15]. The tip of the distil phalanges is dependent on its competent vasculature. Deposition of AGE reduces the flexibility of these vessels. Hence the environment becomes anoxic and favors ischemia. Venous return becomes sluggish and minor injury leads to cuts in the soft skin[16]. The normal commensuals get entry into the subcutaneous tissue and are not removed from the site quickly due to slow movement of PML[17]. These bacteria get time to multiply and secrete their enzymes and toxins which will fully recruit PML. In all of our 150 cases we observed heavy infiltration by PML. The stunted PML have lysosomal enzymes that degrade the normal tissue along with bactericidal activity. The tissues loose their shape and structure permanently and this type of necrosis is known as liquifactive necrosis[18,19]. We also observed that the type of necrosis evident was liquifactive necrosis in all of the cases. In diabetic foot there is predominance of acute inflammation however at places where there is chronic phase or little formation of healing tissue there is presence of other cells also, but their presence is numerically insignificant[20]. Lack of healing tissue suggests that until bacterial load and putrefied tissue is not removed the natural capability of the tissue to regain healing cannot be achieved. The most common microbes implicated in the pathogenesis of diabetic foot are the commensuals of the skin[21]. The gynogenic bacteria recruits PML and uses them to destroy the healthy tissue[22]. In our study the tissue section showed that the bacteria were surrounded by PML and Liquifactive necrosis in all 150 cases. Therefore it is mandatory to remove the putrefied tissue. Once wound debriment is done oxygen and nutrients can be restored by healthy capillaries and the bacterial load is reduced.

CONCLUSION

Since PML are the main defense against normal commensals, every effort must be made to diagnose such cases as early as possible so that the damaging effect of hyperglycemia on innate immunity is reduced and amputation of limb can be avoided. Timely

intervention and minor surgical debriment can improve the quality of life of such patients.

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Address for Corresponding Author:
Dr. Saba Fazle Rabbi,
Assoc. Prof. of Pathology,
Hamdard College of Medicine and Dentistry,
Hamdard University, Karachi.
Cell No. 0300-2219089

Original Article

Visfatin and its relationship with the Severity of Coronary Artery Disease in Pakistani Population

1. Kashif Nisar 2. Anila Jaleel 3. Erum Afaq 4. Jawed Aftab 5. Adnan Zubairi 6. Iqbal Mazahir

1. Lecturer of Biochemistry, Jinnah Medical and Dental College, Karachi 2. Prof. of Biochemistry, Ziauddin University 3. PG Student M.Phil of Physiology, Institute of Basic Health Sciences, DUHS, Karachi 4. Assoc. Prof. of Nuclear Medicine, Ziauddin University 5. Assoc. Prof. of Chemical Pathology, Ziauddin University 6. Prof. of Biochemistry, Jinnah Medical and Dental College, Karachi.

ABSTRACT

Objective: To determine plasma visfatin levels in patients with and without coronary artery disease and to correlate it with the coronary vessels blockage by using angiography.

Study Design: Comparative Cross Sectional Study.

Place and Duration of Study: This Study was conducted at the Department of Biochemistry, Ziauddin University and Jinnah Medical and Dental College, Karachi from June 2009 to November 2010.

Materials and Methods: The study includes 80 subjects (mean age48.8±6.15; 40-55 years age range) who underwent coronary angiography for suspected coronary artery disease. Plasma visfatin levels were determined by using ELISA.

Results: Out of these 80 study subjects, 30 (37.5%) had single vessel CAD, 12 (15%) had two vessels CAD, 24 (30%) had three vessels CAD and 14 (17.5%) had non significant disease. Serum Visfatin levels were higher in three vessel disease (5.82 ± 0.58) when compared with non significant (4.55 ± 1.10) single vessel disease (4.86±0.93) and two vessels disease (5.53± 0.79) respectively but these values were statistically nonsignificant in all four study groups.

Conclusion: Serum Visfatin levels were high in all three study groups when compared with non significant disease group and positive correlation of serum visfatin with the extent of the coronary artery disease was observed.

Key words: Visfatin; coronary artery disease; angiography; single vessel disease; non significant disease.

INTRODUCTION

Coronary artery disease shares a major burden of mortality worldwide. It remains the leading cause of death not only in industrialized nations but countries like Pakistan and India are also listed in the countries where prevalence of CAD is on the rise and surprisingly younger age group is the target in this region. Studies suggest an almost 2.5-fold rise in the prevalence of CAD in two decades—from 3.6% in the 1970s to 9.5% in the 1990s in people aged ⩾35 years in urban India [1]

According to World Health Organization (WHO) estimates, 60% of total world CAD deaths will be in India. India now is on the midway of CAD epidemic and Indians who live in urban areas have higher CAD rate [2] Although CAD rates become half in western populations in the past 30 years, rates doubled in India and no signs of decline in it is evident yet[3]

One out of five middle-aged adults in urban areas of Pakistan may have underlying CAD. Women are more at risk than men. Possibly this high prevalence of CAD in the Indo-Pakistan population is due to a greater vulnerability to the metabolic syndrome. Smoking is the major factor for greater prevalence of CAD in men [4] other reported contributors of CAD in Pakistani population are obesity, high blood cholesterol levels and atherosclerotic disease of vessels [5]

Adipose tissues synthesize and secrete some proteins which are known as adipokines and these include Visfatin, leptin, adiponectin, resistin and many others. Role of adipokines is well established in inflammation [6] Atherosclerotic lesions have been also reported to express these adipokines[7,8]

Visfatin is a newly identified adipokine having high expression in visceral adipocyte. Macrophages of adipose tissue are principle source. It has a molecular weight of 52 kDa and its gene encodes 491 aminoacids. Structurally it is similar to pre-B cell colony-enhancing factor (PBEF) It is widely distributed in bone marrow, liver, spleen, pancreas, heart, kidneys, thymus gland and other tissues. Visfatin is reported to be associated with endothelial dysfunction, atherosclerosis, plaque rupture and the metabolism of glucose and lipid [9, 10, 11, and 12]. However positive correlation has been found between the expression of visfatin and coronary atherosclerosis [13]

MATERIALS AND METHODS

Subjects: A total of 80 subjects aged in between 40-55 years were included in the study who were advised for angiography by the consultant cardiologist for their preliminary diagnosis of CAD. Before angiography detailed history was taken and patients with other cardiovascular diseases, and endocrinological disorders were excluded from the study.

All participants underwent detailed physical examination including measurement of height and weight with standard methods. The study was approved by ethical committee of Ziauddin University. All the participants were explained about the study and they gave written informed consent.

Sampling and assay: Blood samples were obtained by venipuncture at the time of angiography and then centrifuged at 3000rpm for 5 minutes within 20 minutes of its collection and stored at - 70ºC for its future use. Serum visfatin levels were determined by commercially available ELISA kit (Pheonix Pharmaceuticals, Belmont,CA,USA)

Angiography: Angiography was performed on TOSHIBA infinix 2000A. Coronary guide wires were selected while keeping in mind the anatomy and morphology of coronary lesion.

Statistical Analysis: Statistical analysis was performed by using SPSS (Statistical program for social sciences) version 17. Continuous response variables like age, height, weight, BMI, waist circumference, hip circumference, waist hip ratio, and serum visfatin levels were presented by standard error of mean (**s.e.m**) and ANOVA was performed to compare mean level among four study groups according to extent of CAD. Regression analysis was done to estimate relationship of serum levels of visfatin with the extent of CAD. Statistical significance was considered if $p \leq 0.05$.

RESULTS

80 Study participants were subdivided into four study groups that is non significant disease group (Subjects whose coronary arteries are <50 % occluded and this group was considered as controls), single vessel disease group, two vessel disease group and three vessel disease group.

Table No. 1: Physical characteristics of patients with multivessel Coronary artery disease(CAD) Values are expressed as mean and standard error of mean (s.e.m)

	Non Significant (n=14)	One vessel CAD (n=30)	Two vessels CAD (n=12)	Three vessels CAD (n=24)
Age (years)	47.43±1.57	49.13±1.21	49.25±1.51	49.00±1.30
Height (m)	1.61±0.02	1.62±0.01	1.71±0.02	1.65±0.01
Weight (kg)	70.14±3.75	71.77±1.39	77.58±2.51	74.71±1.55
BMI (kg/ m^2)	26.84±1.34	27.15±0.71	26.30±0.54	28.03±0.49
Waist circumference(cm)	85.64±1.53	90.13±1.09	92.67±2.35	94.88±1.29
Hip circumference(cm)	89.50±1.79	91.83±1.33	90.67±1.71	89.29±0.95
Waist hip ratio	0.94±0.01	0.98±0.01	1.06±0.01	1.07±0.01

Table No.2: Serum Visfatin levels in multivesssel Coronary Artery Disease. Values are expressed as mean and standard error of mean (s.e.m).No: of cases are given in parenthesis.

Study Groups	Serum Visfatin Levels (ng/ml)
Non Significant Disease (n=14)	4.55 ± 1.10
Single Vessel Disease (n=30)	4.86 ± 0.93
Two Vessels Disease (n=12)	5.53 ± 0.79
Three Vessels Disease (n=24)	5.82 ± 0.58

Out of 80 study subjects, 30 (37.5%) had one vessel, 12 (15%) had two vessels, 24 (30%)
had three vessels CAD and 14 (17.5%) had non significant disease. (Figure 1)
Overall mean age of subjects was 48.8±6.1. Significant effect of larger waist
Circumference and waist hip ratio ($p<0.001$) was observed. (Table 1)

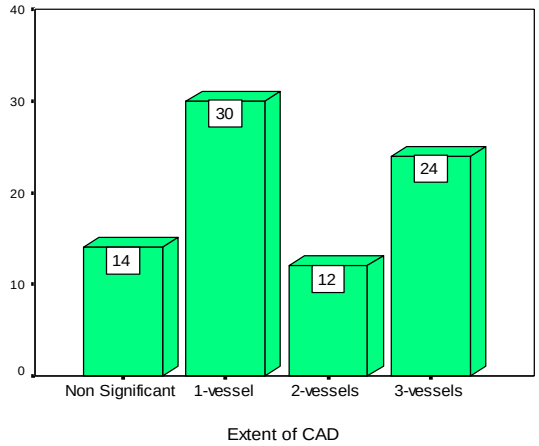

Figure 1: **Pattern of extent of CAD.**

Table -2 shows plasma levels of visfatin in multivessels coronary artery disease. Mean serum visfatin levels were statistically non-significant in all four study groups. Visfatin levels were higher in three vessel disease when compared with non significant group, single vessel disease and two vessels disease.

Moreover, statistically non significant (p value <0.176) positive correlation exists between serum visfatin and extent of CAD (r = 0.153) (Figure-2).

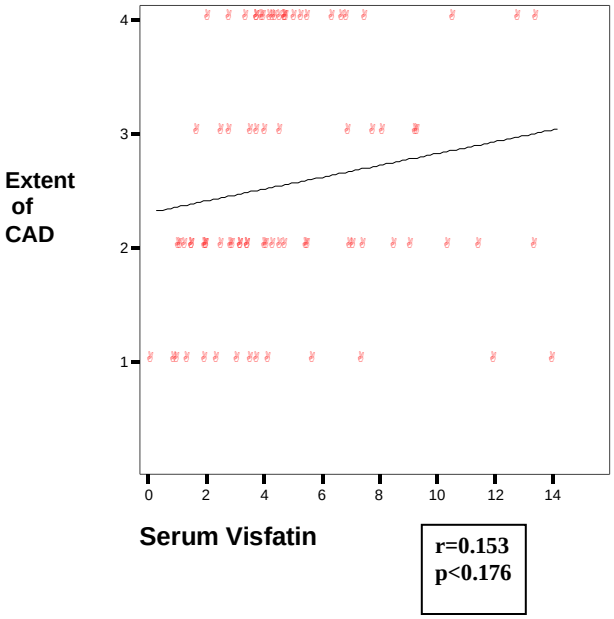

Figure-2: Correlation graph of serum visfatin with the extent of CAD.

DISCUSSION

Adipose tissues are no longer considered as fat store depot but they are recognized as a functional endocrine organ which releases numerous bioactive peptides knows as adipokines. These factors are not only active in adipose tissues but can circulate in blood reaches to distant sites and elicit their biological effects in the regulation of food and energy metabolism, insulin sensitivity, inflammation and vascular homeostasis[14,15] Visafatin is a newly found novel adipokine which is expressed in visceral fat. Obesity and type 2 diabetes mellitus are reported to be associated with high plasma visfatin levels. Visfatin is highly expressed in macrophages within human unstable atherosclerotic lesions, and has been proposed to potentially play roles in atherosclerotic plaque destabilization[16].

Fu et al. 2009 reported significantly higher plasma visfatin levels in CAD patients in Chinese population when compared with the controls and suggested plasma visfatin as a helpful marker of early CAD [17] In another study byYu Qin et al, 2010 demonstrated significantly higher levels of visfatin in obese CAD patients as compared with the controls [18] Kadogluo et al, 2011 also reported significantly high visfatin and hsCRP levels in CAD patients in Greece population [19]

To the best of our knowledge no such study has been carried out in Pakistan which can relate plasma visfatin levels with atherosclerosis and coronary lesions. In our study we demonstrated plasma visfatin levels with the extent of CAD in group of Pakisatni population.

Our findings are not consistent with the data that has been already published. Furthermore our results shows gradual rise of serum visfatin levels in all the four study groups when compared with the number of coronary arteries involved but this gradual rise is statistically non-significant in all four study groups. These findings are consistent with the data presented by Choi et al,2008[20], in which he compared serum lipocalin-2 and visfatin levels in patients of CHD and he concluded that circulating lipocalin-2 levels were significantly higher in patients with CHD compared with the control subjects (82.6±38.7 ng/ml versus 43.8±27.8 ng/ml; P<0.001). However, visfatin levels were not significantly different between patients with CHD and control subjects.

CONCLUSION

Visfatin levels increases in three vessel disease compared with two and single vessel disease but is nonsignificant. However positive correlation exists between visfatin and extent of CAD but is also nonsignificant.

Study on large scale may provide some significant results.

Limitation of the Study: Sample size was small due to budget constraints.

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Address for Corresponding Author:
Dr. Muhammad Kashif Nisar,
Lecturer of Biochemistry
Jinnah Medical and Dental College, Karachi.
drkashif2003@yahoo.com
Cell No.0321-2318813

Original Article

Relationship Between Diagnostic Delay and Stage of Disease in Oral Cancer Patients

1. Afsheen Maqsood 2. Mirza Mohammad Shakir 3. Anwar Ali 4. Yasmin Hashim

1. Lecturer of Oral Pathology 2. Asstt. Prof. of Oral Surgery 3. Assoc. Prof. of Oral Surgery 4. Dr.Ishrat-ul-Ebad Institute of Oral Health Sciences, Karachi 4. Asstt. Prof. of Pathology, Sindh Medical College, Karachi.

ABSTRACT

Background: In spite of the belief that cancer mortality can be reduced if lesions are detected, diagnosed and treated at an early stage. There is a concurrent increase in advanced head and neck cancer patients, because of delayed in medical consultations.

Objectives: The objective of this study is to determine an association of staging and diagnostic delay in oral cancer patients.

Study Design: Descriptive study.

Place and Duration of Study: This study was conducted at the Dow Diagnostic & Research Laboratory (DDRL) of the Ojha Campus, Dow University of Health Sciences from Jan 2009 to April 2011.

Materials and Methods: The information is collected from the record files of DDRL of OJHA campus DUHS. Two hundred and seventy nine patients with an oral cancer are included in the study.

Results: With descriptive statistics, OSCC is mostly found at 4^{th}, 5^{th} and 6^{th} decades of life, with diagnostic delay of $\geq$ 6 months. OSCC is mostly seen in males than in females whereas; Well differentiated squamous cell carcinoma is a common finding in both males and females, with the largest lesion being size 12 cm in size. Buccal mucosa is a commonly affected site in both genders. OSCC is mostly seen in males than in females.

Conclusion: Our findings highlight the importance of early detection and systemized collection of patients verbal statements regarding their initial symptoms of oral cancer.

Key Words: Oral cancer; Diagnostic Delay; Early detection.

INTRODUCTION

Squamous cell carcinoma (SCC) accounts for more than 90% of all malignancies affecting the oro-facial regions. High level of 5-year survival rate upto 80% is investigated when diagnosed in early stages, and comparatively 60% survival rate in metastatic lesions. The advantage of early diagnosis not only increases the survival rate but also enhances the sufferer quality of life by induction of less destructive, damaging and disfiguring interventions.[1]. Advanced oral cancers are mostly due to delay in diagnosis. Inherent alterations in tumor and time interval are the two established causes. Cancers in oral cavity may be symptom less at the initial stages.[2] About 40% patients with oral cancer presented with stage 3 and stage 4.[1] The delay was due to patients rather than clinician delay. Patients either delayed looking for support and start self-remedies and discuss their symptoms to family or friends.[3] Investigators around the globe showed poor prognosis of cancer in young individual than old patients. Younger ones should be positively predisposed by community awareness.[4] Last twenty years has seen increased occurrence of advanced stage cancer in oral cavity has been observed.[3] Extensive management is required in advanced stage oral cancer which increases morbidity and mortality after intervention. A delay in pursuing care could partly be described by tumor associated reasons such as the location of the tumor and the nature of symptom experienced by the patients. In addition, socio-demographic variables, such as socioeconomic class were found to effect patient delay.[5] Current cancer Strategies and a general review have highlighted the matter of fast recommendation and the cancer delay group. Llewellyn et al. [4] stated instructive stages and low socioeconomic position are responsible for late pursuing a medical consultation. Scott et al. similarly establish that low socioeconomic status groups notices oral cancer mostly in an advanced stage[6]. However, resourceful screening by general dentist the most rational group to screen for oral cancer is a substantial step frontward in the efforts to decrease morbidity and mortality causing from oral cancers. Diagnostic delays in oral cancer have been categorized as ‘‘patient delay’’ or ‘‘delay by patients’’ (the period between the patient with initial appointment to a medical consultant concerning a symptom), and ‘‘provider/professional delay’’ or ‘‘delay by the clinicians’’ (the period from the patients with initial appointment to a medical consultant and the final pathological opinion).[7] Continuity of care depends upon the communication among providers furnished by the dental record, particularly in settings where several practitioners are providing care for the individual patient. It has also been recognized that the maintenance of complete and accurate records is a prerequisite for the assessment of the quality of care delivered, and such records provide a basis for the evaluation of the outcome of treatment. The problem of the validity of the medical history recorded in the dental

record has been documented, and indications of other dental record deficiencies have been noted[12]. *The principal goal of the present study is to inspect the delay in diagnosis and severity of oral cancer to govern which justification is satisfactory.

