Osmani Medical Teachers Association Journal

Volume 2: Number 1
January 2003

Teachers Association, Sylhet MAG Osmani Medical College, Sylhet, Bangladesh

Osmani Medical Teachers Association Journal (OMTAJ)

Official organ of the Teachers Association, Sylhet MAG Osmani Medical College

EDITORIAL OFFICE:

Department of Microbiology, Sylhet MAG Osmani Medical College

Telephone : 717051, Extn : 406, 711556

E-mail:somc@gononet.com

Teachers Association, Sylhet MAG Osmani Medical College

Executive Committee

President

Professor Md. Rezaul Karim

Vice President

Dr. MA Matin

Dr. Osul A Chowdhury

General Secretary

Dr. Mustaque Ahmed

Treasurer

Dr. Kazi Akter Uddin

Joint Secretary

Dr. Md. Siraj Uddin

Organizing Secretary

Dr. Fazlur Rahim Kaiser

Members

Dr. Md. Arif Mian

Dr. Md. Ismail Patwary

Dr. Shibbir Ahmed

Dr. Promode Ranjan Singh

Dr. Helal Uddin

Dr. Shamimur Rahman

Dr. Abu Ahmed Adiluzzaman

Dr. Rafiques Salehin

Dr. Shahnewaz Choudhury

Dr. Shamim Akhter Mimi

ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 2 Number 1

Experience of Ramstedt's Pyloromyotomy in Sylhet MAG Osmani Medical College

*MD. SHADRUL ALAM,[a] MRIGEN K. DAS CHOUDHURY,[b] MD. KABIRUL ISLAM[c]

Abstract

Paediatric surgeons commonly encounter infantile hypertrophic pyloric stenosis (IHPS). It is a common cause of vomiting that requires surgery. The operative procedure of choice remains the Ramstedt's pyloromyotomy as a simple effective surgical cure. The purpose of this study was to determine the intraoperative and postoperative complications after Ramstedt's operation. A total of 35 patients with infantile hypertrophic pyloric stenosis were included in the study treated surgically by Ramstedt's pyloromyotomy between 1996 and 2002 in the department of Paediatirc Surgery at Sylhet MAG Osmani Medical College, Bangladesh. The diagnosis of IHPS was established by clinical examination and contrast imaging studies. All patients were successfully operated using this technique. The results obtained were excellent in all, except one (2.85%) case that died on the operation table due to anesthetic hazards. The average operating time was 30 minutes. No complication or morbidity was noticed in 34 (97.15%) among the patients postoperatively. The average length of postoperative stay in this study was 3.2 days. Ramstedt's pyloromyotomy withstood the test of time as the standard operation for IHPS. This is a relatively simple and safe method for correction of IHPS.

[OMTAJ 2003; 2(1): 1-3]

Introduction

Infantile hypertrophic pyloric stenosis (IHPS) is a common cause of gastric outlet obstruction in infants and is one of the most frequent conditions requiring surgery in nowborn.[1] It affects 1 in 450 children of whom 85 percent being boys and having increased risk to first-born infants. The cause remains obscure. It is thought to be multifactorial with both hereditary and perinatal environmental influences.[2] There are many hypotheses for the etiopathogenesis of infantile hypertrophic pyloric stenosis. Various factors associated with this pathology specifically are: immature ganglion cells or decrease in ganglion cells in hypertrophic pyloric muscle;[3] lack of nitric oxide; vasoactive intestinal polypeptide (VIP); hypergastrinemia; subtance P; increased insulin-like growth factor 2 (IGF-2) and platelet derived growth factor-B (PDGF-B) in pyloric muscle in IHPS.[4]

Once considered as an invaribly lethal condition, IHPS is now associated with almost negligible mortality rate. The main reason for this remarkable success is undoubtedly Ramstedt's introduction of pyloromyotomy as a simple, effective surgical cure.[3] Nevertheless, morbidity could not been eliminated totally. Ramstedt's pyloromyotomy has its own complications like duodenal mucosal perforation, wound dehiscence, infection and incisional hernia.[5] We report in this study our experience of treating 35 patients of IHPS with Ramstedt's pyloromyotomy.

Methods

This was a retrospective observational study. The study was conducted in the department of paediatric surgery, Sylhet MAG Osmani Medical College over a period of 7 years from 1996 to 2002. In this study, 35 infants with infantile hypertrophic pyloric stenosis underwent Ramstedt's pyloromyotomy, were included. The diagnosis of IHPS was established by clinical pictures which include: a) non-bilious, projectile vomiting with each feed; b) visible gastric peristalsis from left upper corner towards right side; c) palpable pyloric mass. However, in all cases, a barium meal study was done to confirm the diagnosis.

All the cases were randomly selected. Patients with IHPS at or below the age of 1 year were included in the study. Patients admitted with IHPS having severe electrolyte imbalance, and IHPS with other major surgical problem for which they were admitted were not

[a] Assistant professor
[b] Associate professor
[c] Professor and Head

Department of Paediatric Surgery
Sylhet MAG Osmani Medical College.

* Corresponding author

included in this study. These patients had not undergone previous operations. No other surgical procedures were performed at the time of Ramstedt's pyloromyotomy.

Procedure of the operation

Fluid, electrolyte and acid-base balances were corrected before surgery. The procedure was performed with the patient in supine position under general endotracheal anesthesia. A right upper quadrant transverse incision of approximately 2.5 to 3 cm made over the right rectus muscle and just superior to the liver edge. Atter opening the peritoneum, the liver edge was retracted superioly exposing the greater curvature of the stomach near the pylorus, which was grasped with a noncrushing clamp and brought out through the incision. The pylorus and the first part of the duodenum was stabilized. The serosa on the anterior wall of the hypertrophied pylorus was incised with a scalpel commenced from the duodenal end and extended proximally towards the stomach. Due to lack of spreading clamp, we preferred to use the back of a scalpel handle and mosquito's forceps to complete the myotomy by bluntly splitting the hypertrophied muscle down to the submucosa preventing injury to the mucosa (Figure 1). The anesthesiologist injected air through the infant feeding tube placed into the stomach to check any inadvertent mucosal perforation. The fascial layers were closed with a running absorbable suture. The skin was closed with a subcuticular suture.

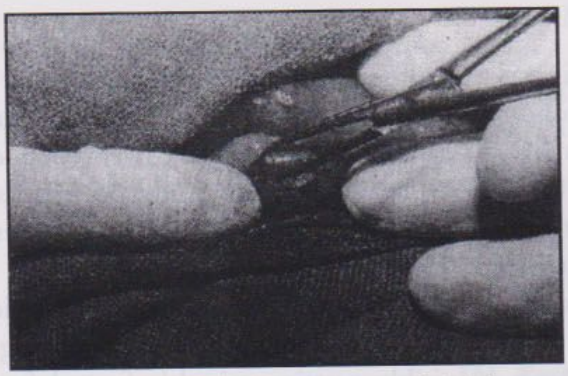

Figure 1: Ramstedt's Pyloromyotomy muscle is being spread showing submucosa bulging through the divided muscle.

Postoperatively, the patients were given clear fluids orally 6 to 12 hours after the surgical procedure and once they were tolerated, they were started on feeds. The patients were discharged approximately 24 hours after the feedings were initiated.

Results

Out of 35 cases studied, there were 30 (85.71%) male and 5 (14.29%) female children (Table-I), and the average weight was 3.5 kg (2.8 kg-4.5 kg). Their ages ranged between 2 weeks to 14 weeks (Table-II) with mean age of 5 weeks. There was no mucosal perforation during operation. The average operating time was 30 minutes (20-50 minutes). No complication or morbidity was noticed in 34 (97.15%) among the patients postoperatively. Only one (2.85%) patient died on the operation table due to anesthetic complication with prematurity. The patients were discharged on the 3rd or 4th postoperative day. The average length of postoperative stay in this study was 3.2 days. The children were followed up at 2 weeks, 1 month, 3 months, and every 6 months after surgery. The cosmetic results were excellent.

Table-I: Sex distribution of the cases (n=35)

Sex	No. of cases	Percentage
Male	30	85.71
Female	05	14.29

Table-II: Age at the time of presentation

Age in weeks	No. of patients	Percentage
2-4 wks	8	22.86
5-7 wks	22	62.86
8-10 wks	4	11.43
> 11 wks	1	02.85

Discussion

In seven years period, 35 infants with infantile hypertrophic pyloric stenosis (IHPS) were selected for Ramstedt's Pyloromyotomy. Success rate was 97.15% in the follow up period. Like other studies, recurrence of vomiting was not reported in any of the cases studied.[6] In this study, majority of the infants presented between 3-7 weeks that was comparable to other studies.[7] IHPS is rare in infants younger than 10 days or older than 11 weeks. Among the sex distribution, 85.71% infants were male in this study similar to other studies reported.

