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Editorial

Beverages – May raise the Blood Pressure and Contributors to Cardiovascular Diseases – A Study

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

New research suggests that drinking sodas and other sugar-sweetened beverages every day may raise blood pressure, but a beverage industry trade group calls the study significantly flawed.

Sugar-sweetened beverages are the No.1 source of added sugars in the American diet, and the research is among the first to link them to higher blood pressure. The study found that the more sugary sodas and other sugar sweetened beverages people drank, the higher their blood pressures tended to be.

Every extra sugar-sweetened beverages drank per day was associated with a 1.6 point rise in systolic blood pressure and a 1 point rise in diastolic pressure. The highest blood pressures were seen in study participants who drank the most sugar sweetened beverages and also had the most added salt in their diets, study co-author J. Brown, PhD, tells WebMD.

"We know that salt is a risk factor for high blood pressure," Brown says, " But our findings suggest that sugar and salt together may be worse than salt alone."

Brown says this finding needs to be confirmed, adding that the research does not prove sugary sodas and other sources of added sugar in the diet to have a direct impact on blood pressure.

That's because the study was observational, meaning the participants were asked to recall what they drank instead of directly comparing participants given a specific amount of sugar sweetened beverages to participants who were not given sugar sweetened beverages.

People who reported drinking the most non-diet sodas and other sugar-sweetened drinks also had the highest overall intake of calories and salt and were the most likely to be obese. Maureen Storey, PhD, of the soda industry group American Beverage Association, agrees the study does not prove a link between sugar-sweetened beverages and elevated blood pressure.

"Finding a very weak association between two things does not establish a cause and effect," she said.

"This study has significant flaws. In fact, the blood pressure changes noted by the authors are inconsequential and well within standard measurement error."

In an interview with Web MD, Storey said there is little evidence that sugar sweetened beverages are unique contributors to cardio-vascular disease. "A calorie is a calorie, and what the data clearly show is that we are eating too much and taking in too many calories, period." She says, adding that Americans are consuming fewer sugar sweetened beverages than they were a decade ago.

The research included close to 2,700 middle aged people in the U.S. and U.K. who were enrolled in a larger health study. The participants reported what they ate and drank for four days, during which time their blood pressures were taken eight time. They also completed a detailed questionnaire examining lifestyle, medical and social issues.

Peoples who reported drinking more than one serving per day of sugar sweetened drinks took in an average of about 400 calories more each day than people who drank no sugar sweetened beverages.

The American Heart Association recommends that women limit added sugars in their diets to no more than 100 calories a day and men limit added sugars to 150 calories.

A typical 12-ounce can of sugar-sweetened soda has about 140 calories and just about all the calories come from added sweeteners "(non-diet) sodas are basically sugar water with or without caffeine." AHA spokesperson Rachel K. Johnson, PhD, tells WebMD. They are the No.1 source of added sugars in a population where the majority of people are overweight."

She concedes that a direct link between soda consumption and obesity and cardiovascular disease would be difficult to prove, but adds that she does not think the science linking sugar sweetened beverages to these health issues has been over played.

Johnson is a professor of nutrition at the University of Vermont.

"I don't think anyone would say that limiting sugar sweetened drinks is the only solution," she says. " But to me, it is an important step in the right direction."

A Soda a day? That's not so bad. A 150 calories blip, burned off with a brisk half-hour walk. But it's not only your waistline that's at stake.

A study released in the journal Diabetes Care found that people with a daily habit of just one or two sugar sweetened beverages anything from sodas and energy drinks to sweetened teas and vitamin water were more

than 25 percent likelier to develop type 2 diabetes than were similar individuals who had no more than one sugary drink per month. Since the overall rate of diabetes is roughly 1 in 10, an increase of 25 percent raises the risk to about 1 in 8. One a day guzzlers in the study also had a 20 percent higher rate of metabolic syndrome, a collection of indicators such as high triglyceride levels suggesting that diabetes is not far off.

"Previous studies have shown that sugar sweetened beverages are strongly associated with weight gain," says lead author Vasanti Malik, a research fellow in the Harvard School of Public Health Department of Nutrition, who says the decision to examine the relationship between sugar sweetened beverages and risk of diabetes was the logical next step."

The researchers conducted a study of studies a meta analysis to reach their conclusion. They identified eight studies with enough data to let them check for a link between sugary drinks and type 2 diabetes and three similar studies of metabolic syndrome. The largest diabetes study, which followed more than 91,000 American women ages 24 to 44 for eight years, made the strongest case for a relationship, and it wasn't just because higher consumption of sweetened drinks added excess calories that turned into pounds. While weight gain is a known diabetes risk factor, the diabetes beverage link persisted even after adjusting for that.

"Other factors independently put you at risk for developing diabetes," says Malik.

The main one is spikes in blood glucose and insulin because sweetened drinks are often consumed quickly and in large quantities and their sugar content is rapidly absorbed. Frequent spiking can lead to insulin resistance, inflammation and hypertension often precursors to diabetes. High-fructose corn syrup, the sugar in many sweetened drinks, is emerging as possibly riskier than other sugars because it seems to produce more belly fat. Fat that accumulates around the middle is closely tied to high blood pressure and other cardiovascular problems.

Americans love sweetened drinks. Consumption climbed to an average of 142 calories a day or nearly one 12-ounce can of soda, in 2006, from 65 in the late 1970s. And many people down far more than that, notes Frank Hu, a senior author of the study and a professor of nutrition and epidemiology at Harvard, which puts them at a much greater risk of diabetes. A report from the Centers for Disease Control and Prevention released earlier this week projects that by 2050, 1 in 3 Americans will develop the disease.

In a study 28 percent of children with hypertension were also reported to have learning difficulties. (Posed by model).

Children who have high blood pressure are four times more likely to have learning disabilities than children with normal readings, according to a study.

U.S researchers said while it was well known that hypertension could increase the risk of heart disease, their study suggested it could also affect mental development in the young. Dr. Heater Adams, of University of Rochester Medical Center, said: "This study found that children with hypertension are more likely to have ADHD (attention deficit hyperactivity disorder).

Although retrospective, this work adds to the growing evidence of an association between hypertension and cognitive function. Around four percent of children in the U.S are now estimated to have high blood pressure. The UK figure is not known because Britain has no standard definition of hypertension in children.

There isn't a defined series of measurements for blood pressure in children. A U.S working group said children with high blood pressure had readings that were higher than 95 percent of their peers who were the same age, height and weight.

The study published in the journal Pediatrics, looked at 201 patients aged between 10 and 18 years old who had been referred to the hypertension clinic at URMC's Children's Hospital. They found 101 had hypertension, or sustained high blood pressure. Of these, 28 per cent had learning disabilities well above the general population's rate of five percent.

Previous studies excluded children with ADHD because medications can increase blood pressure. However, researchers included them this time because it is also possible that the higher rate of ADHD among children with hypertension is a reflection of mental development problems caused by hypertension.

Original Article

Mortality Among Neonates Having Birth Asphyxia at Neonatal Intensive Care Unit P.M.C.H.

1. Ali Akbar Siyal 2. Babar Dahri 3. Juveriya Naquvi 4. Abdul Hameed

1. Prof. of Paeds Medicine 2, 3 & 4. Trainee RMOs, Dept. of Paeds Medicine,
Peoples University of Medical & Health Sciences Nawabshah

ABSTRACT

Objective of study: To see the outcome of birth asphyxia in tertiary care hospital Nawabshah.
Study design: Retrospective descriptive study.
Place and Duration of Study: The study was conducted at neonatal intensive care unit (N.I.C.U) Paediatric ward of People's medical college and hospital Nawabshah from 1st January 2010 to 31st December 2010.
Patients and Methods: Record of patients who were admitted in N.IC.U was used for data collection. Data regarding sex, gestational age (term and preterm), and outcome (discharge, expired) was collected.
Results: During study period 1657 neonates were admitted, of these 1371. Were term infants 286 were preterm infants, there were 1144 males, and 513 Females. Out of 1657, 466 (22%) patients expired, out of these 466 expired patients, 391(83.9%) were term babies and 75 (16.09%) were preterm.
Conclusion: All the patients admitted in our NICU, birth asphyxia was the leading cause of Neonatal admission and mortality. And birth asphyxia stage 3 HIE had the highest mortality.
Key Words: Mortality, neonates, Birth asphyxia, NICU.

INTRODUCTION

There is no universally accepted clinical definition of Asphyxia. Birth asphyxia is a widely used term for clinical diagnosis, but there is a little consensus as to what is meant by it[1]. Each year approximately 4 million babies are born asphyxiated, which results in 1 million deaths and an equal number of serious neurological sequelae, such as cerebral palsy, mental retardation, and epilepsy[2]. It is estimated that around 23% of all newborn deaths are caused by birth asphyxia, with a large proportion of stillbirths[3]. There are many reasons a baby may not be able to take in enough oxygen before, during, or just after birth. A mother may have medical conditions that can lower her oxygen levels; there may be a problem with the placenta that prevents enough oxygen from circulation to the fetus; or the baby may be unable to breath after delivery[4]. Historically, asphyxia was categorized into two grades of severity, Asphyxia Pallida and Livida, indicating varying degrees of affliction. Infants with asphyxia Pallida or pale asphyxia were generally regarded as more severely afflicted, requiring immediate resuscitation[5]. According to the World Health Organization (WHO), between four and nine million newborns develop birth asphyxia each year. Of those, an estimated 1.2 million die and at least the same number develop severe consequences, such as epilepsy, cerebral palsy, and developmental delay[6]. Therefore this is very critical period to reduce the under five mortality and to reach the millennium development goal 4 (MDG4). In our country where most of the newborns are born outside the hospital setting, and even in hospitals there is no proper data collection and registration facility available, it is very difficult to accurately assess the real burden of mortality and morbidity during perinatal period. Epidemiological research is needed to accurately estimate the contribution of birth asphyxia to perinatal morbidity and mortality, especially in community settings where the burden of disease, due to high proportion of unattended deliveries, is likely to be larger than in the hospital setting [7].

This study was conducted to look at the mortality among newborns clinically diagnosed as having birth asphyxia reaching a tertiary care setting.

PATIENTS AND METHODS

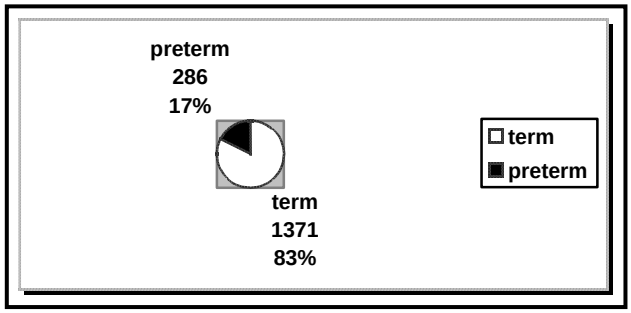
A retrospective study was conducted from the records of patients admitted from January 2010 to December 2010 at NICU Paediatric ward PMCH, the data included was sex, gestational age (term and preterm), outcome (expired, discharged). The patients who left against medical advice (LAMA) were not included. Data was analyzed using SPSS v.15.

RESULT

During our study period , total 2584 neonates were admitted, 1657 patients were admitted due to birth asphyxia, of these 1371 (83%) were term infants and 286 (17%) were preterm infants (fig.1). Out of these 1144 (69%) were males and 513 (31%) (Fig 2). In term infants 571 (41.65%) patients were in stage 1 HIE, 365

(26.62%) were in stage 2 HIE and 435 (31.73%) were in stage 3 HIE. (Table 1 fig 3). While 17 (1.24%) patients were expired in stage 1, 84 (6.12%) patients expired in stage 2 and 290 (21.15%) expired in stage 3 HIE. In preterm infants total admission was 472, 286 (17%) preterm were admitted with birth asphyxia, out of these 211 (73.78%) were discharged and 75 (26.22%) expired (table 2 fig 4). So, the total admission due to birth asphyxia during study period was 1657, out of which 466 (22%) patients expired (fig.5) out of these expired patients 391(83.9%) were term babies and 75 (16.09%) were preterm.

Figure No.1



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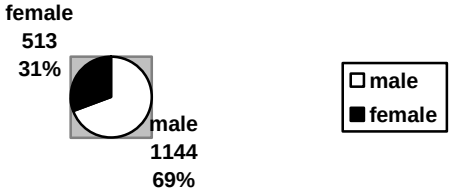

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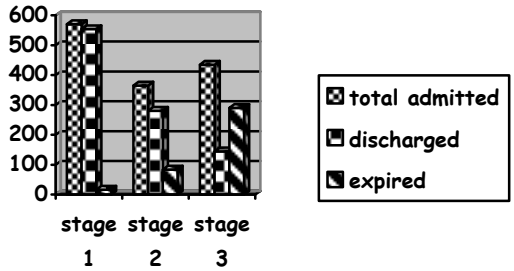

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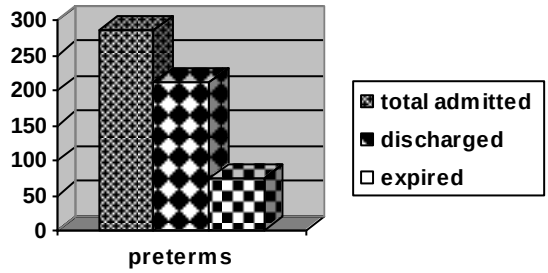


Table No. 01: Birth asphysic in term newborns

	Stage 1	Stage 2	Stage 3
Total admitted	**571 (41.65%**	**365 (26.62%)**	**435 (31.73%)**
Discharged	**554 (40.41%**	**281 (20.50%)**	**290 (21.15%)**
Expired	**17 (1.24%)**	**84 (6.12%)**	**290 (21.15%)**

Table No. 02: Birth asphyxia in preterm

Total admitted	286	%ages
discharged	211	73.78%
expired	75	26.22%

Figure No.5

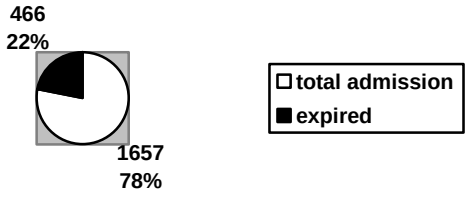
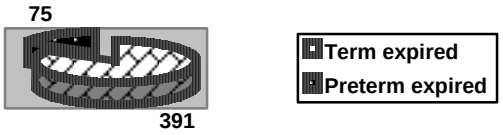


Figure No.6



DISCUSSION

Birth asphyxia is one of the most important causes of neonatal brain injury whose incidence ranges from 3.7 to 9 per thousand deliveries in the west [8]. Majority agree that birth asphyxia is the failure on the part of newborn to breathe spontaneously within one minute after birth [9]. In countries like Pakistan it is even higher because of negligible antenatal care and poor perinatal services. Another main problem is Data from hospitals in Pakistan and NICUs of low resource setting is very limited, and published data is very scanty. Almost 80% of the deliveries take place at home in our community where skilled and trained personnel as well as pediatric supervision are lacking[10].

In our study, 1657 patients with birth asphyxia were admitted during the study period. In our neonatal unit birth asphyxia accounts for the majority of admissions while in study from university of Zambia showed about quarter of neonatal survivors were suffering from Birth Asphyxia [11]. While a study from dhulikhel hospital Katmandu showed Birth asphyxia was one of the commonest causes of admission and mortality in NICU. Babies with HIE Stage III had a very poor prognosis [12] results were similar to our study. Preterm is defined as gestational age less than 37 weeks of gestation measured from the first day of the last normal menstrual period, in our study we admitted 286 (17%) preterm newborns with birth asphyxia, national data on preterm birth asphyxia was not available to match our results with, while a study from Alexandria (Egypt) showed that there was premature admission and death rate were high [13], The percentage of preterm in six countries namely Cuba, Hungary, New Zealand, Sweden, Australia and Japan rated 10.5%, 19.5%, 4%, 4.5%, 10.5% and 2.5% respectively. In the United States, preterm among blacks and whites were 17.8% and 8% respectively [14]. In our study there is a male predominance 1144 (69%), this male predominance is also reported in other studies, and this may be because of preference of parents for the male child.

In our study highest %age of expired patients belonged to stage 3 HIE (21.15%) Study from Tanzania 92.3% of neonates with Mild HIE discharged within seven (7) days while more than half those with severe HIE (51.3%) died and 72% of deaths occurred within first three (3) days of life [15]. similar results were shown in a large community based prospective study in Lahore that nearly 50% of all neonatal deaths in the first week were due to birth asphyxia[16.] However the HIE classification is not mentioned in that study.

CONCLUSION

From our study it is concluded that:

- Birth Asphyxia is still the major cause of hospital admissions in neonates, despite widespread availability of trained staff.

Infants having birth Asphyxia stage 3 HIE have the highest mortality.

RECOMMENDATION

Our recommendations based on our study are:

- All mothers should be offered a proper antenatal care.
- High risk pregnancies should be referred early to centers where NICU facilities are available.

Birth attendants and obstetricians should be trained in early recognition of the newborns that need resuscitation.

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Address for Corresponding Author:
Ali Akbar Siyal,
Prof. of Paeds Medicine,
Peoples University of Medical & Health Sciences
Nawabshah.

Original Article

An Audit of Undescended Testis treated at DHQ Hospital Abbottabad

1. Asif Saeed 2. Muhammad Nawaz 3. Samson Griffin

1. Asstt. Prof. 2. Assoc. Prof. 3. Prof. Dept. of Surgery, Women Medical College, Abbottabad

ABSTRACT

Background: Undescended testis or cryptorchidism which occurs in 2% of boys born at term, is one of the most common congenital abnormalities. Cryptorchidism is associated with impaired fertility and is a risk factor for testicular cancer. There is evidence that post natal germ cell development deteriorates in the undescended testis after the first year and perhaps for this reason, the risk of infertility increases with age. The question of whether the age at treatment has any effect on the risk of testicular cancer is controversial.

Primary management of cryptorchidism is surgery which is usually performed in infancy.

Study Design: A retrospective study.

Place and Duration of Study: This study was conducted at DHQ Hospital Abbottabad from Oct 1998- Dec 2008.

Patients and Methods: Total of 159 patients were treated during this period. Children of all ages were included. The patients were divided into different age groups. Patients were investigated with physical examination, ultrasonography, CT scan and MRI. All patients were treated with open surgical orchidopexy. Pre operative complications were evaluated. Patients were followed up and complications were noted.

Results: The common age group was above 05 yrs 80 patients (50%).Rt side was involved in 82 cases(52%) and Lt side in 54 cases(34%). Inguinal hernia was the most common associated finding 76 cases(48%) with cryptorchidism. The results indicate that age at orchiopexy has an effect on the risk of testicular cancer in boys with an undescended testicle. The risk among those treated at 13 years of age or older was twice the risk among those who were treated at younger ages.

Conclusions: Failure of the testicle to descend through the inguinal canal during the fetal life may be related to enough of a specific type of maternal hormones, failure of testis to respond to inadequate pull from the gubernaculum, or various other factors. Ultrasound can help to identify testicle located in the inguinal canal, but is of limited use for intra abdominal testis. MRI and CT scan can be useful for intra abdominal testis, but they are often difficult to use on small children and have a high rate of false negative results. Many men who were born with undescended testes have reduced fertility, even after orchiopexy in infancy. The most effective treatment is surgery which is usually performed in infancy. Hormonal treatment has the advantage of avoiding anesthesia and being minimally invasive. HCG is the drug of choice. However success rates have been reported to be as low as 10%. The principal major complication of all types of orchiopexy is loss of the blood supply to the testis, resulting in the loss of the testis due to ischemic atrophy or fibrosis.

Key Words: Cryptorchidism, Testicular torsion, Orchiopexy, Retractile testis.

INTRODUCTION

Undescended testis, also called cryptorchidism, is a common condition in which reproductive gland is located outside the scrotum. The condition may be unilateral or bilateral. Cryptorchidism literally means hidden testis. Cryptorchidism occurs more frequently in preterm boys (30 %) and almost is associated with inguinal hernia, although most are not symptomatic.

Incidence is 3-5% in full term boys and 1.8% at one year age. More than 80% of undescended testis are on one side, the other side is usually normal. Diagnosis of this condition is made through physical examination at birth. Generally radiologic imaging is not reliable. Ultrasound can help to identify testicle located in the inguinal canal, but is of limited use for intra abdominal testis. MRI and CT scan can be useful for intra abdominal testis, but they are often difficult to use on small children and have a high rate of false negative results. The most common diagnostic dilemma in otherwise normal boys is distinguishing a retractile testis from a testis that will not descend spontaneously into the scrotum. In minority of cases the bilaterally non palpable testes, further testing to locate the testes, assess their function, and exclude additional problems is often useful. Pelvic ultrasound or magnetic resonance imaging can often, but not invariably, locate the testes while confirming the absence of uterus.

PATIENTS AND METHODS

A retrospective study was carried out in DHQ Hospital Abbottabad from Oct 1998 to Dec 2008. A total of 159 patients were included in this study. Children of all ages were included. The patients were divided into different

age groups. Patients were investigated with physical examination, ultrasonography, CT scan MRI. All patients were treated with open surgical orchidopexy. Mostly single stage orchiopexy was done but in some cases surgery was done in two stages. All surgeries were done under general anesthesia and the patients were discharged the next day. Pre operative complications were evaluated. Patients were followed up and complications were noted. Results were evaluated and thorough search of the literature was done and results compared with the international studies. Conclusions drawn after thorough search of the literature.

RESULTS

The results from the collected data indicate that age of orchiopexy has an effect on the risk of testicular cancer in boys with an undescended testicle; the risk among those treated at 13 years of age or older was twice the risk among those who were treated at younger ages. The principal major complication of all types of orchiopexy is loss of blood supply to the testis, resulting in loss of the testis due to ischemic atrophy or fibrosis. Most of the studies used retrospectively collected data, and all of them were too small to produce conclusive results. In our study, the common age group was between 7-9 yrs(35%) and 20% were between 3-6 yrs. 43% children belonged to educated parents while 57% children were from uneducated class. Torsion of testes was found in 35 (22%) children, orchitis in 25(16%) and inguinal hernia in 76 (48%). Tumor was noted in 7(4.5%) children above 13 yrs where orchidectomy was done with suspicion of malignancy. Rt side was invoved in 82 (52%), Lt side in54(34%) and bilateral cryptorchidism was noted in 23(14%) cases. 118(74%) children were from rural areas while 41 (26%) were from urban area.

Table No 1: Age Wise Distribution

Age (years)	No of cases	Percentage
3-6 yrs	32	20%
7-9 yrs	55	34.6%
10-12 yrs	15	9.4%
13-15 yrs	26	16.35%
16-19 yrs	19	12%
Above 05 yrs	80	60%
Below 02 yrs	06	4%
Above 10 yrs	58	36.5%

Table No 2: Complications

Complication	No of cases	Percentage
Torsion	35	22%
Inguinal hernia	76	48%
Orchitis	25	16%
Tumor	07	4%

DISCUSSION

Cryptorchidism occurs more frequently in preterm boys (30 %) and almost is associated with inguinal hernia, although most are not symptomatic. Incidence is 3-5% in full term boys and 1.8% at one year age. More than 80% of undescended testis are on one side, the other side is usually normal. Diagnosis of this condition is made through physical examination at birth. Generally radiologic imaging is not reliable. Ultrasound can help to identify testicle located in the inguinal canal, but is of limited use for intra abdominal testis. Laparoscopy can be used to localize nonpalpable, undescended testis.
A testis absent from the normal scrotum can be Found anywhere along the "path of descent" from high in the posterior abdomen (retroperitoneal) just below the kidney, to the inguinal ring
Found in the inguinal canal
Ectopic, found to have wandered from that path, usually outside the inguinal canal and sometimes opposite scrotum and femoral canal
Found to have vanished (anorchia)
Testicular descent into the scrotum is influenced greatly by maternal hormones that stimulate pro hormones by the fetal testis. Failure of the testicle to descend through the inguinal canal during the fetal life may be related to enough of a specific type of maternal hormones, failure of testis to respond to inadequate pull from the gubernaculum, or various other factors. A karyotype can confirm or exclude forms of dysgenetic primary hypogonadism, such as Klinefelter syndrome or mixed gonodal dysgenesis.