MATERIALS AND METHODS

The samples were collected from the archive of the Dow Diagnostic & Research Laboratory (DDRL) of the Ojha Campus, Dow University of Health Sciences. All patients were investigated in a retrospective manner by an extensive chart review. Sex, Age, Location, Tumor size, Delay in diagnosis were compared and then they were analyzed to those in the existing literature. The data was collected from the year Jan 2009 to April 2011 from the files of histopathology division. Total of 279 oral squamous cell carcinoma cases were included in this study. Malignant tumors were classified through TNM staging

All OSCC patients from the medical record of DDRL of both sex and all age groups were included in the study. Cases were excluded when the patient file is not located and when information is lacking in the file.

The data was analyzed by SPSS version 16. Descriptive and cross tabs statistics were used to investigate the patients age, sex, tumor site, diagnosis and diagnostic delay and their factors were compared with previous studies.

RESULTS

Two hundred and seventy nine patients were selected from the record of DDRL (Dow Diagnostic and Research Lab) Ojha campus. 54 (18.0%) cases experienced a diagnostic delay. Among 279, 246 (82%) have no data of diagnostic delay recorded.

Table No.1 Diagnostic delay in Months

Diagnostic delay in months	1	2	3	4	5	6	7	8	10	12	18	24	48	Total
Well differentiated Squamous cell carcinoma	01	04	06	02	00	08	01	03	03	04	01	01	01	35 Cases
Moderately differentiated squamous cell carcinoma	01	02	00	04	01	01	00	00	00	03	01	01	00	14 Cases
Poorly differentiated squamous cell carcinoma	00	01	00	00	01	01	00	00	00	02	00	00	00	05 Cases
Total no of cases	02	07	06	06	02	10	01	03	03	09	02	02	01	54

Table No.2: Diagnostic delay in moths correlated with gender

Diagnostic delay in months	Male	Female	Total
1 month	1	1	2
2 months	3	4	7
3 months	4	2	6
4 months	4	2	6
5 months	1	1	2
6 months	6	4	10
7 months	0	1	1
8 months	1	2	3
10 months	3	0	3
1 year	5	4	9
1.5 year	2	0	2
2 years	1	1	2
4 years	0	1	1
Total	31	23	54

One seventy seven (177) patients were male and one hundred and two (102) patients were female. In males 31 cases have diagnostic delay with most common of 6 months to 1 year delay. In females 23 cases have diagnostic delay with common of 2 months, 6 months and 1 year delay. The most common site of tumors in both males and females was buccal mucosa with total of 103 and 39 cases respectively. Well differentiated squamous cell carcinoma was a common diagnosis in both males and females have accounting for 118 and 70 cases respectively, whereas moderately differentiated SCC were 49 and 22 cases respectively, and poorly differentiated SCC was diagnosed in 5 and 7 cases respectively, verrucous carcinoma have seen in 4 cases only in males and schwanoma has seen 1 case in females only. Mild dysplasia was discernable have in 1 and 2 cases in males and females respectively.

Table No.3: Descriptive analysis of diagnosed cases

Diagnosis	Mean	N	Std. Deviation
well differentiated squamous cell carcinoma	6.2340	188	6.14169
moderately differen-tiated squamous cell carcinoma	5.8732	71	6.48940
poorly differentiated squamous cell carcinoma	6.0833	12	7.41569
Schwanoma	8.0000	1	.
verrucous carcinoma	4.5000	4	4.12311
mild dysplastic	14.6667	3	3.05505
Total	6.2079	279	6.26568

Diagnostic delay was commonly found at 40 years of age. Among them 6 months delay is common. Well differentiated SCC is mostly commonly seen with diagnostic delay and maximum tumor size was 12 cm. Most commonly OSCC was found at 4th, 5th and 6th decades of life.

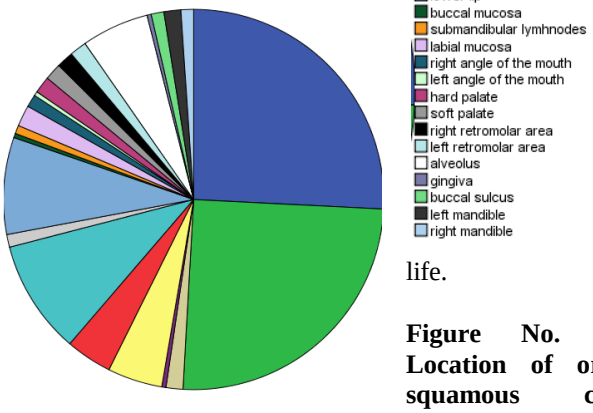

Figure No. 1: Location of oral squamous cell carcinoma

DISCUSSION

Diagnostic delay of head and neck cancers comprises of delay by the patient itself and delay by the professional to provide an ultimate diagnosis.[8]

Two hundred and seventy nine patients are selected from the record, among them fifty-four patients(19.3%) of OSCC with diagnostic delay are enlisted in the study. Patients with large tumors had less specialist delay than those with small tumors.[9] In current years, modern, sophisticated tools were used for finding of mechanisms responsible for growth of oral malignancies; but the role of general dental practioner is of paramount importance in initial detection of oral cancer. Both patient reluctance and lack of general dental practioner vigilance are classically responsible for delayed detection of oral malignancies. Scott and colleagues; found OSCC in upto 30% of patients with delayed pursuing professional advice. Poor understanding of treatment and fear of cancer was the two main factors involved. Hence, before looking professional advice, patients mostly start self-medication and limits their communication with nearby relatives.[1,14] Men were at higher risk of having aggressive tumor when compared to women. However, early stage tumor was higher in females as reported earlier. In our sample, males are more commonly affected than females. Age at diagnosis was not associated with stage of oral cancer, Diagnostic delay is commonly found at 40 years of age and most commonly OSCC is found at 5th and 6th decades of life. Age and gender are not establish to be prognostic, consistent with previous finding.[2] Women reported longer evolution time than men which is in agreement with other studies. Taking into account gender differences are detected in this sample.[11]

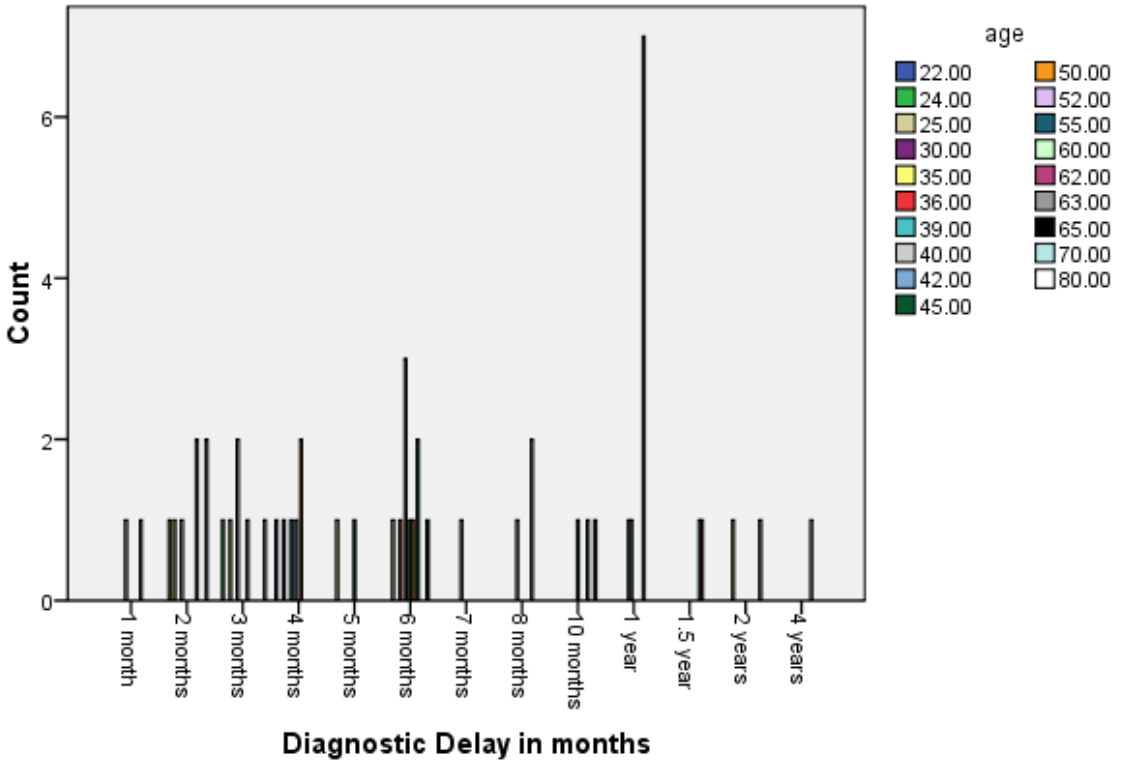

Figure No. 2: Showing diagnostic delay in months correlated with age

Tumors situated in the posterior area of the mouth have been remarked late.[6,18,19] This statement is approved by our study that buccal mucosa is a most common site affected in both genders. No substantial relationship among the age, gender, alcohol abuse, tumor site and patient delay is shown by researchers.[8] In our society, females do not generally practice the potential risk habits such as tobacco smoking whereas these habits are common in males. Common risk behavior in females particularly in the rural area is betel quid chewing. The habit is usually started at a young age[13].

Larger size oral malignancies were detected prior than reduced size lesions. Our study has shown that OSCC ranges from 0.09 to 12 cm, with the diagnosis of well differentiated OSCC. In patients with reduced size tumors, the delay in diagnosis is associated with professional delay, other studies shown that there was no remarkable relationship among tumor size and diagnostic delay.[8] The absence of significant association between age and specialist delay in our study is consistent with the findings from other studies. Neither education nor sex was associated with specialist delay.[9] Wildt *et al.* found a significant positive correlation between older age and increased professional delay.[10]

Conversely, studies from united states investigated that general dental practioner are not skilled about oral cancer detection and avoidance.[4,15,16] Consultation postponed by the patient due to their reluctance for more than 3 months is associated with delay by patients.[5,17] In this retrospective study there are problems of incomplete Data. Detailed clinico-pathologic information need to be recorded. The incomplete files could be upgraded by eventual assessment. Guggenheimer, 1989 stated that oral carcinoma were asymptomatic initially and their signs are mostly misunderstood as other dental problems. Other studies highlighted a factor of deprivation. Due to low socioeconomic status, people are less liable to observe oral cancer in its initial stages and delay pursuing health care consultation.[6,20]Another potential problem is the validity of the crucial delay data which is largely dependent upon subject recall.[10] Because of the retrospective design we cannot make associations between history, examination, sign and symptoms.

The percentage of patient delay of more than 6 months in the present study is nearly equal to that reported in UK by Cooke and Taper- Jones. It has been observed that access to treatment in a public hospital is often delayed and it cannot be attributed only to the patient.[11] As oral cancer patients liked to discuss their symptoms to nearby relatives therefore general public education is beneficial. They need to be helped and educated patient for early consultant advice. The majority would advise earlier for oral cancer if they had been prior educated.[3] Stress and tobacco smoking may be accountable for longer diagnostic delay.[4] Our results shows that diagnostic delay is severely blamed for head and neck cancer patients, and proper history record of first recognition of symptoms is not optimal. It is our duty that the recording of clinical stages will should be undertaken at the first hospital appointment and make cancer registry.

Limitations: The limitation of the study is improper analysis of diagnostic delaying, due to consultant invagiliance.

The regularity of patients dental attendance, was not an inclusion criteria in the present study.

In the study, duration of delay in diagnosis cannot be clearly defining weather it was due to patient or professional delay. The data is retrospective, therefore it was difficult to contact patients and gather information about the symptoms first noticed.

CONCLUSION

The association between staging and duration of delaying in early diagnosis is hampered due to aggressive behavior of oral cancer. In this research there is no association existing between duration of diagnostic delay and advanced stage of oral cancer due to complex clinical behavior, some tumors remain silent until they get advanced. We recommend that professionals must improve approaches to entice and reassure patients to go through routine dental checkup. Finally highlighting on self-examination for early oral lesions can similarly attain certain achievement. However further analysis would be necessary, as present consideration of diagnostic delay in oral squamous cell carcinoma is unsatisfactory.

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Address for Corresponding Author
Dr. Mirza M. Shakir
E-Mail m.shakir@duhs.edu.pk
Address 130/3, P Street Khayaban-e-Sehr
Phase-VII Dha Karachi

Original Article

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

1. Faiza Hasan 2. Rahila Najam 3. Kamran Asadullah

1: Asstt. Prof. of Pharmacology, Sir Syed College of Medical Sciences for Girls, Karachi 2. Assoc. Prof. of Pharmacology University of Karachi 3: PG Student MDS, Dept. of Oral Biology, Dow University of Health Sciences, Karachi.

ABSTRACT

Objective: The purpose of this study was to assess the in vitro antimicrobial activity of calcium hydroxide associated with aqueous 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 Sept. 2007 to March 2009.

Materials and Methods: The microbial strains were evaluated against calcium hydroxide pastes prepared with calcium hydroxide powder mixed with aqueous vehicles. Antimicrobial activity of the vehicles was also evaluated. For such purpose agar diffusion and broth dilution method was used.

Results: The results showed that calcium hydroxide mixed with aqueous vehicles was inhibitory against all the microbial strain tested. Calcium hydroxide pastes also eliminated the Enterococcus faecalis (the most resistant organisms in infected root canals) effectively. The results are statistically significant when calcium hydroxide was mixed with aqueous vehicles ($p<0.05$).

Conclusion: We concluded from our study that aqueous vehicles play a very important role in eliminating the endodontic bacteria particularly Enterococcus faecalis which is very challenging for the endodontists while treating the patient.

Key Words: Calcium Hydroxide, Aqueous Vehicles, Route Canal Treatment

INTRODUCTION

Root canal therapy plays a vital role in the line of dental treatment. Root canal therapy consists of proper cleaning, shaping, irrigation and obturation of root canals which results in the reduction or elimination of bacteria.[1] However, complete elimination of bacteria is very difficult to achieve in clinical practice due to the anatomical complexities of root canals such as accessory canals, canal ramifications, apical deltas, fins and transverse anasmastos.[2, 3] The inter-appointment intra-canal medication is common during root canal treatment procedures to eliminate the bacteria from infected root canals.[4, 5, 6] The application of the medicament is usually common in those cases where there is pain or continuing exudates. Calcium hydroxide was originally introduced in dentistry by Hermann in 1920 and since then it is used widely in dental treatment throughout the world particularly in root canal treatment. The antibacterial effects of calcium hydroxide are due to the damage to the microbial cytoplasmic membrane by the direct action of hydroxyl ions. The hydroxyl ions induce lipid per oxidation that results in the destruction of phospholipids and structural components of the cellular membrane. The alkaline pH of calcium hydroxide is also responsible for the breakdown of ionic bond which maintains the protein structure of the bacterial cell membrane. Hydroxyl ions also react with the bacterial DNA results in the inhibition of DNA replication by splitting the strands of DNA. Availability of calcium ions at the site of action also exerts therapeutic effects through ion channels. 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.[7, 8]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 aqueous 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:

- Distilled water
- Saline
- Anesthetic solution (3%Mepivacaine hydrochloride, used in dentistry)

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 spectrophotometrically to match the turbidity of 0.5 McFarland scale.
- Glass flasks containing 50 ml of BHI agar at 46^0C 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 37^0C 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 spectrophoto-metrically 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 37^0C 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 associated with aqueous 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 + distilled water (21.666mm), calcium hydroxide + anesthetic solution (21mm), calcium hydroxide + saline (20.833mm). Data analyzed by one-way ANOVA (df = 8, 45) showed that calcium hydroxide combined with vehicles had a significant effect on tested microorganisms ($p < 0.05$).

Table 2 shows that the aqueous vehicles such as distilled water, saline, anesthetic solution, had no antimicrobial action except on *Escherichia coli* on which anesthetic solution showed smaller inhibition zones of microbial growth of 3.333 mm.

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

$Ca(OH)_2$ + Vehicles	Candida albicans	Bacillus subtalis	Staphlyococcus aureus	Enterococcus faecalis	Sterptococcus mutans	Escherichia coli	Mean
Distilled Water	23	22	21	22	18	24	21.666
Saline	21	20	21	21	19	23	20.833
Anesthetic Solution	22	22	22	22	16	22	21

$Ca(OH)_2$: Calcium Hydroxide

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

Vehicles	Candida albicans	Bacillus subtalis	Staphlyococcus aureus	Enterococcus faecalis	Sterptococcus mutans	Escherichia coli	Mean
Distilled Water	0	0	0	0	0	0	0
Saline	0	0	0	0	0	0	0
Anesthetic Solution	0	0	0	0	0	20	3.333

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

	Distilled water			Saline			Anesthetic solution		
	Mean (mm)	St.dev	p	Mean (mm)	St.dev	p	Mean (mm)	St.dev	p
Calcium hydroxide + aqueous vehicles	21.67	2.07	0.00	20.83	1.33	0.00	21.00	2.45	0.004
Aqueous Vehicles	0.167	0.408		0.167	0.408		3.33	8.16	

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

$Ca(OH)_2$ + Vehicles	Candida albicans	Bacillus subtalis	Staphlyococcus aureus	Enterococcus faecalis	Sterptococcus mutans	Escherichia coli
Distilled Water	N.G	N.G	N.G	N.G	N.G	N.G
Saline	N.G	N.G	N.G	N.G	N.G	N.G
Anesthetic Solution	N.G	N.G	N.G	N.G	N.G	N.G

$Ca(OH)_2$: Calcium Hydroxide

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

Vehicles	Candida albicans	Bacillus subtalis	Staphlyococcus aureus	Enterococcus faecalis	Sterptococcus mutans	Escherichia coli
Distilled Water	Gr	Gr	Gr	Gr	Gr	Gr
Saline	Gr	Gr	Gr	Gr	Gr	Gr
Anesthetic Solution	N.G	N.G	N.G	N.G	N.G	N.G

Gr: Growth, N.G: No growth

Table 3 shows the comparison of calcium hydroxide pastes with aqueous vehicles against aqueous vehicles alone. According to Newman-Keuls test the results are statistically significant when calcium hydroxide mixed with aqueous vehicles: ($Ca(OH)_2$ + distilled water, $p = 0.00$), ($Ca(OH)_2$ + saline, $p = 0.00$), ($Ca(OH)_2$ + anesthetic solution, $p = 0.004$) ($p < 0.05$).

