Original Article

Spectrum of Causes of Cholestatic Jaundice in Neonates and Infants

Causes of Cholestatic Jaundice

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ABSTRACT

Objective: To determine the causes of Cholestatic jaundice in infants and children.
Study Design: Analytical study.
Place and Duration of Study: This study was conducted at the Department of Pediatrics Naseer Teaching Hospital Peshawar from January 2015 to December 2018.
Materials and Methods: A total of 25 patients presented with Cholestatic jaundice to the department of pediatrics were included in the study. All patients of both gender presented with jaundice in infancy. Data collected from all patients was put on a predesigned proforma. Data was analyzed on SPSS version 14.
Results: A total of 25 patients diagnosed with Cholestatic jaundice were included in the study. Out of 25 patients 15 (60%) were male and 10(40%) were female. Biliary atresia was the most common cause present in 7(28%) cases, followed by galactosemia and progressive familial intrahepatic cholestasis (PFIC) which were 4(16%) cases each. Cytomegalovirus (CMV) infection was found in 3(12%) cases. Alagille syndrome and choledochal cyst were diagnosed in 2(8%) cases each. Caroli disease, Neonatal sepsis and Neonatal hemochromatosis was present in 1(4%) case each.
Conclusion: From this study we concluded that Cholestatic jaundice is a common problem in infants and has diverse causes both medical and surgical. Timely diagnosis is important for the prognosis of disease.
Key Words: Cholestatic jaundice. Direct bilirubin. Infants.

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INTRODUCTION

Cholestatic jaundice is defined as reduced bile formation or excretion resulting in retention of biliary substances within the liver which should be normally excreted into the intestinal lumen in bile [1]. Incidence of Cholestatic jaundice in infants is approximately 1 in 2500 to 5000 live births with different causes[2]. Neonatal jaundice can be due to conjugated or unconjugated hyperbilirubenemia, but conjugated hyperbilirubenemia is always pathological due to cholestasis[3]. Cholestatic jaundice usually presented with prolong jaundice, pale color stool, dark color urineand sometime bleeding disorder [4].

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The first step in diagnosing cholestasis is to find out intrahepatic or extra hepatic cause, and early diagnosis is important for prognosis in some condition as in biliary atresia[5].
Cholestatic jaundice is usually due to metabolic and canalicular dysfunction of different etiologies such as TORCH infection (toxoplasmosis, herpes simplex, cytomegalovirus, Rubella) idiopathic neonatal hepatitis, neonatal hemochromatosis, galactosemia, tyrosinemia, cystic fibrosis, alpha 1-antitrypsin deficiency, hemophagocytic lympho-histiocytosis (HLH)and extra hepatic diseases (biliary atresia, choledochal cyst gall stones)[3] [6].Detail history taking is important for diagnosis and it include details of neonatal screening, any medication, passage of first bowel, onset of jaundice, color of stool and urine, consanguanity, pruritus and previous history of miscarriages and other siblings[7]. Hepatomegaly, splenomegaly and acholia (pale color stool) must be observed as these findings indicate significant cholestasis [8].
Initial approach for diagnosing cholestasis is to do conjugated bilirubin along with aspartate aminotransferase (AST) alanine aminotransferase (ALT) and gamma glutamyl transferase (GTT) level which are variably elevated. Abnormal Synthetic liver functions like prolonged prothrombin time (PT), raised serum ammonia, low albumin level and hypoglycemia shows severe hepatic dysfunction needs urgent referral

to tertiary care hospital. Urinalysis for reducing substances is important to rule out galactosemia [9].

MATERIALS AND METHODS

The study was carried out in the department of pediatrics Naseer Teaching Hospital, Peshawar from January 2015 to December 2018. Patients included in this study were from ward, nursery and OPD of pediatric department. A total of 25 patients were included in the study. All cases included in the study presented with Cholestatic jaundice in infancy.

The data was recorded on a predesigned proforma including detail history, clinical examination and investigations. All cases included in the study were having Cholestatic jaundice. Investigations have been done to find out the causes by performing Complete blood counts (CBC), Liver function tests (LFTS), conjugated and unconjugated bilirubin levels, serum albumin, prothrombin time(PT), urine for reducing substances, serum ferritin level, TORCH screening test, abdominal ultrasonography, echocardiography, HIDA scan and liver biopsy. The study had necessary approval from the Institutional ethical committee and informed consent was taken from the parents/guardian of the subject. The data was transferred and analyzed using statistical package for social sciences (SPSS) version 14. The results were presented in the form of percentages, chi-square test was applied for comparison of proportions with significance of p value less than 0.05.

RESULTS

A total of 25 patients diagnosed with Cholestatic jaundice were included in the study. Out of 25 patients15 (60%) were male and 10(40%) were female.

