PREVALENCE OF CHOLESTATIC JAUNDICE IN CHILDREN – A STUDY IN HOSPITALISED CHILDREN

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ABSTRACT

INTRODUCTION

A study conducted in 58 cases of children who were admitted and evaluated over a period of 2 years October 2013 to November 2015 to find out the prevalence of cholestatic jaundice in children. This study conducted in KGH, AMC, Visakhapatnam.

OBSERVATION

Out of the total cases studied (58) 12 cases were Biliary atresia (20.68%) and 24 cases were hepatitis (41.37%). The various sub groups of hepatitis were hepatitis 'A' 'B', other infections 14(24.13%), neonatal hepatitis 5(8.62%), Malarial hepatopathy 2(3.44%), enteric fever 3(5.17%). Sickle hepatopathy 3(5.17%), IHBA 1(1.72%), hypothyroidism 6(10.34%), Down syndrome 3(5.17%), Gall stone disease 6(10.34%), Drug induced 3(5.17%). Out of 58 cases 0-3 months' age were 28(48.27%), females outnumbered males in many conditions especially in gallstones and drug induced cholestatic jaundice.

AIMS

To study the incidence and etiological causes cholestatic Jaundice in pediatric patients between the age group 0 to 12 years during the period November 2013 to November 2015.

MATERIAL AND METHODS

The present study was conducted in the department of paediatrics, Andhra Medical College, Visakhapatnam between January 2013 to November 2015. During this period 25 cases of Cholestatic Jaundice were taken up for study. Cases from both the sexes ranging from birth to 12 years were included in the present study.

CONCLUSION

The study utilisation of the newly developed "AIIMS clinical scoring index" to differentiate the two main groups of cholestatic disorders, i.e., Biliary atresia and hepatitis and compared the score with the scan patterns of HIDA scan patterns. Finally the present study was analysed and the results compared with the results of other similar studies reported in literature.

KEYWORDS

Biliary Atresia, Hepatitis, Malarial Hepatopathy, Gall Stones, Down Syndrome, IHBA.

HOW TO CITE THIS ARTICLE: Satyakumari K, Devi RS, Rao KS. Prevalence of cholestatic jaundice in children – a study in hospitalised children. J. Evid. Based Med. Healthc. 2016; 3(18), 742-746. DOI: 10.18410/jebmh/2016/168

INTRODUCTION: The term cholestasis was coined by Popper and denotes the physiological state of prolonged elevation of serum levels of conjugated bilirubin. The older term obstructive liver disease of infancy has given way to the terms neonatal cholestasis and cholestasis jaundice of infancy because these terms acknowledge that the pathology may be functional at the level of hepatocyte instead of mechanical obstruction.

Before 1968 most of the infants that have been diagnosed as having cholestasis disorder due to obstruction died before one year age.

Submission 28-01-2016, Peer Review 12-02-2016,
Acceptance 23-02-2016, Published 03-03-2016.
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DOI: 10.18410/jebmh/2016/168

The situation changed dramatically following the report of Kasai journal of paediatric surgery in 1968; describing a surgical procedure named after him allowing some hope to affected children.

The other group with normal stools, a patent biliary tree grouped as "neonatal hepatitis" progressed to end stage cirrhosis. But with the development of newer diagnostic techniques, improvements in nutritional monitoring, availability of unique nutritional solutions and Liver transplantation have all added new dimensions to early diagnosis and management of neonatal hepatitis patients.

Thus with the hope of cure and management of cholestasis disorders began, efforts were made at early diagnosis of these disorders. Thus many biliary imaging techniques like; Oral Cholecystography, IV Cholangiography, US Scan, CT scan, Trans hepatic cholangiography, ERCP and cholescintigraphy were developed.

MATERIAL AND METHODS: The present study was conducted in the department of paediatrics, Andhra Medical College, Visakhapatnam between January 2013 to November 2015. During this period 25 cases of Cholestasis Jaundice were taken up for study. Cases from both the sexes ranging from birth to 12 years were included in the present study.