Table 4 shows that when calcium hydroxide mixed with vehicle it showed no growth of bacteria and the broth appeared transparent as compared to the broth that was turbid containing bacteria. The above table

proved that calcium hydroxide is an excellent antibacterial agent against all microorganisms tested.

Table 5 shows that when only vehicles were mixed in to the test tubes containing bacteria it showed growth in case of distilled water, saline, and the broth was turbid due to the presence of bacteria where as in anesthetic solution the broth appeared transparent.

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]

The aqueous vehicles promote a high degree of solubility when the paste remains in direct contact with the tissue and tissue fluids, rendering it solubilized and resorbed by macrophages. Hence from clinical point of view the root canal must be redressed several times until the desired effect is achieved.[17]

The results of this study suggests that among different vehicles when calcium hydroxide was mixed with distilled water then we observed the largest mean values against all microorganisms tested followed by anesthetic solution and saline. Thus, our study verifies that the use of calcium hydroxide with water is effective in eliminating the bacteria from the infected root canal in endodontic treatment in the first 24 hours as observed also by Ballal et al[19] in 2007. Whereas when vehicles were used as controls, only anesthetic solution showed some antimicrobial activity against *Escherichia coli* as indicted by Pelz et al.[20] and Gocmen et al.[21] in 2008. When calcium hydroxide was mixed with aqueous vehicles then the result was statistically significant ($p < 0.05$).

CONCLUSION

The present study confirmed the in vitro antimicrobial activity of calcium hydroxide associated with aqueous vehicles, and have shown to be effective ones ($p < 0.05$). The significant finding of our study is that Enterococcus faecalis the most resistant microorganism in infected root canals as observed by Ferrari et al.[22] and Pirani et al.[23] also showed good zones of inhibition against the tested paste of calcium hydroxide.

The first step in a study of the effectiveness of intra-canal medicament is the laboratory test. In vitro research to determine the antimicrobial activity depends on the sensitivity of the drug, bacterial source (wild strains or collection species), number of bacteria inoculated, pH of the substrates in plates or tubes, agar viscosity, storage conditions of the agar plates, incubation time and the metabolic activity of the microorganisms. However, in vitro results must be analyzed carefully before their extrapolation to clinical conditions.

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Address for Corresponding Author:
Dr, Faiza Hasan,
Asstt. Prof. of Pharmacology,
Sir Syed College of Medical Sciences for Girls,
Karachi
Cell No.0302-2842608

Original Article

Early Removal of 3 Way Foleys Catheter after Transurethral Resection of Prostate is Beneficial?

1. Javed Altaf Jat 2. Shafique-ur-Rehman Memon 3. Jai Pal Paryani 4. Muhammad Shahzad Laghari 5. Atif Jawed Bhatti

1: Sen. Registrar of Urology 2. Prof. of Urology 3. Asstt. Prof. of Urology 4. Prof. of Urology 5. Resident Urology Dept. Liaquat University of Medical & Health Sciences Jamshoro

ABSTRACT

Objective: To compare the outcome of three way foleys catheter removed on 2nd and 5th day after Transurethral resection of Prostate for BPH regarding postoperative retention of urine , urine culture and hospital stay.

Study Design: Quasi Experimental study.

Place and Duration of Study: This study was carried out in Department of Urology, University of Medical & health sciences Jamshoro from from July 2010 to December 2011.

Materials & Methods: This study consisted of 50 patients were divided in two groups. Group A for catheter was removed on 2nd post operative day of Trans Uretheral resection of prostate and group B for catheter was removed on 5th Post Operative Day of Trans Uretheral resection of prostate, each group consist of 25 patients.Detailed History was taken from all the patients with special regard to the urinary retention. Inclusion criteria were that all diagnosed as case of BPH on the basis of history and investigations. Exclusion criteria included unfit patients for general anesthesia, presented with chronic urinary retention, hematological disorders, pre operative infected urine and concurrent uretheral stricture.

Results: Re-catheterization were in 2 patients (8%) group A and 1 patient (4%) in group B. Post operative urine culture growth of organism (bacteriuria) were 1 patient (4%) in group A and 3 patients (12%) in group B. Duration of hospital stay in group A was 5.68 days as compared to the patients in group B was 8.44 days.

Conclusion: In conclusion, early catheter removal had a dramatic impact on hospital stay. Catheters can be removed early after transurethral resection of prostate with no increase in morbidity and maintain the efficacy of the procedure, resulting in considerable savings to their patients. Our study confirms the safety of an irrigation-free and early catheter removal policy after TURP.

Key Words: Benign prostatic hyperplasia, 3 way foleys catheter, transurethral resection of prostate.

INTRODUCTION

Benign prostatic hyperplasia (BPH) is the most common urological disease of old age[1]. About half of the male population over the age of 50 can be diagnosed with histological BPH, and this prevalence increases with age to about 90% over the age of 80 [2]. Histological BPH leads to anatomical changes in prostate, causing bladder outlet obstruction and secondary physiological and anatomical changes in bladder and in tissue causing symptoms, which then impairs health status [3]. There are various procedures for the management of benign prostatic hyperplasia but transurethral resection of prostate is considered the gold standard and is the most commonly performed procedure in developed world [4,5]. Symptoms of BPE are hesitancy, decreased force and caliber of stream, sensation of incomplete bladder emptying, double voiding, straining to urinate, dribbling and irritative symptoms include urgency, frequency and nocturia [6]. Various modes of treatment for BPH are available i.e. watchful waiting , medical (i.e. drugs like alpha adrenargic blockers, 5 alpha reductase inhibitors are being considered as alternative to surgery), surgical (conventional), and endourological methods like transurethral resection, transurethral incision of prostate[7]. Catheter related urinary tract infection accounts for 40% of nosocomial infections, urinary tract infection is the complication of long-term urinary catheterization [8]. Catheterization increases the risk for urinary tract infection. A single catheterization is associated with upto 5% infection rate, and if the catheter remains in place, there is a 5% increase per catheter day in the rate of associated infection [9]. E.coli is the major cause of catheter associated urinary tract infection and the most common nosocomial pathogen. Urethral meatal flora is an important source of bacteriuria, the likelihood of which increases with the duration of catheterization. It is suggested that the density, but not the prevalence of meatal colonization by potentially pathogenic bacteria is a risk factor for catheter associated bacteriuria [10]. Catheterization during transurethral resection of prostate can cause severe infective disorders, that is, urinary tract infection, bacteriuria, septicemia, epididymitis and urethral strictures[11]. This study is aimed to see whether early catheter removal has any bad outcome as still controversy is presented in available literature.

MATERIALS AND METHODS

This study was conducted at department of urology, Liaquat University of Medical & Health Sciences,

Jamshoro from July 2010 to December 2011. This study consisted of 50 patients were divided in two groups. Group A for catheter was removed on 2nd post operative day of Trans Uretheral resection of prostate and group B for catheter was removed on 5th Post Operative Day of Trans Uretheral resection of prostate, each group consist of 25 patients admitted through the outpatient department, as well as from casualty department of Liaquat University Hospital Jamshoro/Hyderabad. Detailed History was taken from all the patients with special regard to the urinary retention. Inclusion criteria were that all patients after counseling for study and taking voluntary consent and diagnosed as case of BPH on the basis of history and investigations. Exclusion criteria included unfit patients for general anesthesia, presented with chronic urinary retention, hematological disorders, pre operative infected urine and concurrent uretheral stricture.Data was analyzed through SPSS software.

RESULTS

In our study, we compared the results in both the groups regarding the number of patient who underwent retention of urine followed by re-catheterization after removal of 3 way Foley's catheter after 2nd and 5th post transurethral resection of prostate. In group A, 2 patients (8%) went into the retention of urine after removal of Foley's catheter and eventually they require re-catheterization as compared 1 patient (4%) in group B went into the retention of urine and require re-catheterization (Chart No.1).

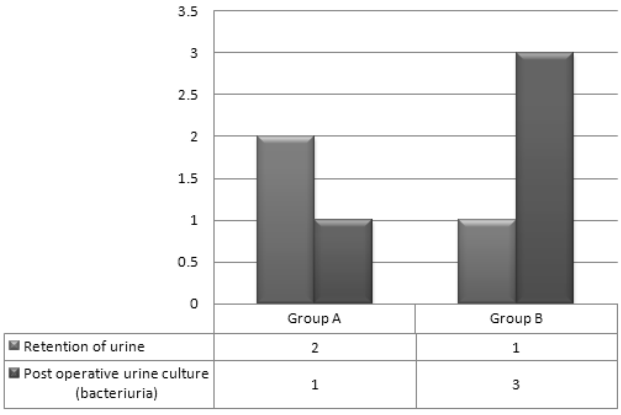

Chart No.1: Comparison of two groups

Retention of urine in both groups were compared by Chi- Square test. A high significance P- value = 0.552 of Chi- test indicates that there is no relationship between groups and retention of urine variables. Post operative urine culture group A, 1 patient (4%) out of 25 patients had positive urine culture growth of organism (bacteriuria), as compared to group B, 3 (12%) patients out of 25 patients had positive urine culture growth of organism (bacteriuria) (Chart No.1). A positive urine culture in two groups is compared by Chi-square test. A high significance P- value = 0.297 of Chi- test indicates that there is no relationship between group and positive urine culture variables. Duration of hospital stay in group A was 5.68 days as compared to the patients in group B was 8.44 days. Compare the means of the duration of hospital stay of the patients of two groups, a low significance value (P- value <0.001).

DISCUSSION

The duration of Foley's catheter drainage after transurethral resection of prostate varies amongst surgeons. In our study 2 patients (8%) out of 25 patients went into retention of urine followed by re-catheterization in group A, as compared to 1 patient (4%) went into retention of urine followed by re-catheterization in group B. In study which was conducted by Koh KBH in which 30 patients whose catheter was removed on 2nd post transurethral resection of prostate [12]. Only 3 patients went into retention of urine followed by re- catheterization. In another study conducted by Dodds et al. in which 41 patients whose catheter was removed on 2nd post operative day of transurethral resection of prostate, 7/41 that 14% of the patients went into retention of urine followed by re-catheterization [13].

In our study only 1 patient in group A had positive urine culture after removal of 3 way Foley's catheter on the 2nd post operative day of transurethral resection of prostate as compared to group B in which only 3 patients had positive urine culture. In the study of Agarwal SK in which 83 patients were included and their 3 way Foley's catheter was removed in 24 hrs shows that only 2 patients have positive urine culture and finally in discussion of his study he stated that the early removal may reduce the incidence of urinary infection, catheter related dysuria and possible urethral stricture formation [14].

Early catheter removal have significant impact on overall duration of hospital stay, as proved in our study with mean of 5.68 days in group A as compare to 8.44 days in group B. However in the study of Bhagia SD reported catheter was removed post operatively TURP at day 2 in 12 patients, at day 3 in 19 patients, day 4 in 3 patients, day 5 in 1 patient, day 6 in 7 patients, day 7 in 7 patients, day 8 in 4 patients, day 9 in 1 patient, day 10 in 4 patients and day 12 in 2 patients and the duration of hospital stay depends upon catheter removed [15]. Some other international studies reported catheter removal following transurethral resection of the prostate is variable, ranging from 24 hours [16] to 5 days[17].

CONCLUSION

In conclusion, early catheter removal had a dramatic impact on hospital stay. Urologist can be reassured that catheters can be removed early after transurethral resection of prostate with no increase in morbidity and

maintain the efficacy of the procedure, resulting in considerable savings to their patients. Our study confirms the safety of an irrigation-free and early catheter removal policy after TURP.

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Address for Corresponding Author:
Dr. Shafique-Ur-Rehman Memon
House No. P-9, Diplai Memon Housing Society
Behind Rajputana Hospital Hyderabad Sindh.
Cell: 0300-3018112

Original Article

Frequency of Congenital Anamolies in Polyhydramnios

1. Bushra Haq 2. Wajid Ali 3. Shahid Shoukat Malik

1. Sen. Registrar of Gynae Unit II, KEMU / Lady Willingdon Hospital, Lahore 2. Sen. Registrar of Radiology, KEMU / Mayo Hospital, Lahore 3. Asstt. Prof. of Community Medicine / Biostat. IPH, Lahore.

ABSTRACT

Abstract: Polyhydramnios is a relatively uncommon but distressing complication associated with pregnancy.
Objective: To find frequency of congenital anomalies with increasing severity of polyhydramnios.
Study Design: Prospective Study.
Place and Duration of Study: This study was conducted in Lady Willingdon Hospital, Lahore from July 2009 to June 2011.
Materials and Methods: Total 170 diagnosed cases of polyhydramnios from 20-41 weeks of gestation were included in the study.
Results: Polyhydramnios was diagnosed in 170 pregnancies. Mild polyhydramnios (AFI 24.0-29.9 cm) was found in 112 (65.88%) pregnancies, moderate (AFI 30.0-34.9 cm) in 38 (22.35%) pregnancies and severe (AFI 35.0 cm or more) in 20 (11.76%) pregnancies. Antenatal detection of anomalies was in 71 (41.76%) fetuses. The prevalence of anomalies was higher in pregnancies with more amniotic fluid. A total of 83 anomalies were detected in 71 fetuses. Pregnancies complicated with severe polyhydramnios had maximum number of fetuses with multiple anomalies. 37 pregnant women out of 170 (21.76%) with polyhydramnios had maternal diabetes. Of these 37 pregnancies 11 (29.72%) had pregestational diabetes, 13 (35.13%) had gestational insulin treated diabetes, 13 (35.13%) had gestational diet controlled diabetes. Anomalous fetuses were present in 5 (13.51%) of diabetic pregnancies with polyhydramnios.There were 7 (4.11%) fetal deaths in pregnancies complicated with polyhydramnios.
Conclusions: This study proves that pregnancies with severe polyhydramnios have a greater frequency of fetal anomalies. Diagnosis of second trimester polyhydramnios should initiate a search for possible associated fetal anomalies and causative factors.
Key words: Polyhydramnios, congenital anomalies, amniotic fluid.

INTRODUCTION

Fetus within the uterus is surrounded by alkaline fluid called amniotic fluid. This fluid is important for its proper growth and development. Normal amniotic fluid level varies in relation to period of gestation. Polyhydramnios refers to an excess amount of amniotic fluid [1].

Polyhydramnios occurs in about 1% of pregnancies [1]. It is defined as " deepest vertical pocket (DP) of more or equal than 8cm" [2] or " amniotic fluid index (AFI) of more or equal than 24cm" [3].AFI is preferred to DP because DP does not allow for an asymmetrical fetus position within the uterus [4].

Polyhydramnios is often indicative of fetal, placental or maternal problems. In polyhydramnios there is an increased risk of perinatal morbidity and mortality . The recent observations indicate a more dominant role of anomalous fetus development in production of polyhydramnios [5].

Congenital anomalies are defined as " gross structural defect present at birth"[6] . Various factors are associated with congenital anomalies. Polyhydramnios is one of them [2].

Aim of Study is to find frequency and ultrasound detection of different fetal anomalies in pregnancies complicated with polyhydramnios to improve counseling for women with polyhydramnios.

MATERIALS AND METHODS

This is a prospective study of singleton pregnancies conducted in Lady Willingdon Hospital, Lahore from July 2009 to June 2011. A total number of 170 pregnant women from 20 to 41 weeks of gestation with ultrasound diagnosis of polyhydramnios were included in the study. 9 women with polyhydramnios who presented in labour ward with established labour were excluded from the study. Each case was evaluated for demographic profile, severity of symptoms and maternal medical disorder. Abdominal examination was performed. Obstetrical ultrasound was done and record was made for fetal biometry, placental localization, liquor volume estimation. Degree of polyhydramnios was measured by Amniotic Fluid Index(AFI). After diagnosis of polyhydramnios congenital fetal anomalies were recorded and classified according to organ system involved by targeted sonography.

AFI was determined by directly measuring the vertical pocket (free of any fetal part) in four quadrants of maternal abdomen. The line of demarcation being linea alba longitudinally and umbilicus transversely. The four quadrant's largest pockets were summed and AFI was measured. Depending upon AFI polyhydramnios was categorized as Mild (AFI 24.0-29.9 cm), Moderate (AFI 30.0-34.9 cm) and Severe (AFI 35 cm or more). Association of fetal anomalies with increasing severity of polyhydramnios was defined according to organ system(s) involved. Record of fetal death was also

made. Anomaly was considered to be present if detected in antenatal period.

Pregnancies complicated by diabetes were also analyzed separately. Gestational diabetes was diagnosed based on standard 100 gm oral glucose tolerance test. Frequency tables and percentages were calculated. Data was analyzed on SPSS.

RESULTS

Table No.I : Degree of polyhydramnios

Degree of Polyhydramnios	Number of Patients	Percentage
Mild Polyhydramnios (AFI 24.0-29.9cm)	112	65.88 %
Moderate polyhydramnios (AFI 30.0-34.9cm)	38	22.35 %
Severe polyhydramnios (35.0 cm or more)	20	11.76 %

Table No.2: Number of anomalous fetuses stratified by severity of polyhydramnios

Fetuses	Mild polyhy-dramnios n=112	Moderate polyhy-dramnios n=38	Severe polyhy-dramnios n=20	Total No n=170
Anoma-lous fetuses	28 (25%)	26 (68.4%)	17 (85%)	71 (41.76%)
Normal fetuses	84 (75%)	12 (31.57%)	3 (15%)	99 (58.2%)

$P < 0.05$

Table No.3: Different organ systems involved

Organ system involved	Mild polyhydramnios n=31	Moderate polyhydramnios n=16	Severe polyhydramnios n=36	Total No. of anomalies n=83
Central nervous system	21	4	10	35
Gastrointestinal system	2	4	8	14
Thoracic	1	1	9	11
skeletal	3	3	3	9
Ventral wall	___	3	3	6
Cardiac	2	1	3	6
Craniofacial	2	___	___	2

Table No.4: Association of diabetes with anomalies in polyhydramnios

Type of diabetes	No. of Patients n=37	No. of Anomalies n=5
Pregestational diabetes	11 (29.72%)	3 (8.10%)
Gestational insulin treated diabetes	13 (35.13%)	1 (2.70%)
Gestational diet controlled diabetes	13 (35.13%)	1 (2.70%)

Polyhydramnios was diagnosed in 170 pregnancies. Polyhydramnios was categorized as mild (AFI 24.0-29.9 cm) in 112 (65.88%) pregnancies, moderate (AFI 30.0-34.9 cm) in 38 (22.35%) pregnancies and severe (AFI 35.0 cm or more) in 20 (11.76%) pregnancies as shown in table 1.