Ultrasonography has been added as the most common diagnostic tool for IHPS, being reliable, non invasive and less expensive. It is dependent, yet, on the level of experience and expertise of the ultrasonologist.[9] Nonetheless, in our study, due to lack of paediatric ultrasound probe we took the help of barium studies to

diagnose IHPS. Pyloromyotomy is usually undertaken after adequate hydration and correction of hypokalemic, hyponatraemic, hypochloremic, and metabolic alkalosis. Before induction of anesthesia, the stomach is decompressed. No matter how long the patient may have been without oral intake, the stomach is likely to be distended with air, gastric secretions, residual feedings, or barium.

In this study, we preferred a right upper quadrant transverse incision. Because of better cosmetic appearance, some among the surgeons choose a supraumbilical curvilinear incision. This incision, on the other hand, is associated with a higher incidence of wound-related complications.[10] Laparoscopy has also been described as a method of performing pyloromyotomy. It requires two or three small incisions for access and has the disadvantages of a prolonged operative time and a higher incidence of perforation of the submucosa.[11,12] Moreover, paediatric laparoscopic instruments were not available in our hospital.

The most likely complication of pyloromyotomy is disruption of the duodenal mucosa. If the duodenum is suspected to have been entered, this can usually be confirmed by milking douodenal content back towards the pylorus. In this situation, we preferred to close the mucosa with inverting absorbable suture and the pyloromotomy reapproximated. A second pyloromyotomy is then done further superiorly. Alternatively, an omental patch is loosely approximated over the mucosal wound and feedings were withheld for 24 hours.[13] In our study, there was no mucosal perforation during operation and no complication or morbidity was noticed in 34 (97.15%) patients postoperatively. Only one (2.85%) case died due to anesthetic hazards, which is similar to the reported studies.[14] The overall results were excellent.

Infantile hypertrophic pyloric stenosis should be diagnosed and treated very early. Over the years, Ramsterdt's Pyloromyotomy has withstood the test of time as the standard operation for IHPS. This is a relatively simple and safe method for correction of IHPS.

References

1. Puri P, Lakshmanadass G. Hypertrophic Pyloric stenosis. In: Puri P (ed). Newborn Surgery. Oxford, England: Butterworth-Heinemann 1996: 266-71.
2. Schwartz MZ. Hypertrophic Pyloric Stenosis. In: O'Neill JA, Rowe MI, Grosfield JL, Fonkalsrud EW, Coran AG (eds). Pediatric surgery, 5th edn. St louis: Mosby 1998: 1111-7.
3. Apte AV, Dhulkotia A, Gangopadhyay AN, Aryya NC. Histopathological examination in the study of idiopathic hypertophic pyloric stenosis. J Indian Assoc Pediatr Surg 2002; 7: 130-3.
4. Oshiro K, Puri P. Increased insulin-like growth factor 2 and platelet derived growth factor system in pyloric muscle in IHPS. J Pediatr Surg 1998; 33: 378-81.
5. Rao N, Youngson GG. Wound sepsis following Ramstedt's Pyloromyotomy. Por J Gung 1998; 78: 1144-6.
6. LWE Van Heurn, P Vos, G Sie. Recurrect vomiting after successful pyloromyotomy. Pediatr Surg Int 1999; 15: 385-6.
7. Kobayashi H, Webster T, Puri P. Age related changes in innervations in hypertrophic pyloric stenosis. J Pediatr Surg 1997; 32: 1704-7.
8. Beasley SW, Hudson I, Hok Psan Yuen, Jones PG. Influence of age, sex, duration of symptoms, and dehydration of serum electrolytes in hypertrophic pyloric stenosis. Aust Pediatr J 1986; 22: 193-7.
9. Chen EA, Luks Fl, Gilchrist BF, *et al.* Pyloric stenosis in the age of ultrasonography: Fading skills, better patients? J Pediatr Surg 1996; 31: 829-30.
10. Besson R, Sfeir R, Salakos C, *et al.* Congenital pyloric stenosis: A modified umbilical incision for pyloromyotomy. Pediatr Surg Int 1997; 12: 224-5.
11. Ford WD, Crameri JA, Holland AJ. The learning curve for laparoscopic pyloromyotomy. J Pediatr Surg 1997; 32: 552-4.
12. AA Shah, AV Shah. Laparoscopic Pyloromyotomy for Infantile Hypertrophic Pyloric Stenosis-A Study of 10 Cases. J Indian Assoc Pediatr Surg 2002; 7: 145-6.
13. Royal RE, Linz DN, Gruppo DL, *et al.* Repair of mucosal perforation during pyloromyotomy: Surgeon's choice. J Pediatr Surg 1995; 30: 1430-2.
14. Hulka F, Harrison MW, Campbell TJ, *et al.* Complications of pyloromyotomy for infantile hypertrophic pyloric stenosis. Am J Surg 1997; 173: 450-2.

ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 2 Number 1

Clinical Manifestations and Bacteriolgical Profile of Septicaemia in Preterm Neonates: Experience from a Tertiary Level Pediatric Hospital

*SYED SHAFI AHMED MUAZ,[a] MAK AZAD CHOWDHURY,[b] MD. ASHRAFUL ALAM,[c] DILRUBA BEGUM[d]

Abstract

This study was carried out to find the common presenting symptoms and signs of septicaemia in preterm neonates along with the causative organisms. Sixty preterm neonates with 45 'confirmed' and 15 'highly suspicious' septicaemia cases were included. Clinical presentations were non-specific in most of the cases, including reluctancy to feeding (90%), lethargy (83.3%), hypothermia (65%), recurrent apnea (60%), abdominal distension (54.6%), and bleeding tendency (50%). Majority (97.8%) of the cultures isolated Gram-negative bacilli, most of them being *Klebsiella pneumoniae* (53.3%), *Pseudomonas aeruginosa* (24.5%) and *Acinetobacter* (15.5%). These isolates were found mostly sensitive to ciprofloxacin and third generation cephalosporins. *Pseudomonas* species were also found highly sensitive to gentamicin. Out of 60 cases, 14 (23.3%) died. Periodic surveillance for agents of preterm septicaemia and finding their antimicrobial sensitivity profiles is recommended.

[OMTAJ 2003; 2(1): 4-9]

Introduction

Neonatal septicaemia refers to the systemic response to infection in the newborn infant, including metabolic and hemodynamic consequences of infection.[1] Despite considerable progress in hygiene, introduction of new antimicrobial agents, and advanced techniques for early diagnosis and treatment of infections and in supportive measures for critically ill neonates, septicaemia remains one of the most important causes of mortality in this age group. Case fatality rates vary from 20% to more than 75% and a substantial percentage of surviving infants have neurological handicaps.[2]

Reports of the epidemiology of neonatal septicemia from our own background situation are few. The epidemiologial data from other developing countries, however, shows important differences in the incidence, risk factors, antimicrobial sensitivity pattern of the pathogens, and mortality from that of developed countries.[3-5] Group B streptococcal disease is the most important cause of neonatal sepsis in Europe and North America,[6] but there is a preponderance of Gram-negative organisms in tropical and developing countries.[7] The epidemiology of neonatal septicaemia within a geographical location, however, also may change with time.[8,9]

Neonatal septicaemia, more especially in preterm neonates, is a life-threatening emergency. So, delays in diagnosis and treatment with appropriate antibiotics may have devastating consequences. Surveillance is therefore needed to identify the common signs and pathogens of neonatal septicaemia along with the antimicrobial sensitivity pattern for the causative agents in a particular area. The purpose of this study was to identify the presenting symptoms and signs of septicaemia in preterm neonates and the organisms causing these infections along with their antimicrobial sensitivity profiles in order to devise an optimal detection and management strategy.

Methods

Site. This hospital based prospective study was conducted in the Special Care Baby Unit (SCBU) of Dhaka Shishu (Children) Hospital from June 2000 to November 2001.

Study population. Neonates with suspected septicaemia were identified and screened based on the presence of one or more clinical sign consistent with possible serious bacterial infection including lethargy, refusal of feeds, abdominal distension, vomiting, groaning, grunting, facial grimace, respiratory distress, hypothermia, fever or sclerema. A thorough history

[a] Assistant Professor, Department of Paediatrics, Jalalabad Ragib-Rabeya Medical College, Sylhet.

[b] Professor, Department of Neonatology, Bangladesh Instiute of Child Health, Dhaka.