Although orchiopexy makes cancer more easily recognizable at an early stage, whether early orchiopexy actually reduces the chance of developing cancer remains the subject of controversy. The risk of malignancy in the undescended testis is 4 to 10 times higher than that in the general population and is approximately 1 in 80 with a unilateral undescended testis and 1 in 40 to 1 in 50 for bilateral undescended testis. The peak age for this tumor is 15-45 yr.The most common tumor developing in an undescended testis is seminoma (65%); in contrast, after orchiopexy, seminomas represent only 30% of testis tumors. About 1 in 500 men born with one or both testes undescended develop testicular cancer, roughly a 4 - 40 fold increased risk. The peak incidence occurs in the 3rd and 4th decades of life. The risk is higher for intra-abdominal testes and somewhat lower for inguinal testes, but even the normally descended testes of an infant whose other testis was undescended has about a 20% higher cancer risk than those of other men.
Many men who were born with undescended testes have reduced fertility, even after orchiopexy in infancy. The reduction with unilateral cryptorchidism is subtle, with a reported infertility rate of about 10%, compared

with about 6% reported by the same study for the general population of adult men. The fertility reduction after orchiopexy for bilateral cryptorchidism is more marked, about 38%or 6 times that of the general population.

At least one contributing mechanism for reduced spermatogenesis in cryptorchid testes is temperature. It seems likely that subtle or transient hormone deficiencies or other factors that lead to lack of descent also impair the development of spermatogenic tissue. An additional factor contributing to infertility is the high rate of anamolies of the epididymis in boys with cryptorchidism (over 90% in some studies). Even after orchiopexy, these may also affect sperm maturation and motility at an older age.

The most effective treatment is surgery. Most pediatric urologist recommend orchidopexy by 1 to 1.5 years or earlier. There is evidence that early damage to the germ cells that produce sperm begins at this age..

Hormonal treatment has the advantage of avoiding anesthesia and being minimally invasive. HCG is the drug of choice. However success rates have been reported to be as low as 10%. A newer hormonal intervention used in Europe is use of GnRH analogs such as Nafaren or Buserelin. The success rates and putative mechanism of action are similar to HCG, but some surgeons have combined the two treatments and reported higher descent rates. Limited evidence suggests that germ cell count is slightly better after hormone treatment. The cost of either type of treatment is less than that of surgery and the chance of complications at appropriate doses is minimal.

Despite the potential advantages of a trail of hormonal therapy, many surgeons do not consider the success rates high enough to be worth the trouble, since surgery itself is usually simple and uncomplicated. Surgery becomes more complicated if the blood supply is not ample and elastic enough to be stretched into the scrotum. In these cases, the supply may be divided, some vessels sacrificed with expectation of adequate collateral circulation. In the worst case, the testis must be "auto-transplanted" into the scrotum, with all connecting blood vessels cut and reconnected (anastomosed). When the testis is in the abdomen, the first stage of surgery is exploration to locate it assess its viability, and determine the safest way to maintain or establish the blood supply. . If the testis is low in abdomen, an orchidopexy is performed laparoscopically.

The principal major complication of all types of orchiopexy is loss of the blood supply to the testis, resulting in the loss of the testis due to ischemic atrophy or fibrosis.

Multi stage surgeries, or auto transplantation and anastomosis, are more often necessary in these situations. One of the strongest argument for early orchiopexy is prevention of testicular cancer.

Long term issues include infertility and tumor genesis.

The goals of treatment include

Improve fertility

Promote easier examination for testicular cancer

Correct associated abnormalities (hernia)

Prevent testicular torsion

Alleviate psychological concerns regarding body image

Reduce risk for injury

CONCLUSIONS

Undescended testis, also called cryptorchidism, is a common condition in which reproductive gland is located outside the scrotum. The condition may be unilateral or bilateral. More than 80% of undescended testis are on one side, the other side is usually normal. The most common diagnostic dilemma in otherwise normal boys is distinguishing a retractile testis from a testis that will not descend spontaneously into the scrotum. . The risk of malignancy in the undescended testis is 4 to 10 times higher than that in the general population and is approximately 1 in 80 with a unilateral undescended testis and 1 in 40 to 1 in 50 for bilateral undescended testis. The most effective treatment is surgery. Hormonal treatment has the advantage of avoiding anesthesia and being minimally invasive. HCG is the drug of choice one of the strongest argument for early orchiopexy is prevention of testicular cancer.

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Address for Corresponding Author:
Dr. Asif Saeed
H No: 113, Street No: 10
Jinnahabad Township,
Abbottabad.
Ph. 0992-380372
Mob. 0333-5037702
E- mail aasif_saeed@yahoo.co.uk

Original Article

Eclampsia: Still A Dreadful Situation

1. Rubina A.D Memon 2. Razia Bahadur Khero 3. Farida Wagan 4. Safia Maqsood

1, 2 & 3. Assoc. Profs. Obs & Gynae 4. Asstt. Prof. Obs & Gynae, Peoples University of Medical & Health Sciences for Women, Nawabshah

ABSTRACT

Objective: To study the prevalence of eclampsia, its related maternal morbidity, mortality and perinatal outcome.
Study Design: Observational Study.
Place and Duration of Study: This study was conducted in the Department of Obstetrics & Gynaecology at Peoples Medical College Nawabshah from 1st January 2009 to 31st December 2009.
Materials and Methods: All the patients admitted with eclampsia were included in this study and they were analyzed according to their age, parity, duration of gestation, timing of convulsions, mode of delivery, complications and feto-maternal outcome.
Results: 107 patients of eclampsia presented during the study period, giving a frequency of 2.43 %. Mean age group involved was 15 – 24 years (47.7 %) and 25 – 34 years (44.9 %) while 7.5 % were > 35 years. Majority of the patients belong to 15 – 24 years age group and found to be statistically significant (p–0.000). Primi gravida (65 %) were highly effected population. 57 % (62) patients had fits in antenatal period while 9.3 % (10) patients had intrapartum and 32 % (35) patients had postpartum fits.
Vaginal was the commonest mode of delivery 49 (45.5 %). Assisted vaginal delivery in 21 (19.6 %), while cesarean section was performed in 37 (34.6 %) patients. 39 (36.44 %) maternal deaths occurred during study period, while 7 materanl deaths were attributed to eclampsia. Regarding the neonatal outcome, 64.5 % (69) were born alive, 20.6 % (22) were IUD and 15 % (16) were died during neonatal period mostly due to prematurity (75.7 %).
Conclusion: Eclampsia is a big challenge in obstetrics, it can lead to very high maternal and perinatal mortality and morbidity. It is a 3rd commonest cause of maternal death in developing countries.
Community health education coupled with availability of emergency obstetric and neonatal care service at doorstep would reduce the incidence of eclampsia and its associated morbidity and mortality in Pakistan.
Keywords: Eclampsia, maternal morbidity and mortality, fetal outcome.

INTRODUCTION

Eclampsia is an unpredictable multi-organ disorder, unique to human pregnancy, characterized by occurrence of generalized convulsions in women with signs and symptoms of pre-eclampsia[1].
It is a potentially fatal disorder of pregnant woman that has been prevalent since the time of Hippocrates. It remains an important cause of maternal mortality throughout the world. It accounts for about 50,000 deaths annually worldwide[2,3].
In Pakistan where the mortality rate is 500/100000, eclampsia is the 3rd leading cause of the maternal death[4].
Hypertensive disorders complicates 10 – 15 % of pregnancies, eclampsia occur in 1.3 % of pregnancies.
In Pakistan and other developing countries, the incidence of eclampsia and its related morbidity and mortality are quite high because of poverty, illiteracy, lack of health awareness and superstitious believes prevents the woman from seeking the medical advises during pregnancy[5]. Incidence of gestational hypertension are also increased in patients with twins (25.9 %) and in patients who had gestational hypertension in previous pregnancy[6].
The risk to the mother and fetus from eclampsia appear to be more related to degree of pre-eclampsia pre-existing the convulsions and number of convulsions prior to the admission[7].
Inspite of its importance for public health, the etiology of this disorder is unknown. It is a multisystemic disorder with various forms and which are believed to result from a failure of the normal invasion of trophoblastic cell, leading to mal-adaptation of maternal spiral arteries[8].
It can also be associated with the hyperplacentation disorder such as diabetes, hydatidiform mole and multiple pregnancies. Nutritional, environmental and genetic factors play a role in maternal systemic reaction that produces the clinical signs and symptoms of the disorder[9].
Objective of our study was to determine the frequency of eclampsia in our setup and observe its maternal and fetal outcome.

MATERIALS AND METHODS

This was a descriptive study of proposive cohort carried out in the Department of Obstetrics & Gynaecology at Peoples Medical College Nawabshah from 1st January of 2009 to 31st December 2009.

Eligible patients included women admitted during the study period with diagnosis of eclampsia and unexplained convulsions occurring during antepartum, intra partum and post partum period.
Exclusion criteria were diagnosed cases of epilepsy and fits due to known other medical disorders.
Patients were analyzed according to their age, parity, duration of gestation, time of convulsions, mode of delivery, complications and fetomaternal outcome.
Physical examination was performed for level of consciousness, assessment of the blood pressure and for any sign of cardio-pulmonary compromise. Abdominal examination was carried out to assess the uterine size in comparisons with gestational age, fetal presentation, fetal viability and for uterine contraction. Vaginal examination was performed to assess the Bishop score and adequacy of pelvis.
Necessary investigations like complete blood count, liver function test, renal function test, coagulation studies, urine detailed report and ultrasound were carried out in all patients. In selected cases CT scan was performed to assess the neurological damage.
All the patients were managed in ward according to hospital protocol and patients with serious complications were shifted to ICU. Pregnancy was terminated after maternal stabilization, patients monitored regularly till they become conscious and ambulant. Maternal outcome were measured in term of death or complications like cerebrovascular accident, cardio pulmonary compromise and heamatological disorders (HELLP syndrome). Perinatal morbidity (Preterms, low birth weight, IUGR) and mortality (still birth and neo natal death) were all recorded.
Data was entered in a pre-designed proforma and analysed through SPSS Software version 10.0. For quantitative variables like age, mean value and standard deviations were calculated and for qualitative variables (gravidity, parity, maternal complications and fetal outcome).

RESULT

Over a period of one year, out of the total 4395 deliveries, 107 (2.43 %) patients were diagnosed as eclamptic and were recruited for further study. Their mean age with ± SD was 29 ± 6.61 years. Women between the ages of 15 – 24 years were 47.7 % (51), 25 – 34 years 44.9 % (48) and 7.5 % (8) were > 35 years. Primigravida were 60.7 % (65), Para 2 – 5 were15 % (16) and para > 5 were 24.3 % (26) respectively.
Antepartum eclampsia was seen in 57.9 % (62) cases, 9.34 % (10) and 32 % (35) were intrapartum and postpartum respectively. Majority 47.7 % (51) cases were seen of age group 15 – 24 years and that was found statistically significant (p-0.000) and primigravida (60 %) were seemed to be at highest risk for developing eclampsia. Vaginal was the mode of delivery in 45.5 % (49), 19.6 % (21) were delivered through assisted vaginal delivery while C-section was performed in 34.6 % (37) cases.

Out of 107, the deranged liver function was found in 16 (15 %) cases, abruptio placentae in 10 (9.3 %), renal failure in 3 (2.8 %), temporary blindness in 2 (1.9 %) cases, HELLP syndrome was found in 2 (1.9 %) cases, pulmonary edema in 3 (2.8 %) cases and CVA in 2 (1.9%) cases. Out of 107 patients, 7 (6.5 %) were died due to one or more than one complication (Table No.1). The cause of death was pulmonary edema 3 (42 %) cases, cardiac arrest in 1 (14.29 %) case, CVA in 2 (28.57 %) cases and renal failure in 1 (14.29 %) case, remaining 93.5 % (100) cases recovered with time.
Total number of maternal deaths during the study period were 38 and eclampsia contributes 18 % of it. Regarding the fetal outcome 64.5 % (69) patients were born alive, 20.6 % (22) were IUDs and neonatal death was noted in 15 % (16) cases and it was mostly due to prematurity 75.7 % (81) (Table No. 2).

Table No.1: Maternal complications seen with eclampsia. (n=107)

Complications	Number N (%)	Final outcome Recovered/expired
Deranged LFT	16 (15 %)	All are Recovered
Abruptio Placentae	10 (9.3 %)	All are Recovered
Renal Failure	3 (2.8 %)	2 Recovered 1 (14.29 %) Expired
CVA	2 (1.9 %)	Both expired (28.57%)
Pulmonary edema	3 (2.8 %)	All expired (42.85%)
Temporary Blindness	2 (1.9 %)	All are Recovered
HELLP Syndrome	2 (1.9 %)	All are Recovered
Cardiac Arrest	1 (0.9 %)	Expired (14.29%)
	107 (100 %)	Mortality 6.5 % (7 Expired) Recovered 93.5 % (100 Pts)

Table No.2: Fatal Outcome

Outcome	No	Percentage %
Alive Baby	69	64.5
IUD	22	20.6
Neonatal Death	16	15
	107	100

DISCUSSION

Eclampsia and Pre-eclampsia accounts for significant maternal and perinatal mortality.
The incidence of eclampsia in Western countries is about 1/16000 pregnancies[10]. In our study, the frequency of eclampsia was 24/1000 pregnancies. Talat

Naz et al reported the frequency of eclampsia 11.5/1000 pregnancies[5], Naseeruddin indicates the prevalence of eclampsia 18/1000 pregnancies[11], while another study at Lahore revealed the frequency of eclampsia 10/1000 pregnancies. The high frequency in our study probably indicate illiteracy, low socioeconomic status, lack of antenatal care, poor healthcare system and late referral of patients by healthcare providers.

Eclampsia has been found more common in third trimester of pregnancy as the term approached[12]. Approximately 50 % of the cases developed fits before the delivery, the remaining 50 % are divided equally between the intrapartum and postpartum period[6]. In our study, the occurrence of eclampsia in antepartum period was 57.9 %.

Ikechebelu JI, Okoli, in their study at Nnewi in Nigeria showed the incidence of antepartum eclampsia was 55.8 %[13]. There is another study conducted by Jamelli RN at JPMC Karachi, she also found the occurrence of eclampsia more in the antenatal period (54.3 %)[14].

Eclampsia is more common in primi gravida and in grand multipara. In our study, the frequency of eclampsia in primi gravida was 59.8 % and in grand multipara 26 %. Sultana et al in her study at Ayub teachong hospital Abbottabad also mentioned more frequency in primi (46 %) and grand multipara (38%)[12].

Control of the convulsions and prevention of further fit is the first goal of management. Magnesium sulphate was used as an anticonvulsant in almost all the patients except in those who were deeply unconscious having respiratory depression, slow reflexes and urine output < 300 ml in 24 hours. Many randomized control trial showed that the efficacy of magnesium sulphate for the control of the fit and prevention of the further fit superior to the diazepam.

Mst Rashida Begum, in her study shows the control of the convulsion and prevention of further fits is good with magnesium sulphate as compared to phenytoin and diazepam[3].

In another study conducted at Dhaka by Begum and Begum, she showed the only loading dose of magnesium sulphate is adequate to control the fits and prevention of the further fits.

The Magpie trial showed that preventive magnesium sulphate for all severe cases pre-eclampsia can reduce the risk of development of eclamspia and maternal death by 58 % and 45 % respectively[16].

Khedun S.M et al, in their study at South Africa also shows the good response in control of convulsion by magnesium sulphate as compared to the diazepam[17].

Control of the hypertension is the second goal after controlling the convulsions to prevent the complications such as cerebrovascular accident, renal failure and placental abruption. Choice is very wide depends upon the availability of drug and the personal experience. We use methyldopa and nifidipine as the first line treatment as the hydraliazine is not available in our setup. Mst Rashida Begum, in her study at Bangladesh used hyraliazine in acute stage followed by oral nifidipine and methyldopa alone or in combination. Similar regimen has been adopted by Khedun S.M in South Africa[17].

In Pakistan, where the maternal mortality rate is 500/100000, eclampsia is the 3rd leading cause of maternal death. Jamelli Rana found 8 % fatality rate during her 5-year study period. We also have the maternal mortality 5.6 % and perinatal mortality 35.5 % due to eclampsia. Similar situation has been observed in many studies in Pakistan.

Bashir et al reported 8.35 to 10.3 % maternal mortality and 55.7 % perinatal mortality in his study at Faisalabad in 1991 – 93[18].

The most common cause of maternal death in our study was pulmonary oedema, while the second commonest cause was cerebrovascular accident. Other causes were renal failure and cardiac failure.

Regarding the perinatal mortality, the most important reason for neonatal death was prematurity related problems.

CONCLUSION

Eclampsia is a big challenge in obstetric and still a major cause of maternal and perinatal mortality & morbidity.

Community based health education, timely referrals of high risk patients coupled with availability of emergency obstetric care and neonatal care services would reduce the incidence of eclampsia and its associated morbidity and mortality in Pakistan.

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Address for Corresponding Author:
Dr. Rubina A.D Memon
Associate Professor Obs & Gynae
Peoples University of Medical & Health Sciences for Women,
Nawabshah.
Phone No: 0300-3200500

Original Article

Effect of Chemotherapy on Serum Lactate Levels in Malignant Neoplasia

1. Kausar Tasneem 2. Muhammad Ahmad 3. Rahida Karim 4. Mudassir Ahmad Khan 5. Amjad Zaman

1. Assoc. Prof. of Biochemistry, KMC, Peshawar 2. Assoc. Prof. of Biochemistry, PMC, Peshawar
3. Senior Registrar of Peads, KMC, Peshawar 4. Prof. of Biochemistry, KMC, Peshawar
5. Asstt. Prof. of Physiology, KGMC, Peshawar

ABSTRACT

Objective: The present study was designed to look at the levels of serum lactate in various malignancies and to observe the effect of chemotherapy on serum lactate concentration in malignant neoplasia as a whole. The study was also intended to look for the difference, if any, in this effect for haematopoietic and non-haematopoietic neoplasias, so as to see whether evaluation of lactate levels could represent an additional and useful parameter in determining the clinical and prognostic aspect of the disease.

Study Design: Observational and comparative study.

Place of Study: This study was conducted at Radiotherapy Department, Jinnah Postgraduate Medical Centre, Karachi

Materials and Methods: In this study 131 patients of Malignant Neoplasia were taken from the out-door patients in which 56 patients of haematopoietic group and 75 patients of non- haematopoietic group. Blood samples of 131 patients suffering from haematopoietic and non-haematopoietic neoplasia and 20 healthy control subjects were collected and analyzed for lactate, pyruvate and the $NADH/NAD^+$ ratio.

Results: Blood lactate, Pyruvate levels and $NADH/NAD^+$ ratio were significantly higher in all groups of neoplasia before chemotherapy when compared with control subjects. The $NADH/NAD^+$ ratio and the levels of blood lactate and Pyruvate decreased significantly with chemotherapy in all groups of patients suffering from neoplasia.

Conclusion: Observation of low levels of these parameters, particularly that of serum lactate, after the course of chemotherapy can be used as an indicator of prognosis and also considered helpful in assessing the effectiveness of chemotherapy in malignancies.

Key Words: Neoplasia, Haematopoietic neoplasia, Non-Haematopoietic neoplasia, Chemotherapy, Lactate, Pyruvate.

INTRODUCTION

Lactate is produced as a metabolic end product during anaerobic glycolysis by the action of enzyme lactate dehydrogenase on pyruvate. Its concentration is dependent upon concentration of pyruvate in the cytosol, cellular pH and the cytosolic ratio of (Nicotinamide adenine dinucleotide reduced / Nicotinamide adenine dinucleotide oxidized) $NADH/NAD^+$ that reflects the redox state of the cytosol.[1]

The excessive accumulation of lactic acid in blood is termed as lactic acidosis.[2] Lactic acidosis in cancer is complex as the regulation of acid production and its utilization is dependent on regulation of several factors.[3] Lactic acidosis can be due to a number of different mechanisms including metastasis and dysfunction of liver, which leads to underutilization of lactate, by process of gluconeogenesis in the liver. The body in order to balance the excess negative lactate ions produced starts retaining positively charged hydrogen ions, and this results in lactic acidosis.[4]

Tumors have been suggested to behave aggressively as vigorous glycolytic systems in which rate of glycolysis is unchecked by oxygen delivery to the tissues.[5] Several workers have confirmed rapid glycolysis in malignant neoplasia, and if this is unchecked it may result in excessive lactate production.[6-10] So far the production of lactate has not been compared in different tumours, nor the effect of chemotherapy on lactate levels assessed.

Therefore, the present study was designed to look at the levels of serum lactate in various malignancies and to observe the effect of chemotherapy on serum lactate concentration in malignant neoplasia as a whole. The study was also intended to look for the difference, if any, in this effect for haematopoietic and non-haematopoietic neoplasias, so as to see whether evaluation of lactate levels could represent an additional and useful parameter in determining the clinical and prognostic aspect of the disease.

MATERIAL AND METHODS

The study included before and after first dose of chemotherapy in patients of different types of malignant neoplasia. They were enrolled from amongst the out-door patients of Radiotherapy Department, Jinnah Postgraduate Medical Centre, Karachi. Twenty normal healthy subjects, of comparable age and socio-economic status, with no family history of cancer, from the staff and students were also included in the study as controls. Patients and control group of both sex of 18 years and above were included. Only those patients and control subjects were included who had no history of diabetes, cardiac or pulmonary or hepatic dysfunction. Informed consent was taken from both patients and control subjects.

Patients apart from having malignant neoplasia, and control healthy subjects suffering from any disease such as diabetes mellitus, hypertension, coronary heart disease or any other acute or chronic illness were not included. Patients already undergoing chemotherapy were excluded from the study.

This was a double controlled study in which the normal healthy subjects served as controls for the cancer patients who had not received chemotherapy; they, in turn, served as controls for patients who had received chemotherapy. Fasting blood samples of 131 patients suffering from haematopoietic and non-haematopoietic neoplasia and 20 control subjects were collected and analyzed for lactate, pyruvate and the $NADH/NAD^+$ ratio. Lactate and Pyruvate levels were determined by colorimetric method using kit supplied by Sigma Diagnostic, USA, while $NADH/NAD^+$ ratio was determined by calculation. Blood was collected for analysis of different parameters before and four (4) weeks after the chemotherapy treatment. The values were expressed as mean ± SEM, and Students "t" test was applied for comparison between different groups with p value less than 0.05 ($P<0.05$) accepted as significant.

