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Original Article

Evaluation of Neonatal Cholestasis: An Experience in a Tertiary Centre of Bangladesh

Salahuddin Mahmud*[1], Jahida Gulshan[2], Mashud Parvez[3], Farhana Tasneem[4], Syed Shafi Ahmed[5]

*[1] *Associate Professor, Pediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Institute of Child Health, Dhaka Shishu (Children) Hospital.*

[2]*Associate professor, Institute of Statistical Research and Training, University of Dhaka.*

[3]*Associate Professor of Histopathology, Bangladesh Institute of Child Health, Dhaka Shishu (Children) Hospital.*

[4]*Assistant Professor, Department of Pediatrics, BIHS General Hospital, Diabetic Association of Bangladesh.*

[5]*Professor and Head, Pediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Institute of Child Health, Dhaka Shishu (Children) Hospital.*

* *drsmbablu@gmail.com*

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ABSTRACT

Background: *A common presenting feature of neonatal hepatobiliary and metabolic dysfunction is cholestatic jaundice. Any infant who remains with jaundice beyond age 2 to 3 weeks must be assessed with fractionated serum bilirubin level. Late referral and lack of exact etiological diagnosis results in poor outcome in a substantial number of cases in Bangladesh.*

Objective: *Retrospective evaluation of infants with cholestatic jaundice in terms of history, common clinical presentation and biochemical profile with etiologies.*

Materials & Methods: The study was conducted in the Department of Pediatric Gastroenterology, Hepatology & Nutrition, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh from July 2014 to June 2016 on 80 infants who were presented with cholestatic jaundice at <3 months of age. Clinical history and physical examination findings were recorded and investigations were done as appropriate.

Results: *Among 80 cholestatic infants, 32 (40%) were extra-hepatic cholestasis & 48 (60%) were intra-hepatic cholestasis. Biliary atresia (BA) & choledochal cyst (CC) in extra-hepatic causes and idiopathic neonatal hepatitis (INH) & TORCH infections in intra-hepatic causes were the commonest. Mean age of onset among extra-hepatic cases were 6.7±2.3 days but age of admission were 94.6±50.4 days and among intra-hepatic cases mean age of onset were 12.4±2.8 days with an age of admission of 82.4±29.0 days. Among children with extra-hepatic cholestasis, female were predominant (Female: male=2.2:1) and among children with intra-hepatic cholestasis, males were pre-dominant (Male: Female=1.6:1). Among the children with extra-hepatic cholestasis, more were term babies [28 (87.5%)] & among the children with intra-hepatic cholestasis pre-term babies [32 (66.6%)] were more. Maternal history of fever [16 (35.3%)] and rash 22 [(45.8%)] were significant in intra-hepatic cases. Persistent pale stool [27 (84.3%)] in extra-hepatic cases and intermittent pale stool [37 (77.1%)] in intra-hepatic cases were significant. Gamma glutamyl tanspeptidase (GGT) (886.87±122.85) & Alkaline phosphatase (ALP) (786.87±122.85) were significantly higher among children with extra-hepatic causes and alanine aminotransferase (ALT) (459.08±59.10) & International normalization ratio (INR) (1.53±0.28) were significantly higher among children with intra-hepatic causes. Most of the cases were presented as acute hepatitis (BA 51.6%, INH 70% & TORCH infections 45.9%), and acute liver failure (ALF) [Galactosemia (100%), intra-hepatic bile duct paucity (100%), progressive familial intra-hepatic cholestasis (PFIC) (100%) and INH (22.9%)].*

Conclusion: *The study demonstrates that although cholestatic jaundice developed early, most of the cases were presented late due to primary health care failure which indicates the need of improvement in primary health care facilities as well as training of primary health care providers in order to be able to diagnose the problem and refer to respective health care facilities to avoid further complications due to late detections.*

Keywords: *Neonatal cholestasis, Biliary atresia, Idiopathic neonatal hepatitis, Liver biopsy (LB).*