[c] Assistant Professor, Department of Microbiology, Sylhet MAG Osmani Medical College, Sylhet.

[d] Lecturer, Department of Microbiology, Sylhet MAG Osmani Medical College, Sylhet.

*Corresponding author

and physial examination was performed and recorded on standard forms. Neonates with severe birth asphyxia, respiratory distress syndrome (RDS), extreme prematurity (<28 weeks estimated gestational age by Ballard examination), gross congenital anomalies and any previous antibiotic therapy were excluded.

Procedures. After initial enrollment patients underwent the following diagnostic procedures: complete blood count, blood culture and C-reactive protein (CRP) estimation. Patients with positive blood culture, categorized as 'confirmed septicemia' and those with clinical diagnosis of sepsis and having positive CRP (>10 mg/l) and band neutrophil ratio of >0.2 categorized as 'highly suspicious septicaemia', were finally enrolled in this study. Sixty preterm neonates with 45 confirmed and 15 highly suspicious septicemia were studied. Study patients were categorized according to the following risk factors for septicaemia: sex (male, female), birth-place (home, hospital, clinic), mode of delivery (normal, forceps-assisted, Caesarian section) and socio-economic status (poor, middle class, higher class). All children were weighed accurately. Gestational age was determined by Ballard examination. Socio-economic status was determined by monthly income of the parents and considered as poor <Taka 5000 per month, middle class Taka 5000 to 10,000 and higher class > Taka 10,000.

Patient management. All cases were initially treated with penicillin and gentamicin or with a third generation cephalosporin in combination with or without gentamicin depending on severity of illness and prescribing physicians' preference. This therapy was later modified depending on the identity and antimicrobial sensitivity of the isolate from blood cultures. Other supportive therapy such as correction of acidosis, maintenance of fluid and electrolyte balance, ventilatory assistance, phototherapy and blood transfusion was given as required.

Data collection. The parents of the neonates were thoroughly explained about the study and then informed consents were taken in a consent form. Then detail history was taken by interviewing the parents and clinical examination was conducted. Findings were recorded in a pre-tested questionnaire.

Statistical analysis. The data were subjected to statistical analysis according to standard procedure. SPSS Win verson 10.1 programme was used for data analysis. Results of the findings were verified by doing standard test for significance like unpaired student's "t" test and Chi-Square (X^2) tests and finding out the p value.

Results

Almost equal numbers of male (31) and female (29) neonates were included in the study. About three-fourths (73.3%) of the neonates belonged to the middle class. Out of total 60 babies, 35 (58.3%) were born at either hospitals or clinics. The mean age of the neonates were 9.92 ± 4.06 days, the minimum and maximum ages of the neonates were 3 days and 19 days respectively. The mean gestational age and the birth weight of the babies were much below the minimum weight of 2.5 kg of full term newborn. The mean birth weight were 1500 gm with a standard deviation of 300 gm (Table-I).

Table I : Baseline charatcteristics of enrolled neonates (n=60).

Birth weight (in grams) ± SD		1.50 ± .3
Mean Gestational age (in weeks)± SD		30.90 ± 1.87
Mean Age (in days)± SD		9.92 ± 4.06
Sex	Male	31 (51.7%)
	Female	29 (48.3%)
Socio-economic class	Lower	10 (16.7%)
	Middle	44(73.3%)
	Higher	06 (10.0%)
Place of Delivery	Home	25 (41.7%)
	Hospital/ Clinic	35 (58.3%)
Mode of Delivery	Normal	27 (45.0%)
	Forceps / C/S	33 (55.0%)

History of illness from mothers/caregivers revealed that overwhelming majority of neonates was reluctant to feed i.e., unable or unwilling to suck breast (Table-II).

History of recurrent apnea and bleeding tendency were found among 36 (60%) and 30 (50%) of the study patients respectively. About two-thirds (65%) were found to be hypothermic on clinical examination. Majority

(54.6%) of neonates had abdominal distension. A significant number (28.3%) of neonates presented with jaundice and 18.3% were found to be dyspnic on examination. Overwhelming majority (83.3%) was lethargic during clinical examination. It is found that 48.3% of the patients had leucocytosis and 38.3% had leucopenia. Thrombocytopenia was present in 65% and toxic granules were found in 28.3% of cases (Table III).

Table II: Clinical profile of the neonates with sepsis (n=60)

Clinical Profile	Number	Percent
Reluctant to feed	54	90.0
Lethargy	50	83.3
Hypothermia	39	65.0
Recurrent apnoea	36	60.0
Abdominal distension	34	54.6
Bleeding tendency	30	50.0
Jaundice	17	28.3
Dyspnoea	11	18.3
Vomiting	07	11.7
Fever	07	11.7
Splenomegaly	07	11.7
Septic foci	05	8.3
Diarrhoea	01	1.7

Klebsiella was found as the most common organism causing septicaemia (53.3%), followed by *Pseudomonas* (24.5%) (Table IV).

Blood culture was found positive in about three-fourths (76.7%) of cases. This laboratory finding indicates that 45 (75%) were confirmed cases of septicemia and other 15 (25%) fell in the highly suspicious group. CRP was found high among 70% of the cases. Third generation cephalosporins, ciprofloxacin and imipenem were mostly sensitive to all the isolates. More than half of the cases were gentamicin sensitive (Table V).

Table III : Laboratory findings of enrolled patients (n=60)

Findings	Number	Percent
Leucocytosis	29	48.3
Leucopenia	23	38.3
Toxic granules	17	28.3
Band form	28	46.7
Thrombocytopenia	39	65.0
High CRP level	42	70.0
Positive Blood Culture	45	75.0

Table IV : Organisms causing sepsis in culture positive patients (n=45)

Organisms	Number	Percent
Klebsiella pneumoniae	24	53.3
Pseudomonas spp.	11	24.5
Acinetobacter	07	15.5
Salmonella spp.	02	4.5
Staphylococci	01	2.2
Total	45	100

Out of total 60 patients, 46 (76.7%) were released from the hospital when they were cured completely, whereas some 14 (22.3%) cases died. [Figure - 1]

Table V: Antimicrobial susceptibility of organisms isolated in blood culture

Antibiotic	Number (%) of the sensitive isolates				
	Klebsiella pneumoniae (n=24)	*Pseudomonas aeruginosa (n=11)*	*Acinetobacter* (n=07)	*Salmonella* spp. (n=9)	*Staphylococcus aureus (n=01)*
Penicillin	-	-	-	-	-
Ampicillin	-	-	-	-	-
Cloxacillin	-	-	-	-	-
Gentamicin	5 (20.8)	5 (45.4)	1 (14.3)	-	-
Netilmicin	12 (50.0)	6 (54.5)	4 (57.1)	-	-
Chloramphenicol	5 (20.8)	2 (18.2)	3 (42.9)	2 (100)	-
Ceftriaxone	17 (70.8)	7 (63.6)	4 (57.1)	2 (100)	
Ceftazidime	18 (75.0)	8 (72.7)	5 (71.4)	-	-
Ciprofloxacin	19 (79.2)	9 (81.9)	6 (85.7)	2 (100)	1 (100)
Imipenem	24 (100)	11 (100)	7 (100)	2 (100)	1 (100)

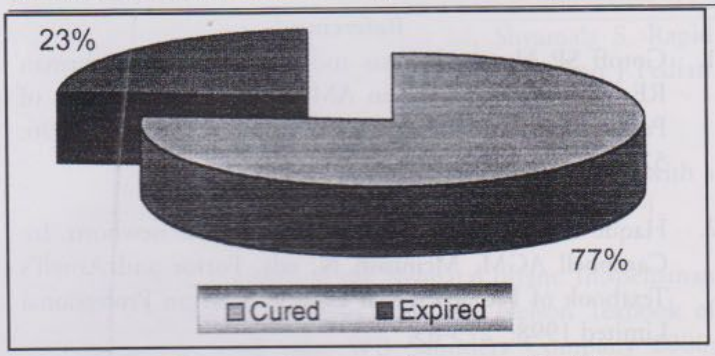

Figure 1: Outcome of treatment (n=60)

Discussion

Neonates are considered immunocompromised host in view of their relatively immature immune defense mechanism. Specifically, they have quantitative as well as qualitative deficiency in their humoral immunity. The preterm neonate is at further risk as transplacental transfer of antibodies starts after 32 weeks gestation.

In the present study, almost equal number of male (31) and female (29) neonates (ratio 1.06:1) were included to make it comparable with other studies (Table I). In a study done by D. Clapp *et al*[10] the male: female ratio was 1:1.17. In another study by Kinney *et al*[11] the male: female ratio was 1:1.27. These findings coincide with the present study.