RESULTS

The distribution of patients and control subjects, between the ages of 18-60 years, on the basis of sex and diagnosis is given in Table No.1. Male to female ratio in control subjects and patient group was 13:07 and 56:75 respectively. The malignant neoplasia group comprised of 56 Haematopoietic and 75 non-haematopoietic neoplasia patients. The patients and control subjects had a mean ± S.E.M of 39.46 ± 1.96 and 37.10 ± 3.65 years respectively. No statistically significant difference was observed in the mean age of patients and control groups. The distribution of patients in different groups on the basis of diagnosis and chemotherapy can be seen in Table No.2. Out of the Haematopoietic group 28 whereas of non-haematopoietic neoplasia patients 38 gave an informed consent to further participate in the study. Only one of the patients in non-haematopoietic neoplasia sub-group left the study without any reason and did not return after giving blood sample before chemotherapy.

Table No.3 describes the comparison of fasting blood lactate and pyruvate levels and $NADH/NAD^+$ ratio in controls and in patients of malignant neoplasia (as whole group), haematopoietic and Non-haematopoietic neoplasia (as sub-group), before and after chemotherapy. Blood lactate, Pyruvate levels and $NADH/NAD^+$ ratio were significantly higher ($P<0.001$) in malignant neoplasia as whole group having both haematopoietic and non-haematopoietic neoplasia patients, before chemotherapy when compared with control subjects. The $NADH/NAD^+$ ratio and the levels of blood lactate and Pyruvate decreased significantly ($P<0.001$) after chemotherapy in malignant neoplasia as whole group and in all sub-groups of patients suffering from neoplasia when compared with levels of the aforementioned parameters before chemotherapy.

Table No.1: Distribution of Patients and Control Subjects on the Basis of Sex and Diagnosis

Subject	Male	Female
Control (n=20)	13	07
Malignant Neoplasia [Whole Group] (n=131)	56	75
Haematopoietic Group (n=56)	36	20
Non-Haematopoietic Group (n=75)	20	55

Note: Whole Group = Haematopoietic and Non-Haematopoietic neoplasia patients.

Table No.2: Malignant Neoplastic Patients Before and After Chemotherapy

Diagnosis	Before Chemo-therapy	After Chemo-therapy
Haematopoietic Neoplasia	28	28
1.Non-Hodgkin's lymphoma	07	07
2.Hodgkin's lymphoma	07	07
3.Lymphoid leukemia	07	07
4.Myeloid leukemia	07	07
Non-Haematopoietic Neoplasia	38	37
1.Breast carcinoma	15	15
2. Lung carcinoma	09	08
3. Uterine carcinoma	07	07
4. Thyroid carcinoma	07	07
Total	66	65

Table-3: Fasting Blood Lactate, Pyruvate and Nadh/Nad$^+$ Ratio in Controls and in Patients with Malignant, Haematopoietic and non-Haematopoietic Neoplasia Before Chemotherapy (B/C) and after Chemotherapy (A/C).

The values are expressed as mean ± SEM. Number of cases is given in parenthesis

	Lactate (mg/dl)		Pyruvate (mg/dl)		NADH/NAD$^+$	
CONTROL (n=20)	6.97 ± 0.59		0.48 ± 0.02		16.82 ± 2.27	
	B/C	**A/C**	**B/C**	**A/C**	**B/C**	**A/C**
Malignant Neoplasia (Whole Group) (n= 131)	54.98 ± 4.18***** (n+ 66)	10.80 ± 0.15† (n= 65)	0.88 ± 0.05***** (n= 66)	0.55 ± 0.01† (n= 65)	70.24 ± 5.53***** (n= 66)	21.81 ± 1.44† (n= 65)
Haematopoietic Group (n= 56)	67.45 ± 6.95***** (n= 28)	10.53 ± 0.23† (n= 28)	0.89 ± 0.08***** (n= 28)	0.57 ± 0.02† (n= 28)	78.80 ± 9.13***** (n= 28)	19.60 ± 1.13† (n= 28)
Non-Haematopoietic Group (n= 75)	46.84 ± 4.72***** (n= 38)	11.00 ± 0.20† (n= 37)	0.85 ± 0.07***** (n= 38)	0.54 ± 0.02† (n= 37)	63.90 ± 7.40***** (n= 38)	23.42 ± 2.36† (n= 37)

Note:

***** P<0.001 as compared to control subjects.

† P<0.001 as compared to patients "before chemotherapy".

Whole Group = Haematopoietic and Non-Haematopoietic neoplasia patients.

DISCUSSION

The microenvironment of a tumour is characterized by oxygen depletion, lactic acidosis and glucose and energy deprivation.[11] Lactic acidosis in cancer patients is not common even when the tumor is a rapid growing one. It often develops suddenly, may in few hours become profound and life threatening.[12] Patients, who harbour tumours but are otherwise healthy, may have compartmentalized areas of hypoxemia. These hypoxic neoplastic tissues elaborate lactic acid. This phenomenon has been identified in patients with myeloproliferative disorders such as acute leukemia,[8,13,14] Hodgkin's lymphomas,[15] lung oat-cell carcinoma,[16] and anaplastic large-cell carcinoma.[17] Within hypoxic tumor regions anaerobic dissimilation of glucose is the sole source of energy generation. The increased need for glucose may aggravate cancer cachexia.[18]

Serum lactate levels in patients with haematopoetic neoplasia in our study were found to be significantly higher (P<0.001) as compared to control group. Malignant cells have a distinct type of metabolism in which the glycolytic sequence and the tricarboxylic acid cycle are poorly integrated, hence the cells tend to utilize from five to ten times as much glucose as do normal tissues, converting most of it into lactate[19]. Lactic acidosis associated with haematopoietic malignancies such as leukemia,[8,17] non-Hodgkin's[20,21] and Hodgkin's Iymphomas[21] in which leukemia cells become hypoxic due to being packed in bone marrow and thus, overproduce lactate.[22,23]

Lactic acidosis occurring in patients having non-haematopoietic neoplasia associated with extensive hepatic metastasis has been attributed to impaired lactate utilization.[1,16,24] However, hyperlactacidemia has also been reported in similar malignancies without hepatic involvement.[25] In our study, we found increased levels of lactate in non-haematopoietic neoplasia which correspond with observations of other research workers.[3,17,26]

Rice and Schwartz[26] showed total correction of lactic acidosis after chemotherapy in a patient who presented with widespread small cell carcinoma lungs and rapidly progressive lactic acidosis. Hayek et al[27] reported a patient with acute lymphoblastic leukemia presenting with severe lactic acidosis and renal tubular dysfunction, both of which were refractory to conventional management, including peritoneal dialysis, but resolved rapidly with appropriate chemotherapy. Cho and his group[28] also reported a case of acute lymphoblastic leukemia with severe lactic acidosis and enlargement of kidney. Hemodialysis and alkalization resulted in no change in blood lactate level. They showed that after starting chemotherapy the lactic acid levels dropped. A group of scientists[29] reported a case of non-Hodgkins lymphoma in which leukemic transformation resulted in elevated plasma lactate concentrations. Our study is also in agreement with the above mentioned researchers and showed a significant decrease in the serum lactate levels in haematopoietic and non-haematopoietic neoplasia patients.

Many of the drugs used to treat malignant tumors are directed towards inhibition of DNA replication. These chemotherapeutic drugs are more toxic to cancer cells than normal cells, because cancer cells divide more rapidly. However such drugs also may inhibit normal rapidly dividing cells such as cells of the bone marrow

or cells in the hair follicles[30]. Pyruvate levels in this study showed almost the same pattern as exhibited by lactate in all groups of patients. The effect of chemotherapy was also similar on these metabolites. This might be due to the fact that effective chemotherapy reduced the number of malignant cells and their activity, leading to decreased glycolysis.

In hypoxia, the phosphorylation in mitochondria is impaired and cellular stores of ATP are depleted. All these homeostatic derangements eventually lead to an increase in $NADH/NAD^+$ ratio, hydrogen ion production, and lactic acidosis.[8,17] Elevated $NADH/NAD^+$ ratio is reported in various types of malignant neoplasia,[3,7,17] which is in agreement with the present study. This $NADH/NAD^+$ ratio dropped significantly after chemotherapy in all groups of patients with malignant neoplasia which is in accordance with the work of different research groups.[1,8,10,13,16,23]

The decline in the concentration of serum lactate, pyruvate and $NADH/NAD^+$ ratio after chemotherapy indicates the fact that chemotherapy not only reduces the number of malignant cells but also decreases glycolysis. As a result the processes, that lead to excessive production of lactate and pyruvate and raise the $NADH/NAD^+$ ratio, are reversed**,** due to effective chemotherapy which reduces the number of malignant cells or stops their activity. It can, therefore, be concluded that the levels of these parameters, particularly that of serum lactate, after the course of chemotherapy can be used as an indicator of prognosis and also considered helpful in assessing the effectiveness of chemotherapy in malignancies.

CONCLUSION

Observation of low levels of these parameters, particularly that of serum lactate, after the course of chemotherapy can be used as an indicator of prognosis and also considered helpful in assessing the effectiveness of chemotherapy in malignancies.

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Address for Corresponding Author:
Dr. Muhammad Ahmad
Assoc. Prof. of Biochemistry,
Peshawar Medical College,
Peshawar.
Email: mahmad29@hotmail.com

Original Article

Distribution of ABO Blood Group in Peptic Ulcer Patients in the Ethnic Population of Balochistan

1. Asghar Hussain 2. Qamar Aziz Siddiqui 3. Sikandar Ali Sheikh

1. Prof. of Physiology, QIMS/CMH, Quetta 2. Prof. of Physiology, BMU, Karachi 3. Chairman & Prof. of Physiology, BMU, Karachi

ABSTRACT

Objective: To find relationship between ABO blood group and peptic ulcer (PU) in the ethnic population of Balochistan.

Study Design: An observational and prospective study.

Place and duration of Study: The study was carried at Bolan Medical College Complex Hospital Quetta for a period of one year.

Patients and methods: 60 peptic ulcer patients confirmed with video endoscope were included. ABO blood group was determined by slide test method.

Result: Out of 60 PU patients 54 were males and 6 females. 18 had blood group O, 24 had group B, 11 had AB and 7 had A blood group. 90% were Rhesus positive. O group was dominant (38.46%) in peptic ulcer patients with antral lesion. In patients having duodenal lesion, B group was prevalent (45.83%). Males were predominant sufferers (75%). The poor and middle class patients were equally affected. The ethnic group Pathan were more affected (36.67%) compared to Baloch and Hazara.

Conclusion: Antral lesions are dominant in O blood group peptic ulcer patients whereas duodenal lesion is common in blood group B. There is a high prevalence in Pathan males. Duodenal lesion is more prevalent compared to antral lesion.

Keywords: Peptic ulcer, ABO blood group.

INTRODUCTION

The pathology of peptic ulcer disease (PUD) was first described by Jean Cruvielhier in 1835 and peptic ulcer was known as La-maladie de Cruvielhier[1]. Genetic and environmental factors play an important role[2]. Stress and pepsin are other important factors[3, 4]. Smoking and diet deficient in Linoleic acid reduces PGE_2 in gastric juice and leads to ulcer[5].

Genetic factor plays a role in the etiology and blood group studies provide a line of evidence. If there is a positive association between a given disease and a particular allele of a well defined genetic locus, the genetically determined trait can be considered important in the pathogenesis of the disorder[1].

There is a strong association of ABO blood groups and certain diseases[6]. The strongest is between duodenal ulcer and blood group O[7]. Specially O group patients of DU are more prone to bleed or perforate[8]. Contrary to this finding in adults, children with chronic DU were not associated with increased incidence of blood group O compared to controls[9]. Similarly cancers of stomach are strongly co related to A group[10]. As a result of this strong relationship between O group and PU patients there is an increase in the incidence of risk by 2.4 times compared to other PU patients with A, AB and B groups[11].

However there is a high prevalence of blood group B in the population of Balochistan[12]. The present study was therefore designed to find out this relationship of ABO blood group in peptic ulcer patients. If proper association is found, this will help in identifying high risk cases where the role of preventive measures will be very important in reducing mortality associated with PU disease.

PATIENTS AND METHODS

This prospective and observational study was carried in the department of gastro-entrology and medicine, Bolan Medical College Complex Hospital Quetta. A detailed proforma was prepared and proper study protocol was designed. Dyspepsia, pain in epigastrium with duration, sex was recorded. For diagnosis of peptic ulcer, endoscopy with video endoscope Petnax SUJNON-EC 200 LR was performed without sedation, using gargles and topical spray. 60 cases, men and women aged 26-70 years were included. ABO blood group was determined according to Dacie[13], by slide test method using antisera by Gamma biological Inc Sanofi diagnostic pasture USA. As only one or two samples were grouped at a time and agglutination was rapid on flat surface, thus slide test method was preferred, no control was used. The agglutination was observed within 5 minutes; in case of doubt agglutination was

checked by viewing the suspension under low power microscope. Blood group control data was used from Balochistan population. The total number was 2000; of these 1260 were males and 740 were females belonging to young and middle age group. They were clinically normal individuals who were randomly selected[12], mostly students and staff members of Bolan Medical College.

Statistical Analysis

Was carried on EPI Info-6 for X^2 (chi square) test and p value was calculated.

RESULTS

The distribution of 60 cases of peptic ulcer, mean age of 47.5 ± 22.5 years. Blood group O was found in 18 patients, group B in 24 patients, while AB was seen in 11 cases and 7 had group A. 90% were Rhesus positive. O group was dominant (38.46%) in peptic ulcer patients with antral lesion. In patients having duodenal lesion, B group was prevalent (45.83%). Males were predominant sufferers (75%). The poor and middle class patients were equally affected. The ethnic group Pathan were more affected (36.67%) compared to Baloch and Hazara.

Table No. 1: Blood Group Prevalence in Peptic Ulcer Compared With Control

Blood group	Control	Peptic ulcer patients	% Increase or decrease on control
O	35%	30%	-5
A	23.2%	11.6%	-11.6
B	31.7%	40%	+8.3
AB	10.1%	18.3%	+8.2

Table No.2: Table showing sum of control and PU patients

Blood group	Control n=2000	Peptic ulcer patients	∑ (sum)
O	700	18	718
A	464	7	471
B	634	24	658
AB	202	11	213
Total	2000	60	2060

Table-3: Expected and Observed values

Blood group	Expected values	Observed values	$\frac{(O-E)^2}{E}$
O1	697.08	700	0.098
O2	20.91	18	3.28
A1	457.28	464	0.036
A2	13.71	7	1.22
B1	638.83	634	0.11
B2	19.16	24	3.71
AB1	206.79	202	0.01
AB2	6.2	11	0.40

X^2 (observed) = 8.864 and $p<0.05$ (chi-square table 2x2, 2 x n)

df= (r-1) (c-1) = 3

In the Chi square table, the df value 3 against C.I. 0.05 = 7.815 (X^2 table)

X^2 (observed) > X^2 (table) shows the relationship is significant.

Table No.4: ABO distribution according to site of lesion

Blood group	O	A	B	AB	Total
Antral lesion	12	3	11	6	32
Duodenal lesion	6	4	13	5	28

Statistical analysis of the data was done using the chi square $p<0.05$ and df = 3. A strong association was found between ABO blood group and peptic ulcer disease when compared to control with significant values shown in (Table-1-3). X^2= 8.864 with a significant $p<0.05$ (Chi square table 2 x 2.2xn) value.

DISCUSSION

The correlation between peptic ulcer and ABO blood group has been studied in different parts of the world [14, 15, 16]. The present study like other studies have shown that relationship exists between ABO blood groups and peptic ulcer. The antral lesion was dominant in O blood group which is in accordance with others.

Bacterial colonization and inflammatory response may be influenced by expression of ABO blood group antigens and blood group O was represented higher among peptic ulcer patients[17]. The adherence to the gastric epithelial cell is mediated by fucosylated blood group antigens associated with blood group O phenotype, suggesting that it might explain the higher frequency of peptic ulceration in patients with blood group O[18].

Thus O group patients are about 35% more likely to develop PU compared to other blood groups. The O group patients of PU have been shown to have hypersecretory ulcers[19].

Association between blood group O with H *pylori* is controversial. Some workers believe in the presence of fucose which is the immuno dominant sugar of H-antigen of blood group O. Adhesins of H *pylori* that bind fucose have been identified[19]. However others have failed to find association between ABO and secretor status[20]. Carefully controlled studies are still required to establish the relationship between ABO blood groups and PU. If this relationship is established, high risk cases can be identified and preventive measures against PU can be undertaken to minimize the mortality and morbidity related to complication of PU. There may be a possibility that other blood groups have some ulcer inhibitory factors which needs to be explored.

CONCLUSION

Blood group O is associated with antral ulcers of stomach. Duodenal lesions were more common in blood group B. The blood group B patients specially of the ethnic group "Pathans" suffering from dyspepsia must be identified and advised diet control and other preventive measures for control of complications of ulcers.

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Address for Corresponding Author:
Prof. Dr. Qamar Aziz Siddiqui,
Department of Physiology,
Baqai Medical University, Karachi
Office Telephone No. Dir. 92-21-4410438 &
4410293-298 Ext. 249
Cell No. 0333-3145734
E-mail Address: drqamer1@hotmail.com.

Original Article

Cetirizine & Loratadine - Comparing Their Antagonist Effects on Isolated Trachea of Rabbit

1. Gulshan Ara Jalbani 2. Madiha Shah 3. Manzoor Ahmed Unar 4. Ali Nawaz Bhurgri

1. Asstt. Prof. of Pharmacy, LUMHS, Jamshoro 2. PG Student, LUMHS, Jamshoro 3. Assoc. Prof. of Pharmacy, CMC, Larkana 4. Lecturer of Pharmacy, LUMHS, Jamshoro

ABSTRACT

Objective: To study and compare the antagonist effects of Cetirizine and Loratadine on histamine induced contractions of isolated trachea of rabbit.

Study Design: Comparative controlled invitro experimental study.

Place and Duration of Study: This study was conducted at The Department of Pharmacology and Therapeutics, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Center (JPMC) Karachi, for the period of six months.

Materials and Methods: Isolated tracheal smooth muscles of twenty four rabbits were used. Fresh Kreb's nutritional solution was prepared for each subject. Tracheal smooth muscles were exposed to standard dilution of Histamine, and then they were challenged with serial dilutions (10^{-18} to 10^{-3} gm /ml) of *Cetirizine* and *Loratadine* separately. Responses as rate and amplitudes of contractions were recorded by 7B Grass Polygraph machine.

Results: Cetirizine inhibit the rate of histamine induced contractions of tracheal muscles from 0.85 to 12.33 % and amplitude from 0.0 to 82.69 %, as concentration of drugs increased. While Loratadine inhibit the rate of histamine induced tracheal contractions from 0.85 to 10.59 % and amplitude from 6.5 to 76.82 % as concentration of drugs increased.

Conclusion: Cetirizine found more potent than Loratadine as inhibitor of histamine induced contraction in isolated tracheal smooth muscles of rabbit.

Category: Basic Sciences**.**

Key Words: Cetirizine, Loratadine and Tracheal smooth muscles.

INTRODUCTION

Seasonal allergic rhinitis is a common disease world wide affecting a significant percentage of the global population. It is a source of great discomfort, and can have a major effect on patient's quality of life. Indeed more than 90% of seasonal allergic rhinitis patients believe that their work productivity is negatively affected by allergy symptoms [1,2].

Histamine is generally considered as the principle mediator of acute inflammatory process and allergic reaction [3], in both the upper and lower respiratory airways [4]. It has important role in gastric acid secretion and function as neurotransmitter and neuromodulator [5]. Histamine is found in all tissues, but in high amount in lungs, skin, gastrointestinal tract mast cells and basophils [6]. It is also found in animals, in plants, as a component of venoms and secretions from insect stings [7]. The effects of histamine are exerted through three well defined classical G protein coupled histamine receptor subtypes termed H_1R, H_2R and H_3R, and the more recently H_4R. Histamine signaling through H_1R is responsible for the majority of the immediate manifestations of allergic disease [8].

Anti-histamines are the classic H_1 receptors mediated response blockers and competitively block the receptor mediated response of target tissues [9]. They are divided into first and second generation anti-histamines. The main distinguishing points between first and second generation anti-histamines are that first generation drugs are widely distributed throughout the body and are more likely to block autonomic receptors and enter the central nervous system readily, while the second generation drugs are less lipid soluble and enter the central nervous system with difficulty or not at all, so they show less sedative and anticholinergic effects [10].

Cetirizine: It is a potent, non-sedative, H_1 receptor antagonist belongs to second generation antihistamines [2, 8]. It is a member of piperizine group of H_1 antagonists[11]and pharmacologically active oxidized metabolite of hydroxyzine. It is minimally metabolized so it may be anti-histamine of choice for patients with hepatic dysfunction and can also be used in elderly patients without dosage reduction. It has a low rate of penetration of the blood brain barrier and is without any significant anti-cholinergic and anti-serotonin effects, used in the treatment of allergy[12].

Loratadine: It is highly potent[3], non-sedative and long acting tricyclic[13], second generation anti-histamine[14], with selective competitive peripheral histamine H_1 receptor antagonistic activity[15], belonging to the pipridine group and structurally related to azatadine[16]. It

is less lipophilic, has no central nervous system activity and is essentially free of sedation[17]. It is proven to be effective in the treatment of seasonal allergic rhinitis, chronic idiopathic urticaria and allergic bronchial asthma[18, 19].

Purpose of study:

The purpose of study was to evaluate and compare the antagonistic effects of Cetirizine and Loratadine on histamine induced contractions of isolated tracheal smooth muscles of rabbit.

MATERIALS AND METHODS

All experimental work was carried out for the period of six months, in the Department of Pharmacology and Therapeutics, Basic Medical Science Institute (BMSI), Jinnah Postgraduate Medical Center (JPMC), Karachi.

Preparation of serial dilutions of drugs: Serial dilutions were made by taking 1 ml of drug and adding 9ml of distilled water to make the ratio 1:9 .In this way serial dilutions of drugs were prepared from concentration 10^{-3} to 10^{-18} gm/ml.

Nutrition solution: In this vitro project Kreb's bicarbonate nutritional solution was used for the perfusion of isolated tracheal tissue. For the preparation of 5 liters of Kreb's bicarbonate solution, following quantities of ingredients were used: Sodium chloride 34:50 gm, Sodium bicarbonate 10.50 gm, D-glucose 10.00 gm, Sodium dihydrophosphate 0.60 gm, Potassium chloride 1.85gm, Magnesium chloride 0.23 gm, Distilled water 5000 ml.

Preparation and isolation of tracheal smooth Muscle: Twenty-four healthy adult rabbits male and female (non-pregnant), approximately 2kg weight were selected and used for the present study. The animals were sacrificed; trachea was removed and transferred to Petri dish containing aerated (oxygenated) Kreb's bicarbonate solutions, where it was cleaned of extraneous tissues. A chain of tracheal section was made by cutting several rings of cartilages and tying them together loosely in such a way that muscles of two rings were at 180^{0} to each other. Chain was suspended vertically in an inner organ bath containing 20 ml Kreb's bicarbonate solution with the help of tissue holder and connected to the 7B Grass Polygraph machine with the help of force transducer. The nutritional solution was continuously aerated 10-12 bubbles of oxygen per minutes and temperature was equilibrate in Kreb's bicarbonate solution for 90 minutes. Bath solution was changed after every 15 minutes. The drugs were added in small quantities (1ml) at each interval to inner organ bath from lower concentration 10^{-18} gm/ml to higher concentration 10^{-3} gm/ml according to experimental protocol and response from each dilution was recorded on Grass Polygraph under resting tension of 1 gm.