1. INTRODUCTION:

Jaundice, occurring in 2.4% to 15% of newborns, is a yellow discoloration of the skin, sclera, mucous membranes, and bodily fluids, is a common clinical finding in the first 2 weeks after birth.1-6 Jaundice is, most often, the indirect/unconjugated bilirubin variety that resolves spontaneously without intervention.5 However, persistent jaundice is unusual and can be the sign of serious hepatobiliary and metabolic dysfunction. When jaundice continues beyond 2 weeks, one must consider cholestasis or conjugated hyperbilirubinemia in the differential diagnosis. 6,7

By definition, Cholestasis is reduced bile formation or flow ensuing in the retention of biliary substances inside the liver, which, normally, excreted into bile and destined for elimination into the intestinal lumen.8 Neonatal cholestasis is defined as conjugated hyperbilirubinemia occurring in the newborn as a result of reduced bile flow.9 Conjugated hyperbilirubinemia in a neonate is defined as a serum direct/conjugated bilirubin concentration greater than 1.0 mg/dL if the total serum bilirubin (TSB) is <5.0 mg/dL or greater than 20 percent of TSB if the TSB is >5.0 mg/dL. 10 Jaundice in newborns is most commonly physiological or due to ABO/Rh hemolytic incompatibility.11 However, if jaundice is associated with dark urine and/or pale stools, it is suggestive of cholestasis. 9 The presence of pale stools is very sensitive for liver disease and even as an isolated finding should prompt immediate investigation. Acholic or white stools imply complete cholestasis with a consequently worse prognosis. 12

We conducted this study to examine the possible etiologies, important history, common clinical presentation and biochemical profile of neonatal cholestatic disorders in Bangladeshi infants attending a tertiary-care hospital.

2. MATERIALS & METHODS

The study was conducted in the department of Pediatric Gastroenterology, Hepatology & Nutrition, Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh from July 2014 to June 2016. With prior written consent, a total of 80 admitted cases of neonatal cholestasis defined by conjugated bilirubin is higher than 1 mg/dl, if the total serum bilirubin is ≤5 mg/dl, or >20% of total serum bilirubin when it is >5 mg/dl, age <1 year, both sexes were enrolled in this study. Patients ≥1 year, jaundice due to other causes were excluded from the study.

Complete blood count with culture and liver function tests (S. bilirubin total, direct, indirect, Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), Gamma-glutamyl transpeptidase (GGT) and Prothrombine time (PT) were done. Urine was tested for non-glucose reducing substances (NGRS) and for bacterial culture. Ultrasonography of hepatobiliary system (fasting & after feed) was done in all cases. Hepatobiliary scintigraphy (HIDA scan) was done from Institute of Nuclear Medicine, Bangabandhu Sheikh Mujib Medical University after administration of phenobarbitone (5 mg/kg/day orally in two divided doses for at least 5 days). At scintigraphy, absence of radioactivity in the small bowel after 24 hours was taken as absent tracer excretion. The biopsy was done with the help of Automated Biopsy Gun (18G×16 cm, PD 22 mm) under local anesthetics (2% lidocaine) and intravenous midazolam (0.1 mg/kg) with 3 hours fasting. The biopsy specimens were immediately fixed in 10% formal-saline. Biopsy was not done in patients with huge ascites, Hemoglobin <10 gm/dl, platelet count <80,000/cu mm, increased prothrombin time (INR >1.3), prolong bleeding and/or clotting time and lack of parental consent.

Biliary atresia were diagnosed on the basis of clinical (full term with good birth weight and persistent pale stool), biochemical (moderate elevation of serum bilirubin, ALT but high elevation of ALP & GGT), ultrasonographic (non-visualized/contracted/small gall bladder), scintigraphc (absent tracer excretion) and liver biopsy by bile ductular proliferation, portal tract fibrosis and bile plugs in portal triads (Fig-4).