Criteria for Selection of Cases: Cases of cholestatic Jaundice (i.e. direct reacting serum bilirubin greater than absolute value of 1.5 mg/d L or greater than 20% of the total serum bilirubin value) were selected for the present study.

Age group of the patients were from birth to 12 years.

The cases which could stay in the hospital for a minimum period of 15 days for complete work up and combined administration of phenobarbitone 5 days prior to subjecting them for HIDA scan were selected.

After admitting the cases detailed case history was elicited and a complete clinical examination was done. The "AIIMS clinical scoring index" was calculated on every patient.

Aims of the present study are: To study the incidence and etiological causes cholestasis Jaundice in paediatric patients between the age group 0 to 12 years during the period November, 2013 to November 2015.

To subject the cases of cholestasis Jaundice for routine diagnostic investigations.

To study the Hepatobiliary scintigraphic (HIDA) patterns in cholestasis Jaundice

To study the newly developed "AIIMS Clinical Scoring Index" as a simple bedside test to differentiate Hepatitis from biliary atresia.

RESULTS:

To compare the results of the "AIIMS Clinical Scoring Index" with results HIDA scan.

To compare the results of the present study with other similar studies done elsewhere after analysis.

Sl.No.		Diagnosis	No. of Cases	Percentage of cases
1		Biliary Atresia	12	20.68%
2		Hepatitis (24) 41.37%	24	41.37%
	A	hepatitis 'A'B,other infectious hepatitis	14	24.13%
	B	neonatal hepatitis	5	8.62%
	C	malarial hepatopathy	2	3.44%
	D	enteric fever	3	5.17%
3		Sickle hepato pathy	3	5.i7%
4		Intra hepatic biliary atresia	1	1.72%
5		Hypo thyroidism	6	10.34%
6		Downs syndrome	3	5.17%
7		Gall stone disease	6	10.34%
8		Drug induced	3	5.17%

Slno	Age	Male		Female		Total	
		N	%	N	%	N	%
1	0-1year	10	17%	18	31%	28	48%
2	1-4years	3	5%	5	9%	8	14%
3	4-7years	4	7%	4	7%	8	14%
4	7-10years	3	5%	1	2%	4	7%
5	10-13years	3	5%	7	12%	10	17%

p-value; 0.0884(Male babies), P-Value; 0.000069 (Female babies).

The total number of cases between 0-1 year were 28(48%) out of which males were 19(17%) and females were 18(31%). The number of cases between 1-4 years were 8(14%) out of which males were 3(3%) and females were 5(9%). The total number of cases between 4-7 years were 8(14%) cases. The total number of cases between 7-10 years were 4(7%) cases out of which males were 3(5%), females were 1(2%). The total number of cases between 10-13 years were 10(17%) out of which males were 3(5%), females were 7(12%).

In a study of Bhave and Bavdekar[1] in 1996, it was found that infantile cholestasis account for 30% of hepatobiliary disorders seen in children. Yachha, et al. showed that the age of onset of jaundice in BA was 3-12 days and that of hepatocellular causes was 16-24 days.