Method: Experimental subjects were divided into three groups. Eight animals were used in each group and eight experiments were done in each group. The responses were recorded as Rate and Amplitude of isolated tracheal smooth muscle contractions

In group-I, first of all spontaneous contractions of tracheal smooth muscles were recorded than tissue were challenged with a serial dilutions of histamine (from 10^{-18} to 10^{-3} gm/ml) and responses were recorded. From these responses, standard concentration of histamine (10^{-3} gm/ml) was selected, which had produced maximum response.

In group-II, tissues were challenged with serial dilutions of Cetirizine (from10^{-18} to 10^{-3} gm/ml) in the presence of selected standard concentration of histamine (10^{-3} gm/ml) and responses were recorded for each dilution. After taking response of each concentration the tissues were washed and given rest for 3 minutes before applying the next concentration.s

In group III, tissues were challenged with serial dilutions of Loratadine (from 10^{-18} to 10^{-3} gm/ml) in the presence of selected standard concentration of histamine (10^{-3} gm/ml) and responses were recorded for each dilution. After taking response of each concentration the tissues were washed and given rest for 3 minutes before applying the next concentration.

RESULTS

Effects of Cetirizine on Histamine Induced Contractions in Isolated Tracheal smooth muscles of rabbit (Group-II):

Rate: Cetirizine antagonized the rate of histamine induced contractions of isolated tracheal smooth muscles from 0.85 % to 3.70 % non-significantly at the concentrations 10-18 to 10-12 gm/ml and from 7.78 % to 12.33 % significantly ($p<0.001$) at concentrations 10-11 to 10-3 gm/ml. (Table No.1).

Amplitude: Cetirizine antagonized the amplitude of histamine induced contractions of isolated tracheal smooth muscles 0.00 % to 13.33 % non-significantly at the concentrations 10-18 to 10-12 gm/ml and from 30.30 % to 82.69 % significantly ($p<0.001$) at concentrations 10-11 to 10-3 gm/ml. (Table No.2)

Effects of Loratadine on Histamine Induced Contractions in Isolated Tracheal smooth muscles of rabbit (Group-III):

Rate: Loratadine antagonized the rate of histamine induced contractions of tracheal smooth muscles from 0.85 % to 5.75 % non-significantly at the concentrations 10-18 to 10-11 gm/ml and from 7.52 % to 10.59 % significantly ($p<0.001$) at concentrations 10-10 to 10-3 gm/ml. (Table No.3)

Amplitude: Loratadine antagonized the amplitude of histamine induced contractions of tracheal smooth muscles from 0.00 to 8.89 % non-significantly at the

concentrations 10-18 to 10-13 gm/ml and from 15.69 % to 76.82 % significantly (p<0.001) at concentrations 10-12 to 10-3 gm/ml. (Table No.4)

Table No.1: Effects of Citirizine on Histamine induced Contractionsin Isolated Trachea of Rabbit (Group-II) (Rate of contraction)

Drug concentration	Agonist		Antagonist		Agonist to antagonist	
gm/ml	Mean	SEM	Mean	SEM	%age	P-value
10^{-18}	29.37	0.46	29.62	0.49	0.85	n.s
10^{-17}	30.87	0.47	30.87	0.47	0.00	n.s
10^{-16}	32.37	0.56	32.12	0.47	0.77	n.s
10^{-15}	35.5	0.46	33.25	0.49	1.33	n.s
10^{-14}	34.5	0.46	34.12	0.44	2.72	n.s
10^{-13}	35.37	0.46	35.00	0.46	3.46	n.s
10^{-12}	36.37	0.41	35.25	0.52	3.70	<0.01
10^{-11}	36.37	0.47	34	0.70	7.78	<0.001
10^{-10}	37.12	0.54	34.62	0.49	9.42	<0.001
10^{-9}	38.00	0.42	35	0.46	7.89	<0.001
10^{-8}	39.00	0.53	35.25	0.70	9.19	<0.001
10^{-7}	39.37	0.53	35.75	0.75	9.19	<0.001
10^{-6}	39.5	0.62	35.37	0.62	10.45	<0.001
10^{-5}	39.25	0.61	35.37	0.82	9.85	<0.001
10^{-4}	39	0.42	34.37	0.59	11.87	<0.001
10^{-3}	38.5	0.46	33.75	0.61	12.33	<0.001

Table No.2: Effects of Citirizine on Histamine induced Contractions in Isolated Trachea of Rabbit (Group-II) (Amplitude of contraction)

Drug concentration	Agonist		Antagonist		Agonist to antagonist	
gm/ml	Mean	SEM	Mean	SEM	%age	P-value
10^{-18}	2.12	0.12	2.12	0.12	0.00	n.s
10^{-17}	2..87	0.12	2.87	0.12	0.00	n.s
10^{-16}	4.12	0.22	4.12	0.12	0.00	n.s
10^{-15}	5.37	0.18	5.37	0.22	0.00	n.s
10^{-14}	6.12	0.22	6.12	0.18	0.00	n.s
10^{-13}	6.87	0.22	6.87	0.22	0.00	n.s
10^{-12}	7.5	0.18	6.5	0.22	13.33	n.s
10^{-11}	8.25	0.25	5.75	0.18	30.30	<0.001
10^{-10}	9.12	0.22	5.62	0.16	38.04	<0.001
10^{-9}	9.62	0.18	5.25	0.18	45.42	<0.001
10^{-8}	10.37	0.18	4.5	0.16	56.60	<0.001
10^{-7}	11.12	0.12	4.12	0.18	62.94	<0.001
10^{-6}	11.87	0.12	3.87	0.12	67.79	<0.001
10^{-5}	12.00	0.00	3.37	0.12	71.91	<0.001
10^{-4}	12.00	0.00	2.62	0.18	77.5	<0.001
10^{-3}	12.25	0.16	2.12	0.12	82.69	<0.001

DISCUSSION

We have observed the effects of Cetirizine and Loratadine on histamine induced contractions of isolated tracheal smooth muscles. We found that Cetirizine has more potent antagonistic action than Loratadine on rates and amplitudes of histamine induced contractions of isolated tracheal smooth muscles. Our observations are in correlation with the results of study of Dobashi (1995), in which he found that cetirizine antagonize the histamine induced contractions in a concentration dependent fashion on smooth muscles of isolated trachea of rabbit [20]. Our results confirmed by the findings of Liu H (2005) study, who observed antagonistic effects of antihistamines on muscarinic induced mucus cell ion

Table No.3: Effects of Loratadine on Histamine induced Contractions in Isolated Trachea of Rabbit (Group-III): (Rate of contraction)

Drug concentration	Agonist		Antagonist		Agonist to antagonist	
gm/ml	Mean	SEM	Mean	SEM	%age	P-value
10^{-18}	29.37	0.49	29.62	0.37	0.85	n.s
10^{-17}	30.25	0.55	30.37	0.46	0.39	n.s
10^{-16}	31.5	0.62	31.37	0.53	0.41	n.s
10^{-15}	31.87	0.54	31.87	0.54	0.00	n.s
10^{-14}	33.75	0.86	33.25	0.61	0.74	n.s
10^{-13}	35.37	0.77	34.25	0.64	3.16	n.s
10^{-12}	36.37	0.70	35	0.5	3.76	n.s
10^{-11}	37	0.63	34.87	0.69	5.75	<0.01
10^{-10}	38.12	0.54	35.25	0.55	7.52	<0.001
10^{-9}	38.37	0.67	35.37	0.77	7.81	<0.001
10^{-8}	39.25	0.52	36	0.59	8.28	<0.001
10^{-7}	39.37	0.62	36	0.62	8.55	<0.001
10^{-6}	39.25	0.61	36	0.59	8.28	<0.001
10^{-5}	39.12	0.83	35.25	0.75	9.89	<0.001
10^{-4}	38.5	0.73	34.62	0.65	10.05	<0.001
10^{-3}	37.75	0.64	33.75	0.64	10.59	<0.001

Table No.4: Effects of Loratadine on Histamine induced Contractions in Isolated Trachea of Rabbit (Group-III): (Amplitude of contraction)

Drug concentration	Agonist		Antagonist		Agonist to antagonist	
gm/ml	Mean	SEM	Mean	SEM	%age	P-value
10^{-18}	2.00	0.00	1.87	0.12	6.5	n.s
10^{-17}	2.50	0.18	2.50	0.18	0.00	n.s
10^{-16}	3.62	0.18	3.62	0.18	0.00	n.s
10^{-15}	4.5	0.18	4.5	0.18	0.00	n.s
10^{-14}	5.25	0.16	5.25	0.16	0.00	n.s
10^{-13}	5.62	0.18	4.87	0.29	8.89	<0.01
10^{-12}	6.37	0.18	5.37	0.18	15.69	<0.001
10^{-11}	7.62	0.18	5.37	0.18	29.52	<0.001
10^{-10}	8.25	0.16	4.87	0.29	44.35	<0.001
10^{-9}	8.62	0.18	5.12	0.22	40.60	<0.001
10^{-8}	9.37	0.26	4.87	0.22	48.02	<0.001
10^{-7}	9.87	0.12	4.62	0.18	53.19	<0.001
10^{-6}	10.12	0.12	4.25	0.16	58.00	<0.001
10^{-5}	10.75	0.16	4.00	00	64.28	<0.001
10^{-4}	11.62	0.18	3.75	0.16	67.72	<0.001
10^{-3}	11.87	0.12	2.87	0.12	76.82	<0.001

transport and rank them on potency in order to Desloratadine > Cetirizine > Fexofenadine > Diphenhydramine > Loratadine[21.] Our observations were in complete agreement with the study of Meltzer EO (1996), who observed that cetirizine provided greater relief of allergic rhinitis symptoms caused by outdoor allergent compared with loratadine [12]. Day JH (1998) also found in his study that cetirizine is more effective in reducing symptoms of seasonal allergic rhinitis than that of loratadine[18].

CONCLUSION

In this present in vitro study, we have observed the effects of second generation anti-histamines Cetirizine and Loratadine on histamine induced contractions of isolated tracheal smooth muscles. We found that Cetirizine has more potent antagonistic action than Loratadine on histamine induced contractions of tracheal smooth muscles.

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Address for Corresponding Author:
Dr: Manzoor Ahmed Unar
Associate Professor,
Deptt: Pharmacology & Therapeutics
Chandka Medical College, Larkana.
Mobile: 0333-7556522

Original Article

Comparison Between Auramine-Rhodamine (AR) And Ziehl-Neelsen (ZN) Staining In Cases of Chronic Granulomatous Lymphadenopathy

1. Niaz Muhammad 2. Chandi Kapoor 3. Muhammad Iqbal 4. Amir Muhammad Babar 5. Zahid Masood 6. Azim Asif Goraya

1. Asstt. Prof. of Histopathology 2. Assoc. Prof. of Haematology 3. Asstt. Prof. of Microbiology 4.Assoc. Prof. of Microbiology 5. Asstt. Prof. of Haematology 6. Sen. Research Officer, PMRC, Bolan Medical College, Quetta

ABSTRACT

Study Design: Experimental study.

Place and Duration of Study: This study was conducted at various hospitals of Quetta.

Materials and Methods: This study includes 103 cases of chronic granulomatous lymphadenitis, with 101 cases of tuberculosis lymph nodes amongst a total of 200 cases of non-neoplastic lymphadenopathy.Their ages ranged from 2 to 79 years. Maximum number of cases were in 10-29 years age group. Females (69.31%) were affected more as compared to males. The commonest presenting symptom was fever. Cervical lymph nodes (83 cases) were the commonest site of involvement whereas 18 cases showed multiple site involvement.

Fluorescent staining of histopatholigical sections from 103 chronic granulomatous lymphadenitis gave positive results in 76 out of 103 (73.78%) cases, however Ziehl-Neelsen staining was positive only in 29 out of 103 (28.15%) cases. The yield of mycobacteria on fluorescent staining was higly significant ($p<0.001$) as compared to Ziehl-Neelsen staining thereby providing the superiority of fluorescent stain.

Result: In a total of 200 cases of non-neoplastic lymphadenopathy 101 cases showed granulomatous lesions, histologically consistant with tuberculosis. Other causes of lymphadnopathy were chronic non-specific lymphadenitis (n=87) viral lymphadenitis (n=8), fungal lymphadenitis (n=2) and acute bacterial lymphadenitis (n=2). Fluorescent staining of histopathological sections from 103 chronic granulomatous lymphadenitis gave positive results in 76 out of 103 (73.78%) cases, however Ziehl-Neelsen staining was positive only in 29 out of 103 (28.15%) cases.

In 101 cases, the finding were consistent with the diagnosis of tuberculous lymphadenopathy. In our study, significantly greater number of cases, 78 out of 101 ($P<0.001$) diagnosed as tuberculous lymphadenitis were in age groups 10-29 years. Female (69.31%) were more affected than males (30.69%). The common presenting symptom was fever. Cervical lymph nodes were commonest site of biopsy. Haemoglobin estimation in 98 cases revealed anaemia in 65 out of 101 (66.32%) patients of tuberculous lymphadenopathy. Erythrocyte sedimentation rate was performed in 63 cases and was raised in 52 (82.53%) cases. In a total of 80 cases in whom X-ray chest was performed, 14 (15.5%) cases revealed foci of tuberculosis.

Conclusion: Thus, in conclusion, this study has highlighted the superiorty of fluorescent stain over ZN stain.

Key Words: Haemotoxylin and Eosin stain, Reticulin stain, Periodic-Acid Schiff stain, Phloxine-Tartrazine stain, Auramine-Rhodamine stain, Ziehl-Neelsen stain, Acid-Fast Bacilli

INTRODUCTION

Tuberculosis is a leading cause of morbidity and mortality not only in developing countries but also in the developed countries due to emergence of human immunodeficiency virus infection [1, 2]. Peripheral tuberculous lymphadenopathy is the commonest form of extra-pulmonary tuberculosis. Whereas cervical lymphadenitis is the commonest form of the tuberculous lymphadenitis, [3, 13].

Histological diagnosis of tuberculosis and to be differentiated from simulating granulomatous lesions of lymph nodes caused by other microbial infections. Bacteriological proof for tuberculosis is always beneficial for making a firm diagnosis either by demonstrating acid-fast bacilli in smear, section or by culture to distinguish it from other granulomatous lesions.[8] In a review of 23 cases of abdominal tuberculosis in Pakistan Institute of Medical Sciences Islamabad, mesenteric lymphadenitis was present in 5(22%) out of 23 cases.[4] In another study done in Karachi and Hyderabad during 1971-1991, 133 patients of abdominal tuberculosis were confirmed histologically. At operation, mesenteric lymphadeinitis was found in 50(38%) patients.[4] Sarfaraz [5] studied 200 resected intestinal specimens at Postgratuate Medical

Institute Lahore, 51 out of 200 cases presented with tuberculous mesenteric lymphadenitis.

The present study was carried out to document the morphological features of tuberculous lymphadenopathy, with comparison between auramine-rhodamine (AR) and ziehl-neelsen (ZN) staining in cases of chronic granulomatous lymphadenopathy.

MATERIALS AND METHODS

The present study included 103 patients of granulomatous lymphadenopathy, with 101 patients of tuberculous lymphadenopathy from various hospitals of Quetta. They were taken from total of 200 patients of non-neoplastic lymphadenopathy seen during this period. Patients of all ages and both sexes were included in the study. The specimens of the lymph nodes were collected irrespective of any specific sites for morphological study. Clinical information regarding history, physical examination and relevant investigations were obtained from the patients and doctor incharge, after detailed gross examination of each specimens, all the sections were stained with Haematoxylin and Eosin (H&E) and reticulin stains. Whereas granulomatous lesions were stained with Ziehl-Neelsen, Auramine-Rhodamine, periodic acid-Schiff, whereas methenamine silver and Giemsa stains were used when required. In non-granulomatous lesions, Gram stain, Congo red and phyloxin-tartrazine stains were used. The sections stained with fluorescent stain were examined under the Zeiss Axioplan fluorescent microscope.

RESULTS

In a total of 200 cases of non-neoplastic lymphadenopathy 101 cases showed granulomatous lesions, histologically consistant with tuberculosis. Other causes of lymphadnopathy were chronic non-specific lymphadenitis (n=87) viral lymphadenitis (n=8), fungal lymphadenitis (n=2) and acute bacterial lymphadenitis (n=2)(Table No.5). Fluorescent staining of histopathological sections from 103 chronic granulomatous lymphadenitis gave positive results in 76 out of 103 (73.78%) cases (Table No.1), however Ziehl-Neelsen staining was positive only in 29 out of 103 (28.15%) cases (Table No.2).

In 101 cases, the finding were consistent with the diagnosis of tuberculous lymphadenopathy. In our study , significantly greater number of cases, 78 out of 101 (P<0.001) diagnosed as tuberculous lymphadenitis were in age groups 10-29 years (Table No.3). Female (69.31%) were more affected than males (30.69%) Figure No.1. The common presenting symptom was fever (Figure No-2). Cervical lymph nodes were commonest site of biopsy (Table-4) Haemoglobin

Table No.1: Comparison of fluorescent (auramine-rhodamine) staining in cases of chronic granulomatous lympahadenopathy

Histopathological findings	Fluorescent positive	Fluorescent negative	No. of cases
Caseous granulomatous Lymphadenitis	61	19	80
Non-caseous granulomatous Lymphadenitis	15	08	23
Total	76	27	103

P = Not significant

Table No.2: Comparison of ziehl-neelsen staining in cases of chronic granulomatous lymphadenopathy

Histopathological findings	Ziehl-Neelsen positive	Ziehl-Neelsen negative	No. of cases
Caseous granulomatous lymphadenitis	20	60	80
Non-caseous granulomatous lymphadenitis	09	14	23
Total	29	74	103

P = Not significant

Table No.3: Distribution of age in cases of tuberculous lymphadenopathy

Age(Years)	No. of cases	Percentage
0-9	7	6.93
10-29	78*	77.23
30 and above	16	15.84
Total	101	100.0

*P<0.001 as compared to 0 – 9 and 30 and above age groups

Table No.4: Site of lymph node biopsy of patients with lymphadenopathy

Site of biopsy	No. of cases	Percentage
Cervical	83	82.18
Axillary	7	6.93
Submandibular	4	3.96
Inguinal	2	1.98
Mediastinal	2	1.98
Mesenteric	1	0.99
Anterior chest.	1	0.99
Pre-auricular	1	0.99
Total	101	100.0

Table No.5: Histopathological diagnosis of patients with lymphadenopathy

Dignosis	No. of cases	Percen -tage
1Chronic-specific lymphadenitis 1 Bacterial a) Granulomatous b) Non-granulomatous 2 Viral lymphadenitis 3 Fungal lymphadenitis	 101 2 8 2	 50.5 1.0 4.0 1.0
II Chronic non-specific Lymphadenitis	87	43.5
Total	200	100.0

estimation in 98 cases revealed anaemia in 65 out of 101 (66.32%) patients of tuberculous lymphadeno-pathy. Erythrocyte sedimentation rate was performed in 63 cases and was raised in 52 (82.53%) cases . In a total of 80 cases in whom X-ray chest was performed, 14 (15.5%) cases revealed foci of tuberculosis (Figure No.3).

Figure No.1: Sex distribution of patients with lymphadenopathy

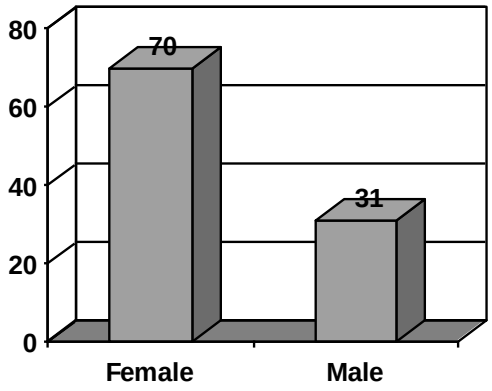


Figure No.2: Presenting complaints of patients with lymphadenopathy

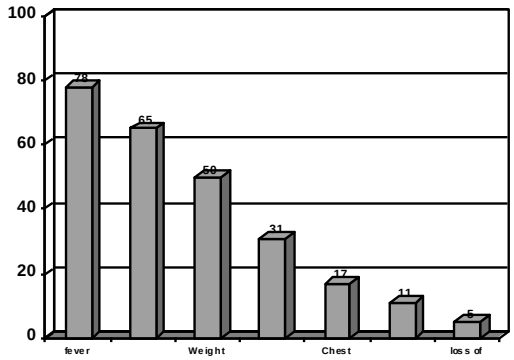
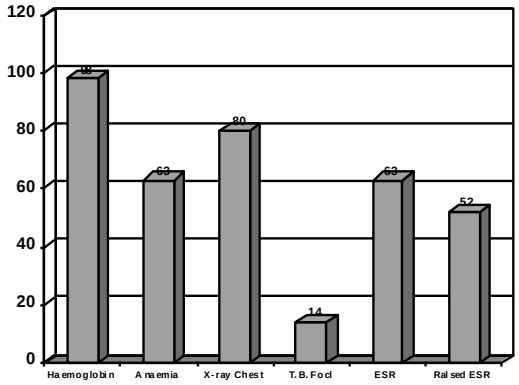


Figure No.3: Investigation of patients with lymphadenopathy



DISCUSSION

Tuberculous lymphadenopathy has been the commonest form of extra pulmonary tuberculosis both in India and Pakistan [3,6,7,14]. In the present study in which 101 cases of tuberculosis formed the major group in a total of 200 (51.5%) cases of non-neoplastic lymphadenopathy were the commonest. The same were the findings of Krishnaswami et al [8] and Dandapat et al [7] .

Maximum numbers of cases of tuberculous lymphadenitis in the present study were of 10-29 years age group. Ahmed [6] has also reported the same age group from Lahore. In India the commonest age group of tuberculous lymphadenitis has been reported to be 21-30 years [7,8] . In United States of America the reported age group was 20-70 years [16].

In the present study females out numbered the males. This is similar to the findings of other workers in the Sub-Continent [6,8] . This could be due to the fact that females in our male dominant society have low nutritional status and are exposed to overcrowding more than the males [6,8].

In this study a large majority of the lymph nodes (83 out of 101) belonged to the cervical group of lymph nodes. The predominance of cervical lymph node involvement in tuberculosis has already been established [3,6,7] . It has been suggested that tonsils, adenoids and waldayers ring provide an easy portal of entry of Mycobacterium lymph node involvements [7].

In this study X-Ray chest was available in 80 cases. Out of these only 14 revealed foci of tuberculosis. Our findings are in accordance with those of Ahmed[6,15] who reported tuberculous lesions in X-Ray Chest in only 3 out of 43 cases. This also suggests that X-Ray Chest has a very limited value in the diagnosis of tuberculous lymphadenitis. Moreover it is also concluded that a normal chest radiography does not rule out the possibility of patient suffering from tuberculous lymphadenitis.

In this study 80 cases showed caseating granulomas whereas 23 had non-caseating granulomatous inflammation. Zeihl-Neelsen staining for acid-fast bacilli was positive in 29 out of 103(28.15%) cases. Different studies have quoted frequency of demonstration of acid-fast bacilli on Ziehl-Neelsen staining varying from (16.97%) to (37.5%) [9,10] However yield of Mycobacterium tuberculosis on fluorescent staining is significantly more (P<0.001) as it was seen in 76 out of 103 (73.78%) cases, there by proving the superiority of fluorescent stain over Zeihl-Neelsen stain has already been reported in many studies. [11,12]

CONCLUSION

Thus, this study has highlights the superiorty of fluorescent stain over Zeihl-Neelsen stain, it is noted that tuberculosis is an important differential diagnosis of cervical lymphadenopathy and cervical lymph node biopsies should be sent for histological as well as for microbiological examination.