Table II shows number of anomalous fetuses (as detected by ultrasound) stratified by severity of polyhydramnios. Antenatal detection of anomalies was in 71 (41.76%) fetuses. The prevalence of anomalies was higher in pregnancies with more amniotic fluid ($P < 0.05$). Thus as hydramnios increased, the frequency of anomalies increased.

Table 3 presents list of anomalies, detected by antenatal ultrasound. A total of 83 anomalies were detected in 71 fetuses. This was due to presence of multiple anomalies in fetuses. Maximum anomalies were detected in central nervous system. Pregnancies complicated with severe polyhydramnios had maximum number of fetuses with multiple anomalies.

Table IV shows association of maternal diabetes with polyhydramnios. Total of 37 pregnant women out of 170 (21.76%) with polyhydramnios had maternal diabetes. Of these 37 pregnancies 11 (29.72%) had pregestational diabetes, 13 (35.13%) had gestational insulin treated diabetes, 13 (35.13%) had gestational diet controlled diabetes. Anomalous fetuses were present in 5 (13.51%) of diabetic pregnancies with polyhydramnios.

There were 7 (4.11%) fetal deaths in pregnancies complicated with polyhydramnios.

DISCUSSION

Polyhydramnios is a relatively uncommon complication associated with pregnancy. The clinical problems associated with polyhydramnios, apart from fetal anomalies are, maternal discomfort, preterm labour, abruptio-placenta and many others. Polyhydramnios is

suspected clinically and confirmed by measuring Amniotic Fluid Index with ultrasound.

The results of this study demonstrate that frequency of anomalies in fetuses increases proportionally to the degree of polyhydramnios complicating pregnancy, which is fairly comparable with other studies [7,8].In present study antenatal detection of anomaly is 41.76% while in study of Paur HU, Viereck V the antenatal detection of anomaly was 48% [2]. The same results are shown by Damato et al although in is study amniotic fluid volume was measured according to DP (Deepest Pool) [9] Esplin et al recommended that diagnosis of second trimester polyhydramnios should initiate a search for possible associated anomalies [10]. Present study shows that 15.49% (11 of 71) anomalous fetuses had multiple anomalies thus a total of 83 anomalies were found.

As far as type of fetal anomalies are concerned, in present study neural tube defects are the largest group, which were 35 (42.16%) out of total 83 anomalies found. These defects are easily detectable by ultrasound in first and second trimester. In study of Stoll et al more frequent malformations associated with polyhydramnios were CNS (central nervous system), GIT (gastrointestinal),cardiac, musculoskeletal and urinary systems [11] .Whereas in review of polyhydramnios by Cardwell, Jacoby and Charles CNS defects comprised 50% of congenital anomalies[12,13]. In present study Anencephaly was most common anomaly detected.

Similarly serious structural abnormalities like septal defects and anterior abdominal wall defects can be easily diagnosed by mid trimester ultrasound [14]. If early diagnosis is made maternal psychological and physical trauma can be reduced by offering early termination of pregnancy.

Apart from fetal malformations, polyhydramnios may also indicate maternal medical disorder. In this study maternal diabetes mellitus was found to be associated in 37 (21.76%) of pregnancies. Uncontrolled diabetes in first trimester leads to congenital anomaly in fetus. Therefore ultrasound examination at 18-20 weeks of gestation should be performed to exclude major structural defects at this stage.[15,16]. Lazebnic and Many found that the anomaly rate was not significantly different between diabetic pregnancies with hydramnios and non diabetic pregnancies with hydramnios[17]. However in present study fetal anomaly detection rate in diabetic mothers with polyhydramnios was 13.51% compared to non diabetic pregnancies.

Idiopathic polyhydramnios in 3rd trimester can cause high maternal morbidity and fetal morbidity and mortality due to excessive abdominal distention, sudden premature rupture of membranes, placental abruption, cord prolapse, fetal malpresentation, postpartum hemorrhage and operative delivery. Pregnancies with severe polyhydramnios are usually delivered at an earlier gestational age and have correspondingly lower birth weights.

Although fetal karyotype may be offered in the setting of polyhydramnios , women should be informed that if no anomaly is detected sonographically, the aneuploidy risk is likely 1% or less.1 In cases where fetal growth restriction coexists with polyhydramnios and malformation, amniocentesis has been recommended[18,19].

CONCLUSION

Polyhydramnios is an uncommon but distressing condition for the patient. Differentiating severe from mild polyhydramnios has prognostic implications.This study proves that pregnancies with severe polyhydramnios have a greater frequency of fetal anomalies. Knowledge of fetal anomalies and potential risks is the basis for counseling parents about the pregnancy outcome. Therefore diagnosis of second trimester polyhydramnios should initiate a search for possible associated fetal anomalies and causative factors.

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Address for Corresponding Author:
Dr Bushra Haq,
Gynae Unit II,
KEMU/ Lady Willingdon Hospital
Lahore.
drbushrahaq@yahoo.com

Original Article

Pomegranate Protects Minocycline Induced Epidermal Pigmentation in the Extremities of Guinea Pigs

1. Sarwath Fatimee 2. Anjum Naqvi

1. PG Student of MPhil Anatomy 2. Head, Dept. of Anatomy, Basic Medical Sciences Institute, Jinnah Post Graduate Medical Centre, Karachi

ABSTRACT

Objective: To investigate the protective effects of Pomegranate on Minocycline induced epidermal pigmentation on the extremities of guinea pigs.

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: 60 adult guinea pigs were divided into 3 groups A B and C, A served as control, B given Minocycline, while C given Minocycline with Pomegranate for 8 weeks, after which their skin was processed for histological examination and pigmentation was observed in Masson Fontana stained sections under light microscope.

Results: The melanin pigmentation deposition observed in Minocycline treated group B, 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 spinosum.

Conclusion: Based on the present study it is conducted that pigmentary changes induced by Minocycline can be protected by taking pomegranate.

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

INTRODUCTION

Skin pigmentary abnormalities are seen as aesthetically unfavorable and have led to the development of cosmetic and therapeutic treatment modalities of varying efficacy[1]. Unwanted cutaneous hyperpigmentation can also produce a significant psychological stress[2]. Drug induced pigmentary alteration are quite common[3]. A variety of drugs have been reported to induce hyperpigmentation[4]. Regarding this, minocycline, a synthetic broad spectrum antimicrobial tetracycline whose common application in the treatment of pneumonia, acne infections of skin genital and urinary systems[5] and rheumatoid arthritis[6] has been associated with cutaneous hyperpigmentation with its prolonged use[7,8].

Hyperpigmentary disorders are often treated with hydroquinones, retiniods and tyrosinase inhibitors[9]. Increasing consumer interest in skin care and treatment products derived from natural sources has driven increased research into novel skin depigmentating agents[10].

Pomegranate (Punica granatum, Punicaceae) a traditional Chinese medicine[11] has been extensively used in the folk medicine of many cultures[12-14]. Some previous studies cited by Moawad et al[15] had proved that the products of pomegranate tree (Including peels, juice, leaves, seeds, flowers etc) have medicinal and industrial importance. Pomegranate is a rich source of polyphenoic compounds anthocyanins (such as cyanidine, delphinidin) and hydrolysable tannins (such as ellagic acid, gallagic acid), which account for 92% of antioxidant activity of the whole fruit[16]. Its main constituent, ellagic acid, a naturally occurring polyphenol, when applied topically suppresses U-V induced pigmentation in brownish guinea pigs, as it has a high affinity for copper at the active site of tyrosinase enzyme[17-19]. Tyrosinase is the rate limiting enzyme for melanin synthesis[10] which synthesized by melanocytes situated in the basal epidermis and are transferred to the surrounding epidermal keratinocytes.[19,20]The type and amount of melanin synthesis and its distribution pattern in the surrounding keratinocytes determines the actual color of the skin[10]. Therefore, chelating copper at the active site of tyrosinase enzyme inhibits the activity of it[22], which is also being proved by Zho and Goa[23].

In the light of above mentioned studies, this study was conducted to observed the protective effects of pomegranate against the minocycline induced pigmentation in the epidermis and note down the histological changes occurring in this regard.

MATERIALS AND METHODS

This study was conducted in the department of Anatomy, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi, on 60 adult male guinea pigs weighing between 450 – 650 grams, and were divided into 3 main groups A, B and C.

Group A animals were served as control, group B received Minocycline 0.02mg/G body weight/ day orally, and group C received Minocycline 0.02mg/G/day orally along with pomegranate 0.9mg/G body weight/day orally for 8 weeks.

After completion of the experimental period all the guinea pigs were sacrificed under ether anesthesia in a glass container and one skin fragment of two inches size, from both upper and lower limbs and of abdomen were taken from each animal. The fragment from each extremity was fixed in 10% formalin for 24 hours and processed for paraffin embedding, and then paraffin blocks were made in the tissue embedding system. 4 to 5 micron thick sections were cut on rotatory microtome and mounted on albumenized glass slides. After that, they were stained with the Haematoxylin and Eosin and Masson's Fontana stains for histological studies under light microscope and the results were graded and recorded.

RESULTS

In the haematoxylin and eosin stained sections of control group A animals, the epidermis of abdomen and both extremities observed under 40 X showed 3 to 5 layers of cells in addition to stratum corneum and their cytoplasm with nuclei were visualized normal in appearance. The cells in all layers were stained uniformly.

Table No. 1: Distribution of melanin deposition in all epidermal layers indifferent groups

Group	Period 0f Treatment	Treatment Given	Sparse*	Patchy**	Dense***
A Control	8 Weeks	Laboratory diet ad libitum	+		
B Minocycline treated	8 Weeks	0.02mg/G body weight/day(Orally)			+++
C Minocycline + Pomegranate treated	8 Weeks	0.02mg/G body weight/ day + 0.09mg/G body weight/ day(Orally)		++	

[8]Sparse: scatteredly distributed(+),Patchy: patchy distributed,***Dense: uniformly distributed**

Table No. 2: Extension of melanin deposition in all epidermal layers in different groups

Group	Period of Treatment	Treatment Given	Normal*	Grade I**	Grade II***
A Control	8 Weeks	Laboratory diet ad libitum	+		
B Minocycline treated	8 Weeks	0.02mg/G body weight/day(Orally)			+++
C Minocycline + Pomegranate treated	8 Weeks	0.02mg/G body weight/ day + 0.09mg/G body weight/ day(Orally)		++	

***Normal: extended till stratum basale (+) **Grade-I: extended till stratum spinosum (++) ***Grade-II: extended till stratum corneum (+++)**

In the Minocycline treated group B animals, tissues were observed under 40 X and showed all the layers of epidermis of both extremities bearing the same morphology as that of control group A animals, but there is black colored pigment deposition was seen within the cells as well as outside the cells in all the layers of the epidermis.

Meanwhile in the protective group C treated with pomegranate along with Minocycline, the morphology is same as observed in control group A and there is no deposition of any pigment within or outside the cells.

The Masson Fontana stained sections were observed under 40 X. In the control group A animals tissues, the melanocytes were dark black and brown black in color. They were in scattered manner; located in the epidermal basal layer. They were oval to irregular in shape with pale staining cytoplasm. The distribution of melanin pigment deposition was of sparse pattern (+) and extension was of normal grade. (Table 1 and Table 2, Fig 1)

In the Minocycline treated group B animals, the morphology shows no significant changes but the deposition of melanin pigment was of dense pattern (+++) and extension was of grade II. (Table 1 and Table 2, Fig 2).

In the Minocycline and pomegranate treated group C animals, the morphology shows no significant changes as compare to control group A but the deposition of melanin pigment was of Patchy to sparse pattern (++)

and extension was of grade I.(Table 1 and Table 2, Fig 3).

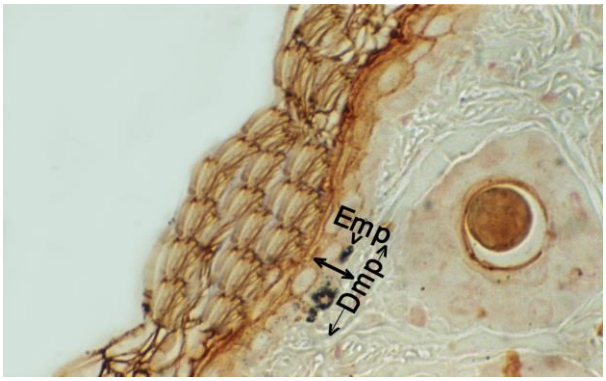

Figure No. 1: Epidermis of group A control animals showing distribution of melanin pigment (Dmp) and extension of melanin pigment (Emp) in Masson Fontana stain, (Photomicrograph 40 X).

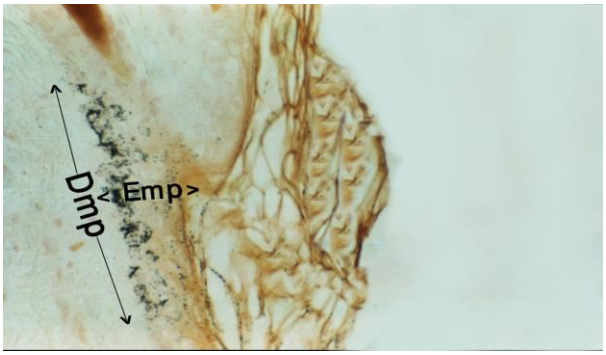

Fig 2: Epidermis of group B Minocycline treated animals showing distribution of melanin pigment (Dmp) and extension of melanin pigment (Emp) in Masson Fontana stain,(Photomicrograph 40 X).

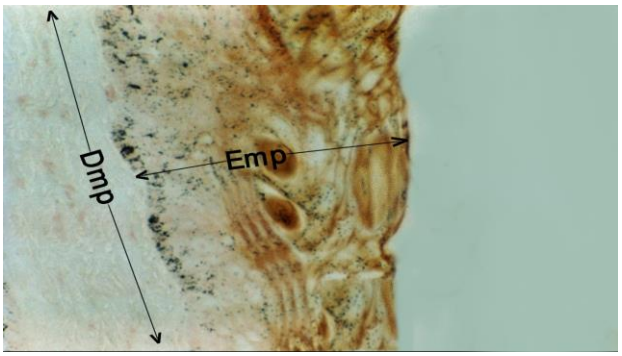

Figure No. 3: Epidermis of group C Minocycline and Pomegranate treated animals showing distribution in melanin pigmentation (Dmp) and extension of melanin pigment (Emp)deposition in Masson Fontana stain.(Photomicrograph 40 X).

DISCUSSION

Pomegranate (punica granatum) has been used extensively in traditional medicines in many countries[12,14,16,17,19]. Its main constituent, ellagic acid, a naturally occurring polyphenol, is reported to have the high affinity for copper at the active site of tyrosinase and inhibits its activity by binding to the copper[17-23]. The tyrosinase is the rate limiting enzyme in the biosynthesis of melanin. Thus inhibiting tyrosinase, inhibit the melanin synthesis proven in various international studies[10,17,18,19,23].

Melanin is synthesized in the melanocyte in which tyrosinase played an important role. As a result of tyrosinase activity, tyrosine is transformed first into 3, 4-dihydrooxyphenylalanine (dopa) and then into dopaquinone, which is converted, after a series of transformations, into melanin. Once formed, melanin within the membrane bounded granules called melanosomes, migrates within the dendrites of melanocytes, and is transferred to the cells of all epidermal layers, whish act as a depot and create the pigmentation of skin[20].

The histological changes in the Minocycline treated group B animals showed densely distributed black brown pigment deposition as compared to the control group A. This black brown pigment is melanin as it is being stained by the Masson's Fontana stain. It would be consider that Minocycline may induce pigmentation as reported by Mounton et al[8] about the mechanism of Minocycline pigmentation which may involve a reactive quinine iminium ion metabolite, iron chelation, or stimulation of melanin production. Burns et al[21] cited Minocycline association with post inflammatory hyperpigmentation in women who have undergone sclerotherapy.The diffuse muddy brown discoloration in the sun exposed areas of skin (type III reaction) induced by Minocycline-stimulated melanocytes that can lead among other things to deposits of melanin or Minocycline melanin complexes at the epidermal basal membrane.[4]

The result of group C Minocycline treated animals along with pomegranate shows that melanin pigment deposition in the epidermal layers had markedly decreased as compare to Minocycline treated group B animals. This is more obvious in the Manson's Fontana stained sections. As the melanin is formed after the conversion of tyrosine into dopa which is the rate limiting step being catalyzed by tyrosinase, therefore, inactivation of tyrosinase leads to the inhibition of melanin formation. Ellagic acid inhibits the melanin synthesis by suppressing tyrosinase enzyme activity as it penetrate into its active site and chelate firmly with copper present there. This had been proven that after the topical application of ellagic acid rich pomegranate extract, the melanin content of skin had been reduced[18]

The result is also in agreement with Kasai et al[19] who reported that the orally administered ellagic acid rich pomegranate extract provides the protective effects on the pigmentation of human skin caused by U-V irradiation.

CONCLUSION

Based on the present study it is conducted that pigmentary changes induced by Minocycline can be protected by taking pomegranate. This suggests that the

result could be considered promising enough in humans who are on Minocycline with pomegranate for long term duration. The present work is under progress for further extended studies.