The mean birth weight was 1.5 ± 0.3 kg. The preterm babies are usually low birth weight (LBW), which is reflected in the findings of the present study.

In a study "Rapid diagnostic tests in neonatal septicemia" undertaken by Chandna *et al*[12] in the neonatal unit of Gandhi Hospital, Hyderabad, and another review study on neonatal sepsis at Lahore,[13] the most frequent clinical features of neonatal sepsis were: lethargy, refusal to feed, fever, hypothermia, vomiting, abdominal distension, diarrhea, jaundice, seizures, respiratory distress (apnea) etc. In the present study, the majority of neonates also presented with reluctance to feed i.e., unable or unwilling to suck breast, recurrent apnea and bleeding tendency, temperature instability including hypothermia, abdominal distension, jaundice and dyspnea in descending order. The clinical features with which the preterm neonates presented with in the present study are also consistent with clinical feature narrated in the standard pediatric text book.[14] In a study done by Stabile *et al*[15], lethargy, convulsion, apnea, hypotonia, sclerema and cyanosis were found to be the common clinical features of the neonates presenting with "proven" and "very probable" sepsis.

The leukocyte count is usually elevated, with a predominance of neutrophils in neonatal sepsis.[14] In the present study also 48.3% of the cases had leucocytosis, which is in line with textbook review stated above. Thrombocytopenia was present in 65% and CRP was found high among 70% cases. These findings (except thrombocytopenia) are comparable with a study done by Haque *et al.*[16] The study by Chandna *et al*[12] revealed that CRP is the most useful single test with a high degree of sensitivity (83%), specificity (42%) and positive predictive accuracy (57%). In another study done by Leonard *et al,*[17] the percentage of thrombocytopenia was found to be low. The high percentage of thrombocytopenia in the present study may be the evidence of disturbance of bone marrow function in the babies with neonatal sepsis.

Blood culture was found positive in almost three-fourth of the cases. This finding is also consistent with the study done by Haque *et al,*[16] in which 66% were found culture positive. In another multicentre study by Shenoi *et al.*[18] 42.8% neonates were culture positive. Chandna *et al*[12] found blood culture positive in 48% of cases of neonatal sepsis.

In developed countries, Group B *Streptococci* and coagulase negative *Staphylococci* are the most common aetiological agents for early- and late-onset sepsis respectively. However, in developing nations these organisms are rare with an entirely different bacterial spectrum. *Escherichia coli* and *Klebsiella* are the most common organisms causing neonatal septicaemia.[19] This notion is proved to be true in case of the present study and other studies done in other developing countries. In the present study, *Klebsiella* was found to be most common organism causing sepsis (53.3%) that was followed by *Pseudomonas* (24.5%). There was no growth of B-*Streptococcus* and *Staphylococcus* was only found responsible in one case. In one study conducted in the same unit in 1998, nearly three fourths (73%) of the isolated organisms from blood in neonatal septicaemia were Gram-negative bacilli. *E. coli* was then the most common organism followed by *Kl. pneumoniae* (23%) and *Pseudomonas* spp. (10%). Among the Gram-positive

organisms *Staphylococcus aureus* was found in 16.7% of the isolates.[20] In their study, done at Saudi Arabia, researchers found *E. coli* in 40.9% and *Klebsiella* in 25% of proven sepsis cases whereas *Staphylococcus* in only 13.6% cases.[21] In another study done at Hyderabad, India, Gram-negative bacilli were found in 71% of culture positive cases.[12] Studies done at developed countries give us an opposite picture. Coagulase negative *Staphylococcus* was found responsible for 63.04% and *Klebsiella* for only 4.34% of "proven sepsis" in a study done at Leeds by Conway.[22] Stabile *et al*[15] in their study done at University of Pediatrics, Rome, Italy found *Staphylococcus* to be responsible for 50% and *Klebsiella* for only 10% of "proven sepsis" cases. Most of the organisms were found sensitive to third generation cephalosporins and ciprofloxacin. Netilmicin and gentamicin were moderately sensitive. A previous study also showed similar sensitivity pattern.[20]

The mean duration of hospital stay was 16.42 ± 5.85 days with a range of 3 to 35 days. The mortality rate was 22.3%, which is comparable to a multicentre study done in Hyderabad, India, where the mortality was also 28% in septicemia of preterm neonates.[23]

The present survey confirms the high case fatality rate in neonatal septicaemia, despite care in a tertiary-level pediatric hospital and use of appropriate antimicrobial therapy. This high mortality highlights the importance of anticipatory guidance for parents at home, particularly those with a LBW infant and early clinical suspicion on the part of practioner.

Due to the small sample size and hospital-based design of this study, we recommend additional community-based studies on local patterns and antimicrobial sensitivity of pathogens of neonatal septicaemia in order to formulate rational antibiotic use policies. There is also a need for community-based case-control studies with larger sample sizes to identify risk factors and design preventive measures for neonatal septicaemia. Moreover, in light of the rising incidence of antimicrobial resistance worldwide, we recommend that patterns of antibiotic usage and antimicrobial susceptibility of isolates be reviewed periodically.

References

1. Gotoff SP. Neonatal sepsis and meningitis. In: Behrman RE, Kliegman RM, Arvin AM, eds. Nelson Texbook of Pediatrics, 15th Edition. WB Saunders Company, 1996: 528-37.
2. Haque KH. Infection and immunity in the newborn. In: Campbell AGM, Mcintosh N, eds. Forfor and Arneli's Textbook of Pediatrics, 5th Edition. Pearson Professional Limited 1998: 273-89.
3. Darmstadt GL, Black RE, Santosham M. Research priorities and postpartum-care strategies for the prevention and treatment and postpartum-care strategies for the prevention and treatment of neonatal infection in less developed countries. Pediatr Infect Dis J 2000; 19: 739-50.
4. Polin RA, St. Geme JW III. Neonatal sepsis. Adv Paediatr Infect Dis 1992; 7: 25-61.
5. WHO Young Infants Study Group. Bacterial etiology of serious infections in young infants in developing countries: results of a multicenter study. Pediatr Infect dis J 1999; 18: S17- S22.
6. Fisher G, Horton RE, Edelman R. Summary of the neonatal institutes of health workshop on group B streptococcal infections. J Infect Disease 1983; 148: 163-6.
7. Sharma PP, Halder D, Dutta A. Bacteriological profile of neonatal septicaemia. Ind Paediatr 1987; 11: 1010- 7.
8. Saha SK, Rikitomi N, Ruhulamin M, *et al.* The increasing burden of disease in Bangladeshi children due to *Haemophilus influenzae* type b meningitis. Ann Trop Paediatr 1997; 17: 5-8.
9. Glandstone IM, Ehrenkranz RA, Edberg SC, Baltimore RS. A ten-year review of neonatal sepsis and comparison with the previous fifty year experience. Paediatr Infect Dis J 1990; 9: 819- 25.
10. Clapp DW, Kliegman RM, Baley JE, *et al.* Use of intravenously administered immune globulin to prevent nosocomial sepsis in low birth weight infants: report of a pilot study. J Pediatr 1989; 115: 973- 8.
11. Kinney J, Mundorf L, Gleason C, *et al.* Efficacy and pharmacokinetics of intravenous immune globulin administration to high-risk neonates. Am J Dis Child 1991; 145: 1233- 8.

12. Chandna A, Rao MN, Srinivas M, Shyamala S. Rapid diagnostic tests in neonatal septicaemia. Indian J Pediatr 1988; 55: 947- 53.

13. Aman MFS, Khan SR. Neonatal Sepsis: a review with a study of 50 cases. J Tropical Pediatr 1987; 33: 133- 4.

14. Gotoff SP. Infections of the Neonatal Infant. In: Behrman RE, Kligman RM, Arvin AM, eds. Nelson Texbook of Paediatrics, 16th edn. WB Saunders Company 2000; 538-52.

15. Stabile A, Sopo SM, Romanelli V, Pastore M, Pesaresi MA. Intravenous Immunoglobulin for prophylaxis of neonatal sepsis in premature infants. Arch Dis Child 1988; 63: 441- 3.

16. Haque KN, Remo C, Bahakim H. Comparison of two types of intravenous immunoglobulins in the treatment of neonatal sepsis. Clin Exp Immunol 1995; 101: 328- 33.

17. Leonard Col, Weisman E, Stoll BJ, *et al.* Intravenous immune globulin therapy for early-onset sepsis in premature neonates. J Pediatr 1992; 121: 434- 43.