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Address for Corresponding Author:
Dr. Niaz Muhammad
Asstt. Prof. of Histopathology
Bolan Medical College, Quetta
Cell No.0343-8215910

Original Article

Frequency of Ventricular Arrhythmias during First 24 hours of Acute Myocardial Infarction in Patient Thrombolysed with Streptokinase

1. Zulfiqar Ali 2. Shahid Mahmood 3. Nouman Maqbool 4. Sohail Tufail 5. Muhammad Taimur 6. Muhammad Sikandar Aslam

1. Specialist Sen. Reg., Emergency & Trauma Center, Rashid Hospital Dubai, UAE 2. Assoc. Prof. of Surgery, FUMC, Rawalpindi 3. Asstt. Prof. of Orthopaedic, FUMC, Rawalpindi 4. Consultant Cardiologist, Sialkot Medical Complex Hospital, Sialkot 5. Reg. of Surgery, FUMC, Rawalpindi 6. 4th Year Medical Student, FUMC, Rawalpindi.

ABSTRACT

Objectives: To asses the frequency of ventricular arrhythmias during first 24 hours complicating first episode of Acute Myocardial Infarction in patients thrombolysed with Streptokinase.

Study Design: Cross-sectional, prospective, observational & quatitative study.

Place and Duration of Study: This study was conducted at Sialkot Medical Complex for six months from March 2010 to August 2010.

Patients and Methods: 200 consecutive patients with acute myocardial infarction who received streptokinase were assessed for ventricular arrhythmias. Monitoring of the patients for ventricular arrhythmias for 24 hours from the time of admission was done. Arrhythmias from the cardiac monitor's memory noted & documented. Ventricular arrhythmias studied were ventricular fibrillation (VF), sustained ventricular tachycardia, accelerated idioventricular rhythm, non-sustained ventricular tachycardia & premature ventricular beats > 10 beats per hour. Findings were recorded on a specially designed proforma. The data were then entered in the computer for analysis & conclusions were drawn.

Results: Reperfusion arrhythmias were observed in 20% of the patients (40/200) in first 24 hours after thrombolytic therapy presenting with first acute myocardial infarction. All the patients included in the study showed the ECG criteria of STEMI and positive quantitatively Troponin T test. Inferior Wall MI was the most common type of acute MI. All the patients received IV streptokinase as thrombolytic agent. The patients with Sustained VT (33%) received cardioversion & IV amiodarone. Non-sustained VT were managed by observation only (77%). A total of 35 patients survived in first 24 hours, five died.

Conclusions: Reperfusing arrhythmias are commonly observed in first 24 hours after streptokinase therapy for acute myocardial infarctions. Most of the non-sustained reperfusion arrhythmias are left untreated and requires observation only but sustained ventricular arrhythmias (VF, VT) can be life-threatening and therefore must be considered for treatment. Electrical cardioversion is preferred over pharmacological treatment in case of sustained ventricular arrhythmias. Survival can be maximized if these arrhythmias are recognized and managed efficiently.

Key Words: ventricular arrhythmias, cardioversion, acute myocardial infarction.

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death woldwide[1]. World health organization (WHO) predicts that the current figure of 7.1 millions deaths from CAD globally will jump to 11.1 millions in 2020. At least 50% of these deaths will occur in South Asian counries[2] like India, Pakistan, Sri Lanka and Bangladesh. Clinical manifestations of CAD include acute coronary syndromes and chronic stable angina. Acute coronary syndrome (ACS) representing acute myocardial ischemia is further categorized on the basis of index ECG and cardiac biochemical markers into ST elevation myocardial infarction (STEMI), non-ST elevation myocardial infarction (NSTEMI) and unstable angina (UA)[3]. STEMI is not only prevalent but also associated with higher mortality than the other two subsets (NSTEMI and UA) of the ACS. In the US, one million new myocardial infarctions are added to the existing pool of more than 70 million prior infarctions[4]. One third of the patients who experience STEMI die and about half of them do so within first four hours of the onset of symptoms.

Advancements in the management of STEMI with optical medical treatment like aspirin, beta blockers and ACE inhibitors as well as reperfusion therapies like fibrinolysis and primary percutaneous coronary intervention (PCI) has undoubtedly contributed to the decline in mortality over the last 30 years. Nevertheless, early mortality rates are still unacceptably high[5]. Majority of early deaths after STEMI are caused by ventricular arrhythmia. In order to make a significant impact on the early Post MI mortality, early recognition and prompt treatment (electrical or pharmacological) of ventricular arrhythmias are mandatory. Several studies

have been performed to know the frequency of ventricular arrhythmias and their subsequent relation with mortality in patients recovering from myocardial infarction[6,7]. But such studies in South Asian patients who are the main victims of CAD globally are very few. The mainstay of the management of STEMI in Pakistan is fibrinolysis with streptokinase as tissue plasminogen activator (TPA) and primary PCI are not preferred choices due to economic reasons. The aim of this study is to establish the frequency of ventricular arrhythmias, the most important cause of early mortality, in post myocardial infarction patients treated with streptokinase during the first 24 hours.

PATIENTS AND METHODS

200 consecutive patients with acute myocardial infarction who received streptokinase were assessed for ventricular arrhythmias. Monitoring of the patients for ventricular arrhythmias for 24 hours from the time of admission was done. Arrhythmias from the cardiac monitor's memory noted & documented. Ventricular arrhythmias studied were ventricular fibrillation (VF), sustained ventricular tachycardia, accelerated idioventricular rhythm, non-sustained ventricular tachycardia & premature ventricular beats > 10 beats per hour. Findings were recorded on a specially designed proforma. The data were then entered in the computer for analysis & conclusions were drawn.

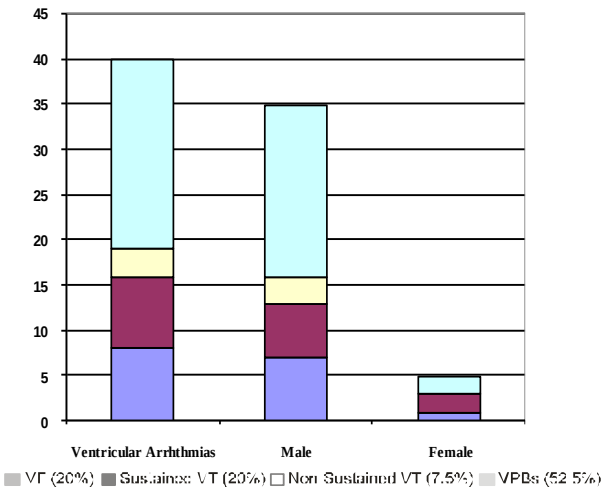
Study design: It was a prospective cross-sectional, observational study done at Cardiology Department, Sialkot Medical Complex Sialkot from March 2010 to August 2010. Ethical approval was taken from Board of Governors of Heart Care Society Sialkot and ethical committee of Sialkot Medical Complex before the commencement of study.

Inclusion Criteria: All the patient with myocardial ischemia and time of onset of symptoms to therapy is ≤12 hours, ST segment elevation ≥1mm in contagious limb leads or ≥2mm in contagious chest leads, presumably new-onset LBBB & with first myocardial infarction were included in the study.

RESULTS

Figure 1 show the characteristics of ventricular arrhythmias in first 24 hours in those patients thrombolysed with streptokinase at our centre. In our study, four types of ventricular arrhythmias were seen in those patients receiving streptokinase as thrombolytic agent for acute myocardial infarction in first 24 hours. The most common ventricular arrhythmias were VPBs (52.5 %) followed by VF (20%), Sustained VT (20%), and Non-sustained VT (7.5%) respectively.

Figure 1 showing post MI vent. arrhythmias



The mean age for all the ventricular arrhythmias was found to be 53.4 years with slightly younger age for males than females (M: F, 52.9: 57 years). On the other hand, VF occurred in patients with comparatively older age (65.3 years) than other ventricular arrhythmias (non-sustained VT 55 years, VPBs 52.8 years, and sustained VT 49.4 years). There were striking findings related to sex distribution that most of those ventricular arrhythmias were in male group (M: F, 87%: 13%). The ventricular arrhythmias were also recorded more in patients with cardiovascular risk factors (75%) than those with no risk factors (25%). Quantitative Troponin T was positive in all patients during the course of the disease progression.

Table 1: Characteristics of ventricular arrhythmias in patient's thrombolysed with streptokinase

Characteristics	**VF (n=8)**	**Sustain-ed VT (n= 8)**	**Non-sustained VT(n= 3)**	**VPBs (n= 21)**
Age (Mean) 53.4 yrs (M=52.9yrs, F=57yrs)	65.3 yrs	49.4 yrs	55 yrs	52.8 yrs
Sex				
Male (n=35, 87%)	7 (17%)	6 (15%)	3 (7%)	19(47%)
Female (n=5, 13%)	1 (2%)	2 (5%)	-	2 (5%)
Risk factor profile				
DM (n=15)	4	3	1	5
HTN (n=9)	1	1	-	6
DM+HTN (n=6)	1	1	-	4
No HTN/DM (n=10)	2	3	2	6

Type of Acute Myocardial Infarction on presenting ECG				
Antero Septal (n=6)	1	3	-	2
Anterior Wall (n=7)	1	1	-	5
Inferior Wall (n=14)	2	3	-	9
Infero Posterior (n=2)	-	-	1	1
Antero Lateral (n=2)	-	-	-	2
Postero Lateral (n=1)	-	-	1	-
Extensive (n=5)	2	1	1	1
Global (n=3)	2	-	-	1
Quantitative Troponin T	All positive	All positive	All positive	All positive

Reperfusion arrhythmias are frequently observed in patients receiving thrombolytic therapy for acute MIs and many of them need simple observation but sustained arrhythmias can become life-threatening and must be treated. All the patients with VPBs (n= 21) were simply observed. Patients with VF (n=8) were defibrillated immediately. Patients with sustained VT received electrical therapy (62.5%), drug therapy (25%), and observation only (12.5%) respectively. In general most of our patients (54%) with ventricular arrhythmias in post-thrombolysis period were observed as the most common rhythm was VPBs (52.5%). Electrical therapy (33%) was offered to lethal and sustained arrhythmias and some stable patient were also managed with drug therapy (13%). Majority (87.5%) of the patients survived and the mortality rate in first 24 hours after admission was 12.5%. VF was the most common cause of death (80%), followed by Sustained VT (20%). Unfortunately two of the patients develop embolism in the lower limbs which were successfully removed under local by the surgeons.

Table 2: Treatment of ventricular arrhythmias in 24 hours post-thrombolysis period

Treatment Option	**VF (n=8)**	**Sustained VT (n= 8)**	**Non-sustained VT (n= 3)**	**VPBs (n=21)**
Observation (22/40) 55%	-	1	1	20
Drug Therapy (5/40) 13 %	-	2	2	1
Electricity (13/40)32%	8	5	-	-

DISCUSSION

Reperfusion arrhythmias are seen more than 25% of the patients after thrombolytic therapy for acute myocardial infarction[8]. In our study 20% of the patients suffered ventricular arrhythmias in first 24 hours which is very much similar to most of the studies in the literature[9]. It is documented that accelerated idioventricular rhythm is frequently seen as reperfusion arrhythmia after thrombolytic therapy[10, 11]. In our study, VPBs were the most common ventricular arrhythmias seen after streptokinase therapy, followed by VF, sustained VT, and non-sustained VT respectively. Inferior wall MI was the most common type of acute MI seen in our patient but most of the life-threatening arrhythmias like VF were seen more commonly in extensive MI or global MI than any regional myocardial infarction. This explains that more extensive the myocardial damage, more lethal the arrhythmias are and more chances of sudden cardiac arrest[12]. One of the limitations in our study is lack of follow-up for most of the patients. But we believe that our study opens the doors to search for the long term mortality at 30 days and one year in patients with post-thrombolysis ventricular arrhythmias[13]. Additionally, it is not clear that sustained ventricular arrhythmias were either associated with acute myocardial infarctions or related to reperfusion state after streptokinase therapy. Few studies where patients were randomized to streptokinase and placebo reveals that incidence of arrhythmias were same in two groups[14].

CONCLUSION

Reperfusion arrhythmias are commonly observed in first 24 hours after streptokinase therapy for acute myocardial infarctions. Most of the non-sustained reperfusion arrhythmias are left untreated and requires observation only but sustained ventricular arrhythmias (VF, VT) can be life-threatening and therefore must be considered for treatment. Electrical therapy is preferred over pharmacological treatment in case of sustained ventricular arrhythmias. Ventricular arrhythmias are directly related to infarct size, extensive the infarct, fatal the arrhythmias and vice versa. Survival can be maximized if these arrhythmias are recognized and managed efficiently.

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Address for Correspondence Author
Dr. Zulfiqar Ali MRCP, MRCSEd A&E, EMDM
Specialist Senior Registrar
Emergency & Trauma Center,
Rashid Hospital Dubai, UAE.
Consultant Emergency Medicine MOH, UAE
Teaching Faculty, Dubai Medical College
Tel: +971507928004
Email: dr.alizulfiqar@yahoo.com

Original Article

Cause of death in exhumed bodies: An experience in upper Sindh, Pakistan

1. Haresh Chand 2. Kanwal Kumar 3. Rashid Ahmed Pathan 4. Zawar Hussain Khichi 5. Ghulam Qadir Kaheri 6. Khurshid Ahmed Abbasi

1. Asstt. Prof. of Pathology 2 & 3. Asstt. Prof. of Forensic Medicine 4. Assoc. Prof. of Forensic Medicine, CMC, Larkana 5. Prof. of Forensic Medicine, GMMMC, Sukkur 6. Prof. of Paeds Medicine, CMC, Larkana

ABSTRACT

Background: - Exhumation is conducted around the globe when foul play is suspected. In developed world and in some developing countries this procedure is also carried out for identification purposes as well as in insurance claims, and some other civil suits.

Objective: To determine the cause of death in exhumed bodies.

Study design: Prospective, descriptive.

Place & Duration of Study: The Study was conducted in the department of Forensic Medicine, Chandka Medical College, Larkana (CMCL) from Jan:2001 to Dec:2010.

Materials and Methods: A total of 125 bodies were exhumed in various districts of upper Sindh by exhumation board, constituted by Director General Health Services Hyderabad. At the site of graveyard, bodies were digged out. After identification of deceased by near relatives, the bodies were thoroughly examined, viscerae taken for histopathological and chemical analysis, and cause of death determined by consensus in almost all cases.

Results:- The most common cause of death was firearm injuries 37 (29.6%), followed by blunt trauma 15 (12%), sharp weapon injuries 09 (7.2%), drowning 09 (7.2%), poisoning 07 (5.6%) strangulation 06 (4.8%), infanticide 06 (4.8%). In about 1/3 of cases cause of death could not be decided due to advanced stage of decomposition.

Conclusion: Majority of victims were young males & firearm injury was the commonest cause of death.

Key Words: Exhumation, Cause of Death, firearm injuries

INTRODUCTION

Exhumation is lawful disinterment of dead body or human remains from the grave or earth.[1,2] Dead bodies are buried in two general contexts, one is legally interred bodies in cemetery, while unlawful burials, being the act of person / gangs involved in concealing the heinous crimes, are found at some places other than cemetery.[3] Exhumation is performed mostly in criminal cases, but it is also conducted rarely in civil suits.[3] It is highly objectionable and illegal to disturb human remains without authorization of state machinery in every country[4], except in Israel where it is completely forbidden by Jewish law.[5] Exhumation is unwelcome and highly charged issue particularly for family members and friends of deceased, hence utmost care should be taken during whole procedure to avoid law and order situation.[1,6] There are multiple purposes of exhumation, the prime being the determination of cause of death when foul play is suspected.[7] In these circumstance, it should be performed as early as possible before skeletonization of body, as clue about cause of death is inferred from soft tissues in majority of cases[8], whereas exhumation, some times conducted for identification purpose through DNA test, can be undertaken even after centuries.[9] Movement from original grave to subsequently acquired family plot, repatriation overseas to be buried along with other family members, shifting of graves en mass to another new graveyard when old one is required by State for some vital public projects are other rare purposes of exhumation in different countries.[6]

Although common perception is that main cause of death of decreased in exhumed bodies is due to violence and this has been supported by two studies done in Pakistan.[2,10] Hence this study was conducted in various districts of upper part of Sindh province to prove this hypothesis or otherwise because no such study has been done here before.

MATERIALS AND METHODS

This was the prospective descriptive study conducted with the approval of ethical committee of Chandka Medical College Larkana (CMCL). A total of 125 bodies were exhumed in various districts of upper part of Sindh during the period of ten years from January 2001 to December 2010 by exhumation board constituted by Director General Health Services Sindh, comprising of Medical Superintendent as Chairman, Police surgeon, Forensic expert, Pathologist and Lady doctor in case of female bodies as members. All team members, accompanied by police escort under the supervision of Judicial Magistrate to control the emergency situation, used to reach the graveyard early in the morning. Before starting the procedure of

exhumation, consent, identification of grave, shroud, and body by heirs or near relatives were the mandatory requirements. The examination of the body was performed (both external and internal) which included the following protocol.

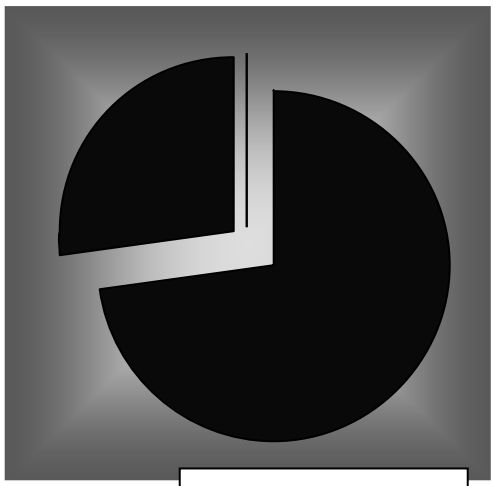
a. Identification of sex from external appearance and in case of decomposition from bones.
b. Age from teeth or from skull sutures.
c. In case of firearm injuries, presence of bullets, pellets, wads, evidence of entry & exit wound.
d. External & internal injuries were seen in the region of neck especially, hyoid bone status and cervical vertebral fractures in cases of compression to the neck.
e. Collection of viscerae in 10% formalin for Histopathological examination.
f. Collection of viscerae in normal saline for chemical examination in suspected poisoning.
g. Collection of soil samples from different sites around the shroud of the body and distant from the grave as control in suspicious poisoning cases only.

The body was to be handed over to concerned authorities for reburial at the end of examination. After doing all above steps, opinion was formed regarding cause of death by the exhumation board based upon the examination of body, reports of Histopathologist and Chemical examiner. The board took unanimous decisions in almost all cases. Data was analyzed using Statistical Package for Social Sciences (SPSS) version 13.

RESULTS

A total of 125 bodies were exhumed during the study period. There were 91 males (72.8%) and 34 females (27.2%), with a male / female ratio of 2.7:1 as shown in figure-1. The age ranged from 0-65years.

Figure 1: Pie chart showing sex distribution



The majority of [illegible] years age, representing 63. [illegible]e ages of 8.0% bodies were in between 0-15 years(TableNo.1).

Regarding cause of death, in 37 (29.6%) bodies it was firearm injuries, while in about equal number of bodies, cause remained undecided. (Table-2). In all death causes, male gender out numbered the females expect infanticide where both sexes were in equal number (Table – 3)

Table No. 1: showing age distribution (n=125)

Age group	No.	Percentage
0 – 15 years	10	8%
16 – 30 years	79	63.2%
31 – 45 years	24	19.2%
46 – 65 years	12	9.6%
Total	125	100%

Table No. 2: showing cause of death (n=125)

Cause of death	No.	Percentage %
Fire-arm injuries	37	29.6%
Blunt Trauma	15	12%
Drowning	09	7.2%
Sharp weapon Injuries	09	7.2%
Poisoning	07	5.6%
Strangulation	06	4.8%
Infanticide	06	4.8%
Indeterminate	36	28.8%
Total	125	100%

DISCUSSION

Mode of disposal of dead bodies in Pakistan is mostly burial as Muslims are in majority; hence requests for exhumation are more common as compared to India where cremation of corpse is the common practice.[11] In this study, all the 125 exhumations were of criminal nature, whereas in previous national studies, one conducted by Qazi et al,[2] and another by Hussain et al,[10] have also shown all exhumations, related to criminal cases. In our study, male victims were in majority, with male to female ratio of 2.7:1 whereas Qazi et al,[2] Hussain et al,[10] Grellner & Glenewinkel,[12] Kremer & Sauvageau,[13] have shown male female ratio as 2.5:1, 1.53:1, 2.83:1 & 2:1 respectively. The male predominance may be explained by their indulgence in violent activities and in the society women and children are usually spared.[14, 15] This Study showed the majority of cases in younger age group of 16-30 years (63.2%). Our results are similar as observed by Qazi et al,[2] who have also shown younger victims to be 62.8%. The predominance of younger age persons is also shown by Hussain et al

Table No. 3: Cause of death, Sex wise distribution (n=125)

	Cause of Death								
	Fire-arm Injuries	Blunt Trauma	Sharp Weapon Injuries	Drowning	Strangu-lation	Infanticide	Poisoning	Undetermined	Total
Male	26	9	9	8	4	3	6	26	91
	11	6	0	1	2	3	1	10	34
Female	37	15	9	9	6	6	7	36	125

(41.8%).[10] However our results are in contrast to one study conducted in Canada[13] where majority of cases of exhumation are of older persons over the age of fifty. Involvement of younger persons of our sub-continent, in the productive and prime years of life is due to erratic, aggressive behavior and these persons are more vulnerable to fast changing social trends and culture patterns and they do not care of consequences in case of disputes[14]. In this study death of deceased had occurred by firearm injury in significant number of cases (29.6%). Our results are lower, as compared to study by Hussain et al[10] at Peshawar who reported firearm injury in 44.2% of cases as the cause of death. Firearm Fatalities are no doubt common in our upper part of Sindh, but even more common in Peshawar which is due to easy availability of deadly weapons without license and further more Pukhtuns keep the sophisticated weapons as a tradition.[16] In this study death due to violent acts other than firearm injury was seen in 41.6% of cases. This finding is in agreement with Hussain et al[10] who observed 39.5% of deaths due to these violent acts. Tribal feuds, matrimonial disputes, eloping of young girls for free will marriages leading to honor killing are the main reasons behind these fatalities in this region. In our study out of 125 cases, cause of death was established in 89 cases (71.2%), in remaining 36 cases (28.8%) cause could not be established. Failure to reach the cause of death in such a large number of cases in our study region is early putrefactive changes due to hot atmospheric temperature, water logging and salinity. The lengthy codal procedures, apathy of police, large number of pending cases in judiciary are also responsible for unnecessary delay and negative results.

CONCLUSION

1. Firearm injury followed by blunt trauma, sharp weapon injuries due to violence constitutes the common cause of death in this study.
2. Majority of victims are young males

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Address for Corresponding Author:
Dr. Haresh chand
Assistant Professor of Pathology
Chandka Medical College Larkana
Mobile: 0333-7541954

Original Article

Atherosclerotic Lesions In Relation To Occupational Physical Activity---A Human Autopsy Study

1. Amjad Naeem 2. Azhar Masud Bhatti 3. Syed Muddasar Hussain

1. Prof. of Pathology, Akhtar Saeed Medical and Dental College Lahore 2. Addl. Director, EPI, Punjab
3. Asstt. Prof. of Forensic Medicine, KEMU, Lahore.