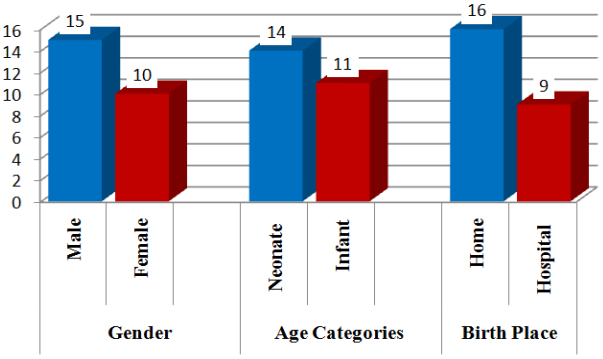

Figure No.1: General Characteristics of Neonates and Infants

Similarly 14(56%) were neonate (< 28 days) and 11 (44%) infants (>28 days) where, minimum age of presentation with jaundice was 21 days and maximum age of 3 months with average of 37.44 days. Biliary atresia was the most common cause present in 7(28%) cases, followed by galactosemia and progressive familial intrahepatic cholestasis (PFIC) which were 4(16%) cases each. Cytomegalovirus (CMV) infection was found in 3(12%) cases. Alagille syndrome and choledochal cyst were diagnosed in 2(8%) cases each. Caroli disease, Neonatal sepsis and Neonatal hemochromatosis was present in 1(4%) case each (table 1).

Table No.1: Causes of Cholestatic jaundice in neonates and infants

Diseases	No of cases	percentages
Biliary atresia	07	28%
Galactosemia	04	16%
PFIC	04	16%
CMV infection	03	12%
Allagille syndrome	02	8%
Choledochal cyst	02	8%
Caroli disease	01	4%
Neonatal sepsis	01	4%
Neonatal hemochromatosis	01	4%

DISCUSSION

Many disorders in neonates and infants can present with Cholestatic jaundice and early diagnosis and treatment is very important for prognosis. Biliary atresia is one the most common cause of Cholestatic jaundice as reported in our study which is 28%. Hoerning et al study performed in a tertiary care center also revealed biliary atresia the most common cause in 40% of cases [10]. Average age of patients with biliary atresia was 50 days. All patients were referred to specialized unit for surgical management. Galactosemia was the 2nd most common cause found in 4(16%) cases. Galactosemia is one of the most common metabolic disease causing Cholestatic jaundice in infants as found in other studies like Gottesman et al which revealed galactosemia in 36.49% of metabolic cases [11]. All patients of galactosemia were put on lactose free milk with significant improvement of jaundice. PFIC is also the 2nd most common cause of cholestasis in our study found in 16% of cases.Many studies had near same results as revealed in Kamath BM et al, Fischler B et al and Ruth ND et al found PFIC in 11.75%, 12.9% and 16% respectively [12, 13 14]. Cytomegalovirus (CMV) infection is present in 3(12%) cases, which were treated with gancyclovir for 6 weeks with significant improvement. CMV infection as a cause of cholestasis are different in other studies ranges from 2 to 7% in some studies and up to 34%in other studies [15, 16]. This high frequency of CMV hepatitis may be due to high incidence in some countries. Alagille syndrome was present in 2 cases which contributes to 8% of all cases. Both patients were having dysmorphic features (triangular face, broad face, hypertelorism, deep set eyes)pulmonary stenosis and Cholestatic jaundice. Gottesman et al found Alagille syndrome in 6% of cases close to our results [11]. Choledochal cyst was found in 2 cases (8%).Hitch et al and bazlul et al found choledochal cyst in 3.5% and 6.5% of cases

respectively which are nearly to our findings [17, 18]. Neonatal sepsis, Caroli disease and neonatal hemochromatosis were present in 01 case each contributing 4% in each case. Rafeey et al found neonatal infection in 3.28% of cases, while Ipek et al found in 9.78% of cases. This high incidence may be due to variation of neonatal sepsis incidence in different areas[19,20]. One patient of neonatal hemochromatosis was admitted with hepatic failure and was died after 3 days of admission.

CONCLUSION

From this study we concluded that Cholestatic jaundice is a common problem in infants and has diverse medical and surgical causes. Timely diagnosis is important for the prognosis of disease.

Recommendation: It has been recommended that infants presented with persistent jaundice must be investigated for cholestasis as many causes are treatableif diagnosed timely.

Author's Contribution:

Concept & Design of Study:	Rifayat Ullah Afridi
Drafting:	Irfan Khan
Data Analysis:	Sher Bahadur
Revisiting Critically:	Shezad Najeeb and Irum Naz
Final Approval of version:	Shadman and Kifyat Ullah Afridi

Conflict of Interest: The study has no conflict of interest to declare by any author.

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