To identify the intra-hepatic causes of cholestasis, TORCH screening, thyroid function test and HBsAg were done. If Cytomegalovirus (CMV) IgM positive or IgG >10 fold than normal then urinary CMV PCR was done. Katyotyping was done in one suspected case of Down's syndrome and Galactose-1-phosphate uridylyltransferase (GALT) assay only in NGRS positive cases. Intra-hepatic bile duct paucity was diagnosed by characteristic biopsy finding and PFIC (Type I/II) was diagnosed by low or normal GGT as DNA testing not available here. When all test results were insignificant for any condition, then termed as idiopathic neonatal hepatitis.

A preformed semi structured data collecting form was used as a data collection instrument. Data were collected by the researcher and analyzed by Statistical Package of Social Science (SPSS) version 11.5 programme. Data was analyzed by Z test for proportion testing. A right tailed p-value of <0.05 was considered as significant.

3. RESULTS

All the children were <1 year of age. Out of 80 children, 48 (60%) were intra-hepatic causes & 32 (40%) were extra-hepatic causes (Fig-1). Intra-hepatic causes includes idiopathic neonatal hepatitis (INH) 20 (25%), TORCH infection 19 (23.7%), hypothyroidism 2 (2.5%), galactosemia 2 (2.5%), intrahepatic bile duct paucity 2 (2.5%), down's syndrome with hypothyroidism 1 (1.2%), UTI with sepsis 1 (1.2%) and PFIC 1

*Corresponding author:
Dr. Salahuddin Mahmud
Associate Professor, Dhaka Shishu (Children) Hospital, Dhaka.
Email: drsmbablu@gmail.com
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(1.2%). Biliary atresia 30 (37.5%) and choledochal cyst 2 (2.5%) were extra-hepatic causes.

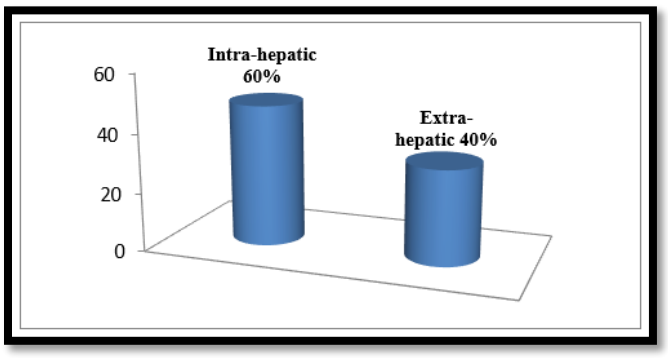

Fig-1: Percentage of Intra-hepatic & Extra-hepatic cholestasis

In intra-hepatic causes, males were pre-dominant (Male:Female=1.6:1) & extra-hepatic causes female were predominant (Female:male=2.2:1) and that was stastistically significant (p=0.002) (Fig-2 & Table-I).

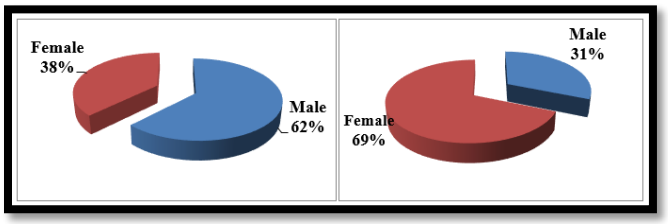

Fig-2: Sexual pre-dominance of intra-hepatic & extra-hepatic cholestasis

In intra-hepatic cases, mean age of onset were 12.4±2.8 days but age of admission were 82.4±29.0 days. Among extra-hepatic cases mean age of onset were 6.8±2.3 days but age of admission were 99.6±52.6 days & that was not statistically significant (Fig-3 & Table-1).