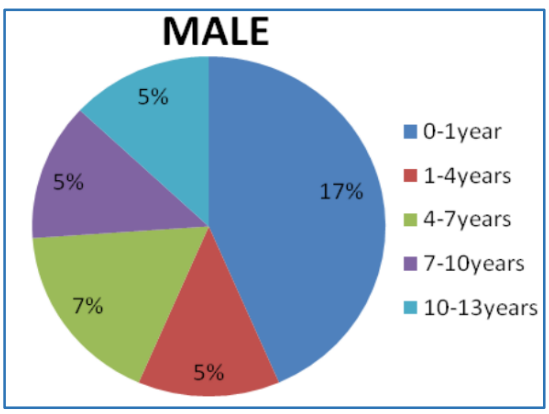

Fig. 1

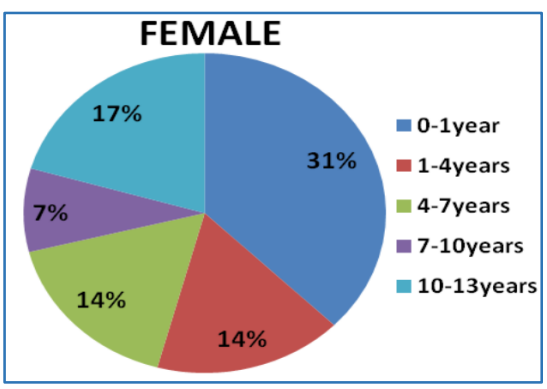

Fig. 2

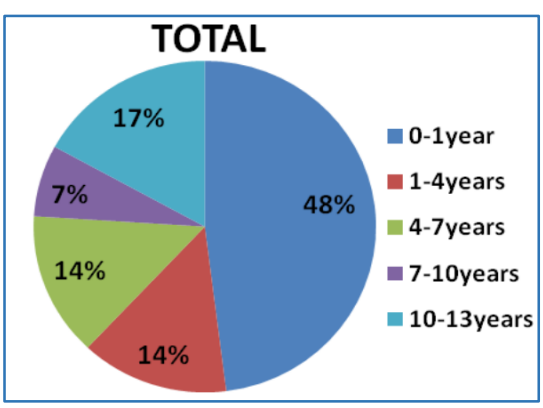

Fig. 3

Sl. No.	Maternal History	No. of cases	Percentage
1.	Maternal febrile illness	16	27.58
2.	Maternal Exanthema	4	6.8
3.	Advanced Maternal age more than 35 years	20	34.48
4	Nil significant	18	31.03
Maternal and antenatal history in the present study			

P-Value 0.0135

Sl. No.	Findings	Male		Female	
		N	%	N	%
1.	Jaundice	23	39.6%	35	60.34%
2.	PEM	18	31.03%	26	44.82%
3.	Anemia	10	17.24	17	29.31%
4.	Edema	2	5.17%	5	8.62%
5.	Dysmorphic features	2	3.44	1	1.72%
6.	Ocular abnormalities	1	1.72%	1	1.72%
7.	Delayed milestones	2	3.44	3	5.17%
General examination findings					

P-Value 0.00001 (Male babies).
P-Value 0.00001(Female babies).

OBSERVATIONS: Jaundice was observed in all the male and female patients, Protein energy malnutrition was found in 18 cases (31.03%) in males and 26 cases (44.82%) in females. Anaemia was found in 17 cases (29.31%) In females and 10 cases (17.24%) in males* Oedema was noticed in 5(8.62%) in females and 4 cases (6.89%) in males, Dysmorphic features were noted in 1 case (1.72%) in females and 2 cases (3.44%) in males. Delayed milestones were noted in 2 cases (3.44%) in females and 2 cases (3.44%) in males.

Sl. No.	Stool Colour	Biliary Atresia	Hepatitis
1.	Persistently Acholic Stools	(10)83.33%	(4)16.66%
2.	Occasional Acholic Stools	(2)16.66%	(12)50%
3.	Persistently Normal	(0)0%	(8)33.33%
Stool colour			

Stool Colour: In biliary atresia persistently acholic stools were noted in 10 cases (83.33%), occasional acholic stools were found in 2 case (16.66%) and persistently normal colour stools were found in none (0%). In hepatitis occasional acholic stools were found in 12 cases (50%), persistently normal coloured stools were found in 8 cases (33.33%) and persistently acholic, stool was found in 4 cases (16.66%). Presence of stool pigment excluded extrahepatic biliary atresia, while its absence was suggestive of extrahepatic, Biliary atresia.