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Address for Corresponding Author:
Dr. Sarwath Fatimee
Anatomy Department,
Basic Medical Sciences Institute,
Jinnah Post Graduate Medical Centre, Karachi.
Cell # 0092-302-2100393

Original Article

Intestinal Tuberculsis - 5 years experience in Tertiary Care Hospital

1. Abdul Razaque Qazi 2. Syed Qaiser Husain Naqvi 3. Farkhunda Jabeen Dahri

1. Assoc. Prof., Surgical Unit-III 2. Asstt. Prof. of Pathology 3. Asstt. Prof. Surgical Unit-III, Peoples University of Medical & Health Sciences Hospital Nawabshah

ABSTRACT

Background; Abdominal tuberculosis (TB) is a common disease in developing countries and reemerging in the west. This disease is still diagnostic dilemma for physicians and surgeons, as it mimics many abdominal diseases.
Objective: To evaluate the clinical presentation and management of abdominal tuberculosis in our set up.
Study Design: Prospective study
Place and Duration of Study: This study was conducted in surgical unit III, Peoples University of Medical & Health Sciences Hospital Nawabshah, from July 2006 to June 2011.
Materials and Methods: Total 70 patients were included in this study from 205 suspected cases. The cases were either previously diagnosed or diagnosed during operation performed for intestinal obstruction, peritonitis or appendicitis. Patients were confirmed on the basis of histopathology, cultures and AFB.
Results: Age of the patients ranged between 6 to 38 years. Male to female ratio was 1.3:1. Abdominal pain and weight loss were the most common symptoms. Common presentation was intestinal obstruction and peritonitis. Majority of patients underwent resection and anastomosis and limited right hemicolectomy.
Conclusion: It has been emerged from our study that abdominal TB presents with different clinical features which are nonspecific and often diagnosed during laparotomy. Majority of patients underwent resection and anastomosis and limited right hemicolectomy.
Key Words: Abdominal tuberculosis, Intestinal obstruction, Peritonitis, Resection and anastomosis

INTRODUCTION

Intestinal Tuberculosis is a common and major health hazard in Pakistan just like other countries where ignorance, poverty, overcrowding and malnutrition are prevalent. The disease starts as transverse ulcers in the intestine or hyperplastic mass lesion usually affecting ileocaecal region[1,2].

Intestinal TB is one of the common sites of extapulmonary involvement (11%) [3]. Abdominal TB occurs from ingestion of food contaminated with tubercle bacilli causing primary intestinal TB, ingestion of sputum containing tuberculous bacteria from primary pulmonary focus causing secondary intestinal TB. Other roots are cervical lymph nodes and retrograde spread from fallopian tubes, it can affect any part of gastrointestinal tract from mouth to anus. The sites most affected oftenly are the ileum, proximal colon and peritoneum[3].

The protean clinical manifestations and varied complications of abdominal TB continues to challenge the diagnostic acumen and therapeutic skills of all physicians[4].

The disease commonly presents insidiously with abdominal pain, fever, night sweets, vomit, diarrhea or constipation. Common complications are intestinal obstruction, perforation and malabsorption. Surgical treatment is required when it causes intestinal obstruction or peritonitis due to perforation[5].

The main objective was epidemiological observation, clinical features, diagnosis, and planning of surgery in diverse presentation of abdominal TB.

MATERIALS AND METHODS

This study has been carried out in surgical unit III, Peoples University of Medical & Health Sciences Hospital Nawabshah. Total 70 patients with varied presentation of abdominal TB were recruited in this study, patients under the suspicion of abdominal TB were thoroughly evaluated .Careful history and physical examination was performed. Patient's age, sex and socioeconomical status recorded. Details with special reference to their symptoms of abdominal pain, nausea, vomiting, altered bowel habits, anorexia and weight loss were obtained. Patients were looked for anemia, abdominal distension, tenderness and mass. Their nutritional status was also evaluated by clinical methods and biochemical investigation.

Blood CP, ESR, total proteins and other routine blood investigations were performed.

Chest x ray, abdominal x ray and US of abdomen were routinely performed to observe the changes characteristic for abdominal TB. In selected cases CT scan, Laparoscopy, Barium follow through and Barium enema were also done to establish the diagnosis.

Patients admitted in emergency with acute intestinal obstruction or perforation was diagnosed only during exploratory laparotomy.

The operative findings were recorded regarding presence of strictures, ileocaecal lump, ascitis and other

gross features of abdominal TB. The specimens were sent for histopathology.

The patients were monitored post operatively and remained under follow up and antitubercular regimen continued for nine months

RESULTS

Among 70 patients, 40 were males and 30 were females thus average male to female ratio was 1.4 t0 1. Age varied from 20 to 50 years average age was 27.5 years.

Among 70 patients with diagnosis of abdominal TB, 38(54%) patients presented with acute intestinal obstruction, 12(17%) with recurrent abdominal pain and altered bowel habit, 8(11%) with lump in right iliac fossa with subacute intestinal obstruction, 5 (7%) with distension of abdomen due to ascitis, 3(4%) with peritonitis due to perforation of gut and 2(2.8%) with enlargement of mesenteric lymph nodes with abscess formation.

Two patients were presented with pain in right iliac fossa along with fever operated upon on the presumptive diagnosis of acute appendicitis.

Most patients were significantly anaemic, ESR was elevated in many patients significantly.

Evidence of active or old pulmonary TB was seen only in 15(21 %) on chest x ray.

In 42 patients diagnosis was made during explorative laparotomy. Specimen sent for histopathogy.

Table No.1: Clinical Features

Symptoms	No of Patients	Percentage
Abdominal Pain	62	88.5%
Weigh Loss	48	68.5%
Constipation	42	61.4%
Anorexia	41	60.8%
Fever	29	41.4%
Vomiting	25	35.7%
Constipation alternating with Diarrhea	12	18.1%
Night Sweats	11	15%
Pulmonary involvement	10	14%

Table No. 2: Types of Procedure

Procedure	No of Patients	Percentage
Resection of part of ileum & Anastomosis	34	48.5%
Righ Haemicolectomy	21	30%
Adhesionolysis	9	12.8%
Biopsy of Lymphnode & omentum	70	100%
Drainage of Abscess	4	5.5%
Ileostomy	2	2.8%

Table No. 3: Operative Finding

Multiple Structure	32	45.7%
Single Stricture	8	11.4%
Enlarge Lymphnodes	48	68.5%
Ascitis	15	21.4%
Ileocecal Mass	8	14.2%
Adhesions & Bands	6	8.5%
Abscess	4	5.5%

DISCUSSION

Despite the fact that abdominal tuberculosis (TB) is a common disease in Pakistan, it is ill understood and is being neglected all too often by physicians and surgeons. Majority of the patients with abdominal TB come from poverty stricken and remote areas where initially they are being misdiagnosed and treated in appropriately. As a result disease becomes advanced and often patients are being referred to our hospitals with complications like intestinal obstruction, peritonitis and ascitis[6].

Patients with abdominal TB may present with different clinical features which may mimic many abdominal diseases, therefore if it is not clinically suspected, it may culminate in fearsome complications[7].

The diagnosis of abdominal TB is indeed challenging. Even in highly endemic region the accuracy of clinical diagnosis is 50 %.[8].

Abdominal TB can occur at any age but is predominantly disease of young adults.

In our series all patients were between 6 to 38 years with average of 27.5 years. This is consistent with other studies of this region 26.5[9].

In our series males were more commonly affected than females ratio was 1.3;which was some what differ from other studies like Parokash et al showed that F:M = 2;1[10]. Hughes and Shukla reported F:M 1.6:1.17[11] . In our study abdominal pain was the commonest symptom (88.5%) followed by weight loss (68%). Hematological tests revealed moderate degree of anemia and raised ESR in majority of patients.

Intestinal TB is common among the people of low socioeconomic group. Banergee B.N had shown that incidence was more among the refuge living in the slums of Calcutta[12].

In our study evidence of active or previous focus found in 15 cases. S. Sircar et al has shown 16% of patient with abdominal TB found to have coexisting pulmonary TB[13]. Most common site of abdominal TB is ileocaecal region, it is mainly attributed to abundance of payer's patches. Due to stasis there is prolonging contact of bacteria with mucosa and more phagocytic activity. It may present in ulcerative form in which long standing ulcer cause fibrosis and later stricture formation or in hyperplastic form where extensive chronic inflammation, fibrosis, bowel adhesions, nodal enlargement often presents with mass in right iliac fossa.

Surgery is not recommended, either for confirming the diagnosis or as the first line approach to the management of uncomplicated abdominal TB. How ever patients with acute and sub-acute intestinal obstruction, who do not respond to conservative measures, must be treated surgically[14]. Diseased segment of bowel with adequate free margins are removed, avoiding extensive resection. Surgery is also needed in patients with a free perforation associated with abscess formation[15].

In our study admitted 40 patients with acute and subacute intestinal obstruction and in 10 patients we found lump in right iliac fossa. In majority of the patients there were coexisting anaemia, anorexia, weight loss and fever. All these cases underwent vigorous resuscitation followed by laparotomy. In 33 patients multiple strictures found in ileum, diseased segment resected and anastomose performed.

In 10 patients we detected lump involving ileocecal part of intestine. These patients subjected to limited ileocecal resection. In all these cases specimen sent for histopathology to make 100% confirmation of TB and antitubercular treatment given for 9 months.

In our series 10 patients presented with peritonitis due to perforation .in 8 cases resection and anastomose performed in remaining 2 cases due to severe contamination diseased part of ileum resected and ileostomy performed, patients were kept on antitubercular treatment and nutrition support, ileostomy restored after 2 months.

Biopsy from perforation site and closure can be done in early cases but chances of leak and fecal fistula formation is high (due to closure of perforation over disease bowel) so resection is better option.

In 6 patients exploratory laparotomy revealed straw colored fluid with tubercle in the peritoneum, greater omentum and bowel wall. Fluid evacuated and sample sent for culture and AFB, omental biopsy was taken and abdomen was closed. Adhesionolysis in these patients may prove to be counter productive due to friability of gut which can easily get perforated, and it is associated with high mortality. 2 patients had massive ascitis, ascetic tap done under US and sent for cultures and AFB.

TB can involve mesenteric lymph nodes and often results in massive enlargement of lymph nodes and abscess formation, these patients presents with general symptoms of fever, malaise and weight loss. It may presents with features of acute Appendicitis[14]. In our study we found 4 cases where clinical features were abdominal pain, fever and weight loss. All these patients underwent open drainage of abscesses and subsequently kept on antitubercular treatment after having histopathological evidence in hand.

CONCLUSION

Abdominal tuberculosis presents with different clinical features which are nonspecific and often diagnosed during laparotomy. In current study abdominal pain with loss of weight, constipation and anorexia were the leading presentations. Majority of patients underwent resection and anastomosis and limited right hemicolectomy.

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Address for Corresponding Author:
Dr. Abdul Razaque Qazi,
Associate Professor, Surgical Unit III,
PUM&HS, Nawabshah.
Cell # 03003216581

Original Article

Frequency of Streptococcus Pneumoniae, Haemophilus Influenzae and Moraxella Catarrhalis Causing Lower Respiratory Tract Infection in Local Population

1. Pushpa ValiRam 2. Karam Ali Mirjat 3. Izhar Fatima

1. Asstt. Prof. of Pathology, Dow Medical College, Karachi 2. Asstt. Prof. of Pathology, Dow Medical College, Karachi 3. Asstt. Prof. of Pathology, Dow Medical College, Karachi.

ABSTRACT

Objective: To see the frequency of Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis causing lower respiratory tract infection and sensitivity pattern of the isolated organisms to various antibiotics.
Study Design: Experimental Study.
Place and Duration of Study: This study was conducted at the Dept. of Microbiology Basic Medical Sciences Institute, JPMC, Karachi, from January, 2001 to September, 2001.
Materials and Methods: A total of one hundred clinically suspected cases of lower respiratory tract infections attending OPD or admitted to the wards of Jinnah Postgraduate Medical Centre (JPMC) and Civil Hospital, Karachi were included in the study.
Results: Out of 100 cases 53% cases were positive for bacterial pathogens. Of the positive cases. S. pneumonae was 35.9%, H.infuenzae 30.2% and other bacteria were 34.9%, in rest of the cases no bacterial pathogen was isolated. Age range in this study was 15-90 years and mean age was 38 years. Smokers have higher frequency i.e., 65.5% as compared to non-smokers in which 47.9% cases were positive for bacterial pathogens. Higher the number of pus cells /HPF (high power field) in sputum greater was the positivity of bacterial pathogen. Sensitivity pattern to antibiotics of different organisms was also seen in this study.
Conclusion: The goal of the study was to see the behavior of the frequent organisms on the culture and to see the antibiotic sensitivity of lower respiratory tract specimen for the treatment. It requires increased number of patients with more advanced testing system.
Key Words S.pneumonae, H.influenzae, M.cattarrhalis, lower respiratory tract infections**.**

INTRODUCTION

Respiratory tract infections (RTI) are common in our part of world due to poverty, overcrowding, poor hygienic conditions, pollution and irrational use of antibiotics. Acute RTI of viral and bacterial origin such as the common cold, pharyngitis, bronchitis, bronchiolitis, pneumonia and bronchopneumonia, pose serious problems owing to their great prevalence, associated with high mortality rates and economic costs.[1]

Common respiratory tract infections in adults in the community include acute exacerbation of chronic bronchitis (AECB), community acquired pneumonia (CAP) and acute sinusitis (AS). The most common bacterial pathogens isolated from a range of respiratory tract infections are S.pneumoniae, Haemophilus influenzae (H.influenzae) and Moraxella catarrhalis (M.catarrhalis).

Community acquired lower respiratory tract infections (LRTI) are very common and the range of causative pathogens is similar to that for community acquired pneumonia. The overall incidence is 40-50 cases per 1000 population per year.[2] Lower respiratory tract infections (LRTI) are commonly classified as either bronchitis or pneumonia, and these infections are associated with an extremely high morbidity in the community, as well as a high mortality in those patients that require hospitalization. Therefore, such infections place a huge burden, both economically and as a user of health services, on the entire health care system.[3]

The incidence of pneumonia in the developing countries is up to ten times higher than that in developed countries such as United States of America.[4] Comprehensive studies of the disease in the pre-antibiotic era showed mortality rates of about 1 per 1000 per year; over 80% of the cases were due to Streptococcus pneumoniae (S.pneumoniae).[5]

Purpose of Study: The purpose of this study was:

- To see the frequency of Streptococcus pneumoniae, Haemophilus influenzae and Moraxella catarrhalis causing lower respiratory tract infection.
- To see the sensitivity pattern of the isolated organisms to various antibiotics.
- Detection of β-lactamase production.

MATERIALS AND METHODS

This study was conducted in the Department of Microbiology, Basic Medical Sciences Institute, Jinnah

Postgraduate Medical Centre, Karachi, from January 2001 to September 2001.

Inclusion Criteria: All the patients ≥ 14 years of age suspected of lower respiratory tract infection were included in the study.

Exclusion Criteria:

- Specimen that contains only saliva.
- Patients already on antibiotic treatment.
- Patients below 14 years of age.

Early morning samples were collected in sterile containers, from the patients with clinical signs of lower respiratory tract infection. , macroscopic examination and Gram's staining and Ziehl Neelsen staining were done to see whether it was representative of lower respiratory tract infection and to exclude mycobacterium tuberculosis respectively.

The samples were inoculated onto Blood agar, Chocolate agar and on MaConkeys agar and incubated at 35° C for 24 to 48 hours suspected colonies were identified by standard methods.for the confirmation of S.pneumonia, optochin susceptibility and bile solubility and for *H.influenzae* satellitism, DNAase test and discs of X, Vand XV factor were used. β- lactamase production was tested by chromogenic cephalosporin (nitrocefin) discs.

RESULTS

A total of one hundred clinically suspected cases of lower respiratory tract infections attending OPD or admitted to the wards were included in the study.

Table No.1: Age wise Distribution of Patients with Lower Respiratory Tract Infections (n=100)

Bacterial pathogenesis	No. of cases	Percent
Positive for bacterial pathogen	53	53%
Negative for bacterial pathogen	47	47%
Age Group (Years)	Positive Bacterial Pathogen	
15 – 29 (n=53)	15	28.3
30 – 49 (n=53)	29	54.7
≥50 (n=53)	09	17.0
Age range	**15-90 years**	
Mean age	**38 years**	

Table No.2: Relationship of Smoking with Positive Culture

Smoking	No. of cases	Culture +ve		Culture –ve	
		No	%	No	%
Smoker	29	19	65.5%	10	34.5%
Non smoker	71	34	47.9%	37	52.1%

Table-1 shows the number of cases that were positive for bacterial pathogens and distribution of age, out of 100 cases 53% cases were positive, age range in this study was 15-90 years and mean age was 38 years. In 15-29 years age group, bacterial pathogens were positive in 28.3%, in age group 30-49 years bacterial pathogens were positive in 54.7%, followed by age group 50 and above in which 17% cases were positive for bacterial pathogens. Table-2 shows relationship between LRTI and smoking habits of the patients. Smokers have higher frequency i.e., 65.5% as compared to non-smokers in which 47.9% cases were positive for bacterial pathogens. Demographic data was analyzed in this table. Incidence of LRTI in different socio-economic groups was shown positive culture in lower middle class group showed a slightly higher percentage i.e., 50% as compared to other groups.

Table No.3: Demogramphic of Lower Respiratory Tract Infection in Different Social Groups

Socio-economic status	No. of cases	Culture +ve		Culture – ve		P value
		No.	%age	No.	%age	
Poor	63	33	52.3	30	47.7	0.954
Lower middle	29	16	55.2	13	44.8	
Middle	8	4	50.0	4	50.0	
Occupation						
House wife	30	13	43.3	27	56.7	0.084
Skilled worker	17	6	35.3	11	64.7	
Unskilled worker	08	04	50.0	04	50.0	
Students/ jobless/retired	13	7	53.8	6	46.2	
Patients						
Hospitalized	53	36	67.9	17	32.1	0.003
Non-hospitalized	47	17	36.2	30	63.6	

*Statistically significant

Table No.4: Frequency of Lower Respiratory Tract Infection in Normal and Compromised Respiratory Tract

Past history of respiratory illness	No. of cases	Culture +ve		Culture - ve		P value
		No	%	No	%	
Yes	17	14	82.4	03	17.6	0.017*
No	83	39	36.2	44	53.0	
Gram staining status leucocyte / HPF						
< 15	38	05	13.2	33	86.8	0.010
15 – 20	22	12	54.5	10	45.5	
> 20	40	36	90.0	04	10.0	

*Statistically significant.

Occupation had little role in causing LRTI. Incidence of bacterial pathogens in hospitalized and non-hospitalized patients was compared and was found to be more 67.9% in hospitalized as compared to 36.2% in non-hospitalized patients, (Table-3). In table-4, frequency of LRTI in cases who had no past history of respiratory disease was low i.e. 36.2% as compared to cases who had previous history of respiratory disease i.e., 84.4%. In table-4, relationship between pus cells per HPF and culture positive for bacterial pathogen was seen and it

was observed that <15 pus cells/HPF had 13.2% cases positive for bacterial pathogen. Pus cells 15-20/HPF had 54.5% cases positive for bacterial pathogen and specimens in which there were >20 pus cells/HPF, 90% cases were positive for bacterial pathogen.