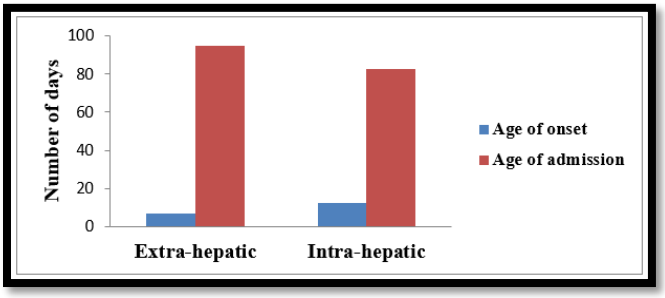

Fig-3: Relationship between age of onset with admission

Intra-hepatic cholestasis were more in Pre-term 32 (66.6%) than term 16 (33.3%) baby. But extra-hepatic cholestasis were more in term 28 (87.5%) than pre-term 4 (12.5%) baby. Intra-hepatic cholestasis were more in pre-term baby & extra-hepatic cholestasis were more in term baby and that was statistically significant (p=0.00) (Table-1).

Table-1: Ante-natal, Natal & Post-natal history of Cholestatic infants:

Maternal	Extra-hepatic cholestasis (n=32)	Intra-hepatic cholestasis (n=48)	P value
Fever	4 (12.5%)	16 (35.3%)	**0.011**
Rash	01 (3.1)	22 (45.8%)	**0.000**
Pruritus	01 (3.1)	6 (12.5%)	0.05
Family (Consanguinity)			
Present	00 (0.0%)	10 (20.8%)	**0.000**
Absent	32 (100%)	38 (79.2%)	
Infants			
Age of onset (days)	6.8±2.3	12.4±2.8	**0.124**
Age of admission (days)	99.6±52.67	82.4±29	**0.117**
Sex			
Male	10 (31.3%)	30 (62.5%)	**0.002**
Female	22 (68.8%)	18 (37.5%)	
Gestational age			
Term	28 (87.5%)	16 (33.3%)	**0.000**
Pre-term	4 (12.5)	32 (66.6%)	

Consanguinity was present in 7 cases of INH, 2 cases of galactosemia and 1 case of intra-hepatic bile duct paucity. So, consanguinity present in 10 (20%) cases of intra-hepatic cholestasis but absent in extra-hepatic cholestasis and that was statistically significant (p=0.000)). Regarding ante-natal history, maternal fever was less in extra-hepatic [4 (12.5%)] cases & more in intra-hepatic [16 (35.3%)] cases and that was statistically significant (p=0.002). Maternal rash was also less

in extra-hepatic [1 (3.1%)] cases but more in intra-hepatic [22 (45.8%)] cases. That was also statistically significant (p=0.000). Maternal pruritus was more in intra-hepatic [6 (12.5%)] cases but less in extra-hepatic 1 (3.1%) cases. That was not statistically significant (p=0.05) (Table-1). Table 2 shows the clinical presentation of the cholestatic infants.

Table-2: Clinical presentation of Cholestatic infants:

Clinical Characteristics	Extra-hepatic cholestasis (n=32)	Intra-hepatic cholestasis (n=48)	P value
Jaundice	32 (100%)	48 (100%)	…….
Dark urine	24 (75%)	29 (60.4%)	0.176
Persistent pale stool	27 (84.3%)	11 (22.9%)	**0.000**
Intermittent pale stool	05 (15.6%)	37 (77.1%)	**0.000**
Hepatomegaly	27 (84.4%)	44 (91.7%)	0.311
Splenomegaly	18 (56.2%)	36 (75%)	0.079
Ascites	06 (18.7%)	07 (14.6%)	0.620

All (both extra-hepatic & intra-hepatic) cholestasis (100%) had history of jaundice and passage of pale stool. Persistent pale stool was more in extra-hepatic [27 (84.3%)] cases & intermittent pale stool was predominant in intra-hepatic [37 (77.1)] cases. Both were statistically significant (P-0.00) (Table-2). Dark urine was present in 24 (75%) cases of extra-hepatic cholestasis and 29 (60.4%) cases of intra-hepatic cholestasis and that was not statistically significant (p=0.176). Hepatomegaly was found in most of the cases of cholestatic infants. Splenomegaly & ascites were found in 18 (56.2%) & 06 (18.7) cases of extra-hepatic cholestasis and 36 (75%) & 07 (14.6%) cases of intra-hepatic cholestasis. These were not statistically significant (Table-2). Table-3 shows the finding of Liver function tests of Cholestatic infants.