Sl. No.	Report	Males		Females		Total	
		N	%	N	%	N	%
1.	Biliary Atresia	6	10.34%	6	10.34%	12	20.68%
2.	Hepatitis Picture	14	24.13%	10	17.24%	24	41.37%
Hida scan reports							

Observations: Biliary atresia had an equal sex incidence with males 6 cases (10.34%) and females 6 cases (10.34%). Total biliary atresia cases were 20.68%. Neonatal hepatitis picture on HIDA scan was seen 24 cases (41.37%) with a sex incidence of males 14. (24.13%) and females 10 cases (17.24%).

Sl. No.	Criteria	Score
1	**Age of the Patient:** <6 weeks >6 weeks	 2 1
2	**Jaundice:** Fluctuating (mild to moderate] Severe (more than 8 mg%)	 2 1
3	**Stool:** Normal to light yellow Mostly clay coloured	2 1
4	**Urine:** Normal or light yellow Mostly Dark yellow	 2 1
5	**Liver:** Soft and smooth Firm with leafy edge	 4 1
AIIMS clinical scoring index		

Score:
More than 10: Hepatitis.
Less than 10: Biliary Atresia, and other conditions.

ACS showed a sensitivity of 91.5%, a specificity of 76.3%, positive predictive value of 89.2%, negative predictive value of 80.5% and overall diagnostic accuracy of 86.6%. ACS is reliable to distinguish NH from EHBA at bed side.

After obtaining the parents' consent all the cases were subjected to routine laboratory investigations, All the cases were subjected to HIDA SCAN procedure. All the cases were subjected to a combined administration of phenobarbitone and Betamethasone for a period of 5 days before subjecting the cases to HIDA scan.

Rationale for the Administration of Pre Scan Phenobarbitone: Phenobarbitone is a choleretic agent which increases the bile flow and thus reduces the false positive diagnosis of Biliary atresia.

Rationale for Administration of Pre Scan Betamethasone: Steroids are known cholerectic agents which stimulate bile flow.

They increase bile volume.

They decrease bile viscosity by Na, K. ATPase and water retaining property.

Steroids also act as anti-inflammatory agents to reduce oedema and collagen deposition.

Steroids help in stabilization of RBC cell wall thus reducing their break down and bilirubin load.

Amount of Drugs Administered:

Phenobarbitone: 5mg/kg/day orally, for 5 days.

Betamethasone: Equivalent to 2.2 mg of prednisolone per kg.per day for 5 days.

Preparation of Patient for HIDA SCAN: The patient is kept fasting for 4-6 hours. Because milk and food stimulates release of cholecystokinin (CCK) causing gall bladder to contract not allowing dye to enter the gall bladder.

Method of Obtaining Scan Films: Imaging is done by a large field of view gamma camera with a parallel hole low energy collimator. The patent is so positioned so that liver occupies right upper portion of field of view. Images are taken for 500,000 counts each every 5 minutes for first 30 minutes and every 10 minutes for next 30 minutes. Additional images are taken as needed.

Features of a Normal Scan: Early images show liver, cardiac and vascular activity that fades as hepatic uptake increases. Gall bladder is not visualized.

Gall bladder and common duct/bowel activity is seen by 60 minutes. Gall bladder uptake should precede bowel visualization.

Minimal renal activity may occasionally be seen.

Features of Scan in Neonatal Hepatitis: In neonatal hepatitis due to hepatocellular inflammation and oedema, uptake of radio isotope is diminished resulting in more back ground activity when compared to hepatic activity and greater renal excretion. However once taken up by liver there is quick excretion of isotope into the intestines as there is no mechanical block in the hepatobiliary passages. However severe hepatitis may cause oedema to compress hepatobiliary channels thus delaying excretion. A 24 hours' film is taken to differentiate hepatitis from biliary atresia.