Table No.5: Distribution of 53 Lower Respiratory Tract Bacterial Pathogens

Total Positive specimens	S. pneumoniae	H. influenzae	Miscellan-eous**
53	19 (35.9%)	16 (30.2%)	18 (33.9%)

****Miscellaneous LRT bacterial pathogens:**

Bacterial Isolated	No. of cases	Percent
Pseudomonas species	12	22.6%
Klebsiella pneumoniae	03	5.6%
Proteus species	01	1.9%
Staphylococcus aureus	01	1.9%
Acinetobacter	01	1.9%

Table No.6: Sensitivity Pattern of Common Lower Respiratory Tract Isolates

Antibiotics	Organism Isolated	
	Strep. Pneumoniae (n=19)	H. influenzae (n=16)
Penicillin	16 (84.2%	4 (18.7%)
Amoxycillin-clavulanic acid	19 (100%)	13 (81.2%)
Chloramphenicol	19 (100%)	14 (87.5%)
Ciprofloxacin	18 (94.7%)	15 (93.7%)
Erythromycin	10 (52.6%)	14 (87.5%)
Co-trimoxazole	3 (15.7%)	12 (75.0%)
Tetracycline	6 (31.1%)	7 (43.7%)
Ceftriaxone	19 (100%)	16 (100%)
Vancomycin	19 (100%)	16 (100%)
H. Influenzae positive	16	
β-lactanase positive	25%	

Distribution of pathogenic organisms was shown in table-5. From a total of 100 cases of LRTI, 53% were positive for pathogenic bacteria, out those 19% were due to S.pneumoniae, 16% were due to H.influenzae and 18% were due to miscellaneous bacterial pathogenic organisms. Distribution of miscellaneous bacterial pathogens was; Pseudomonas 22.6%, Klebsiella pneumoniae 5.6%, Proteus, Staph.aureus and Acinetobacter species were found to be 1% each. Sensitivity pattern of S.pneumoniae and H.influenzae was shown in Table-6. S.pneumoniae was 100% or near 100% sensitive to Ciprofloxacin, Ceftriaxone, Chloramphnicol, Vancomycin and Amoxicillin-Clavulanic acid, 84.2% sensitive to Penicillin, 31% sensitive to Tetracycline and only 15.7% sensitive to Co-trimoxazole. H.influenzae was 100% sensitive to Ceftriaxone and Vancomycin, 93.7% to Ciprofloxacin, 87.5% sensitive to Erythromycin and Chloramphenicol, 81.2% sensitive to Amoxicillin and Clavulanic acid, 75% sensitive to Co-trimoxazole, however, sensitivity to Tetracycline and Penicillin were shown to be 43.7% and 18.7% respectively. β-lactamase production in 16 cases of H.influenzae was shown and comprised of 25% cases.

DISCUSSION

Respiratory tract infections (RTI) were very common in our population; there was no current data available about the most frequent organisms which lead to wrong prescription of antibiotics, selective suppression of normal flora and emergence of resistant strains. Out of 100 clinically suspected patients with LRTI 53% had bacterial pathogens indicated that 47% of patients may not be suffering from LRTI or the etiology could be viral, fungal or of atypical bacterial origin. Several studies had shown that yield of fastidious bacteria such as S.pneumoniae and H.influenzae was zero when any specimen from respiratory tract was collected after antibiotic therapy.[6, 7] The highest incidence of LRTI was seen in the age group of 30-49 years which were the most productive years of one's life. This was in contrast to the study of Macfarlane (1993)[2] and his co-workers in which it was observed by studying 480 adult population over a period of one year; the incidence of LRTI was 2-4 times higher in people aged 60 and over. Woodhead (1995)[7] in his studies had observed that the incidence of LRTI is 15 fold higher in those over 70 years than in younger patients. This study had shown results different from international figures due to the fact that our environment is highly polluted and individuals of 30-49 years age group belonging to lower socio-economic class were exposed more to these pollutants, hence had been at greater risk to get LRTI.

Smokers were more susceptible (52.1%) to LRTI as compared to nonsmokers. These results were comparable to the study carried out by Almirall and his colleagues.[8] It was concluded from the study of 205 male and female patients that the risk of community acquired pneumonia attributable to the consumption of any type of tobacco was 32.4% of cases, in subjects without a history of COPD, the population attributable to risk of tobacco was 23%. The incidence of LRTI seen in hospitalized patients is significantly higher (67.9%) as opposed to 36.2% in non- hospitalized patients. The hospitalized patients included individuals who were clinically suspected of pneumonia or pleural effusion, chronic obstructive pulmonary disease, acute exacerbation of chronic bronchitis and asthmatic patients since they were more prone to secondary LRTI involving secondary pathogen such as Pseudomonas and Klebsiella species.[6, 9] Shaheen (1994)[10] and Sethi (2000)[11] had noted that individuals who had previous LRTI particularly in childhood have compromised respiratory tract. They could not achieve maximal lung

growth (Shaheen, 1994)[10] and were more prone to subsequent LRTI. This study also supplemented the same as 82.4% individuals with compromised respiratory tract developed infection against 36.2% of normal patients.

Gram stain can provide a basis for determining the extent to which identification and susceptibility testing of organisms recovered from specimens should be performed.[12] Sputum microscopy suggested that presence of pus cells was a good indicator for LRTI. Only 13% culture positive were seen in individuals who had < 15 pus cells/HPF as opposed to those who had > 15 pus cells/HPF 54.5%. If the pus cells are more in a sputum sample, higher is the rate of infection and subsequently LRTI, as it was reviewed by Niederman et al (1993).[13] Socio-economic status, number of siblings, maternal smoking, preterm labour, passive smoking from the atmospheric pollutants have been associated with childhood lung disease and there is failure to achieve maximal lung growth and subsequent LRTI.[14] These factors were not established in this study because the majority of the patients belonged to poor, and lower middle class.

Fang et al (1990)[15] studied 359 cases collected from multiple centers had shown that the most frequent etiologic agents were S.pneumoniae (15.3%), H.influenzae (10.9%). In 32.9% the etiology was undetermined which was comparable to this study. This study was also comparable to the study done by Macfarlane et al (1993)[2] in which out of 206 patients, 113 bacterial pathogens were isolated which included 30% S.pneumoniae, 7.7% H.influenzae, 4.3% viruses, approximately 1% cases were due to atypical pathogens. Total bacterial pathogens were accounted 41% of LRTI, whereas in this study the percentage was slightly higher. This was due to some opportunistic/secondary pathogens i.e. Pseudomonas species and Klebsiella pneumoniae. The most common pathogen in our setup was S.pneumoniae (35.9%) followed closely by H.influenzae (30%) while no M.catarrhalis was isolated which could be compared with the study of Lieberman and his co-workers (1996)[16, 17] in which etiology of community acquired pneumonia was identified in 80.6%, S.pneumoniae in 42.8%, M.pneumoniae 29.2%, C.pneumoniae 17.9%, Legionella 16.2%, Viruses 10.1%, C.burnetii 5.8% and H.influenzae 5.5% other causes were 6%.

In another study carried out by French Study Group Moine and his co-workers (1994)[18,19] found out S.pneumoniae, gram negative enterobacteriaceae and Staphylococcus aureus were commonly encountered bacterial pathogen which was in contrast to the present study, M.catarrhalis was not isolated in the present study. This might be due to shift in the pathogenicity in local set up.

It was very fortunate to know that the incidence of resistance among S. pneumoniae and H. influenzae to first line drugs such as penicillin/cephalosporin is either nil or very low. Among S.pneumoniae higher resistance is seen against Co-trimoxazole which was 84% and Tetracycline 69%. Same was true for H.influenzae as resistance to Co-trimoxazole and Tetracycline was 25% and 56% respectively .Same resistence pattern was found by Lebowitz et al in their study[20].

In the present study β-lactamase producing H.influenzae were found to be 25% which was comparable to a study carried out by Parker (1983)[10] who observed incidence of H.influenzae producing β-lactamase to be 18-22%. We must keep a constant vigilance and monitor the sensitivity pattern, so as to keep a check on resistance.

In a study carried out by Seaton and his co-workers (2000)[21] observed by studying 412 adult patients (> 15 years) in whom an episode of respiratory tract infection had been described, during which H.influenzae was isolated, were analysed. Seventy three (17.7%) isolates of H.influenzae were resistant to amoxicillin. Resistance was associated with recent hospitalization and antibiotic exposure in the community. He suggested that hospitalized patients probably received antibiotics during their admission although acquisition of the organism or the beta lactamase via plasmids from other gram negative organisms in the hospital could be a factor. An increasing number of clinical Haemophilus isolates were now resistant to penicillin.

CONCLUSION

The majority of the cases were positive for bacterial pathogens commonest was s S.pneumonae followed by H.influenza. Isolated pathogens were sensitive to Penicilins, Quinolones and erythromycin group and were resistant to Co-trimoxazole and Tetracycline. The study group was small but it suggested that the future development could be, to take a larger group with varied socio-economic status and also look for the other etiological agents(e.g. viruses), study the causes for behaviour of M.catarrhalis and also study the emergence and re-emergence of LRT pathogens.

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Address for Corresponding Author:
Dr. Pushpa ValiRam,
Asstt. Prof. of Pathology,
Dow Medical College, Karachi

Original Article

Role of Rapid Antigen Detection Test (RADT) and Throat Culture in the Diagnosis of Streptococcal Pharyngotonsillitis

1. Karam Ali Mirjat 2. Pushpa ValiRam 3. Izhar Fatima

1. Asstt. Prof. of Pathology, Dow Medical College, Karachi 2. Asstt. Prof. of Pathology, Dow Medical College, Karachi 3. Asstt. Prof. of Pathology, Dow Medical College, Karachi.

ABSTRACT

Objective: To observe the sensitivity and specificity of the rapid antigen detection test and throat culture in the diagnosis of pharyngo tonsillitis.

Study Design: An Experimental study

Place and Duration of Study: This study was conducted in microbiology department, basic medical sciences institute, Jinnah post graduate medical centre, National institute of child health, and civil hospital Karachi, from May 2003 – April 2004.

Materials and Methods: A total of 300 children attending OPD's and admitted (250 suspected and 50 Normal as control cases) of age group 5 – 15 years were included in this study and this age group was again divided into three sub groups I.e: first group from 5 – 8 years, second group was from 9 – 12 years, and the third group was from 13 – 15 years.

Results: Rapid antigen detection test carried out was based on immuno - chromato graphic membrane assay procedure, a total of 24 positive antigen detection test from suspected 250 cases and 5 from 50 control cases were isolated and these isolated (RADT positive) cases were again confirmed by throat culture. The Bacitracin sensitivity and catalase tests were also performed.

Conclusion: The Rapid antigen detection test (RADT) is a rapid way of diagnosing the group A, Beta hemolytic streptococci, result can be obtained within 5 – 10 minutes so the treatment may be started accordingly, while the throat culture is still considered as the Gold standard for the diagnosis of group A beta hemolytic streptococcal pharyngotonsillitis. The positive as well as negative RADT cases were confirmed by the culture.

Key Words: Group A, Beta hemolytic streptococci, Rapid antigen detection test, throat culture, Pharyngotonsillitis.

INTRODUCTION

Streptococcus C and G (non group A) are responsible for community and food borne causes of acute pharyngitis[2]. Pharyngotonsillitis is one of the most common respiratory disease in the community, particularly during childhood. Approximately 28-40% of these infections estimated to be caused by Group A beta hemolytic streptococcus (GABHS) which is considered the important etiological pathogen in terms of sequelae and complications .

Since streptococcal pharyngitis can lead to rheumatic disease and its sequelae, and to suppurative complications, it is a potentially serious medical problem[1].

Group A streptococcal pharyngitis is more common during the winter and rainy months, and occurs most frequently in school going children. Typically, the age group between 5-15 years old with a sudden onset of high fever and a sore throat. The symptoms may be accompanied by headache, malaise, nausea, vomiting and abdominal pain. Physical examination reveals an erythematous pharyngeal exudative tonsillitis, tender cervical lymph adenopathy. Palatal petechiae may be present and papillae of the tongue may be prominent and erythematous, giving the appearance of a "strawberry tongue". During winter months in temperate climates, upto 20% of asymptomatic school age children may be group A streptococcal carriers. Group A beta hemolytic streptococci are ordinarily spread by direct person-to-person contact, most likely through droplets of saliva or nasal secretions, crowding increases transmission and outbreaks of pharyngitis which are common in institutional settings, the military, schools and families. Outbreaks resulting from human contamination of food during preparation have also been reported[3].

If this study was compared with the study done in Eskischiv, fenleey, the organisms isolated was 13.16%, which is more than this study (Atindis et al., 2004)[4].

We have compared the male children with the female suffering from tonsillitis and pharyngitis. Pharyngitis was seen more in male 11 (6.6%) and in female children the pharyngitis is more 6 (7.1%) than tonsillitis, which was 3 (3.6%), while among 166 male children the number of cases positive for tonsillitis were 4 (2.4%). This is again in contrast that male/female ratio is 1:1 (Thomas et al., 2002)[5].

The American Academy of Paediatrics and the Infectious Disease Society of America recommended confirmation of negative rapid antigen detection test results with a throat culture (Bourbeau and

Heiter, 2003)[6].

Group A, Beta hemolytic streptococcal pharyngitis is an important cause of childhood morbidity and the cause of acute rheumatic fever (Aujard et al., 1995)[7].

Culture isolation of Group A, Beta hemolytic streptococcal organisms from the pharynx is the standard method, but rapid antigen detection testing is now widely available (Hall et al., 2004)[8].

Rapid testing has many benefits i.e. early treatment within 48 hours after onset can provide symptomatic relief (Herbeck et al., 1993)[9].

MATERIALS AND METHODS

A total of 300 subjects (250 suspected children and 50 healthy children as control) from 5-15 years of age were included and subjects were divided into three groups; 5-8 years, 9-12 years and 13-15 years respectively.

Methods: Two throat swabs were taken from the patient one for the Rapid test and the other immersed in the transport media (Brain Heart Infusion broth) for further processing in the laboratory. Culture was performed in the laboratory on Blood agar and after inoculation, the plates were incubated at 37°C for 24-48 hours. On the next day, Gram's staining of the growth was carried out, and Microscopy was done. A bacitracin disc of 0.04 U was impregnated on the inoculum on Blood agar plate and zone of inhibition was observed on the following day. Catalase test was performed according to the standards mentioned, which was found negative, and finally the drug sensitivity was carried out.

The rapid antigen detection test was performed according to the standards mentioned. The type of the test performed was immuno-chromatographic membrane assay to detect the Streptococcus pyogenes group A antigen from throat swab.

Principles of the Procedure (RADT): To perform the test, a throat swab is inserted into the test device. Extraction reagents are added from dropper bottles. The swab is rotated three times clockwise. After a one minute incubation, the test device is closed to bring the extracted sample in contact with the test strip. Strep A antigen captured by immobilized anti-Strep A reacts to bind conjugated antibody. Immobilized rabbit anti-goat IgG captures the second visualizing conjugate. A positive test result is read visually in 5 minutes. A negative Strep A Test result, read in 5 minutes, indicates a presumptive negative for the presence of Group A Streptococcal antigen (Binax, 2004)[10].

Interpretation: The test is interpreted by the presence or absence of visually detectable pink-t~purple coloured lines. A positive result will include the detection of both a Sample and a Control line, while a negative assay will produce only the Control line. Any other test result indicates an invalid assay (Binax, 2004)[10].

Limitations of the procedure: Strep A test does not differentiate between viable and non-viable organisms. Patients that have recently been treated for Strep A similar infections may give positive results for a period of time following effective treatment due to the presence of Group A strep antigen in non-viable organisms. Pharyngitis can be caused by organisms other than Group A streptococcus, further diagnostic testing, including culture, should be performed if laboratory findings are inconsistent with clinical presentation. Strep A test will not differentiate asymptomatic carriers of Group A Streptococcus from those exhibiting streptococcal infection. A negative result can be obtained if the amount of extracted antigen is below the sensitivity of the test. Culture confirmation is recommended for all Strep A test negative test results. A single swab that is used both to inoculate a culture plate and to perform the rapid test may have reduced sensitivity in the Strep A test (Bin ax, 2004)[10].

Comparison Between RADT and Throat Culture

Name of Test	Type of Test	Sensitivity and Specificity
Throat Culture	Specimen obtained by throat swab of posterior tonsilIopharyngeal area and incubated on to a 5% sheep blood agar plate to which a bacitracin (0.04U) is applied. Result in 24-48 hours.	Sensitivity 97% Specificity 99% (Results depend on the technique, medium, incubation)
Rapid Antigen Detection Test (RADT)	Detects presence of Group A, Streptococcal carbohydrate on "a Throat swab (change in colour indicates A, positive result). Result available within minutes in office test.	Specificity 95% Sensitivity 80-100% (Depend on the test)

(Vincent et aI., 2000)[5].

RESULTS

Table 1 shows that the number and the percentage of the positive isolated cases were same i.e. 24 (9.6%) in suspected (250) cases and 04 (8.0%) among 50 healthy subjects, which shows the sensitivity of the test and its correlation with culture.

Table No.1: Comparison of %age between RADT and Culture cases.

Children	RADT +ve cases	%	Culture +ve cases	%
Suspected (n=250)	24	9.6	24	9.6
Healthy (n=50)	04	8.0	04	8.0

Table 2 shows the positive cases for group a beta hemolytic streptococci i.e. 24 (9.6%) out of 250 suspected cases and negative cases for GABHS i.e. 226 (90.4%) out of 250 suspected cases.

Table No.2: Distribution of group A and B Streptococci in Pharyngitis and Tonsillitis (n=250)

Bacterial pathogen	Cases	Percent
Positive for GABHS	24	9.6
Negative for GABHS	226	90.4

Table 3 shows the positive isolates among male children (n=166) was 15 (9.04%) and female children (n=84), 9 (10.7%) showing the distribution of GABHS according to the sex.

Table No.3: Distribution of Gabhs According to Sex by Radt

Isolates from children	Cases	Percent
Male (n=166)	15	9.04
Female (n=84)	09	10.70
Total (n=250)	24	9.60

DISCUSSION

Streptococcal pharyngotonsillitis has been a matter of medical concern over the years, particularly because of its potential for causing serious problems such as rheumatic fever and suppurative complications. The prevalence of acute pharyngotonsillitis caused by GABHS is approximately 28% to 40% worldwide; most are known to be susceptible to penicillin. This percentage also varies from region to region[1].