Table-3: Liver function tests of Cholestatic infants:

Liver Function Tests	Extra-hepatic cholestasis (n=32)	Intra-hepatic cholestasis (n=48)	P value
S. total bilirubin (mg/dl)	8.26±3.49	12.72±1.49	0.176
Direct bilirubin (mg/dl)	4.40±1.76	3.78±0.73	0.076
ALT (U/L)	160.62±66.18	459.08±59.10	**0.000**
Alkaline phosphatase (U/L)	786.87±122.85	317.50±70.00	**0.000**
GGT (U/L)	886.87±122.85	212.60±42.68	**0.000**
INR	1.18±0.12	1.53±0.28	**0.000**

Serum total & direct bilirubin was high in all types of cholestasis. ALT (459.08±59.10) was much more in intra-hepatic cases and alkaline phosphatase (786.87±122.85) & GGT (886.87±122.85) were much higher in extra-hepatic cases. INR was normal (1.18±0.12) in extra-hepatic cases but slightly raised in intra-hepatic cases (1.53±0.28) (Table-III). All were statistically significant (p=0.00) (Table-3). Hepatobiliary scintigraphy was found positive in 32 (100%) infants of extra-hepatic causes. Because of lack of parental consent, coagulopathy, huge ascites etc. liver biopsy was done only in 40 out of 80 cases (Table-4 & Fig-4).

Table 4: Liver biopsy findings of studied subjects (n=40)

Findings	Diagnosis	Frequency (%)
Ductular proliferation, prominent bile plug, marked portal fibrosis	Biliary atresia	24 (60%)
Disruption of normal liver architecture, chronic inflammatory cell infiltration, giant cell transformation	Idiopathic neonatal hepatitis	14 (35%)
Paucity of interlobular biliary tract	Intra-hepatic bile duct paucity	2 (5%)

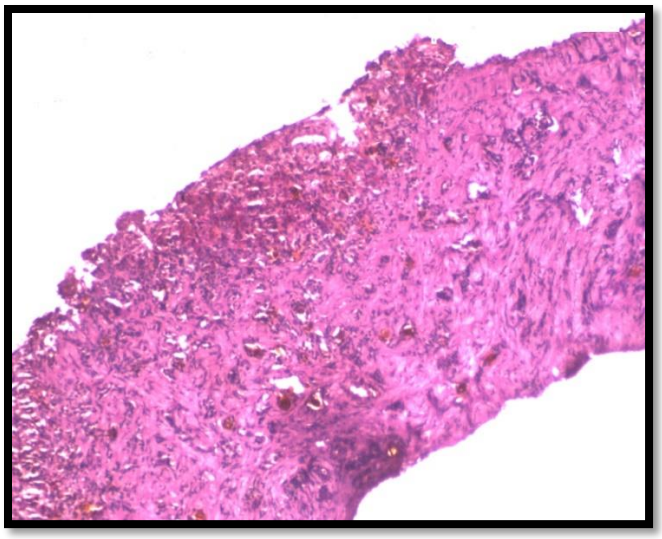

Fig-4: Biliary atresia. Significant ductular proliferation, cholestasis and portal fibrosis. (H&E x100)

Among all children, biliary atresia (BA) 30 (37.5%) were the commonest followed by idiopathic neonatal hepatitis (INH), 20 (25%), TORCH infections 19 (23.7%), 2.5% of choledochal cyst, hypothyroidism, galactosemia, intra-hepatic bile duct paucity each and 1.2% of down's with hypothyroidism, UTI with sepsis & PFIC each of cases (Fig-5).