18. Shenoi A, Nagesh NK, Maiyaa PP, Bhat HR, Subba Rao SD. Multicenter randomized placebo controlled trial of therapy with intravenous immunoglobin in decreasing mortality due to neonatal sepsis. Ind Paediatr 1999; 36: 1113- 8.

19. Kuruvilla KA, Thomas N, Jesudasan MV, Jana AK. Neonatal group B streptococcal bacteremia in India: ten years' experience. Acta Paediatr 1999; 88: 1031- 2.

20. Ahmed ASMNU, Chowdhury MAKA, Hoque MM, Darmstadt GL. Clinical and bacteriological profile of neonatal septicaemia in a tertiary level pediatric hospital in Bangladesh. Ind Pediatr 2002; 39: 1034- 9.

21. Haque KN, Zaidi MH, Bahakim H. IgM enriched intravenous immunoglobulin therapy in neonatal sepsis. Am J dis Child 1988; 142: 1293- 6.

22. Conway SP, Gillies DRN, Doherty A. Neonatal infection in premature infants and use of human immunoglobulin. Arc Dis Child 1987; 62: 1252- 6.

23. Shenoi A, Nagesh NK, Maiya PP, Bhat SK, Subba Rao SD. Multicentred randomized placebo controlled trial of therapy with intravenous immunoglobulin in decreasing mortality due to neonatal sepsis. Ind Pediatr 1999; 36: 1113- 7.

ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal
Volume 2 Number 1

Psychiatric Morbidity Among Patients of Thyroid Dysfunction

ASHFAQUE UZZAMAN CHOUDHURY[a]

Abstract

There is no epidemiological data of psychiatric morbidity among the patients with thyroid disorders in our country, although thyroid disorders and its presentation are very common. A cross-sectional study was carried out for six months in thyroid clinic of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. A total of 260 patients of age group below 10 to 60 years were taken as samples. Among them 33.46% (87/260) were male and 66.54% (173/260) were female patients. Total psychiatric morbidity was found 69.62%, diagnosed on the basis of Diagnostic and Statistical Manual of Mental Disorder-IV (DSM-IV) criterion. Among the hyperthyroid group, anxiety disorder was 67.50%, in hypothyroid group, depressive disorder was 33.33% and among the euthyroid group, non-specific symptoms were predominating (35.55%). Analysis of socio-demographic data revealed that age incidence of thyroid disordered patients were most in third (38.08%) and second decades (26.93%). The urban involvement was slightly more (53.85%) than the rural population (46.15%). But none of these variables had any statistical significance in psychiatric morbidity. Although main treatment was with thyroxin replacement or with anti-thyroid drugs but about 42.31% required treatment with psychotropic drugs.

[OMTAJ 2003; 2(1): 10-13]

Introduction

Thyroid gland is one of the most sensitive organs in the body. It responds to many stimuli and is in a constant state of adaptation.[1] In our country a great number of people have been suffering from thyroid dysfunction. The psychiatric manifestation of thyroid disease has long been recognized.[2] There is uncertainty, however, about the prevalence of thyroid disorder among the mentally ill patients. The different thyroid states can have varied presentations. In hyperthyroidism, there are always some psychological symptoms, including restlessness, irritability and distractibility which may be so marked as to resemble anxiety disorder.[3] Thyroid crises may result in acute delirium and other symptoms of toxic psychosis.[4] When thyroid deficiencies begin, it leads to mental slowness, apathy and complaints of poor memory. There is decreased psychomotor activity. Personality changes are common, most often depression, but sometimes paranoid ideation and frank psychosis are present. The relationship between thyroid and psychiatric disease may have a number of facets. Thyroid disorders are known to manifest occasionally as isolated psychiatric disorders.[5] In our country, there is no such recognized study on psychiatric morbidity among thyroid patients. This study has been undertaken to identify the psychiatric morbidity, the mode of presentation and to compare the socio-demographic variables between psychiatrically ill and psychiatrically normal thyroid dysfunction patients.

Methods

The patients were selected through systematic random sampling from the diagnosed thyroid dysfunctional patients. By adopting this method, 260 patients were interviewed. Among them, 87 were male and 173 were female. A semi-structured questionnaire, consisting socio-demographic data with symptomatology, was used to interview every alternate patients attending thyroid clinic OPD and suffering from thyroid disorders, irrespective of hyper-, hypo- or euthyroid state. A thorough physical and mental state examination was done. Psychiatric disorders were diagnosed clinically on the basis of DSM IV diagnostic criteria. Before going for actual data collection, pre-testing was carried out among five percent of the sample and the questionnaire and the methodology was finalized.

Results

Two hundred sixty patients with thyroid disorders were selected. The age range of the patients were from 5 to 60 years (mean 26.91 SD+ 1.29). Eighty seven patients were male and one hundred seventy three patients were female. The male female ratio was 1:2.

[a] Lieutenant Colonel,
Combined Military Hospital, Chittagong Cantonment

There was no significant difference between male and female thyroid patients in relation to psychiatric disorder. The results were analyzed to see psychiatric morbidity among the thyroid disorder patients. Among the total 260 patients, psychiatric morbidity was 69.62%. Along with this, socio-demographic parameters were studied among the patients.

Majority of the patients (33.08%), with or without psychiatric morbidity and having thyroid disorders, were from the third decade (21-30 Years). (Table I)

Table I : Age wise distribution of thyroid dysfunction patients

Age in years	With psychiatric Morbidity (n=181)	Without psychiatric Morbidity (n=79)	Total (n=260)
<10	2(1.10%)	4(5.06%)	6(2.3%)
11-20	50(27.60%)	20(25.31%)	70(26.93%)
21-30	60(33.14%)	26(32.9%)	86(33.08%)
31-40	39(321.55%)	17(21.51%)	56(21.54%)
41-50	23(12.70%)	7(8.61%)	30(11.54%)
51-60	7(3.87%)	5(6.33%)	12(4.61%)

X^2 = 4.887 P<0.05

There was no signficant difference between male and female thyroid patients in relation to psychiatric disorder.(Table II)

Table II : Sex wise distribution of thyroid dysfunctions.

Morbidity	Male (n=87)	Female (n=173)	Total (n=260)
With Psychiatric Morbidity	60968.97%)	121(69.96%)	181(69.62%)
Without Psychiatric Morbidity	27(31.03%)	52(30.06%)	79(30.38%)

X^2 = 0.068 P<0.05

Table III: Habitat distribution of patients with thyroid disorder.

Habitat	With Psychiatric Morbidity (n=181)	Without Psychiatric Morbidity (n=79)	Total (n=260)
Urban	60995(52.69%)	45(56.96%)	140(53.85%)
Rural	86(47.51%)	34(43.04%)	120(46.15%)

X^2 = 0.443 P<0.05

Habitat distribution was more among the urban (53.85%) than the rural (46.15%) groups though the difference was not statistically significant (P>0.05). (Table III)

Table-IV: Distribution of Psychiatric disorder among thyroider patients (hyper/hypo/euthyroid) by sex.

Psychiatric Disorder	Male Value (%)	Female Value (%)	Total (n=260) Value (%)
Anxiety disorder*	33 (55)	50 (41.32)	83 (85)
Depressive disorder **	14 (23.33)	28 (33.14)	42 (18.10)
Bipolar mood disorder***	03 (05.0))	13 (10.74)	16 (08.83)
Somatoform Disorder ****	05 (08.33)	17 (14.04)	22 (12.15)
Schizophrenia disorder	01 (1.66)	05 (04.13)	06 (03.31)
Delusional disorder	01 (1.66)	03 (02.47)	04 (02.20)
Personality disorder	01 (1.66)	00(00)	01 (0.05)
Others	02 (3.33)	05 (04.13)	07 (03.86)

X^2 = 16.782 P< 0.05

* X^2= 1.15(P>0.05)
** X^2= 0.02 (P>0.05)
***X^2= 14.22 (P<0.05)
**** X^2= 1.39 (P>0.05)

Adjustment disorder = 3
Dissociative disorder =1
Sleep disorder =1
Schizo-affective disorder =1
Psychosis = 1

Most of the patients (85%) were suffering from anxiety disorder, followed by depressive disorder, somatoform disorder and bipolar mood disorder. Among the bipolar disorders females are suffering more than that of males, the difference is statistically significant. (Table IV)

Table-V Statistical Analysis of Anxiety and Depressive disorders among Hyper and Hypothyroid Patients.