In countries where rapid detection tests are routinely used, a controversy exists regarding weather or not a confirmatory culture is necessary when the results are negative. Although most of the doctors do not usually follow this procedure, most of the medical societies have recommended the back up cultures[1].

The use of a rapid detection test, plus a bacterial culture for the negative results, is currently considered the most effective clinical strategy, increasing the marginal costs only slightly (it increases the initial costs, but lowers the global cost when considering the prevention of complications of the non-treated rapid test undetected cases[1].

Although several studies have shown that the rapid test, applied alone, does not have sufficient sensitivity to eliminate the need for cultures[1].

Some researchers have demonstrated that the more recently available rapid tests can be more sensitive than bacterial culture, particularty the immune assay based tests, which can give results in a few minutes[1].

Interestingly, bacterial culture has been considered by many as the "Gold Standard" method of GABHS detection, however, according to recent studies, this would be a high cost choice in relation to its effectiveness[1].

According to the American Academy of Paediatrics and the American Heart Association, a positive rapid antigen detection test may be considered definitive evidence for the treatment of Streptococcal pharyngitis. A confirmatory throat culture should follow a negative rapid antigen detection test when the diagnosis of Group A beta hemolytic streptococcal infection is strongly suspected[3].

In the present study, sensitivity of the rapid test was 100% and was confirmed by throat culture. This is approximately the same as in other studies[11]. A disadvantage of culturing a throat swab on blood agar plates is the delay (overnight or longer) in obtaining the culture results[12].

Culture of a throat swab on a sheep blood agar plate remains the standard for the documentation of the presence of Group A streptococci in the upper respiratory tract and for the confirmation of the clinical diagnosis of acute streptococcal pharyngitis. Several variables impart on the accuracy of the throat culture results, the manner in which the swab is obtained has an important impact on the yield of streptococci from the throat culture[12].

Throat swab specimen should be obtained from the surface of both the tonsils (or tonsillar fossae) and the posterior pharyngeal wall. Other areas of the oropharynx and mouth are not touched before or after the approprate areas have been sampled. In addition a false negative result may be obtained if the patient has received antibiotics shortly before or at the time the throat swab specimen is collected[12].

It has also been reported that the use of anaerobic incubation and selective culture media may increase the proportion of positive cultures. Another variable that can impart on the yield of the throat culture is the duration of incubation. Once plated, cultures should be incubated at 35-37°C for 18-24 hours before they are read. However, the period can be extended for upto 48 hours[12].

The throat culture has always been considered the "gold standard" for diagnosing the presence of Group A Streptococci. The manner in which the throat swab is obtained has an important impact on the accuracy of throat culture results[13].

CONCLUSION

The RADT is a rapid way of diagnosing the GABHS the result can be obtained within 5-10 minutes and so the treatment may be started accordingly.

While the throat culture is still considered as the Gold Standard for the diagnosis of GABHS pharyngitis. The positive as well as the negative RADT should be confirmed by the culture.

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Address for Corresponding Author:
Dr. Karam Ali Mirjat,
Asstt. Prof. of Pathology,
Dow Medical College, Karachi

Original Article

Frequency of Diseases among Flood Affected Individuals at Relief Camps of Karachi Pakistan

1. Tariq Kamal Jafri 3. Kiran Mehtab 3. Muhammad Faizan 4. Uzma Khalid Patel 5. Syeda Afsah Hashmi 6. Usaid Farooq 7. Aqeel Abdul Zohaib Ahsan 8. Zohaib Ahsan 9. Salman Ishaque Sheikh 10. Kehkashan Azeem 11. Yusha Zakai 12. Maliha Mehtab 13. Rabia Hasan

1. Asstt. Prof. of Physiology, SMC, DUHS, Karachi 2. Asstt. Prof. of Community Medicine, SMC, DUHS, Karachi 3,4,5,6,7,8,9,10,11,12 &13. Final Year MBBS Students, Sindh Medical College, DUHS, Karachi.

ABSTRACT

Objective: To determine the frequency of diseases among flood affected individuals and facilities available at relief camps of Karachi Pakistan

Study Design: A cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Community Medicine, Sindh Medical College, DUHS, Karachi from July 2010 to Nov. 2010.

Materials and Methods: A cross sectional study was conducted and data was collected by using a structured questionnaire. A sample size of 300 flood affected individuals were drawn by using convenient sampling methods from four different flood camps located in Karachi.

Results: Out of the 300 cases studied 46.0% had malaria, 90.5% of malarial patients admitted that they did not use mosquito repellents or nettings to protect themselves. About 27.3 % suffered from diarrhea and 26.7% had skin infections. Adequate water supply was supplied to 66.7% of the patients.

Conclusion: This study concluded that malaria had higher frequency at relief camps of Karachi followed by diarrhea and skin infections.

Key words: flood affected, frequency, diseases, Pakistan

INTRODUCTION

In 2010 Pakistan floods began in July following heavy monsoon rains in the Khyber Pakhtunkhwa, Punjab, Sindh, Balochistan regions of Pakistan, affected the Indus River basin. one-fifth of Pakistan's total land area was underwater.[1,2,3] The number of individuals suffering from massive floods exceeds 13 million, more than the combined total of individuals affected by the 2004 Indian Ocean tsunami, the 2005 Kashmir earthquake, and the 2010 Haiti earthquake, according to the United Nations statement 9th August, 2010.[4] In mid-September, according to the Federal Flood Commission, the damage caused by the floods revealed 1,781 deaths, 2,966 people with injuries, and more than 1.89 million homes destroyed.[5]

The Aid agencies had warned that outbreaks of diseases, such as gastroenteritis, diarrhea, and skin diseases due to lack of clean drinking water and sanitation can pose a serious new risk to flood victims.[6,7] Already been pointed out that there is growing concern over rising cases of acute diarrhea, malaria and skin diseases.[8]

On 14th August, the first documented case of cholera emerged in the town of Mingora, striking fear into millions of stranded flood victims, who were already suffering from gastroenteritis and diarrhea[9,10,11] and Pakistan also faced a malaria outbreak.[12]

The risk factors for disease epidemics and deaths in disasters are associated primarily with population displacement complicated by inadequate provisions of safe water and proper sanitation, degree of crowding, an underlying health status of the population, inaccessibility to healthcare services and local disease ecology.[13] The risk of communicable disease outbreaks is more common in the recovery phase than in the acute phase of the disaster.[14]

Water-borne diseases that could result in diarrhea are cholera, typhoid, dysentery and gastroenteritis. Diarrhea illnesses have been recognized as the most lethal infections after disasters with population displacement.[14]

The frequency of vector-borne diseases is potentially increased during post flood period as experienced by Karachi in 2010 which observed an increase in malaria cases over non-disaster periods[15]. On 15th August 2010, the Pakistan Health Department mobilized medical teams to conduct daily clinical examinations on the flood victims and health teams to inspect flood relief centers with regard to prevent and control communicable diseases. These activities were continued throughout the post-flood phase which was up to a month, until 15th October 2010, after the flood water receded. The purpose of this study to determine frequency of diseases and services available to flood affected individuals at relief camps in Karachi so that

appropriate measures can be taken to reduce the frequency of diseases among flood affected individuals.

MATERIALS AND METHODS

A cross sectional was conducted during the months of June to September and data was collected of 300 individuals by using convenience sampling. A structured questionnaire was designed to obtain information after taking consent from the study participants. The camps included were located at Gulistan-e-Jauhar, Malir, Razzakabad and Gulshan-e-Maymar. The study participants were individually interviewed for demographic, socioeconomic and diseases and services available at relief camps.

The data was entered an analyzed by using Statistical Package for Social Sciences (SPSS) version 16.0.

RESULTS

Out of the 300 individuals studied, 46.0% had malaria, 27.3 % suffered from diarrhea and 26.7 % had skin infections.

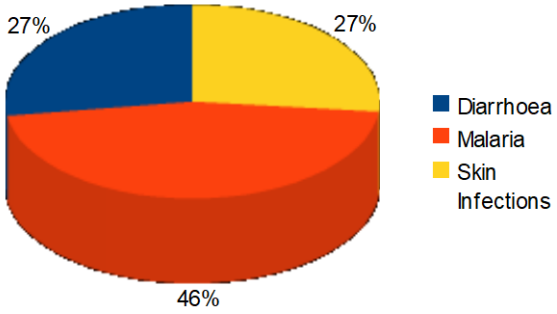

Figure 1: Frequency of diseases among flood effected

Result showed Malaria had the highest occurrence in the relief camps surveyed with a frequency of 46.0%.

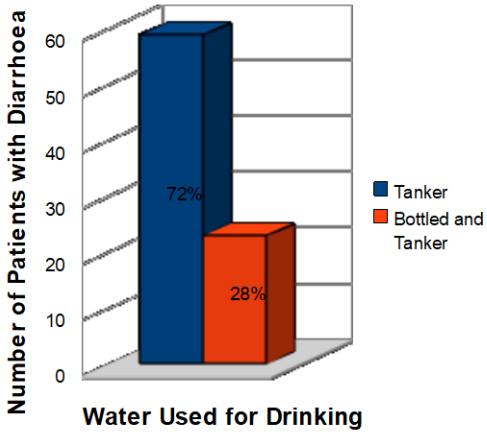

Figure 2: Type of water used for drinking

Result shows 72% of diarrhea patients were continuously ill because of drinking contaminated tanker water

Services available at relief camps:

Only 48.3% of the diseased people were provided with adequate medications, a worrying figure of 45.3% had inadequate medicine supply and 6.3% did not receive any medications at all. Regarding checkups, 79.3% of the patients were satisfied with being regularly checked by doctor whereas 20.7% were found discontented. About 100% people were satisfied that the food they were taking was hygienic. Adequate water was supplied to 66.7% of the individuals to meet their daily demands whereas 33.3% had complaints of inadequacy of water supply. When asked about the contamination of water supply, only 35.3% said that it was contaminated whereas 64.7% stated it was clean. About 5% of the people disagreed on having a specified site for disposal of house hold wastes. About 55.7% said that the disposal site was at a safe distance from their dwelling site. About 100% people agreed on having proper toilets in their camps out of which 89% were satisfied with their sanitation whereas 11% were not satisfied

Practices of individuals at relief camps:

A staggering 90.5% of malarial patients admitted that they did not use mosquito repellents or nettings to protect themselves. Among those suffering from skin conditions, 62.5% used only tanker water while 32.5% used both tanker and tap water for bathing and washing clothes. About 37.3% of the diseased did not wash their hands before eating or after using the toilets, whereas 62.7% said they did wash. About 51% of the affected people did not use any method for purification of water. Out of the remaining 49%, it was seen that 28.3% used boiling, 12.3% chlorine tablets, 6% filtering and 2.3% used lengthy storage in pots as methods of purification of water.

DISCUSSION

Diarrhea had the second highest incidence in Karachi relief camps, with a frequency of 27.3% among 300 individuals. The highest occurrence of 35.7% was noticed in Gulistan-e-Jauhar camp, where 73.2% of the inhabitants drank tanker water and 12.5% drank either tanker or bottled water. Patients presenting during flood-associated epidemics were more severely dehydrated than those presenting during non-flood periods. This may be caused by an increase in the number of cases of secretory diarrhea or to the inherent difficulty of seeking medical attention during a flood situation. Unexpectedly, none of the affected mentioned any sanitary issues yet our team personally assessed and concluded that the washrooms and surroundings did not fulfill the proper sanitary requirements. Also unexpected was the complete satisfaction with the hygiene of their food. Diarrhea disease outbreaks, which are potentially fatal, have been reported in other countries after the flooding periods as a result of consuming contaminated potable water.

Cholera had been found to be responsible for more than 16,000 diarrheal cases in the West Bengal flood disaster in 1998 and partly responsible for more than 17,000 cases in the Bangladesh flood disaster in 2004.[16,17]

In Mozambique in 2000, diarrhea was one of the prominent illnesses observed during the post-flood

period. When the Hurricane Katrina hit the United States in 2005, diarrheal illness was reported among the evacuees. During the Johore flood disaster in 2006, a total of 1,996 acute gastroenteritis cases and 46 food poisoning cases (diarrhea as one of the main symptoms) were reported. Following the Muzarabani, Zimbabwe flooding in 2007, 46 cases of diarrhea and 14 cases of dysentery were recorded by World Vision International. In 2008, widespread flooding in southern Angola caused an upsurge in cholera, with 150 deaths and 4,500 cases of the waterborne disease treated. Flooding has been shown to cause epidemics of vector-borne disease. The same monsoon rainfalls which caused flooding also resulted in pools of stagnant water which acted as favorable breeding sites for the mosquitoes. Malaria therefore showed an overall highest occurrence of 46% in the relief camps surveyed.

99.3% of the patients agreed on the presence of a substantial number of mosquitoes in the vicinity of water bodies, yet 90.5% of them denied the use of mosquito repellents or netting of any kind.

In Sri Lanka, the floods in 1934 were followed by a malaria epidemic during which 1,000,000 people were affected and at least 125,000 died. Malaria outbreaks have been reported in Muzarabani, Zimbabwe where preceding the floods in 2007, the World Vision International had recorded 85 cases of malaria. After the Namibia floods in 2009, malaria cases have increased, with 2,000 known to have contracted the disease of which 25 have died. Crowding, as a consequent of population displacement during disasters, facilitates the spread of communicable diseases especially those of an airborne and direct contact modes of transmission. Non-specific skin infections were the third highest incidence of disease, with 26.7% detected among the flood victims resulting mainly from direct skin contact with the contaminated tanker water or affected person. The majority of the cases, 49.4%, were reported in Malir camp where 42.9% and 50% of the sufferers used tanker water for bathing and washing clothes respectively, while 47.6% and 33.3% used either tanker or tap water for bathing and washing clothes respectively. A sad lacking of personal hygiene was also observed among the patients, regarding the number of times they bathed and washed their clothes weekly.

After the Hurricane Katrina struck in New Orleans, some of the evacuees were found to suffer from bacterial dermatologic conditions, whereas fungal infections were the main skin infections diagnosed among the rescue workers. During the floods occurring in Johore, Malaysia in 2006, skin infections consisted of 25.9% of the cases of communicable diseases, ranking second in incidence.

CONCLUSION

The study concluded that malaria had the highest frequency in the relief camps of Karachi, with diarrhea and skin infections coming up second and third respectively. The increased risk of these diseases is associated primarily with contamination of water supply, specifically tanker water, followed closely by inadequate medications and treatment as well as a lack of personal hygiene.

The study shows improper sanitation played an important part in this epidemiology; the patients seemed unaware of this. It can thus be safely assumed that better anticipation of the needs of the flood victims could have been made and managed through enhanced public health control programmer by reinforcing the existing stocks of medications, oral rehydration salts (for treating diarrhea), increased medical staff, family hygiene kits and water treatment units.

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Original Article

Lab Diagnosis and Evaluation of Fungal Keratitis

1. A.H. Fazle Rabbi 2.Saba Fazle Rabbi 3.S. Mohsin Turab 4.Shah Nawaz Jamali

1. Eye Specialist of Ophthalmology, LRBT, Karachi 2. Assoc. Prof. of Pathology 3. Assoc. Prof. of Pharmacology & Therapeutics 4. Asstt. Prof. of Pharmacology & Therapeutics, Hamdard College of Medicine and Dentistry Hamdard University, Karachi.

ABSTRACT

Objective: This study is aimed to evaluate the usefulness of Sabouraud dextrose agar in the confirmatory diagnosis of suspected cases of fungal keratitis.

Study Design: Pre-designed prospective study of corneal scrapings obtained after detailed slit-lamp examination and documentation from all patients seen for non-viral microbial infective keratitis.

Place and Duration of Study: This study was conducted in the Department of Ophthalmology, JPMC, Karachi from July 2008 to June 2011.

Materials and Methods: 128 cases of non-viral microbial infective keratitis. Corneal scrapings of 128 patients with microbial keratitis Smears of corneal scrapings were stained with Gram's Method and inoculated specimens on Sabouraud dextrose agar (SDA) and incubated for 3-4 days.

Results: In a series of suspected cases of fungal keratitis,119/128 (75% patients) had positive results for fungus in corneal scrapings by direct microscopy using Grams staining method and culture on Sabouraud dextrose agar (SDA). 43% males and 32% females had Candidial keratitis and 11% males and 7% females had Fusarium infection. Other samples showed presence of Gram positve cocci on smears and were negative for SDA.

Conclusion: Fungal keratitis continue to be an important cause of ocular morbidity, Since it becomes difficult to clinically diagnose and differentiate between bacterial and mycotic keratitis in complicated cases. It is better to use a standard culture medium like Sabouraud agar (SDA) when confirming ocular mycosis.

Key Words: Fungal keratitis, Ocular mycosis, Sabouraud agar, Candidia and Fusarium

INTRODUCTION

Fungal infections of cornea "mycotic/fungal keratitis" have been reported from different parts of the world[1]. In tropical region during hay forming season most common isolated fungi are Aspergillus, Fusarium and Candida[2]. Candidial keratitis is closely related to insufficient tear secretion, defective eye closure or systemic illness like Diabetes Mellitus and is closely related to minor trauma including contact lens wear[3]. The stromal keratitis caused by Candida closely resembles bacterial keratitis clinically. Clinical features include irregular, feathery margins, a dry, rough texture, and satellite lesions [4]. Microbiological investigation must be carried out when ocular mycosis is suspected due to a risk of complete loss of vision[5]. Fungal keratitis accounts for 30-40% of all cases of microbial keratitis in developing countries[6,7]. Treatment of microbial keratitis is aimed at rapid eradication of the infecting organisms with control of inflammation and tissue damage, thereby preserving the transparency of the cornea[8]. Effective treatment depends on efficient identification of the infecting microorganisms[9]. A major factor in the improved management of fungal infection has been the ability to detect fungus, thus facilitating the selection of appropriate therapy[10]. While some of the clinical features of fungal keratitis are suggestive of fungal infection, none of them can be considered absolutely pathognomic of a fungal infection. Deep seated mycosis may end up as endophthalmitis with complete loss of vision and destruction of eye. Therefore, microbiology workup in keratitis is required before initiating any treatment[11]. Despite the advent of many new techniques, culture remains the cornerstone of diagnosis of most ophthalmic mycoses. Sabouraud dextrose agar (SDA) has been the preferred culture medium for fungus by physicians[12].