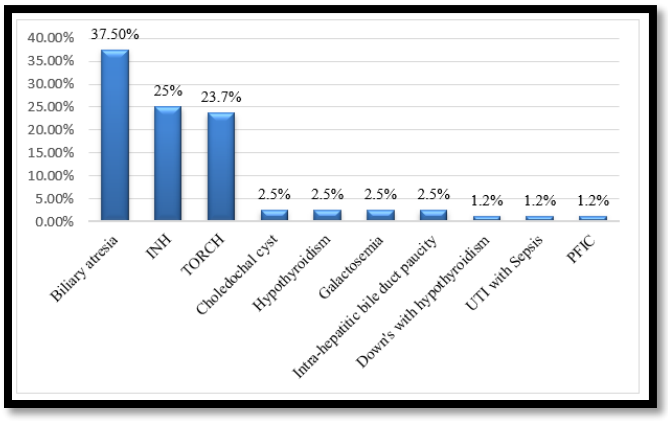

Fig-5: Etiology of neonatal cholestasis

Most of the cases presented as acute hepatitis (BA 51.6%, INH 70.9%, TORCH 45.9% and 100% in choledochal cyst, hypothyroidism, Down's syndrome with hypothyroidism & UTI with sepsis). Galactosemia (100%), intra-hepatic bile duct paucity (100%) and progressive familial intra-hepatic cholestasis (PFIC) (100%) were presented as acute liver failure (ALF) along with INH (22.9%). On the other side, biliary atresia (26.6%), TORCH infection (16.6%) and INH (6.2%) were also presented as chronic liver disease (CLD) (Fig-6).

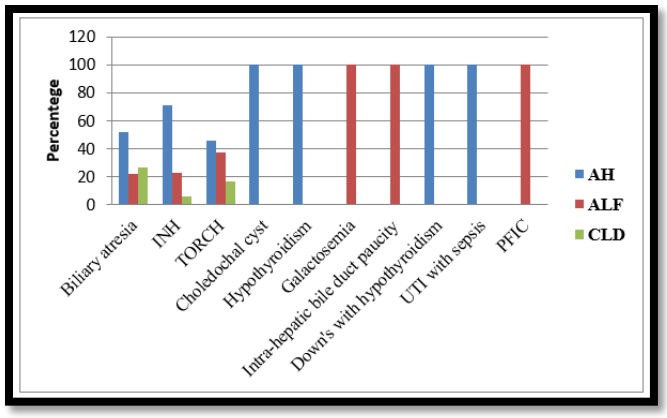

Fig-6: Clinical form of different cholestasis cases

4. DISCUSSION

The causes of cholestasis in young infants are many and early diagnosis and initiation of appropriate therapy is important, because the effects of this disorder are usually very serious.13 Even when treatment is not available or effective, literature shows that infants with progressive liver disease usually benefit from efforts to provide optimal nutritional support and medical management of complications. 14

In the present study mean age of admission was 99.6±52.6 days but mean age of onset was 6.8±2.3 days in extra-hepatic group. In intra-hepatic group, mean age of admission was 82.4±29.1 days but mean age of onset was 12.4±2.8 days. The findings support the fact that delay in referral of biliary atresia (BA) as well as neonatal hepatitis syndrome (NHS) to appropriate centers is still a major problem in Bangladesh. The same fact applies for many parts of South Asia. 13-20 A study in India shown that mean age of admission 120.8±60.5 days in BA and 65.9 ±39.2 days in NHS. 17 Another study in Bangladesh stated a even greater mean age of admission (160.13±60.11 days) with smaller mean age of onset (3.92±2.43 days) in case of BA and a mean age of admission 120.8±60.1 days with a mean age of onset 6.5±4.5 days in neonatal hepatitis group.18 Among all cholestasis, recent studies reported a stated the near similar results on median age of admission (64.2 days in Sri Lanka, 2.9 months and 78 days in India) 13, 15 3.5 months and 3.4 months in Bangladesh)13, 15, 16, 20. In most cases, due to mild nature of jaundice, health-care providers incorrectly diagnose the infants as having 'breast milk jaundice'. 16 Wrong diagnosis, false reassurance by the appearance of pigmented stool, early hospital discharge and parental refusal of referral might play as the key factors for delayed hospital admission. 7 To help reduce the average age for diagnosis of biliary atresia, several groups in Japan and Taiwan have developed pilot programs in which stool color cards are given to mothers of newborns which could be tried in Bangladesh or other countries having similar problems. 20