Psychiatric Disorder	Hyperthyroid (n=80)	Hyperthyroid (n=90)	Total (n=260)
Anxiety	54(67.50%)	10(11.11%)	64(37.66%)
Depressive Disorder	2(2.5%)	30(33.33%)	32(18.82%)

X^2 = 55.1 P< 0.05
$X2$ = 16.78 (P< 0.05)
X2 = 38.3 (P< 0.05)

The anxiety disorders and the depressive disorders were prominently present in hyper- and hypothyroid patients respectively and were statistically highly significant. (Table V)

Discussion

In Bangladesh, the people are not very much interested to give their proper psychiatric history, specially where he/she has reported for her known thyroid complaints. Social stigma seems to be more pronounced when asked about the family history of psychiatric illness from the female patients. Among the total patients, 69.62% of the sample met the Diagnostic and Statistical Manual of Mental Disorder-IV criteria for a psychiatric diagnosis. This reflects the higher prevalence of psychiatric morbidity among the thyroid dysfunction patients than in the general population which is 6.5% in our country.[6] A recent study was carried out in the department of Psychiatry, University of Pisa, Italy with the thyroid disorder patients. The presence of psychiatric disorders were assessed by means of a structured clinical interview for DSM-III. The percentage of patients with psychiatric diagnosis, out of a total 93 thyroid patients, was 63.2%.[7] Our study corresponds with the study results of University of Pisa, Italy.

Age wise distribution of the patients showed 33.08% were from the third decade, followed by second (26.92%) and fourth decade (21.54%). This finding corresponds with the result that the thyroid disorder is common in the second and third decades of life but the range is wide.[8] The prevalence of psychiatric morbidity among female with thyroid disorders were 69.94% and among males were 68.97%. It was likely that the psychiatric morbidity was more among the female patients, since the ratio of thyroid disorder is higher among females but actually it did not happen. This paradox could partly be due to the fact that females are less frequently brought for the treatment than their male counterpart in our country. Again the male-female ratio of psychiatric patients is almost equal in our country which is probably due to male dominated family where females are more neglected and chronically remain underreported.[9]

In case of social background, the psychiatric morbidity among urban population was 52.49% and rural background was 47.51%. There was slightly more preponderance among the urban population in this study though the finding was not statistically significant. Certain factors like easy accessibility, location of the hospital, economic factor, urban people's better health consciousness and better information about the health service may explain the preponderance of the urban patients.

Among the total hyperthyroid patients in this study males were 44.5% and females were 55.5%. Most prevalent psychiatric disorder fulfilling the diagnostic criteria of DSM-IV among the both groups was anxiety disorder (67.50%), bipolar mood disorder (7.50%), depressive disorder (2.5%), somatoform disorder (2.5%) and delusional disorder (3.75%). The finding of anxiety disorder in hyperthyroidism is quite significant and corresponds with the famous study of Kathol *et al*[10] who found 80% of the hyperthyroid had generalized anxiety.

In the study among hypothyroid patients males were 37.78% and females were 62.22%. About 33.33% patients were found to be suffering from depressive disorder, 11.11% anxiety disorder, 8.88% bipolar mood disorder, 15.56% somatoform disorder and 2.2% schizophrenia. A good number of patients with psychiatric symptoms included vague somatic complaints, minor affective symptoms and cognitive impairment of different degrees. The symptoms of hypothyroidism are less distinctive than those of hyperthyroidism. Depression and impairment of attention and memory seem to be more common in hypothyroidism.[7,11] Findings of this study corresponds with those of previous studies.

In this study, quite a good number of patients with thyroid disorders were in euthyroid condition. Among them male were 21.11% and female were 78.98%. This group presented with various psychiatric disorders and symptoms but the predominant were non-specific psychiatric symptoms not fulfilling diagnostic criteria (33.33%) followed by anxiety disorder (21.11%) and depressive disorder (11.11%). Most of the euthyroids were with simple diffuse goitre and were more concerned about their external physical aesthetic condition. Many of them, although within the normal range of thyroid level, were towards hyper- or hypothyroid borderline level which also could be related with the expression of those symptoms.

This study reflected that among the thyroid

dysfunction individuals, maximum patients were suffering from anxiety disorders and depressive disorders. It was also evident that among the hyperthyroid group, most of the patients were suffering from anxiety disorders. In contrast, among the hypothyroid group most were suffering from the depressive disorder. This differences was statistically highly significant (P<0.001) and correlates with the findings of the previous studies.

Among the studied group, about forty two percent patients, received psychotropic drugs. This includes B-blockers, anxiolytics antidepressants, and antipsychotics in different doses, either alone or along with thyroid hormones or antithyroid drugs. It is obvious that severe psychiatric disturbances including many florid psychotic symptomatology, can be the most prominent manifestation of hypothyroidism, hyperthyroidism as well as the euthyroid patients. So screening laboratory tests of thyroid function can often required to be done routinely in psychiatric units. Regarding replacement therapy, clinical judgment is of prime importance so that the person is neither under replaced with unresolved symptoms, nor over replaced with the emergence of hyperthyroidism. A close liaison between the psychiatrist and the endocrinologist should result in a favourable treatment outcome.

The psychiatric morbidity among patients of thyroid dysfunction is very common, but its varied presentation, diagnostic dilemma and appropriate treatment approach requires special skill and consideration. It was found that a subtle thyroid dysfunction led a tremendous increase in psychiatric morbidity. Due to non-specific symptoms and signs, serious consequences and possibility of improper treatment may result from overlooking actual thyroid status by the psychiatrist group or by over enthusiastic treatment of psychiatric symptoms by non-psychiatric professionals. The thyroid test, particularly T^3, T^4 and TSH remains the key investigations that can be used by a skilled clinician to augment, not supplant, good clinical judgment. It was seen that the possibility of enormous number of undiagnosed and improperly treated patients of psychiatric morbidity among thyroid dysfunction are existing in our country. In spite of certain unavoidable limitations findings of the present study is representable in our social context and will demand notice and interest for further study.

Acknowledgement

Prof. MA Sobhan, Chairman of the dept of Psychiatry, BSMMU, for guidance and valuable suggestions. Maj (Dr) M. Kumrul Hasan for constant assistance and support during the study. Dr. Faridul Alam, Thyroid Clinic, BSMMU for continuous support in collecting samples. Dr. Shoeb for papers and information.

References

1. Cotran RS, Vinay K, Robins SL. Robins Pathologic Basis of Diseases. 4th ed. New York :1214-30.
2. Carrey MWP, Shirley M, BF Shiffield. Thyroid function screening in psychiatric inpatients. Br J Psychiatry 1981; 138: 154-6.
3. Gelder M, Dennis G, Richard M. Oxford Textbook of psychiatry. 2nd ed. London: Oxford 1995: 379-81.
4. Harold KI, J Sadock, Benjamin. Comprehensive Textbook of Psychiatry. 6th ed. New York: Lippincott 1995:199-200.
5. Tappy L, Randin JP, Schewed P, Wertheimer J, Lemarchand BT. Prevalence of thyroid disorder in psychogeriatric in-patients: A possible relationship of hypothyroidism with neurotic, depression but not with dementia. J Am Geriatr Soc 1987; 35(6): 526-31.
6. Chowdhury AKMN, Alam MN, Ali SMK. Dasherkandi project studies: Demography, morbidity and mortality in rural community of Bangladesh. BMRC Bulletin 1981; 7(1): 22-39.
7. GPA Placidi, M Boldrini, A Patronilli, E Fiore, L Chiovato, G Perugi, D Marazzite. Prevalence of psychiatric disorders in thyroid diseased patients. Neuropsychobiology 1998; 38: 222-5.
8. Lishman, Alwyn W. Organic Psychiatry. 3rd ed. New York: Blackwell 1995:507-15.
9. Hossain CS, Shahabuddin M, Aminul H. Referral pattern of psychiatric patients of Pabna mental hospital. Bang Med J 1993; 1: 9-12.
10. Kathol RG, Delahunt JW. The relationship of anxiety and depression to symptoms of hyperthyroidism using operational criteria. Gen Hos Psych 1986; 8 (1): 23-8.
11. Gelder, Michael, Dennis G, Richard M, Philip C. Oxford Textbook of Psychiatry. 3rd ed. London: Oxford 1999: 403-4.

ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal
Volume 2 Number 1

Effect of Chlorpromazine on Selected Liver Function Parameters in Psychiatric Patients

*MD. REZAUL KARIM,[a] GOPAL SHANKAR DEY,[b] DIPENDRA NARAYAN DAS,[c] M KUTUB UDDIN CHOWDHURY.[d]

Abstract

Chlorpomazine (CPZ) is a recognized cause of hepatotoxicty. Reports of increased bilirubin output found in experimental animals with acute CPZ treatment. But no alterations in the normal bilirubin conjugation have been documented. In patients with psychiatric illness, CPZ is used almost routinely. A panic works among the physicians whether the prolonged use of this drug causes any hepatotoxicity, particularly in terms of bilirubin conjugation or haem metabolism. Hypotensive effect of chlorpromazine also has to be considered in some cases of elevated blood pressure. Considering the above point of view, this was a prospective study carried out among 102 psychiatric patients to observe the hepatic dysfunction, measured by manifestation of clinical jaundice and /or increased bilirubin level in the serum. Patients were treated with CPZ from 600mg to 200mg for a period of 10 days, sometimes with gradual tapering, considering the intensity of psychiatric illness. Only 2 (1.96%) of the patients found to develop clinical jaundice with mild increase in the serum bilirubin, though concomitant viral hepatitis could not be excluded. From this simple study, it can be assumed primarily that chronic use of CPZ in optimum doses cause no hepatic dysfunction detected through the selected parameters, although a case control study with greater population is recommended to validate the findings.

[OMTAJ 2003; 2(1): 14-16]

Introducton

Chlorpromazine (CPZ) is an antipsychotic drug of phenothiazine group, has the essential mechanism by their ability to block central dopamine receptors. It is usually used to treat acute schizophrenia and mania, and to prevent relapse in chronic schizophrenia. They are also useful in the management of disturbed behaviour due to acute confusional states. The drug has many unwanted side effects, particularly cholestatic jaundice, for which regular review of their use has been recommended.[1] Jaundice was observed in patients shortly after the introduction of CPZ. Commonly occurring during the second to fourth week of therapy, the jaundice generally is mild and pruritus is rare. The reaction is probably a manifestation of hypersensitivity, because eosinophilic infiltration of the liver as well as eosinophilia occur, and there is no correlation with dose.[2] Phenothiazine-induced jaundice is classified as a form of cholestatic hepatocanalicular hepatotoxicity and as an acute liver disease.[3] In a study in rat it was found that acute CPZ treatment with 25mg per kg intravenously produced haemolysis and resulted in increased bilirubin output. Both unconjugated bilirubin and gamma-azopigment, found primarily in obstructed rat-bile, were seen. On the other hand, a chronic CPZ treatment for 4 and 8 days with 25mg per kg intraperitoneally increased bilirubin output without elevating plama Hb-level and increased the fraction of monoconjugated bilirubin in bile; the 8-day chronic treatment regimen also caused unconjugated bilirubin appear in bile; the 8-days with Hb level and increased the fraction of monoconjugated bilirubin in bile; the 8-day Chronic treatment regimen also caused unconjugated bilirubin to appear in bile.[4] CPZ has been considered to have a unique side effect of producing hypotension and the effect of hypotension is more pronounced with parenteral administration.[2] This was a prospective observational study to evaluate the effects of CPZ in psychiatric patients in respect to its hepatotoxicity as well as hypotensive effects.

Methods

A total of 102 patients with psychiatric illness in a psychiatric hospital setting in Sylhet were enrolled into the study. Patients were treated with chlorpromazine on admission following the severity of illness and the dose was gradually tapered in most of the cases. In some

[a] Professor

[b] Associate Professor
Department of Psychiatry, Sylhet MAG Osmani Medical College.

[c] Medical Officer

[d] Social Welfare Officer
Shah Jalal Mental Health and Research Centre, Sylhet.

* Corresponding author

patients the admission dose of CPZ was maintained throughout the treatment period. Any presentation of clinical jaundice was observed on each follow up visit. In case of any clinical jaundice, serum bilirubin level of the patient was measured following standard protocol. Blood pressures of the patients were recorded on every follow up visit and the hypertensive patients, including high normal blood pressures, according to WHO,[5] were considered to see hypotensive effect of CPZ. Fall of BP by > 10mm Hg on either systolic or diastolic pressure was considered as response to the drug during the course of treatment.

Result

Ages of the patients were from 14 to 60 years having a mean age of 26.7 ± SD 8.97. The highest enrollment of the patients (71/102, 69.6%) were among 21-30 years age group (table I).

Table I : Age groups of the enrolled patients

Age group	Number of Patients	Percent
10-20 Yrs	15	14.7
21-30 Yrs	71	69.6
21-40 Yrs	09	8.8
≥ 41 Yrs	07	6.9

The highest number of patients included in the study had substance abuse disorder (SAD) (61/102, 59.8%) followed by chronic schizophrenia (20/102, 19.6%) (table II). In Most of the patients (55/102, 53.9%) the dose was gradually tapered, some (13/55, 23.6%) treated with static dosage schedule as on admission and one was shifted to Halop (Haloperidol) on follow up. None of this group (treated on admission with with 600mg CPZ) had any observable clinical jaundice (table III).

Table II: Psychiatric disorders included in the study

Sl no	Psychiatric disorder	No (%) enrolled
01	SAD[a]	61 (59.8)
02	Chronic Schizophrenia	20 (19.6)
93	Acute Psychosis	06 (5.9)
04	MDP[b]	04 (3.9)
05	BAD-M[c]	03 (2.9)
06	MDP-M	02 (2.0)
07	Paranoid Psychosis	02 (2.0)
08	SAD+ Psychosis	01 (.0)
09	SAD+ Chr. Schizophrenia	01(1.0)
10	Cannabis Psychosis+Chr. Schizophrenia	01 (1.0)

[a]SAD (Substance Abuse Disorder), [b]MDP (Manic Depressive Psychosis), [c]BAD-M (Bipolar Affective Disorder-Manic)

Table III : Relationship of clinical jaundice with the treatment schedule used

Dose of CPZ on admission	No (%) of the patients Total (n=102)	Tapered gradually	Static	Others	Clinical jaundice
600 mg	55 (53.92)	41 (74.55)	13 (23.63)	01 (1.82)*	00(00)
500 mg	01 (0.98)	01 (100)	00(00)	00(00)	00(00)
400 mg	40 (39.21)	19 (47.50)	17 (42.50)	04 (10.0)**	01 (2.50)
300 mg	04 (3.93)	02(50.00)	02(50.00)	00(00)	01 (25.0)
200 mg	02(1.96)	01 (50.0)	01 (50.0)	00 (00)	00(00)

* Shifted to Halop (haloperidol) after 7 days
** Raised to 600 mg (3 Patients after 7/10 days), and stopped on development of clinical jaundice (1 patient)

A total of 02 (1.96%) among the study cases were observed to develop clinical jaundice. One of them was a 25- year old male, admitted with SAD, started with 400 mg CPZ and developed hyperbilirubinaemia (serum bilirubin 1.5 mg/dl) on 8th day of admission when CPZ was stopped. The other patient developing jaundice was 26-year old male admitted with chronic schizophrenia, starting treatment with 300mg CPZ, reduced to 200mg after 7th day, but developed jaundice (4.4mg/dl) after about three months. In both the cases, patients could not be screened for viral hepatitis.

Regarding hypotensive effects of CPZ, a total of 9 patients were observed having either hypertension or high normal blood pressure, and all of them were recorded reduced blood pressure after 10th follow-up day (table IV).

Table IV: Record of hypotensive effect of CPZ

Sl no	Patient age	Disease suffering	Dose (mg) of CPZ On admission	Dose (mg) of CPZ On10th day	BP in mm Hg On admission	BP in mm Hg On 10th day
01	30 yrs	Chr. schizophrenia	400	400	130/90	115/75
02	22 yrs	Chr. schizophrenia	600	200	140/90	110/75
03	21 yrs	SAD	400	400	130/90	110/70
04	30 yrs	Chr. schizophrenia	600	600	130/80	110/70
05	40 yrs	Acute psychosis	400	600	130/90	130/80
06	28 yrs	Chr. Schizophrenia	200	200	130/90	120/70
07	25 yrs	SAD	600	400	130/80	115/70
09	22 yrs	SAD	600	300	130/80	120/75

Discussion

Chlorpromazine is a frequently used antipsychotic drug having hepatotoxicity and also found to have some hypotensive effects. In the present study, we found clinical jaundice only in 2 (1.96%) patients which is

apparently insignificant. Moreover, the follow-up examinations of the patients could be recorded only for 10 days and the concurrent hepatitis virus infections were also not screened. Therefore, the chlorpromazine-induced hepatoxicity can be ignored in cases with short-term treatment. Hypotensive effects were recorded in the patients, particularly those having high normal blood pressure or hypertension. This was a very small study among psychiatric patients with obvious limitations. So a study with larger study population, preferably case-control study, is recommended to conclude about hepatic dysfunction with chlorpromazine use in psychiatric patients.

References

1. Lloyd GG. Principles of Medical Psychiatry. In: Haslett C, Chilvers ER, Hunter JAA, Boon NA, eds. Davidson's Principles and Practice of Medicine. 18th ed. UK: Churchill Livingstone 1999: 1080-1.