MATERIALS AND METHODS

In a pre-designed prospective study was done at ophthalmic unit at JPMC, Karachi. The corneal scrapings were obtained after detailed slit-lamp examination and documentation from all patients seen for non-viral microbial infective keratitis. A common protocol for diagnosis was used in all cases. Corneal scrapings were obtained by qualified cornea specialists from the base and edge of the ulcer using a sterile surgical blade (No.15 on a Bard Parker handle) under topical anesthesia and slit-lamp magnification. Gram's stain was included as a part of the standard protocol for microscopic evaluation of corneal smears. Gram's stained smears were examined at ×400 and ×1000 magnification. Smears were examined by light microscope. Scrapings for smears were collected prior to those for culture. Sabouraud Dextrose Agar was used to inoculate the corneal scrapings. SDA was incubated at 25^0C and colonies were studied after 4 days.

RESULT

Total number of patients enrolled in the study was 128, out of which 74 were males and 54 females. Among 128 suspected cases of fungal keratitis 119 (93%) showed grey white fungal colonies. 9 cases (7%) which had appeared to be Gram positive cocci on Gram's staining could not be cultured on SDA also as shown in table # 1. 96% cases had candidial keratitis which were 43% males and 32% females. 23% cases of fusarium out of which 11% were males and 7% females was also isolated from the studied population.

Table No.1: Percentage of Male and Female in different micro-organism

Micro-organism	Male	Female	Total patients=128
Candida group	55 (43%)	41(32%)	96 (75%)
Fusarium species	14 (11%)	09 (7%)	23 (18%)
Gram positive cocci	05 (4)	04 (5%)	09 (7%)

DISCUSSION

The stromal keratitis caused by Candidia albicans mimics bacterial keratitis clinically[13]. Direct microscopic detection of fungal structures in ocular samples permits a rapid presumptive diagnosis but at time vague especially deep seated fungus in the stroma[14,15]. Use of corticosteroids in such cases would aggravate the infection as growth of fungal colonies is augmented by topical steroids[16]. Once fungi enter the host tissue it becomes very difficult to treat it by medication alone and the chances of endophthalmitis are increased manifold. In such complicated and severe cases attempt is made to remove antigenic/infectious agent and necrotic debris along with antifungal prior and after surgery. Therefore microbiological investigation of suspected ocular mycosis is mandatory to reach conclusive diagnosis before starting topical corticosteroids[17, 18, 19]. For Candida, Fusarium etc SDA is the recommended culture medium. The fungal colonies are visible on SDA after incubation of 3-4 days. Colonies of Candida appear as grey white on SDA[20]. In our study we made early identification of fungal elements on staining corneal scrapings with Gram's stain and inoculated the samples on SDA for 3-4 day also. The most frequently isolated fungi are the Fusarium, Aspergillus, and Candida[21]. C. albicans is the most frequent cause of fungal keratitis[22].

CONCLUSION

Fungal infections of the eye continue to be an important cause of ocular morbidity, particularly in the developing world. Since it becomes difficult to clinically diagnose and differentiate between bacterial and mycotic keratitis it is better to use a standard culture medium like Sabouraud agar (SDA) when confirming ocular mycosis. Understanding ocular infections will improve the outcome and reduce chances of fatality like endophthalmitis.

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Address for Corresponding Author:
Dr. A.H. Fazle Rabbi,
Eye Specialist of Ophthalmology,
LRBT, Karachi.
Cell No. 0300-2219089

Original Article

Single Stage Primary Closure of Bladder Exostrophy VS Two Stage Closure: Experience of 18 Patients

1. Asif Abbas Khawaja 2. Muhammad Aslam 3. Muhammad Imran

1. Asstt. Prof. of Pediatric Urology 2. Sr. Registrar of Paediatrics Surgery 3. Sr. Registrar of Paediatrics Urology, Children Hospital Complex & Institute of Child Health, Multan

ABSTRACT

Objective: To study the outcome and complications of single stage primary repair of Bladder Exostrophy and compare it with two stage repair.

Study Design: Descriptive study

Place and Duration of Study: The study was carried out at Paediatric Urology Dept, Children Hospital Complex & Institute of Child Health, Multan from 1st January 2008 to 30 December 2009.

Patients and Methods: We retrospectively reviewed the records of all patients operated for primary single stage and two stage repair of Bladder Exostrophy. Patients were divided into two groups based on the type of surgery performed. Group I consist of patients with single stage complete repair and group II consist of patients with two stage repair. Data of both groups was entered on a proforma and surgical outcome, complications and urinary continence was noted.

Results: There were total 18 patients 13 male, 3 female, Group I (3male 5female) and Group II (10 male). Age ranges from two days to one year in group one with mean age of four months and in group two age ranges from four days to one year with mean age of six months.

Average surgery time, bloodloss and anaesthesia recovery time was slightly higher in Group I but the complications like wound infection, wound dehience and reoperation rate was also more in Group I as compared to Group II. Long term outcome like VUR, continence interval was similar in both groups.

Conclusion: Single stage primary repair offers the advantage to correct the defect in one sitting and psychologically comfortable for the parents but it needs greater surgical experience and complications are higher in male patients. In our current setup single stage complete repair is suitable in female patients but in males two stage repair is more appropriate with satisfactory results.

Key Words: EEC (Exostrophy Epispadias Complex, VUR (Vesico Ureteral Reflux), Cantt-well Ransley Urethroplasty, Pelvic osteotomy, Urinary continence.

INTRODUCTION

Exostrophy Epispadias Complex (EEC) of genitourinary malformations can be as simple as glandular epispadias or an overwhelming multi system defect such as clocal exostrophy.

The first account of Bladder exostrophy is ascribed to Asyro Bablonia sources dating from 1st and 2nd millennia BC; however first clear description of Bladder Exostrophy is attributed to Schenck in 1595[1]. Its incidence has been estimated as between 1 in 10,000 to 1in 50,000 [2]and male ratio female is 5:1 to 6:1. The etiology of Bladder Exostrophy is not known but reports from two centers suggest possible hormonal cause[3] of the complex. A possible genetic basis for development of EEC is being explored.[4]

In Classic Bladder Exostrophy, most abnormalities are related to the defects of abdominal wall, bladder, genitalia, pelvic bones, rectum and anus. Abdominal wall shows triangular defect occupied by exostrophy bladder and posterior urethra, limited inferiorly by inter-symphysial band and laterally by divergent recti. There is diastasis of pubic symphysis along with external rotation of anterior and posterior pelvis. As a result there is wide separation of crural attachments, prominent dorsal chordee and shortened urethral groove. In females the vagina is short, orifice is stenotic, clitoris is bifid and labia, mons pubis, and clitoris are divergent.

Although a myriad of operations for exostrophy have been proposed and attempted, these operations can be broadly categorized into two approaches. First approach includes operations for urinary diversion and the second includes procedures to reconstruct the bladder either in multistage or in a single stage. In single stage procedure pelvic osteotomy is followed by primary bladder reconstruction, anterior urethroplasty with penile disassembly technique in male, pubic approximation and fixation, abdominal closure and skin coverage. In two stage repair pelvic osteotomy is followed by primary bladder and posterior urethra repair, pubic approximation and abdominoplasty in first stage . Bladder exostrophy is converted into complete epispadias in this stage. Anterior urethroplsty is prformed one year later after primary repair with modified Cantt-well Ransley urethroplasty.

The single stage approach offers the advantage to correct penile bladder and abdominal defect in one setting, but it requires greater expertise and complication rate is high, whilst the two stage operation offers the advantage of less complication and the results are equally satisfactory.

The purpose of this study is to compare the advantages and disadvantages of single stage complete repair versus two stage closure of primary bladder exostrophy.

PATIENTS AND METHODS

This study was carried out at Children Hospital Complex, Multan during two years period from 1st January 2008 to 30th December 2009. There were 18 children (5 females 13 male). Children included in this study ranges from 2 days to one year. Patients with associated exampholos, previous failed repair and small dysplastic bladder template unsuitable for primary repair were excluded from this study.

All patients presenting to out door or referred from other hospitals were considered. Common presenting symptoms were visible abdominal and genital defect with continuous leaking of urine from this defect.

Complete history was taken along with general physical examination performed. Blood tests Complete blood examination, Complete Urine Examination, serum urea, creatinine, Sodium and Potassium, x-ray chest x-ray KUB and Ultrasound abdomen performed in all patients. Bladder template was also assessed under anesthesia for suitability of closure regarding size, surface and elasticity. Bladder mucosa was immediately protected by thin moist plastic sheet which was continuously irrigated and changed frequently to prevent mucosal ulceration.

Patients were divided into two groups based on the type of surgery performed for closure of defect.

First group 8 patients (5 females 3males) were operated by single stage complete repair i.e bilateral posterior pelvic osteotomy, cystoplasty, abdomino-plasty, pubic approximation, total penile disassembly and anterior urethroplasty by modified Cantt-wel Ransley technique. Second group 10 patients (all male) two stage repair was done i.e bilateral posterior pelvic osteotomy, cystoplasty, abdominoplasty, pubic approximation and bladder neck repair early while total penile disassembly and anterior urethroplasty by modified Cantt-wel Ransley technique one year after primary repair was done.

After surgery patients were monitored in PICU for 24 hours and then moved to Pediatric Urology ward. Post operatively gallows were applied for 14 to 21 days in 15 patients and hipspica in 3 patients. Intravenous broad spectrum antibiotics were given for nine to ten days. All patients were discharged on low dose antibiotics and called for follow up in outdoor at 2 weeks, 6 weeks, 3 months and then after every 3 months for 2 years. During follow up wound was examined to see any dehiscence, uretheral fistula formation, motor and sensory system of lower limbs were also examined. Voiding history was taken and continence interval, bedwetting during day and night was noted. In every follow up Complete Urine examination and culture sensitivity, serum urea, Creatinine and Ultra-sonography of abdomen was done. Micturation cystouerthrography at six months & DTPA renal scan was done yearly to see bladder capacity, vesico ureteral reflux and any deteoriation in renal function. Data of both groups of patients was recorded on proforma and compared.

RESULTS

There were eight patients in group I (three males and five females) and ten patients in second group II (all male). Age ranges from two days to one year in group one with mean age of four months and in group two age ranges from four days to one year with mean age of six months.

Table No.1: Early Outcome of Surgery

	Group I	**Group II**
Surgery time	M 4.5 to 5 hours	M 2.5 to 3 hrs (stage I)
		M 1.5 hours (stage II)
Blood loss	M 100 to 150 ml	M 50 to 70 ml (stage I)
	F 80 to 100ml	M 15 to 20ml (stage II)
Anesthesia recovery	15 to 20 mints time	15 to 18 mints
Ventilator support needed	M 1	Nil

Table No.2: Comparison of Complications

	Group I	**Group II**
Infection (superficial)	3(37.5%) 1M(12.5%)2F(25%)	2(20%)
Wound dehiscence		
Abdomen (Complete)	1 M(12.5%)	None
Abdomen (normal)	1 F(12.5%)	1 M(10%)
Bladder (Complete)	1 M(12.5%)	None
Urethra (Complete)	1 M(12.5%)	None
Uretheral fistula	1 F(12.5%)	2 M(20%)
Osteotomy Complications		
Wound infection	1 F(12.5%)	None
Skin excoriation	2F (25%)	3M(30%)
Foot drop	None	1(10%)
Sepsis (shock)	1M (12.5%)	None
Re-operation	2 (25%) (1 M12.5%,1F12.5%)	None

Comparison of average surgery time, blood loss, recovery from anesthesia and needing ventilator for group I and group II are shown in the table 1.

All females were managed with single stage complete repair as female urethroplasty needed 30 to 40 minutes of surgery. In male approximately 1.5 hours is needed to perform urethroplasty and the surgical expertise required to complete this delicate operation is much greater in male patients as compared to female patients.

Comparison of complications between the two groups is shown in table 2.

Table No.3: Long Term Outcome

	Group I	Group II
Continence interval		
2.5 to 3 hours	5 (3F, 1M)	6 (M)
2 to 2.5 hours	1 (F)	2 (M)
1.5 to 2 hours	2 (1F)	2 (M)
Less than 1 hour	1 (1M)	None
Clean Intermittent Catherization (CIC)	3 (2F, 1M)	2 (M)

In, Group I, one male patient went into septic shock and was on ventilator for 8 days. He survived the sepsis but had complete dehiscence of repair and needed major reconstructive surgery later. Majority of patients with superficial infections healed with conservative treatment. In Group II, two patients developed peno-pubic area fistula after second stage repair. Both patients healed spontaneously with conservative treatment.

Bilateral posterior pelvic osteotomy was successfully done with no major complication. Pubic bones approximation was nearly complete. Skin excoriation occurred in 3 patients which healed spontaneously. One patient develop (male) in group II developed left foot drop after surgery which recovered partially with physiotherapy.

Comparison of results regarding continence and need for Clean Intermittent Catherization (CIC) one year after complete repair are shown in table 3.

In patients with single stage complete repair 2 females developed partial urethral stenosis and was later managed by CIC. All 8 patients developed Vesico-ureteral reflux of (5 of grade 3, 3 of grade 4) and managed conservatively. No incidence of recurrent Urinary tract infection was noted.

In 10 patients with two stage repair, all developed vesico-ureteral reflux (six of grade 3 and 4 with grade 4) & managed conservatively. No incidence of recurrent Urinary tract infection was noted

DISCUSSION

Primary closure is the most logical treatment of Bladder Exostrophy with restoration of abdominal wall defect and preservation of renal function. Preoperative assessment and post-operative care is the key for successful surgery.

Efforts to reconstruct the genitourinary system have been tried for over hundred years. Primary closure cannot be achieved when there is hard fibrotic bladder with a small capacity. Trendelenburg (1906)[5] for the first time attempted to reconstruct an exostrophic bladder to achieve urinary continence but his patients did not gain satisfactory continence. Such discouraging results let to abandonment of the functional reconstruction and cystectomy with uretero-sigmoidostomy became the treatment of choice. Young[6] in 1942, Ansell [7] in 1971 and Montagnani[8] in 1982 reported several patients with single stage functional bladder closure. Because of lower rate of urinary continence 0% to 45% and high incidence of renal damage 90% due to bladder outlet obstruction, reconstructive surgical efforts were directed toward staged bladder reconstruction, an approach pioneered and advocated by Dr. Robert Jeffs.[9]

To gain satisfactory results from surgery certain points must be considered. Early operative treatment and in newborns with a wide pubic diastasis anterior or posterior pelvic osteotomy are major factors in maintaining a large bladder volume. Schmidt[10] reported experience of bilateral posterior pelvic osteotomy series of patients in 1993 that osteotomies assist closure and enhance anterior pelvic support which may improve later urinary continence. Purves [11](2007) performed combined vertical iliac and horizontal in nominate osteotomy in staged bladder reconstruction and reported satisfactory results. Similar findings were noted by Salman Riaz[12] at Agha Khan University hospital in 2005. Our experience of osteotomy (posterior pelvic in 17, anterior iliac in one)was also satisfactory. It helped in closure of abdomen and contributed towards achievement of continence. There were no significant complications except one patient who developed left foot-drop which late rimproved.

The single stage anatomic approach offers the advantage to correct the penile, bladder, and bladder neck abnormalities in one setting.[13] In a review of records of patients evaluated for the genital complications following complete repair of bladder exostrophy from 1996 to 2003 at myo clinic, Minnesota by Husmann, [14] 9 patients were noted to have serious genital injuries including complete loss of glans and corporal bodies and penile urethra. Baired[15] after reviewing records of 38 patients at Brandy Urological institute with previous failed primary closure or delayed closure reported very high complication rates, lot of patients needed additional surgery and continence rate at best was reported as 50%. In our experience of 8 patients with single stage repair, two females had superficial wound infection one male developed sepsis and complete dehiscence of wound. These findings dampen our enthusiasm for this procedure. These new techniques currently the Mitchell[16] or CPRE technique have a lower complication rate and urinary continence

can be achieved for many of these patients without the need for further bladder neck reconstruction.

After unsuccessful primary treatment in patients with EEC, the options for a surgical solution to preserve the upper urinary tract, to achieve complete continence and to reconstruct the genitalia are limited. Stein[17] from Germany (1999) reviewed 128 patients after unsuccessful or unsatisfactory primary closure and concluded that first operative intervation in patients with bladder exostrophy determines their fate. Similar results were reported by Osterling[18] at John Hopkins (1987) after review of 144 patients. In our experience in patient with complete dehience of wound, secondary repair was difficult, continence interval short and bladder was small in capacity which later needed augmentation cystoplasty. But our experience with 5 females & 2 male patients was excellent and both healed successfully with minimal complications. In females single stage repair has shown good results. There are no serious early complications and long term outcome like urinary continence rate is also satisfactory.

Since 1970 the staged reconstruction of bladder exostrophy has yielded consistent surgical success. Baker[19] in 1998 at John Hopkins reported early abdominal closure in two stages with bilateral pelvic osteotomy, bladder, abdomen and posterior urethra at first stage and after 1 year anterior urethra closure by modified Canttwell Ransley technique in patients suitable for primary closure. This approach usually results in a continent, voiding patient with pleasing external genitalia and preserved renal function. Our experience of 10 male patients with two stage repair was satisfactory with no serious complications and good long term outcome. Two stage repair with pelvic osteotomy has shown world wide good results with minimal complications, satisfactory cosmetic appearance after closure and urinary continence rates are good.

Baka[20] in 2000 reported a series with two stage repair continence rate of 75% in patients with classic bladder exostrophy. Similarly Baired [21]in 2006 after reviewing the record of 131 patients reported that patients with a good bladder template who develop sufficient bladder capacity after successful primary closure can achieve acceptable continence without bladder augmentation and intermittent catherisation.

Single stage closure saves the patient from second surgery and anesthesia and psychologically comfortable for the parents, but it needs greater surgical expertise with prolong anesthesia time. We recommend that such surgery should only be done in specialized institutions with pediatric and neonatal intensive care units. Although our experience with male patients for single stage repair is limited (2 Patients) but complications were high as compared to females. Two stage repair require two separate surgeries with anesthesia and prolong hospital stay but the results were good even in male patients. We therefore recommend that single stage complete repair of Bladder Exostrophy may be done with satisfactory results in females but for primary closure in males two stage repair is more appropriate.

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Address for Corresponding Author:
Dr. Asif Abbas Khawaja,
Assistant Professor Pediatric Urology,
Children Hospital Complex Multan
Contact: 0300-6335715
Email Address: dr_asif_kh@yahoo.com
Postal Address: 204/B, Jameel Abad,
Airport Road, Multan.