Biliary atresia had been reported to be more common in female infants 15 and this study also showed similar results. This study showed that females were common in extra-hepatic group (Female:male=2.2:1) and males in intra-hepatic (Male:Female=1.6:1) group which differs from the findings of Hamid et al. who reported a Male predominance of all cholestatic (83% in extra-hepatic & 78% in intra-hepatic) infants or Nahid et al. who stated that male were 10 (52.6%) and rest (47.4%) female in extra-hepatic cases. Among intra-hepatic cases, 22 (66.7%) were male and rest 33.3% were female. 18, 20

In the present study, 28 (87.5%) infants of term and 4 (12.5%) infants of pre-term among extra-hepatic cholestesis. On the other side, 16 (33.3%) infants of term and 32 (66.6%) infants of pre-term in intra-hepatic cholestasis which is similar to the findings of Hamid et al. (Out of 12 patients in biliary atresia, 11 (91.6%) were term and only 1 (8.4%) was pre-term. Among intra-hepatic group, larger number of babies were pre-term 10 (56%) and 8 (44%) out of 18 babies were term).18 Nahid et al. also presented similar findings (Pre-term babies were more common in intra-hepatic 16 (41%) cases but absent in extra-hepatic cases. Term babies presents an opposite result)20. However, all these studies are based on very small sample sizes and further studies are required to explore the nature of complications and to understand the problem.

In the present study, history of consanguinity of marriage was present in 10 (20.8%) cases of intra-hepatic cholestasis but absent in extra-hepatic cholestasis which is similar as the findings of Nahid et al. (Consanguineous marriage was present in intra-hepatic 10 (16.7%) cases but absent in extra-hepatic cases.). 20 This is an important findings because a positive family history or history of consanguinity is very important for galactosemia, tyrosinemia, PFIC and Alagille syndrome.

Regarding ante-natal history, maternal fever & rash were less in extra-hepatic [4 (12.5%) & 1 (3.1%)] cases and more in intra-hepatic [16 (35.3%) & 22 (45.8%)] cases. Maternal pruritus was more in intra-hepatic [6 (12.5%)] cases but less in extra-hepatic [1 (3.1%)] cases. Hamid et al. also reported the near similar result (Maternal fever & rash were less in extra-hepatic [2 (16.7%) & 0 (0.00)] cases and more in intra-hepatic 5 (27.8%) & 2 (11.1%) cases) 18. Maternal pruritus were much less in both type of cholestasis cases. These were not statistically insignificant (p=0.79, p=0.65 & p=0.83). Congenital infections are usually originate from mother's womb. So, maternal history of fever & rash are closely related to TORCH infections. Maternal history of pruritus may suggest PFIC or Alagille syndrome.

Jaundice and pale stool were present in all 80 (100%) cases of cholestasis. Persistent pale stool was more in extra-hepatic [27 (84.3%)] cases & intermittent pale stool was predominant in intra-hepatic [37 (77.1)] cases. Nahid et al. [extra-hepatic 21 (100%) & intra-hepatic 34 (88%)] and Hamid et al. [extra-hepatic 11 (91.7%) & intra-hepatic 15 (83.3%)] also described similar results. 18, 20

Hepatomegaly was found in almost all cases [(extra-hepatic 27 (84.4%) & intra-hepatic 44 (91.7%)] of cholestasis. Karim et al. [(extra-hepatic 14 (87.5%) & intra-hepatic 32 (86.5%)], Nahid et al. [(extra-hepatic 21 (100%) & intra-hepatic 39 (100%)] and Luthufdeen et al. [50 (83.3%)] also observed the similar result16, 20, 15. Splenomegaly was was not significantly associated with type of cholestasis but Nahid et al. stated a statistically significant (p=0.002) association between the two. Ascites was not significantly associated with type of cholestasis in the present study. Recent earlier studies on Bangladesh by Hamid et al. and Nahid et al. also showed a similar result.18, 20