ABSTRACT

Objective: To assess the severity of different atherosclerotic lesions in relation to occupational physical activity in our population.

Study design: Prospective descriptive observational study.

Place and duration of study: Mortuary of King Edward Medical University Lahore and Department of Pathology Allama Iqbal Medical College Lahore. The duration of study was completed in one and a half year.

Materials and Methods: A total of 130 human autopsies were carried out at random. The age range was between 8 and 85 years. Heart, aorta coronary arteries and renal arteries were collected from dead bodies. One to four areas of tissue were taken from aorta and each arteries in all cases. Sections were prepared from paraffin blocks. These were stained with Haematoxylin and Eosin stain. Special stain were also performed to differentiate all the components of atherosclerotic lesions.

Results: The fatty streaks were present in a predominant number of cases in Grade-II and Grade-III than in Grade-I physically activity cases. The fibrolipid plaques, complicated and classified lesions were seen predominantly in Grade-I than in Grade-II and Grade-III physically active cases on percentage basis.

Conclusion: In this study the severity of different atherosclerotic lesions is noted in Grade-I, Grade-II and Grade-III physically active subjects according to their occupational activities. This basic data gives indication and guideline for prevention and control of atherosclerotic process by increasing physical activity in life style of our population.

Key wards: Physical activity, Atherosclerosis, aorta, Coronary arteries, Renal arteries.

INTRODUCTION

It has been observed that clerks are twice as prone to fatal coronary occlusion than postmen[1]. It was suggested that sustained physical activity above a certain critical threshold was protective against coronary heart disease[2]. It is also reported that 2-4times higher incidence of coronary heart disease and its complications in 5288 middle aged sedentary males when compared to their physically active counterparts[3]. Short bursts of activity repeated several times a day may be equally or more beneficial than prolonged exhaustive exercise. To be effective, physical exercise should be regular and continuous throughout life[4]. It has been shown that coronary proneness in young bus-drivers as compared to young conductors is due to the higher weight and higher lipid levels[5].

MATERIALS AND METHODS

A total of one hundred and thirty human autopsies were carried out during this study. Ninety were males and forty females. The age range was between 8 and 85 years. The autopsies were done in the mortuary of the King Edward Medical University, Lahore.

Selection of Dead Bodies

All the dead bodies included in this study were examined in the interval which ranged from 4-10 hours between the death and autopsy. The dead bodies of men, women and children were included at random i.e on the basis of availability. In each case the relevant history was obtained from the closest relatives of the deceased. Autopsies were performed. The heart, aorta, coronary arteries and renal arteries were included in this study.

Performa for relevant history and autopsy findings.

1. Name
2. Date of birth (Exact/Application)
3. Date of death
4. Sex
5. Place of Residence
6. Occupation.
7. Any Medical Care before death.
8. Mode of death :- Accidental death, non-accidental death
9. Was any diagnosis made before death, if yes, clinical diagnosis.

Heart, aorta, coronary arteries and renal arteries were collected.

Grading of Atheroma

Cross sections of coronary arteries were graded by one of the four scores according to the degree of atheromatous narrowing, Grade-I, upto 25% narrowing, Grade-II, 26-50% narrowing, Grade-III, 51-75% narrowing and Grade-IV greater than 75% narrowing. Complete occlusion with haemorrhage, ulceration, thrombosis and calcification were recorded separately. In addition, major degree of narrowing in each branch was noted; isolated areas of narrowing were specified as "Focal" and distance from origin of artery was noted. In all the 130 autopsies aorta, coronary arteries and renal arteries were examined. 1-4 sections were taken from aorta for histological examination from the following sites.

1. Arch of aorta.
2. Above the celiac artery level (thoracic).
3. At renal arteries level (abdominal)
4. Below renal arteries level (abdominal).

In addition, 1-4 sections from each of the coronary arteries and renal arteries were taken, For histological examination tissue processing was done. On the average 7-8 slides were prepared from each block by taking ribbons of tissue. The paraffin section were stained using Haematoxylin and Eosin stain, von kossa's staining technique, periodic acid Schiff (PAS) reaction, Toludine blue stain and Peral's Prussian blue stain.

RESULTS

The range of physical activity was evaluated from the occupational activities in case of males. In case of females the nature of daily routine house work was interrogated and range of physical activity was considered. In addition to that any other type of physical activity such as exercise or involvement in the games was noted in both males and females.

The different categories of atherosclerotic lesions such as fatty streaks, fibrolipid plaques, complicated (ulceration, haemorrhage and thrombosis) and calcified lesions were noted. Fibrolipid plaques, complicated and calcified lesions were named as the raised lesions. The atherosclerotic ulcers were seen with ragged edges. No case of aneurismal dilatation or rupture of aorta was observed during the study.

In a total of 130 cases in whom aorta, coronary arteries and renal arteries were collected 45 cases showed the history of sedentary habits (Grade-I), 51 cases showed the history of moderate activity (Grade-II) and 34 cases showed the history of strenuous activity (Grade-III). The fatty streaks were present in a predominant number of cases in Grade-II and Grade-III than in Grade-1 physically active cases. The fibrolipid plaques, complicated and calcified lesions were seen predominantly in Grade-I than in Grade-II and Grade-III physically active cases on percentage basis. (Table No.1), (Figure No.1).

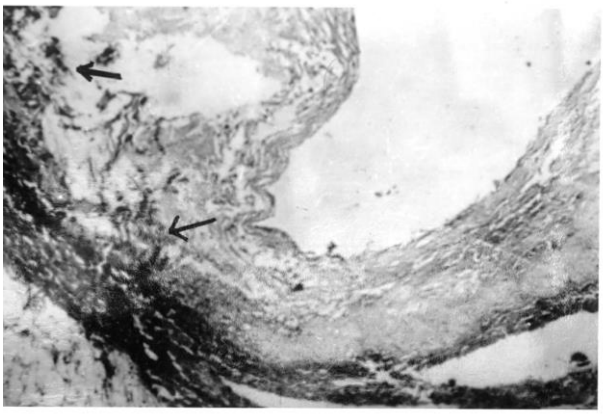

Figure No.1: Photomicrograph of coronary artery showing atherosclerotic narrowing with denegation of elastic lamina in sedentary subject.

DISCUSSION

In this study the fatty streaks were present in the predominant number of cases in Grade-II and Grade-III Verhoeff's elastic tissue stain x 80 than in grade-I physically active cases. Fatty streaks showed correlation with more physically active cases. The fibrolipid plaques, complicated and calcified lesions were seen in a predominant number of cases in grade-I than in Grade-II and grade-III physically active cases.

Exercise was associated with reduced overall atherosclerotic involvement and it was suggested that moderate exercise may prevent or retard coronary heart disease in primates[6]. It was observed that death due to the coronary atherosclerosis was highest amongst[7]. Supporting these findings declared that those who retired had an 80% greater risk of coronary heart disease than those who had not[8]. It showed that coronary proneness in young bus drivers as compared to young conductors was due to the higher weight and higher lipid levels[5]. After 13 weeks moderate exercise programme there was increase in high density lipoprotein – cholesterol level[9]. It has also been established that increasing the number of miles per weeks increases plasma high density lipoprotein-cholesterol while decreasing levels of low density lipoprotein – cholesterol, very low density low density lipoprotein – cholesterol and percent body fat[10]. It was supported these findings but added that high density lipoprotein – cholesterol level decreases within days of stopping exercises, and high-density lipoprotein-cholesterol have an independent protective effect on ischemic heart disease[11,12,13]. On the other hand it is suspected that there was no effect of exercise on serum cholesterol level[14].

During physical activity, the output of cholesterol and bile acids in the bile increases. This causes higher

faecal loss of sterols which may lead of lower cholesterol levels in peripheral tissues and in the bile. There is also release of unsaturated fatty acids from the adipose tissue during exercise alongwith linoleic acid dependent LCAT enzyme[4]. On the other hand it is indicated that classical risk factors for coronary heart disease do not improve with increased physical activity and fitness[15].

Table No.1: Number and percentage distribution of atherosclerotic lesions in aorta, coronary arteries and renal arteries in relation to history of occupational physical activity

Blood vessels	Fatty streaks						Fibrolipid Plaques						Complicated lesions						Calcified lesions					
	IN						IN						IN						IN					
	I		II		III		I		II		III		I		II		III		I		II		III	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No	%	No	%	No.	%	No.	%	No.	%	No.	%
Thoracic Aorta	22	48.9	38	74	20	58.8	22	48.9	13	25.5	6	17.6	11	24.4	7	13.7	3	8.8	6	13.3	3	5.9	1	3..0
Abdominal Aorta	17	37.8	31	60.8	14	41.2	42	93.3	24	47.1	13	38.2	26	57.8	16	31.4	7	20.6	14	31.1	8	15.7	4	11.8
Anterior descending LT. C.A	4	9.0	10	19.6	5	14.7	37	82.2	23	45.1	9	26.5	10	22.2	6	11.8	2	5.9	3	6.7	2	3.9	-	-
Circumflex Lt. C.A	3	6.7	8	15.7	4	11.8	37	82.2	24	47.1	12	35.3	5	11.1	3	5.9	1	3.0	1	2.2	-	-	-	-
Rt. C.A	-	-	2	3.9	1	3.0	3	6.7	2	3.9	1	2.9	1	2.2	-	-	-	-	-	-	-	-	-	-
Rt Renal Artery	8	17.8	21	41.2	12	35.3	18	40.0	10	19.6	4	11.8	9	20.0	5	9.8	1	3.0	6	13.3	3	5.9	-	-
Lt. renal artery	8	17.8	21	41.2	12	35.3	10	22.2	7	13.7	3	8.8	7	15.6	3	5.9	1	3.0	5	11.1	2	4.0	-	-
Rt. Common iliac artery	-	-	7	58.3	4	50.0	10	100	7	58.3	4	50.0	9	90.0	5	41.7	1	12.5	6	60.0	3	25.0	1	12.5
Lt. common iliac	-	-	7	58.3	4	50.0	10	100	7	58.3	4	50.0	7	70.0	5	41.7	1	12.5	5	50.0	3	25.0	1	12.5
Mean incidence in all vessels		**15.3**		**41.4**		**33.3**		**63.9**		**35.4**		**26.7**		**34.8**		**17.9**		**7.7**		**20.8**		**9.4**		**4.4**

I = Sedentary II = Moderate activity III = Strenuous Activity.

It has been established that physical activity and exercise training have important roles in preventing atherosclerotic coronary artery disease. Managing select Coronary artery disease risk factors, including elevated triglyceride levels, low HDL-C. hypertension, glucose intolerance, hypertension, obesity, and possibly cigarette use. Treating patients with coronary artery disease, heart failure and claudicating[16,17]. It has also bee seen that exercise training results in a faster heart rate recovery in patients with heart failure, heart rate recovery, as a simple marker of rehabilitation[18]. A regular physical activity program reduces BP, arterial stiffness, and abdominal fat; increases curio respiratory fitness; and delays arterial wall remodeling in pre-pubertal obese children[19]. On the other hand it has been seen that Cardiopulmonary exercise testing with gas exchange measurements in likely to be a value in diagnosing and quantifying both overt and occult myocardial ischemia and its reversibility with treatment[20,21]. Again it is also suggested that physical activity was weakly associated with a reduced risk of ischemic stroke among middle-aged adults. The association may be due to links between physical activity and other risk factors or due to chance[22,23]. But in a comparative study it is established that the earlier age of acute myocardial infarction is South Asians can be largely explained by higher risk factor levels at younger ages[24]. A recent study from 2 Indian cities indicates that daily moderate intensity exercise such as brisk walking from 35 to 40 minutes was associated with more than a 50% reduction in risk for CHD. Physical activity increased insulin sensitivity and high density lipoprotein cholesterol, lowers blood pressure, improves endothelial function, and reduces the risk of type 2 diabetes mellitus, hypertension, and central adiposity, these risk factors are highly prevalent in South Asians. Hence, there is an urgent need to promote moderate-intensity physical activity for South Asians[25-29].

CONCLUSION

In this study the severity of different atherosclerotic lesions is noted in Grade-I, Grade-II and Grade-III physically active subjects according to their occupational activities. This basic data gives indication and guideline for prevention and control of atherosclerotic process by increasing physical activity in life style of our population.

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Original Article

Congenital Hypothyroidism: An Underestimated Clinical Entity

1. Masud Iqbal Babar 2.Rashid Mahmood 3.Hafiz Yar Muhammad 4. Ghulam Mustafa 5. Shehzad Ali Bukhari

1. Asstt. Prof. of Paeds Medicine 2. Prof. of Paeds Medicine 3. Assoc. Prof. of Community Medicine 4.Demonstrator of Community Medicine 5. Chief Consultant of Paeds Medicine, Sheikh Zayed Medical College, Rahim Yar Khan

ABSTRACT

Objective: The aim of study was to determine the clinical features of Hypothyroid Children in various age groups residing in Rahim Yar Khan.

Study Design: Prospective, descriptive, study, over a span of one year.

Place and Duration of Study: This study was conducted in Pediatrics department at Sheikh Zayed Hospital and Medical College Rahim Yar Khan from 1st March 2010 to March 2011 .

Materials and Methods: The thirty children of both sexes in age group of 1 day – 12 years presenting with clinical features, suspicion of Hypothyroidism were included in study. Children with subtle as well as full fledged sign and symptoms of hypothyroidism were considered for further evaluation. The clinical history, feeding pattern and clinical examination of these cases were recorded. Their blood was examined for T4, T3 and TSH. The X-rays of chest, X-rays of Skelton, particularly X-ray wrist and X-ray knee joint were obtained. Serum cholesterol, glucose, electrolytes (Na^+ & K^+) and perchlorate ($KClO_4$) discharge test were obtained. Thyroid scintigraphy was done for isotope uptake. Ultrasonography for thyroid position, its size and detection of solid and cystic lesions was performed.Cardiac monitoring was gained by E.C.G. The data analysis was done by software SPSS 16.

Results: All children with clinical features and investigations in favor of hypothyroidism were kept in four groups according to the age. The sluggish behavior, bradycardia, typical coarse faces and TSH in values above normal range were consistent findings in all thirty (n=30) cases.

Conclusion: Congenital Hypothyroidism is usually under diagnosed that leads to mental retardation in a child. Therefore any child having suspicion of hypothyroidism should be evaluated by thyroid functions test (TFT), including new born screening.

Key Words: Congenital Hypothyroidism, TFT, Children, New born screening.

INTRODUCTION

Congenital hypothyroidism (CH) has worldwide prevalence of 1:2,000 to 1:4,000 newborns.[1] It is the commonest cause of mental retardation in children.[2] The clinical features may not present in the early infancy due to trans-placental passage of small quantity of thyroxin; therefore the clinical diagnosis is usually missed at even established maternity centers.[3] Congenital hypothyroidism in 85% of the cases is due to thyroid dysgenesis while in the remaining 10-15% the dyshormonogeneses is present.[4] Thyroid dysgenesis may occur as agenesis in 40% of cases and ectopic or rudimentary in the remaining 40% of cases. Congenital hypothyroidism presents as syndromic, nonsyndromic, familial, endemic and sporadic. The familial cases like Pendred's syndrome are autosomal recessive.[5] In Down syndrome the occurrence of hypothyroidism is 1:400[6]

The meticulous clinical examination of the new born and any infant with delayed milestones is an early essential step for the detection of hypothyroidism. The epiphyseal center for the lower end of femur develops under the influence of thyroid hormone. In our setup even at the basic health unit the simplest investigation is X-ray of the knee joint for location of epiphysis center of femur in a new born which can detect the hypothyroidism. Thyroid hormone is also essential for the growth of body tissues, particularly brain, in fetal life.[7] Thereafter the absence of this epiphyseal center in the presence of clinical features like hoarse cry, hypothermia and bradycardia must warrant the sampling for TSH(Thyroid stimulating hormone) .The aim of our study is to emphasize the importance of clinical presentation, X-rays, TFT and new born screening to diagnose CH for early intervention by starting oral thyroxin to reduce mental retardation cases in our community.The new born thyroid screening tests has entirely changed the spectrum of mental retardation in children in the countries where this strategy has been applied for the last many decades.[8]

MATERIALS AND METHODS

The thirty children of both sexes in age group of 1 day – 12 years having clinical features suspicion of hypothyroidism referred to pediatrics unit Sheikh Zayed

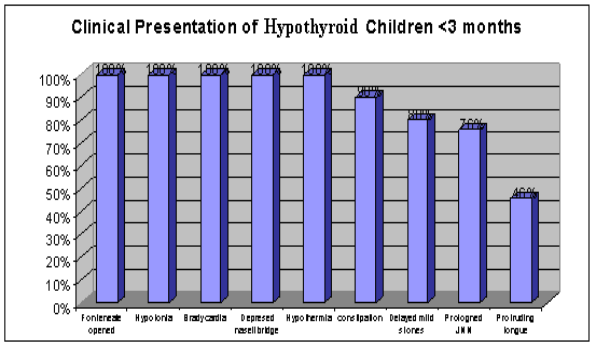
Hospital Rahim Yar Khan were included in the study. The transient hypothyroidism and Down syndrome cases were excluded. The four groups were constructed according to the age. The maternal history, birth history, feeding, developmental milestones, weight and height with clinical sign and symptoms were recorded on a Proforma. The new born babies born in labor room of this hospital presenting with apneic spells, hypothermia, bradycardia and hoarse cry were immediately transported to nursery of the pediatrics unit, managed and evaluated for the study. The other clinical features like prolonged icterus neonatarum, opened fontnellae, feeding and developmental milestones were assessed in the cases in postnatal period. Constipation, pallor, periorbital edema, coarse skin, sleepiness, poor appetite, hearing defects, intelligence quotient (IQ), schooling, social activities, were the features considered in other groups. Goiter size was evaluated according to WHO grading i.e.; grade I and grade II.

Their blood was evaluated for T4, T3 and TSH. The-rays of chest, X-rays of Skelton, particularly X-ray wrist and X-ray knee joint were obtained. Serum cholesterol, glucose, electrolytes (Na^+ & K^+) and per chlorate ($KClO_4$) discharge test were obtained. Thyroid scintigraphy was done for radioisotope uptake. Ultrasonography for thyroid position and description of lesion was performed. Cardiac monitoring was gained by ECG. Hearing was assessed by distraction method. These cases were referred for audiometry. Pure Tone Average (PTA) audiometry, otoacoustic emission (OAE) testing/Auditory brainstem response (ABR) were recommended. The data analysis was done by SPSS16.

RESULTS

Among the thirty children seventeen (n=17) were male and thirteen (n=13) were female with the male to female ratio of M:F 1:3. They were in age range of 1 day –144 months. The mean weight (group 1, <12 months) was 3.8786 kg. ± 1.54331 std, and the mean height was 56.07 cm ± 6.604 std. The mean weight (group 2, 13-36 months) was 10.500 kg ± 1.3228 std, the mean height was 83.33 cm ± 5.686 std; the mean weight (group 3, 37-60 months) was 12.400 kg ± 9.6177 std, the mean height was 92.00 cm ± 1.414 std; the mean weight (group 4, 61-144 months)was 21.500 kg ± 4.37526 std, the mean height was 106.12 cm ± 7.549 std .All the children were short stature. The figure 1 depicts the clinical features of a ten year hypothyroid, whose carpal bones are showing only two ossification centers on X-ray wrist, therefore his bone age was < 1 year(figure 2). The sign and symptoms of hypothyroid children in different four age groups are shown in graphs 1,2,3,4 respectively. The TSH was above the

Graph No.1



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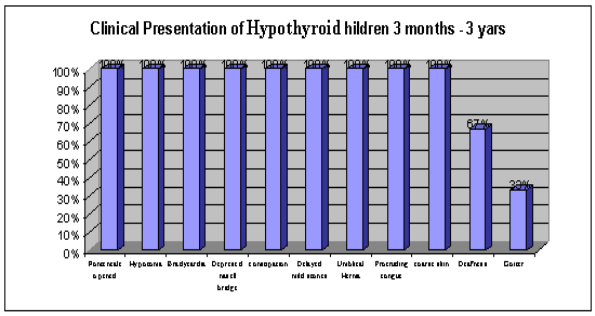

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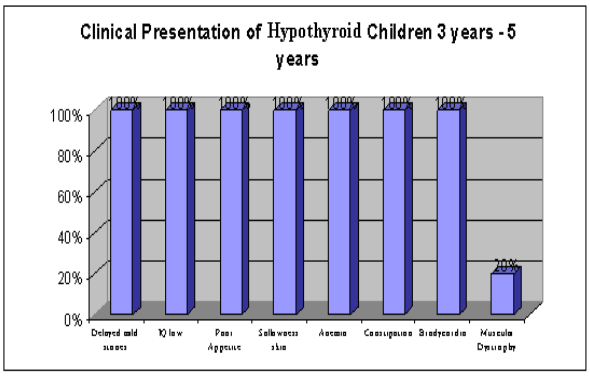

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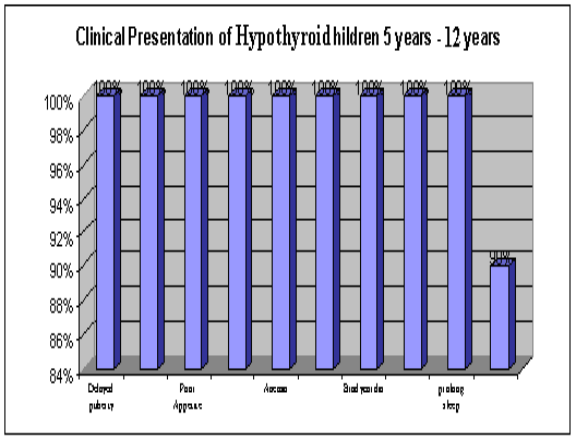

normal reference range of 20 Uml/l and serum cholesterol was also above 200 mg in all cases. The per chlorate discharge was > 40% in three (n=3) cases. The clinical presentation of hypothyroid children different age groups are shown in the graphs.

Figure No. 1: A ten year hypothyroid

Figure No.2: X-ray wrist for bone age

DISCUSSION

Congenital Hypothyroidism is one of the commonest endocrine disorders in children.[9] The prevalence of disease in Pakistan has been reported 1:1000.[10] The occurrence is even higher 1:140 in Down syndrome. The endemic hypothyroidism has been recorded in the northern areas of Pakistan like Gilgat and Sawat.[11] UNICEF, in 1994, has declared Pakistan[12] as one of the severely affected regions of the world regarding iodine deficiency disorders (IDD) but another study has shown the severity was not much. Rahim Yar Khan is a plane area at a distance from the sea and there is no exact record of iodine deficiency in this area. In the study therefore the endemic hypothyroidism is less commonly seen but the sporadic cases due to maternal thyroid disease, familial like pendred's syndrome have been seen.[13] The clinical features in the study have a pivotal role in the diagnosis of congenital hypothyroidism right from the delivery of the new born to adulthood. Most of the studies on IDD depend upon the evaluation of TFT but this study has highlighted the importance of clinical features and X-rays Skelton.[14] Of course this approach will be suitable in our undeveloped areas where facilities for TFT and other advance investigations are lacking. However later on TFT may be obtained but there will be no delay in commencing the thyroid hormone replacement.