2. Baldessarini RJ, Tarazi FI. Drugs and the treatment of Psychiatric disordes. In: Hardman JG, Limbird LE, eds. Goodman & Gillman's the Pharmacological basis of Therapeutics, 10th ed. New York: Mc Graw Hill 2001: 485-520.

3. Regal RE, Billi JE, Glazer HM. Phenothiazine-induced cholestatic Jaundice. Internet Mental Health. www.mentalhealth.com.

4. Knodell RG. Effects of chlorpromazine on bilirubin metabolism and biliary secretion in the rat. Gastroenterol 1975; 67 (4): 965-72.

5. Kumar P, Clark M. Cardiovascular diseases. In: Kumar and Clark Clinical Medicine. 5th ed. UK: WB Saunders 2002: 818-9.

ORIGINAL ARTICLE

The Osmani Medical Teachers Association Journal Volume 2 Number 1

Isolation and Antibiogram of *Escherichia coli* from Urinary Tract Infection in Sylhet Town

*BELAL MAHMOOD,[a] ABDUS SATTAR,[b] RAFIQUL ISLAM,[c] MOOSA M A QAIYUM[d]

Abstract

The study was carried out within the central town of Sylhet for a period of one year. One hundred patients were included randomly with suspicion of urinary tract infection of which females were predominant (72%). Specimens of clean-catch mid-stream urine were cultured to isolate *Escherichia coli* following standard protocol. Isolates were confirmed using specific antisera. Age distribution reveals the highest incidence (41%) among 21-30 years age group of the female cases. Patients of this age group (21-30 years) were clinically symptomatic in contrast to those above 50 years. The antibiotic susceptibility result showed high sensitivity to gentamicin (89%) followed by ceftriaxone (77%) and ciprofloxacin (61%). These results were remarkably different from those of amoxicillin and co-trimoxazole which were resistant by 86% and 83% respectively. Regular monitoring of susceptibility pattern of the urinary isolates is recommended.

[OMTAJ 2003; 2(1): 17-19]

Introduction

Urinary tract infection (UTI) is the most common bacterial infection encoutered by the physicians. The term urinary tract infection means presence or invasion of microorganism and multiplication into a previously sterile urinary system.[1,2]

The increased incidence of resistant organisms, including those resistant to multiple antibiotics has attracted the attention of many workers to the phenomena of transferable drug resistance.

Drug resistance may be genetic or non-genetic.

[a] Associate Professor, Department of Microbiology

[b] Lecturer, Department of Microbiology North East Medical College, Sylhet.

[c] Assistant Professor, Department of Biochemistry Sylhet MAG Osmani Medical College, Sylhet

[d] Associate Professor, Department of Paediatrics North East Medical College, Sylhet.

* Corresponding author

Genetic resistance may be due to either chromosomal mutations or encoded on plasmids (R^+ factors).[3] Plasmids (R-factors) are responsible for 60-90% of drug resistance with the remainder being due to mutations of the chromosomes. R-factors are transmissible to other bacterial cells by conjugation, transduction and transposition.[3,4] In 90% of cases transfer of drug resistance, is due to conjugation.[3-5]

The present study was undertaken to investigate the age-sex distribution and antibiotic sensitivity pattern of *Escherichia coli,* which has been isolated from patients suspected of urinary tract infection.

Methods

One hundred patients of Sylhet town were investigated at a random survey. The Patients were of both sexes and of different age groups. The study period was from October 2001 to September 2002.

Each individual was instructed to collect the "clean-catch" midstream urine sample in a sterile container having a metallic cap. The samples were at once put onto culture media by the standard-loop semiquantitative technique. MacConkey agar was used throughout the lab study. The culture plates were incubated aerobically at 37°C overnight (18-24 hours). Colonies of the *Escherichia coli* was recognized as lactose fermenters on Mac Conkey's agar media. Further tests were done to confirm the identification of bacterium, like Gram's stain and motility test.

Any urine samples showing equal or more than 10^5 colony forming units per milliliter were considerd as significant. Each isolated strain was stored in small sterilized glass tube following standard protocol. All the samples were kept stored at 4°C, until further use.

The isolates of *E. coli* were subjected to antibiotic sensitivity which was based on modified Kirby-Bauer Method.[6,7] Antibiotic disks were placed on the nutrient agar media plate which has been incoulated

with *E. coli*. It was followed by incubation at 37°C for 18-24 hours. The diameter of the zone of inhibition of control organism as well as test organism was compared with respective standard table for zone diameter. The results were expressed as sensitive (S) and resistant (R).

Control strain used was *E. coli* -25922 (ATCC). Senstive to all antibiotic *E. coli* K12.

Serotyping

Serotyping of the *E. coli* strains were done with the collaboration of International Center for Diarrhoeal Diseasses and Research, Dhaka (ICDDR, B). Serotyping kits (commercially available antisera kit, Denlea Scihen, Tokyo, Japan) specific for all poly- and mono-valent antibody reagents specific for all types of *E. coli* were used. Serological reactions were performed by the standard slide agglutination test.

Results

The study population included 100 patients who were suffering from urinary tract infections.

Among the total study population, 52 (65%) were female and 28 (35%) were male.

The isolation rate of *Escherichia coli* was the highest (41%) in 21-30 years age group followed by 11-20 years (23%). (Figure 1)

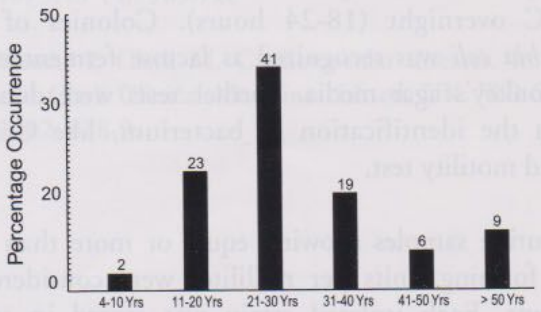

Figure 1: Frequency of isolation of *Escherichia coli* from UTI patients of different age groups in female population

The antibiotic susceptibility pattern of *E. coli* isolates show that 83% were resistant to amoxycillin. To cotrimoxazole, 83% were resistant. To ceftriaxone and ciprofloxacin, 77% and 61% of the isolates were sensitive respectively.

To nalidixic acid, 77% of the *E. coli* strains were resistant. Almost 98% of the isolates were sensitive to gentamicin. (Figure 2)

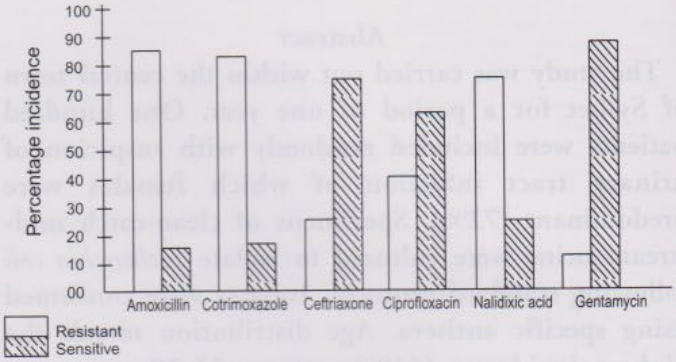

Figure 2: Sensitivity pattern of the *Escherichia coli* isolates against commonly used antibiotics

Discussion

Urinary tract infection (UTI) is the most common bacterial infection encountered by physicians. These pathogens can affect the humans throughout their life span. Out of several pathogens *E. coli* ranks the highest, nearly 80-85%.[8] In the present study, significant bacteriurea was considered as an important criteria in the diagnosis of urinary tract infection.[8,9] The results clearly show that female population had a higher incidence of UTI (72%). These findings suggest that females suffer more from UTI than the male, because of the vulnerable anatomical position of short female urethra allowing bacteria from vagina to enter urinary bladder. Interestingly the average age distrbiution in male and female population did not differ in this study which suggests that *E. coli* has no predilection over age distribution in terms of sexes.

The highest incidence of UTl in female was found among the age group 21-30 years. A similar study, conducted in Sylhet town, showed the evidence of bacteriuria more in pregnant women than the nulliparous women and it also showed the incidence rises with increasing number of pregnancies.[5] The evaluation of *E. coli* in pregnant women was not conducted in the present study. The findings of the susceptibility test to amoxicillin of the isolates suggest that drug resistance was very high and possibly it is plasmid mediated. Plasmid (R^+-Factor) are responsible for 60-90% of drug resistance with the remainder being due to mutation of chromosomes.[3] The other resistant drugs of high