It is difficult to differentiate BA from other causes of cholestasis by biochemical tests. In the present study, Serum total & direct bilirubin was high in all types of cholestasis but that was not statistically significant, however Nahid et al. observed the significant results in both total (p=0.004) & direct (p=0.03) bilirubin aspects.18 ALT was much more in intra-hepatic (459.08±59.10 U/L) than extra-hepatic (160.62±66.18) cases and alkaline phosphatase & GGT were much higher in extra-hepatic (786.87±122.85 & 886.87±122.85 U/L) than intra-hepatic (317.50±70.00 & 212.60±42.68) cases. All were statistically significant (p=0.00). Nahid et al. 20 observed that ALT was significantly higher in intra-hepatic (192.82±109.43 U/L) cases than extra-hepatic (109.31±56.82 U/L). GGT were significantly higher in extra-hepatic (695.47±535.17 U/L) cases than intra-hepatic (516.42±628.79 U/L). On the other side, no significant (p=0.993) difference was observed by Hamid et al. (ALT in extra-hepatic cases were 129.75±71.02 U/L and intra-hepatic cases were 130.0±78.16 U/L)18. Karim et al. also observed the same phenomena.16 No significant difference was observed in ALT [extra-hepatic 219.1 (201.1) & intra-hepatic 294.4 (222.7) U/L] and alkaline phosphatase [extra-hepatic 767.1 (389.5) & intra-hepatic 618.2 (549.9) U/L]. INR was normal (1.18±0.12) in extra-hepatic cases but slightly raised in intra-hepatic cases (1.53±0.28). Karim et al. 16 was found the same results. INR 1.3 (0.3) in extra-hepatic cases and 1.8 (0.8) in intra-hepatic cases. Nahid et al. 20 observed INR raised in both extra-hepatic (1.55±63) and intra-hepatic (2.05± 1.82) cases. In every cases of cholestasis, early diagnosis is very important for best outcome. In case of BA, KASAI (hepatoportoenterostomy) should be done within 2-3 months of age. For the prevention of acute liver failure, chronic liver disease or cirrhosis in every cases of cholestasis, early diagnosis & prompt treatment is very important for saving of life. High ALT may be an early important indicator for intra-hepatic cases and much raised GGT is a crucial indicator for extra-hepatic cases of cholestasis.

Hepatobiliary scintigraphy was found positive in 32 (100%) infants of extra-hepatic causes. Same results were observed by Nahid et al. 20 In all extra-hepatic [19 (100%) cases scintigraphy was found positive.

Limitations of study:

The main limitation of the present study is that was a single-centre study with a limited sample size.

5. CONCLUSIONS

The typical presenting feature of neonatal liver disease in an infant is Cholestatic jaundice and it is commonly clinically confused with the more common prolonged unconjugated hyperbilirubinemia. A careful history, thorough physical examination, and fractionation of serum bilirubin are recommended in any infant with jaundice seen after 2 weeks of life especially with dark urine, pale stool & hepatomegaly. Though jaundice developed early, most cases at Dhaka Shishu Hospital in Bangladesh were presented late and this delayed diagnosis of neonatal cholestasis creates difficulties for successful treatment. Early detection of cholestasis and subsequent prompt diagnostic evaluation by a pediatric hepatologist is essential for successful treatment and optimal prognosis.

6. RECOMMENDATIONS

Hence the future challenges to deal with neonatal cholestasis in Bangladesh are manifold. Firstly, health care providers need to be aware of an infant with prolonged cholestatic jaundice and pale stools. For early detection, serial examination of stool with stool color card is crucial. Secondly, infants suspected of having BA should be managed in a centre with appropriate medical and surgical expertise. Finally, liver transplantation service in Bangladesh should be established so that more children with end stage liver failure can receive life-saving surgery.

7. ACKNOWLEDGMENTS

None.

8. CONFLICTS OF INTEREST

The authors do not declare any conflict of interest in relation to this article.

9. FUNDING

None.

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