Surprisingly more than thirty percent (n=10)children were diagnosed in outpatient department for treatment of other ailments. A few cases were brought for medical certificates to get the financial help from the Government sector provided to disabled children. It is pity that the children of twelve years or even more then twelve year age were still in the lap of their parents. These children were taken as innocent and generous "God given Bhola". They were brought up as such without looking the advice of clinician. The different studies have focused the clinical assessment as a main diagnostic tool in congenital hypothyroidism. Thyroid hormone replacement is the main stay of treatment. Luckily the treatment is cheaper as compared to treatment of other endocrinal disorders.[15]

Dwarfism is difficult to diagnose and treat in other endocrine disorders in children.[16] The limitation of treatment by growth hormone due to high cost and unavailability to poor patients is one of the drawbacks in the treatment of short stature children. However the replacement of thyroid hormone in the early stages of congenital Hypothyroidism can prevent the stigmata of dwarfism in hypothyroids.

Thyroid hormone replacement in the form of tablet thyroxin can also prevent the neurodeficit like nerve deafness and mental retardation. Maintainence therapy and strict follow-up are prudent. Initially the follow-up should be at 2and 4 weeks after starting of therapy, then every 1-2 months for the first year, and 2 weeks after change of doses. The prognosis, particularly neurological depends upon the age of hypothyroid at the time of initiation of thyroid homone. The earliest start of Thyroxin in early neonatal life can prevent nerve deafness and mental retardation.[17] New born screening for congenital hypothyroidism is an urgent need in our country.[18] The new born screening program had been launched in developed countries since decades.[19] This strategy has reduced the incidence of mental retardation in those countries due to in born errors of metabolism.[20]

CONCLUSION

Congenital Hypothyroidism is usually under diagnosed that leads to mental retardation in a child. Therefore any

child having suspicion of hypothyroidism should be evaluated by thyroid functions test (TFT) including new born screening. Least but not the last the clinical features plus bone age on X-rays be enough to start thyroid hormone replacement till the availability of TFT.

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Address for Corresponding Author:
Masud Iqbal Babar
Asstt. Prof. of Paeds Medicine,
Sheikh Zayed Medical College, Rahim Yar Khan
14-A, New Officer Colony,
Rahim Yar Khan
Cell No.0300-6726410
Office: 068-5877680
068-9230165
E-mail: masudbabar@yahoo.com

Original Article

Prevalence of Hepatitis B Virus in Blood Donors

1. Saadat Parveen 2. Muhammad Ashraf 3. Muhammad Zafarullah

1. Classified Pathologist, CMH, Multan 2. Asstt. Prof. of Paeds Surgery, Children Hospital, Multan
3. Assoc. Prof. of Ophthalmology, NMC, Multan

ABSTRACT

BACKGROUND: There is no treatment available once get infected with hepatitis B virus. Transfusion of blood contaminated with HBV is one of the major risk factors for increasing its Seroprevalence.
Objective: To determine the prevalence of Hepatitis B virus in healthy blood donors .
Study Design: A prospective descriptive study
Place and duration of study: This study was conducted in department of pathology Combined Military Hospital Multan during a period of three years from 01.07.2007 to 30.06.2010.
Patients and Methods: A total number of 18042 blood donors in between 18-55 years of age were screened for transfusion related carriers of infectious diseases including hepatitis B virus by ELIZA technique.
Results: Hepatitis B virus suface antigen was detected in 561 (3.1%)
Conclusion: Seroprevalence of hepatitis B is high even in healthy and young blood donors. Therefore every donor should be screened for it.
Key words: Hepatitis B, Serological screening, Transfusion related infectious diseases.

INTRODUCTION

Hepatitis is one of the leading causes of morbidity and mortality world wide especially in developing countries like Pakistan [1]. Hepatitis B viral infection is going to increase since its discovery in 1963 [2]. It has infected over two billions individuals all over the world and more than half million die each year [3]. Hepatitis B surface antigen was first time demonstrated by Blumberz as serological markers for HBV in 1963 [4]. Contaminated blood transfusion of as little as 0.01ml is main culprit of spread of this infection [5]. As there is no treatment available after getting infected with HBV. Special precautions should be taken to check its' transmission.

PATIENTS AND METHODS

This study was carried out in Hematology section of department of Pathology Combined Military Hospital, Multan during a period of three years from 1st July, 2007 to 30th June 2010. All healthy blood donors coming for blood donation between 18-55 years of age were included in study. Screening of all donors for transfusion transmissible infections including Hepatitis B was carried out by ELIZA. Positive individuals were informed and advised not to donate their blood. Results were recorded on predesigned proforma. At the end of study, record of hepatitis B positive cases was analyzed separately.

RESULTS

During three years, 18042 persons came for blood donation. 16138 (90%) were male and 1804 (10%) female. Age was between 18-55 years. Hepatitis B surface antigen was positive in 561 (3.1%).

Table No. 1: Male to Female Ratio in Screened Persons

Male	Female
90%	10%

Table No. 2: Hepatitis B Prevalence in various age groups.

Age in Year	Percentage
18-25	1.8%
25-35	3.8%
35-45	3.8%
45-55	2.9%

Table No. 3: Prevalence in Gender

Male	Female
3.9%	2.8%

DISCUSSION

Viral hepatitis is widely seen all over the world and is one of the most challenging health problem with very high end stage morbidity and mortality [6,7]. In this study 3.1 % of otherwise healthy blood donors were serologically positive for Hepatitis B surface antigen. In an international study by Andrgachen and colleagues published in Biomed central, HBV seroprevalence rate in healthy blood donors is 4.7% [8]. Taguchi etal in Pubmed Journal reported 1.8% in surgical patients [9]. According to Erden and colleague it is 6.6% in patients coming in out patient clinic at Istumbol University Hospital, Turkey. In local studies between 2% to as

high as 14% in blood donors and 3.6%-18.6% in general population [10]. HBV seropositivity in blood donors reported by Chaudhary[11] Hashmi[12], Tanweri[13], Bulkhari[14], Rehman[15], Bhatti[16] and Rehman K[17] is 2%, 2.1%, 2.6%, 3.4%, 3.5%, 6.5% and 14% respectively. In general population it is reported by Abbas[18] and Gondal[19] as 3.6% and 18.6% respectively.

RECOMMENDATIONS

On the basis of findings in this study following recommendation are laid down.

1) Awareness in public and health professionals about hepatitis B, its risk factors and prevention.
2) Screening for HBV surface antigen and vaccination at mass level.
3) Vaccination and regular check of antibody status in all health care providers.
4) Complete screening before blood donation.
5) Use of disposable items and their destruction by incinerator after use on positive patients.
6) Separate non disposable equipment for positive patient and proper sterilization after use.

CONCLUSIONS

Seropveralence of hepatitis B virus is high and more in developing world. No treatment is available after getting infected. Main protective measure is vaccination. Screening before blood donation and transfusion may help in reducing its spread.

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Address for Corresponding Author:
Saadat Parveen
236, Forte Colony Shershah Road,
Multan Cantt.
Cell: 0300-8639700

Original Article

Asymptomatic Spontaneous Bacterial Peritonitis in Liver Cirhosis With Ascitis

1. Ashok Kumar 2. Shamsuddin Shaikh 3. Ubedullah Shaikh

1. Asstt. Prof. of Medicine 2. Prof. of Medicine 3. PG Student of Surgery, Peoples Medical College, Nawabshah

ABSTRACT

Objective: To asses the frequency of asymptomatic spontaneous bacterial peritonitis in liver cirrhotic patients with first presentation of ascities.

Study Design: A descriptive case series study.

Place and duration of Study: This study was conducted at the Department of Medicine, Peoples Medical College Nawabshah from 1st September 2007 to 28th February 2008.

Patients and Methods: In this study 100 patients of cirrhosis with ascities . There were 52 (52%) females and 48 (48%) males. Detailed history was taken from all the patients. The diagnostic criteria were the presence of sign and symptoms of chronic liver insufficiency e.g pallor, jaundice, clubbing, palmar erythema, gynecomastia, spider navie, visible veins, splenomegaly, edema or ascities etc. Laboratory investigations include CBC, LFTs, PT, total protein, Ascitic fluid D/R etc. and specific investigations especially ultrasound of abdomen as diagnostic modality and for assessment of cirrhotic patients with ascities.

Results: All patients fulfilling the inclusion criteria. Age ranging from a minimum of 20 years to 80 years with mean ages of patients was 44.99 ± 14.29 years. There were 52 (52%) females and 48 (48%) males. Twenty one (21%) patients positive for spontaneous bacterial peritonitis because of WBC ≥500 and neutrophils ≥ 250 /mm³ while 79 (79%) patients who had WBC ≤ 500 and neutrophils < 250 /mm³ were spontaneous bacterial peritonitis negative. SBP positive, 8 (38 %) were females and 13 (62 %) males. Average systolic and diastolic blood pressure was found 110 ± 9.32 mmHg and 80 ± 62.98 mmHg, mean pulse rate 83.30 ± 5.81 /min, mean hemoglobin 9.14 ± 1.89 g/dL, total leucocytes count 6408.85 ± 2333.69 /mm, platelets 191.32 ± 54.59 $x10^9$/L, total biluribin 1.99 ± 1.33 mg/dL, total proteins 5.96 ± 0.46, SGPT 134.53 ± 267.06 Unit/L, alkaline phosphatase 314.34 ± 200.85 Unit/L, ascitic fluid proteins 1.35 ± 0.83g/dL, ascitic fluid neutrophils 282.58 ± 48.73/mm, ascitic fluid lymphocytes 43.09 ± 19.38/uL, ascitic fluid RBC 1465.25 ± 2653.35/uL and average duration of stay in hospital was 8.23 ± 4.4.

Conclusion: In this study clearly showed a high percentage of asymptomatic SBP in cirrhotic patients with ascities. This is quite high in comparison with national and international studies. Thus in future studies should be conducted determining the factors associated with high frequency.

Key Words: asymptomatic, spontaneous bacterial peritonitis, Ascitic fluid.

INTRODUCTION

Spontaneous bacterial peritonitis (SBP) is an acute bacterial infection of previously sterile ascitic fluid without demonstrable cause [1,2]. Spontaneous bacterial peritonitis occurs in both children and adults. Ascities is a common complication of cirrhosis and associated with poor quality of life, increased risk of infections and renal failure and a poor long term outcome [3]. SBP is the third leading cause of death in patients with cirrhosis and ascities[4]. The prevalence of SBP in patients with ascities ranges between 10-30% but in Pakistan it varies from 32.20-64.5% [5]. SBP associated with an impaired defense mechanism against infections present in cirrhotic patients, such as a depressed phagocytic activity of the reticulo endothelial system , an impaired leukocyte function, reduced serum complement levels and low antibacterial activity of the ascitic fluid [6]. SBP are mainly due to aerobic , gram –ve bacilli usually present in the intestinal flora. SBP was first described in 1970 and up to the present the mortality rate has been decreasing from 80% to 30%, due to prompt diagnosis and early starting adequate treatment[7]. Clinical features of SBP are abdominal pain, distention, fever and local tenderness.

Aim of this study to asses the frequency of asymptomatic spontaneous bacterial peritonitis in liver cirrhotic patients with first presentation of ascities.

PATIENTS AND METHODS

This study consists of one hundred patients. This descriptive case series study was carried out in department of medicine at Peoples Medical College Nawabshah, from 1st September 2007 to 28th February 2008. Inclusion criteria were all cirrhotic patients with ascities, greater than 18 years of age and either gender,

presenting to tertiary care center. Patients with hepatic encephalopathy, patients receiving anti biotics one week before admission, GI bleeding and acute renal failure were excluded from this study.

Detailed history was taken from all the patients. The diagnostic criteria were the presence of sign and symptoms of chronic liver insufficiency e.g pallor, jaundice, clubbing, palmar erythema, gynecomastia, spider navie, visible veins, splenomegaly, edema or ascities etc. Laboratory investigations include CBC, LFTs, PT, total protein, Ascitic fluid D/R etc. and specific investigations especially ultrasound of abdomen as diagnostic modality and for assessment of cirrhotic patients with ascities. Detailed Clinical examination of the patient was done. Follow up of all these patients was done.1st visit after 6 month and 2nd visit after one year to assess any complication and inquiry about resumption to work. Results were prepared with help of tables and graphs. Data was analyzed through SPSS software.

RESULTS

This study was comprised of 100 patients of with cirrhosis of liver with ascities fulfilling the inclusion criteria. There was wide variation age ranging from a minimum of 20 years to 80 years with mean ages of patients was 44.99 ± 14.29 years. There were 52 (52%) females and 48 (48%) males (Table 1).

The majority of the patients 86 (86%) were of poor class while 14 (14%) patients belonged to middle class (Chart 1). Twenty one (21%) patients positive for spontaneous bacterial peritonitis because of WBC ≥500 and neutrophils ≥ 250 /mm³ while 79 (79%) patients who had WBC ≤ 500 and neutrophils < 250 /mm³ were spontaneous bacterial peritonitis negative (Chart 2) .

When compared the proportion of gender in SBP positive, 8 (38 %) were females and 13 (62 %) males. Average systolic and diastolic blood pressure was found 110 ± 9.32 mmHg and 80 ± 62.98 mmHg, mean pulse rate 83.30 ± 5.81 /min, mean hemoglobin 9.14 ± 1.89 g/dL, total leucocytes count 6408.85 ± 2333.69 /mm, platelets 191.32 ± 54.59 x10^9/L, total biluribin 1.99 ± 1.33 mg/dL, total proteins 5.96 ± 0.46, SGPT 134.53 ± 267.06 Unit/L, alkaline phosphatase 314.34 ± 200.85 Unit/L, ascitic fluid proteins 1.35 ± 0.83g/dL, ascitic fluid neutrophils 282.58 ± 48.73/mm, ascitic fluid lymphocytes 43.09 ± 19.38/uL, ascitic fluid RBC 1465.25 ± 2653.35/uL and average duration of stay in hospital was 8.23 ± 4.43.

Most common examination findings 88 (88%) patients had edema, palor in 80(80%) patients, jaundice was in 33 (34.7%) patients, dehydration in 5 (5.4%) patients , clubbing was found in 2 (2.1%) patients, koiloynychia found in 9 (9.4%) patients, palmar erythema was present in 46 (46.9%) patients, palmer erythema found in 28(28.9%) patients , gynecomastia found in 16 (16.2%) patients, spider navie had in 78 (78.8%) patients, visible veins were seen in 78 (78.8%) patients.

Table No.1

Variable	Number of Patients	Percentage
Gender		
• Male	48	48%
• Female	52	52%
AGE GROUP		
• 20- 30 years	11	11%
• 31 - 40 years	15	15%
• 41 - 50 years	26	26%
• 51 - 60 years	30	30%
• 61 - 70 years	13	13%
• 71 - 80 years	5	5%

Chart No.1: Socioeconomic Status

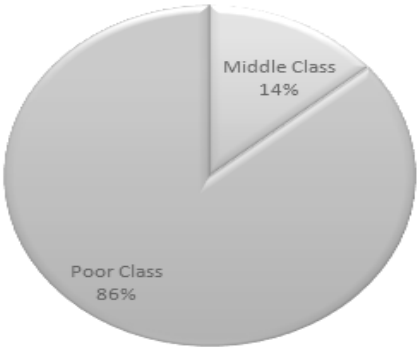
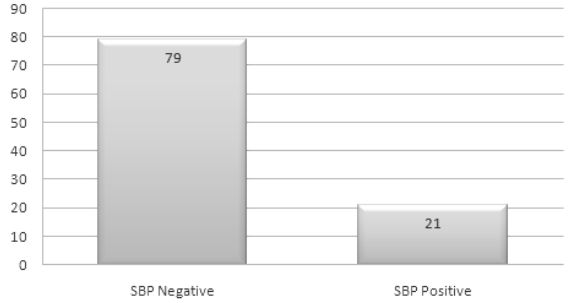


Chart No.2: Distribution of Spontaneous Bacterial Peritonitis.



DISCUSSION

Spontaneous bacterial peritonitis (SBP) is the infection of the ascitic fluid that occurs in the absence of a visceral perforation and in the absence of an intraabdominal inflammatory focus such as abscess, acute pancreatitis or cholecystitis and inoculation.

In our study were 52 % male and 48% female, male to female ratio was 1.03:1 . However the male to female ratio given by Khan Z [8] is 1.1:1. The age ranged from 20 to 80 years with mean age 44.99 ± 14.29 years which is comparable to other study where the mean age was 51.1±11.7 year [9]. In our study majority of the patients were found low socio economic class 86% while middle class 14% where as Khan TM et al 10 reported the reasons for increased frequency of SBP in this study may be due to the low socio-economic conditions, malnutrition and high prevalence of infectious diseases.

The frequency of SBP in our study was 21 %. It correlates with a local study conducted by Khan showed the frequency of asymptomatic spontaneous bacterial peritonitis in chronic liver disease patients with first presentation of ascities was 9.3% [11] . Sarwar S et al, another study from Pakistan, showed figure of 38% which is quite different from present study [12].The clinical parameters were further supported by laboratory investigations which revealed WBC ≥500 and neutrophils ≥ 250 cells/mm^3 positive in 21% patients of SBP. Laboratory finding given by Evans showes that the prevalence of spontaneous bacterial peritonitis in the population of 427 cirrhotic outpatients as defined by neutrocytic ascities (absolute neutrophil count ≥250 cells/mm3) was 3.5% [13].

Ascitic fluid polymorphonuclear cell count is an easy and single best test in establishing the diagnosis of SBP regardless of the fact whether a discriminative value of 250 or 500/cmm is used[14] .Our study were shows mean ascitic fluid proteins 1.35 ± 0.83 gm/dl, ascitic fluid neutrophils 282.58 ± 48.73 /cmm and ascitic fluid lymphocytes 43.09 ± 19.38 /cmm. In the study of Mustafa MG showed ascitic fluid protein was 1.1 ± 0.3 g/dL and ascitic fluid neutrophil 1261 ± 1073 /cmm in the spontaneous bacterial peritonitis[15] . In cirrhosis, the hepatocytes change into fibrosis due to continued inflammation by the inciting agent and lose their capacity to synthesize proteins.

In our study the edema 88% and palor 80% were the commonest presentation followed by spider navie had in 78 (78.8%) patients, visible veins were seen in 78 (78.8%) patients, jaundice was in 33 (34.7%) patients, palmar erythema found in 28(28.9%) patients and testicular atrophy found in 11 (11.2%) patients. However in study of Evans LT et al [16] the patients presented with jaundice (81 %), abdominal pain (78.12%), fever (46.8%) , tenderness (87.5%) and patients with SBP may remain asymptomatic (3.5%)

CONCLUSION

In this study clearly showed a high percentage of asymptomatic SBP in cirrhotic patients with ascities. This is quite high in comparison with national and international studies. Thus in future studies should be conducted determining the factors associated with high frequency.

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Address for Corresponding Author:
Dr. Ashok kumar
Flat No 1, Pak Plaza Trunk
Bazar Nawabshah (SBA)
Mob: 03003025348
Email: drashokfcps@yahoo.com

Original Article

The Role of Medical Man in Cases of Burns

1. Alvina Raja 2. Abdul Hamid 3. Delawar Khan 4. Salma Abbassi 5. Umair Jadoon

1. Asstt. Prof. of Forensic Medicine, AMC Abbottabad 2. Prof. of Forensic Medicine, FMC Abbottabad 3. Assoc. Prof. of Forensic Medicine, AMC, Abbottabad 4 & 5. Lecturers of Forensic Medicine, AMC, Abbottabad

ABSTRACT

Objective: Injuries caused by burns are a common occurrence in our country. Burn always evoke source of interest for forensic curiosity. The victim of burns needs a detailed scrutiny to evaluate the intentional status whether suicidal, homicidal or accidental to provide justice and to satisfy the weeping souls.

Design of Study: A retrospective study.

Place and Duration of Study: This study was conducted in the patients of burn at AMC from March 2005- May 2008.

Materials and Methods: All of the patients were included irrespective of sex and age. Record of burn patient was taken on performas in which their age, sex, type of burn, percentage of burn, causative agent and reason of burning were noted.

Result: Total 53 patients were included in the study. Among them 47 sustained accidental, 5 patients homicidal and 1 suicidal burns. Out of 47 accidental cases 7 patients died, 4 out of 5 homicidal cases died and only one suicidal case revived.

Conclusion: The patients who are registered as accidental or suicidal burns are not always so. A probe into the history of patients can bring out the key to truth. Moreover timely assessment of critical clinical conditions of patient is necessary to avail them their rights of justices.

Key Words: Burn, Medico-legal, Accident, Homicide, Suicide.

INTRODUCTION

status, education, type of burns sustained, percentage of area involved, fatality, cause regarding accidental, Homicidal cases are always masked by accidental or suicidal burns but by probing out the truth, medical professionals can contribute their servings to provide justice in order to keep peaceful society, by participating in reaching the real culprits of crime and preventing the further occurrence of similar crimes.

The cause and risk of burn injuries as well as the risk of burn death are influenced by age, sex, education status, economic circumstances, geographic location, season of year, occupation and prevalence of deliberate suicidal bomb blast causing homicidal burning. 73 percent of all the burns related deaths result from house fires and death rate is higher among children and elderly. Flame and chemical injuries are predominating type of burn in patients admitted in hospitals as compared to scalds which are though the most frequent form of burn injury, far less require admission.

The severity of burns ultimately related to cause and intension of burn. Thermal injury causes coagulation necrosis of the skin and underlying tissue to variable depth. It also has deleterious effect on all other organs of the body to the extent organ dysfunction and death. According to the severity burns can be classified into:

1. 1st degree: Involves only skin epidermis with vasodilatation of arterioles and capillaries resulting in erythemia which is painful.
2. 2nd degree: Involves detachment of epidermis from dermis resulting in blister formation with a surrounding area of hyperemia which is again a painful condition.
3. 3rd degree: Involves entire thickness of skin both epidermis and dermis with massive necrosis and heal by scar formation but there is no pain.
4. 4th degree: Burn involves deeper tissues, subcutaneous tissues, muscles and bones.

To calculate area involved and see the extent of burns surgical "Rule of Nines" is sufficient.

A large area involved maybe more dangerous to life than a deeper, more localized burns. It is generally considered that 30-50 percent involvement of the total body surface is incompatible with survival.

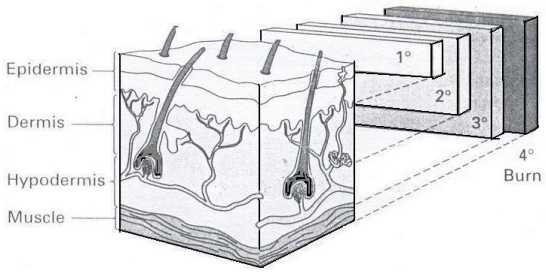

Fig. 1. Schematic demonstrating the correlation of depth-of-injury nomenclature with anatomic structures of the skin.

MATERIALS AND METHODS

In this study, 53 cases of burn are included in Ayub Teaching Hospital from March 2005 to May 2008. Their record regarding age, sex, socioeconomic suicidal and homicidal are taken on performa specially designed for this purpose. 47 out of 53 cases were accidental, 5 were homicidal and 1 was suicidal. Female: Male ratio was-32:21.All Homicidal cases were females. Majority of them belonged to lower socioeconomic group and low education. More extensive and deep burns were seen in homicidal cases.

RESULT

T0tal 53 patients were included in the study. Among them 47 sustained accidental, 5 patients homicidal and 1 suicidal burns. Out of 47 accidental cases 7 patients died, 4 out of 5 homicidal cases died and only one suicidal case revived.

Age (yrs)	Accidental burns		Homicidal burns		Suicidal burns		Total
	Female	Male	Female	Male	Female	Male	
0-10	5	9	-	-	-	-	14
11-20	11	8	3	-	1	-	23
21-30	7	2	2	-	-	-	10
31-40	1	-	-	-	-	-	02
41-50	-	-	-	-	-	-	-
> 60	2	2	-	-	-	-	04
Total	26	21	5	-	1	-	53

Female to male ratio among accidental cases is 26:21, but among homicidal cases and suicidal there are 100% females.

DISCUSSION

The forensic pathologist is concerned with the cause of burns and fatal cases and must recognize the type of the burn whether the burn he finds could cause fatal result and whether the distribution of burns is consistent with the H/O case. It is obvious from the study that women always remained helpless at the hands of men and suffered rather fatal forms of violence and even at those critical times they are held under threat to utter the truth about their cause of violence.

Homicidal cases in our study are a special field of study. We have seen that all women with an age from 15-30 years were with more than 60 percent burns. Otherwise in accidental cases people of all the ages were seen and they had rather lesser degree of burns covering almost 5 to 30 percent area. It is also seen that all homicidal cases were initially registered as accidental but later on after taking proper history in the absence of any influencing agents (relatives) they uttered reality.

In taking dying declaration, the role of doctors is vital for the safety and well being of human and society. Due to amendments in criminal procedure code 1898 which essentially addresses itself to grievous hurt by burn resulting and especially to cases where such injuries cause the death of the injured person. It also enjoins the concerned medical men to record the statement of burnt person immediately on arrival to ascertain the circumstances and cause of burn injuries. This statement is considered accepted in evidence as dying declaration, if the injured person expires due to these injuries.

It is seen that even with most extensive burns some period of survival is common and that period is sufficient to make a statement. In one case the driver of a chemical tanker which caught fire, survived 24 hours with full thickness skin burns involving his entire body, except for the soles of his feet.

It is also clear that incidence of homicidal burns are far less in region of Abbottabad or Hazara as compared to Rawalpindi

Again the point to be noted that lower socioeconomic group is related with low literacy rate which intern is the basis of carelessness in accidental cases. Suicidal cases should always be scrutinized. Circumstances surrounding the case give rise to suspicion until suicide is considered.

CONCLUSION

More meticulous medicolegal scrutiny is required in every case of burning and timely promptly taking statement of person without external influence can bring about remedy in the prevention of homicidal cases. So a sour part of truth can be changed into a sweet candy.

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Address for Corresponding Author:
Alvina Raja,
Asstt. Prof. of Forensic Medicine,
Ayub Medical College, Abbottabad.
0333-5035613

Original Article

Prevalence of Abnormal Body Mass Index Among Students of a Private Sector Medical College in Pakistan

1. Abdul Najeeb Khan 2. Muhammad Jalal 3. Alvina Raja 4. Jan-e-Alam 5. Nighat Perveen 6. Zara Akmal 7. Rabia Asif

1. Assoc. Prof. of Physiology, FMC, Abbottabad 2. Asstt. Prof. of Biochemistry, FMC, Abbottabad 3. Asstt. Prof. of Forensic Medicine, AMC, Abbottabad 4 & 5. Asstt. Profs. of Physiology 6 & 7. Lecturers of Physiology, Frontier Medical College, Abbottabad

ABSTRACT

Objectives: To determine the status of BMI among the students of Frontier Medical College, Abbottabad and to find out the frequency of different BMI groups.

Design of Study: Cross-sectional questionnaire based study.

Place and Duration of Study: This study was conducted from 01.11.2010 till 10.03.2011 in Frontier Medical College, Abbottabad.

Materials and Methods: A cross- sectional questionnaire based study was conducted in Frontier Medical College Abbottabad. Body weight and height of 400 students were measured and then their body mass index (BMI) was calculated. Keeping in view the WHO cut-offs, Under weight, Overweight and Obesity were defined.

Results: 9.75 % of students fell in the underweight category. About 63.25 % were in normal range. 21 % were Overweight while no less than 6 % formed the various categories of obesity

Conclusion: A significantly high proportion of students (36.75 %) were either over weight, obese or underweight. This is an alarmingly high percentage keeping in view the fact that all of them were 18-22 years of age. The students must be advised to take more care of their health status

Key Words: Body mass index, Obesity, Underweight, Overweight

INTRODUCTION

Body Mass Index (BMI) is the ratio between the body weight and the height of a person and is calculated as,

BMI = Weight in Kg/Height m^2

Abnormality of this index, therefore, may be due to an unduly increased or decreased body weight with respect to the height. While the formula, previously called the *Quetelet Index* dates back to the 19th century, the new term "body mass index" for the ratio and its popularity date to a paper published in the July edition of 1972 in the Journal of Chronic Diseases by Ancel Keys. The interest in measuring body fat began due to obesity becoming a discernible issue in prosperous Western societies. BMI was explicitly cited by Keys as being appropriate for population studies, and inappropriate for individual diagnosis. Nevertheless, due to its simplicity, it came to be widely used for individual diagnosis, despite its inappropriateness[1,2]

BMI provided a simple numeric measure of a person's "fatness" or "thinness", allowing health professionals to discuss over and under-weight problems more objectively with their patients. However, BMI has become controversial because many people, including physicians, have come to rely on its apparent numerical authority for medical diagnosis, but that was never the BMI's purpose; it is meant to be used as a simple means of classifying sedentary (physically inactive) individuals with an average body composition.[3]

In clinical terms, a BMI between 25 and 29.9 Kg/m^2 is called overweight, and a BMI greater than 30 Kg/m^2 is called obese. BMI is not a direct estimate of adiposity and does not take into account the fact that some individuals have a high BMI due to a large muscle mass. When greater quantities of energy (in the form of food) enter the body than are expended, the body weight increases, and most of the excess energy is stored as fat. Therefore, excessive adiposity (obesity) is caused by energy intake in excess of energy output.[4]

The medical establishment has generally acknowledged some shortcomings of BMI. Because the BMI formula depends only upon weight and height, its assumptions about the distribution between lean mass and adipose tissue are not always exact. BMI sometimes overestimates adiposity on those with more lean body mass (e.g., athletes) while greatly under-estimating excess adiposity on those with less lean body mass. A study in June, 2008 by Romero-Corral et al examined 13,601 subjects from the United States (Third National Health and Nutrition Examination Survey [NHANES III]) and found that BMI-defined obesity was present in 21% of men and 31% of women. Using

body fat percentage (BF%), however, BF%-defined obesity was found in 50% of men and 62% of women. Thus BMI showed poor sensitivity.[5]

The reason the BMI is used for screening the health of the general population is due to the strong correlation between being overweight or obese and having health problems, chronic disease and premature death. People who are overweight or obese have an increased risk for Hypertension, Type 2 diabetes, Coronary heart disease, Stroke, Osteoarthritis, some cancers, Sleep apnea and respiratory problems. Over the past few decades, there has been a dramatic increase in the prevalence of obesity in many countries. The World Health Organization (WHO) estimates that more than 1 billion adults worldwide are overweight; of these, at least 300 million are obese [6]. Adipose tissue has been increasingly recognized as an active endocrine organ, capable of releasing a large number of cytokines and bioactive mediators that play important roles in the pathogenesis of many obesity-related diseases [7].

Relationship between an abnormal BMI and increased mortality has been studied by a large number of researchers in recent past. [8,9,10,11]

Body weight and height relationship and its association with physical activities are considered to be indicators of a life style and health status [12].A national representative survey indicates that, according to the Asian-Pacific BMI cut-off values, as much as 25% population of Pakistan is overweight and about 10% is obese [13]

The prevalence of underweight, overweight and obesity among young adults and college students has previously been documented.[14,15]

Such studies in Pakistan have largely been confined to a specific area situated in the southern part of the country.[16,17] Our present study was carried out in Frontier Medical College Abbottabad, which is situated in northern mountains. Aim of the study was not only to find out the BMI abnormalities of adolescent students but also to note if there is any gross difference in the results obtained from these geographically farthest apart medical institutions.

MATERIALS AND METHODS

This study was conducted from 01.11.2010 till 10.03.2011 in Frontier Medical College, Abbottabad, Pakistan. It was a cross-sectional questionnaire based study. The study population included four hundred medical students of Frontier Medical College, Abbottabad. Every student was personally inquired about all the items of the data and body weight and height were measured. BMI was calculated by dividing weight in kilograms by height in meters square.

Following are the BMI cut-off points recommended by WHO,

<16.00 kg/m2 (severe underweight)
16.00- 16.99 kg/m2 (moderate underweight)
17.00-18.49 kg/m2 (mild underweight)
18.50-24.99 kg/m2 (normal range)
25.00-29.99 kg/m2 (pre obese)
30.00-34.99 kg/m2 (obese class I)
35.00-39.99 kg/m2 (obese class II)
≥ 40.00 kg/m2 (obese class III)

However, for practical purposes, the participants of our study were classified into the following four groups as well,

<16.00 kg/m2 -18.49 kg/m2 (underweight)
18.50-24.99 kg/m2 (normal range)
25.00-29.99 kg/m2 (overweight)
30.00-34.99 kg/m2 - ≥ 40.00 kg/m2 (obese)

RESULTS

The questionnaire was provided to 400 students. All of them responded adequately and so were included in the study. Two hundred and Forty (60%) of them were males and remaining one hundred and sixty (40%) were females.

Mean height of students was 168.52 ±62cm. For males it was 172.91± 4.6cm and for females160.37 ± 6.2 cm. The difference was statistically significant (P <0.01)

Mean weight of students was 66.98 ± 10.6kg. That for male students was 71.77±11.2 kg

While for female students it was58.11±8.9kg. The difference was statistically significant (P <0.01)

Mean BMI of students was 22.80±3.2. Again, for males the mean BMI was 23.63±3.5

and for females 21.27±2.9.

According to the results obtained, 39 out of 400 students (9.75%) were underweight, 253 students (63.25%) were normal, 84 students (21%) were overweight or pre-obese, while 24 students (6%) were obese (Table-1).

Putting these results together, the total percentage of students with an abnormal BMI was as high as 36.75%. In males at it stood at38.08% while in females at 34.28% (Table-2). The precise details of the possible 8 groups according to WHO cut-off points were also tabulated (Table-3)

DISCUSSION

It is clear from our study results that the medical students, be it males or females, are not careful about maintaining their body weight. Being overweight simply means to be in a preobese state, which if not properly taken care of, eventually culminates into obesity and this obesity is strongly associated with hypertension, ischemic heart disease, diabetes type-II, osteoarthritis and various types of cancers. A study published by JAMA in 2005 showed that "overweight" people had a similar relative risk of mortality to "normal" weight people as defined by BMI, while "underweight" and "obese" people had a higher death rate [18].

Table No.1: Percentage wise BMI distribution of students

Gender	Underweight < 16.00-18.49 kg/m2	Normal 18.50-24.99 kg/m2	Over weight 25.00-29.99 kg/m2	Obese 30.00-≥40.00 kg/m2	Total
Males(260)	4.22%(11)	61.92%(161)	24.61%(64)	9.25%(24)	100%
Females(140)	20%(28)	65.72%(92)	14.28%(20)	0%(0)	100%
Both(400)	9.75 %(39)	63.25%(253)	21%(84)	6%(24)	100%

Table No.2: Percentage of Healthy and Unhealthy students

Gender	Healthy		Unhealthy	
	Number	Percentage	Number	Percentage
Males	161	61.92%	99	38.08%
Females	92	65.72%	48	34.28%
Total	253	63.25%	147	36.75%

Table -3: BMI categories according to WHO cut-off points

Gender	Underweight			Normal 18.50-24.99 kg/m2	Over weight 25.00-29.99 kg/m2	Obese			Total
	Severe < 16.00 kg/m2	Moderate 16.00-16.99 kg/m2	Mild 17.00-18.49 kg/m2			I 30-34.99 kg/m2	II 35-39.99 kg/m2	III ≥40.00 kg/m2	
Males	0	3	8	161	64	21	3	0	260
Females	0	11	17	92	20	0	0	0	140
	0	14	25	253	84	21	3	0	400

Our study result showed that there are as much as 23% of students who form the overweight category. These are in synchronicity with a number of such studies carried out earlier, including one by Oguntibeju et al [19], giving the percentage of overweight students at 20%, and another one by Jaffar et al [13]calculating it at 25%.

Our study results, however, are highly contradictory to the two earlier studies conducted in Karachi: one in a medical university[16] giving the underweight category 29% whereas overweight category only 8% proportion. Another public sector Medical college[17] calculating it to the same level i.e. 29% and 12.6% respectively.

Now, this is very significant. According to these results, in the most southern medical institutions of the country, there is pronounced dominance of underweight students (29%) while those falling in Preobese and obese category are mere 10% or so. In our study carried out up north in mountains of Abbottabad this ratio is almost reversed i.e. only 10% are underweight while as much as 23% are definitely over weight (Pre obese and obese put together). It may be because of the general health status of the people living in these two locations; bulk of the students involved in these studies belongs to these cities and the surrounding areas. It is suggested that more research work in this regard be undertaken in other institutions, especially those located in the central regions of Pakistan.

Since most of the studies have been conducted in populations of European origin, relationship between BMI and the overall risk of death among Asians, who account for more than 60% of the world population, remains unclear. The definitions of overweight (BMI ≥25.0) and obesity (BMI ≥30.0) are based essentially on criteria derived from studies that involved populations of European origin. The validity of these criteria in Asian populations has yet to be determined. Studies have shown that for a given BMI, Asians generally have a higher percentage of body fat than do Europeans. On the basis of these observations, it has been proposed that the BMI cutoff points for overweight and obesity should be lower for Asian populations than they are for European populations (suggested cutoff points for Asians, ≥23.0 for overweight and ≥27.5 for obesity),although a 2004 consensus statement from the WHO concluded that the available data were not sufficient to support Asian-specific cutoff points to define overweight and obesity[20].The optimal weight range associated with a minimal risk of death in Asian populations remains controversial [21].Revision of the cut-off points for Asians, if however, may be considered for the people belonging to South East Asia, in whom the body frame is generally smaller than that of the rest of Asians

CONCLUSION

We believe that preobesity, eventually leading to frank obesity, with all its sequels, is the real threat to the long term health status of these students. Regular exercise, careful selection of nature and amount of food, and keeping an eye on the weight measuring scales is all that is required.

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Address for Corresponding author
Dr. Abdul Najeeb Khan
Associate Professor
Department of Physiology
Frontier Medical College,
Abbottabad
03009689817, 0992381926
drabdul.najeeb@gmail.com

Original Article

Presentation of Complications of Chronic Liver Disease at a Tertiary Care Hospital

1. Tariq Muhammad Khan Tareen 2. Ijaz-ul-Haque Taseer 3. Umer Ejaz Malik 4. Sarmad Ali Naqvi

1. Sen. Registrar of Medicine Unit-I 2. Research Director, PMRC Research Centre 3. PG Student of Medicine 4. PGR of Medicine, Nishtar Medical College & Hospital, Multan

ABSTRACT

Objectives: To see presentations of various complications of chronic liver disease at a tertiary care hospital.
Study Design: Retrospective study
Place and Duration of Study: This Study was conducted at Medical Unit 1, Nishtar Hospital, Multan for a period of 6 months from 01-01-2010 to 30-06-2010.
Patients and Methods: Patients admitted at Medical Unit 1, Nishtar Hospital, Multan were included in the study. The medical record of these patients was checked. The data obtained were entered in SPSS-11 and analyzed.
Results: A total number of 50 patients were studied, 30 (60%) were male and 20 (40%) were female. Age of the patients ranged from 36-58 years. Mean age of the patients was 45.39 ± 4.77 years. All the patients presented with fatigue, generalized weakness, oedema feet, anorexia and nausea. Twenty (40%) patients presented with jaundice. Abdominal distension was present in 42 (84%) patients. Twenty two (44%) patients were having altered consciousness. Twenty three (46%) patients presented with haemetemesis and 28 (56%) with malena. Low grade fever was present in 26 (52%) patients. Epistaxis was present in 2 (4%) patients. Previous history of jaundice was present in 40 (80%) patients and history of alcohol intake was present in 12 (24%) cases.
On examination, all the patients were found emaciated with protuberant abdomen. Twenty (40%) were clinically jaundiced. Oedema feet was detected in 48 (96%) patients. Palmar erythema was present in 26 (52%). Hepatic flaps were present in 24 (48%) patients. Shifting dullness and fluid thrill was present in 46 (92%) patients and engorged paraumblical veins were present in 36 (72%) patients. Splenomegaly was seen in 36 (72%) patients.
Laboratory investigations revealed raised serum bilirubin in 26 (52%) patients and level of bilirubin was 3-6 mg/100 ml in most of the cases. ALT levels were raised in 33 (66%) patients above the twice of the upper limit of the normal value. Serum alkaline phosphatase was raised only in 1(2%) of patients. Platelet count was below 70000 in 32 (64%) patients. Anti HCV and HBsAg were detected in 38 (76%) and 12 (24%) patients respectively. Prothrombin time was prolonged ≥5 seconds (than control) in 36 (72%) patients. Serum albumin was less than 3 g/100 ml in all cases.
Abdominal ultrasonography revealed coarse echotexture with nodular liver in 46 (92%) patients. Ascites was detected in 48 (96%) patients. Two patients (4%) had hepatic mass.
Upper GI endoscopy revealed esophageal varices in 33 (66%) patients, fundal varices in 12 (24%) patients, gastric ulceration in 17 (34%) patients and duodenal ulceration in 11 (22%) patients.
Conclusion: Patients of chronic liver disease present in tertiary care hospital at a very late stage of the disease and most common presentations are ascites, hepatic encephalopathy, upper GI bleeding and low grade fever. Awareness may be created to motivate the patients to report to tertiary care hospital at an early stage, so that development of these complications can be managed at the very initial stage.
Keyword: Chronic liver disease, complications, cirrhosis.

INTRODUCTION

Chronic liver disease is an important issue through out the world. It is mostly post viral in Pakistan[1]. Among hepatotropic viruses hepatitis B virus and hepatitis C virus are most important which may lead to chronic liver disease[2-4].

Patients of chronic liver disease usually report to tertiary care hospital when the disease has progressed to advance stage and has been declared untreatable by the hakeems, quacks and healthcare pesonnels at primary level. The progressive deterioration in chronic liver disease can not be stopped but the disease process may be delayed and early development of life threatening complications may be checked, provided the patient comes to tertiary care hospital at an early stage. Mortality in liver disease is directly related to its complications. The present study was designed to see the presentation of various complications of chronic liver disease at a tertiary care hospital.

PATIENTS AND METHODS

The present study is a retrospective study conducted in admitted patients at medical unit-I Nishtar Hospital Multan. The data was collected for 6 months from 01-01-2010 to 30-06-2010. A total of 50 patients were studied. The data were entered in SPSS-11 and analyzed.

RESULTS

A total number of 50 patients were studied, 30 (60%) were male and 20 (40%) were female. Age of the patients ranged from 36-58 years. Mean age of the patients was 45.39 ± 4.77 years. All the patients presented with fatigue, generalized weakness, oedema feet, anorexia and nausea. Twenty (40%) patients presented with jaundice. Abdominal distension was present in 42 (84%) patients. Twenty two (44%) patients were having altered consciousness. Twenty three (46%) patients presented with haemetemesis and 28 (56%) with malena. Low grade fever was present in 26 (52%) patients. Epistaxis was present in 2 (4%) patients. Previous history of jaundice was present in 40 (80%) patients and history of alcohol intake was present in 12 (24%) cases.

On examination, all the patients were found emaciated with protuberant abdomen. Twenty (40%) were clinically jaundiced. Oedema feet was detected in 48 (96%) patients. Palmar erythema was present in 26 (52%). Hepatic flaps were present in 24 (48%) patient. Shifting dullness and fluid thrill was present in 46 (92%) patients and engorged paraumblical veins were present in 36 (72%) patients. Splenomegaly was seen in 36 (72%) patients.

Laboratory investigations revealed raised serum bilirubin in 26 (52%) patients and level of bilirubin was 3-6 mg/100 ml in most of the cases. ALT levels were raised in 33 (66%) patients above the twice of the upper limit of the normal value. Serum alkaline phosphatase was raised only in 1(2%) of patients. Platelet count was below 70000 in 32 (64%) patients. Anti HCV and HBsAg were detected in 38 (76%) and 12 (24%) patients respectively. Prothrombin time was prolonged ≥5 seconds (than control) in 36 (72%) patients. Serum albumin was less than 3 g/100 ml in all cases.

Abdominal ultrasonography revealed coarse echotexture with nodular liver in 46 (92%) patients. Ascites was detected in 48 (96%) patients. Two patients (4%) had hepatic mass.

Upper GI endoscopy revealed esophageal varices in 33 (66%) patients, fundal varices in 12 (24%) patients, gastric ulceration in 17 (34%) patients and duodenal ulceration in 11 (22%) patients.

DISCUSSION

Jaundice predicts bad prognosis in cirrhotic patients [5]. In present study jaundice was noticed in 20 (40%) patients which shows considerable liver cell dysfunction. Pathak et al[6] in their study described raised serum bilirubin in 57.5% of cases while in our study it is in 40% of the cases. The difference is because he has conducted this study in alcoholics and might have included acute on chronic case of alcoholic disease so his percentage is a bit high. Distension of abdomen in cirrhotic patients is usually due to fluid in the peritoneal cavity. This ascites may be due to portal hypertension, sodium retention by the kidneys, arteriolar vasodilatation of the splanchnic blood vessels, increased splanchnic and hepatic lymph formation and most commonly due to hypoalbuminea [7]. Abdominal detension in our study was seen in 98% of cases and it has been described in 66.7% in another study[8]. But in their study number of cases of chronic liver disease were only 30. Therefore, the figure is low as compare to our study. Moreover, in our study, the cases were all admitted patients which were almost all in decompansated state and serum albumin was less than normal in all of our study cases, so ascites was present in 98% of cases and points towards advanced stage of disease. Hepatic encephalopathy is a neuropsychiatric state(usually reversible) that complicates chronic liver disease[9-10]. It can occur in porto systemic shunting, with increased level of amonnia and presence of false neurotransmitters in brain. In our study 44% of the patients have hepatic encephalopathy while study conducted by Khokhar and Niazi[11] it was 18%. Here again the low frequency of hepatic encephalopathy is due to less number of study cases, moreover this study was conducted in urban educated population of Islamabad which is more health conscious than our population in southern Punjab. Abdominal ultrasonography revealed coarse texture with nodular liver in 46 (92%) of patients. Ascites was detected in 48 (96%) patients. Two patients had hepatic mass. Upper GI bleeding in our study was 46% while in study conducted by Khokhar and Niazi[11] it was 36% it may be due to the reason that they might have taken the cases which may be at initial stage and has not undergone decompansation. In our study 76% cases were positive for Anti HCV and 24% of the cases in our series were positive HBsAg. Low platelet count which is seen in 64% of the cases in our study might be due to hyperspleenism.

CONCLUSION

Patients of chronic liver disease present in tertiary care hospital at a very late stage of the disease and most common presentations are ascites, hepatic encephalopathy, upper GI bleeding and low grade fever.

Awareness may be created to motivate the patients to report to tertiary care hospital at an early stage so that development of these complications can be managed at the very initial stage.

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Address for Corresponding Author:
Tariq Muhammad Khan Tareen,
Medical Unit-I,
Nishtar Medical College & Hospital,
Multan.