Features of Scan in Biliary Atresia: In biliary atresia because the hepatobiliary channels are obliterated, there is no excretion of radio isotope into the intestines even after 24 hours in spite of good hepatic uptake. Thus 24 hour films are taken before labelling the case as biliary atresia.

OBSERVATIONS: The sex incidence in extra hepatic biliary atresia was males 5(41.66%) and females 7(58.33%). The sex incidence in intra hepatic biliary atresia was females 1(100%). The sex distribution of hepatitis was male 6(42.85%), female 8(57.14%). Neonatal hepatitis males 4(80%), female 1(25%). Malarial hepatopathy was in male 1(50%), females 1(50%). Enteric fever hepatopathy was in males 2(66.66%), females 1(33.33%), Sickle hepatopathy was in males 2(75%) females 1% (25%), and Down's syndrome in 3(100%) males only, hypothyroidism males 3(50%), in females 3(50%), Gall stone disease 2(33.33%) in males, 4(66.66%) in females, Drug induced in males 1(33.33%) and 2(66.66%) in females.

DISCUSSION AND COMPARISONS: The study of cholestasis jaundice in paediatric age group has not widely reported. The following studies were taken up for comparison.

Early Onset Conjugated Hyperbilirubinemia in newborn Infants. This study was conducted by Filiz Ticker et[2] al was published in Indian journal of paediatrics[3], May, 2006, volume 73. 42 babies were taken up for this study.

Diagnostic Evaluation of Cholestasis in Infants and Young Children in Alexandria. This study was conducted by A Abdel Moniem Deghady, M Abdel-Kader was published in the internet journal of paediatrics and neonatology 2005 volume 6 November [4]1. Cases of cholestasis jaundice belonging to both sex was taken up for study.

Evaluation of Cholestatic Jaundice in Young Infants. This study was conducted by John Matthai[5] and Sarah Paul was published in Indian paediatrics 2001; 38:893-898. 36 infants were taken up for this study belonging to both sexes

Neonatal Hepatic Cholestasis with Particular Regard, For the Use of Radio Isotopes in Its Diagnosis. This is study was conducted by MUSSA[6] et al and was published in Minerva--Pediatrics 1991 May; n3 (5)I357-70. 54 cases of cholestasis jaundice belonging to both sexes were taken up for study.

Cholestatic Disorders of Infancy-Aetiology and Outcome: T All India Institute of Medical Sciences, New Delhi: Study involving 35 cases of cholestasis jaundice during 1991, 1992 and was published in recent advances in paediatrics volume-3.

This study was done by Motal[2] et al during a 10-year period and was published in journal of-Tropical Paediatrics. 1990 Oct.; 36(5):218~22 145 cases of cholestasis jaundice of both sexes were taken up for study.

Sl.No.		Diagnosis	No. of Cases	Percentage of cases
1		Biliary Atresia	12	20.68%
2		Hepatitis (24) 41.37%	24	41.37%
	A	hepatitis 'A'B,other infectious hepatitis	14	24.13%
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7		Gall stone disease	6	10.34%
8		Drug induced	3	5.17%

As shown in the above data maximum number of cases (41.37%) of all cholestatic jaundice cases belong to the category of Neonatal hepatitis syndrome with its sub groups.

Where nearly 20.68% belong to the category of biliary atresia and its sub groups. 1.72% are due to intra hepatic biliary atresia. 5.17% of cases are due to sickle hepatopathy.

Malarial hepatopathy occupies 3.44%, Hepatitis 'A' 'B' 24.13%, Enteric fever 5.17%, Downs syndrome 5.17%, Hypothyroidism 10.34%.

The other important diseases within the hepatitis group for which aetiology could be made out were HAV infection, Malaria, enteric fever, hypothyroidism, and Down syndrome.

Sl. No.	Study	Males	Females
1	Present	39.6%	60.4%
2	A abdelmoniemdegadhy[4]	48.5%	51.5%
3	John mattai	55.5%	44.5%
4	MUSSA etal	63%	37%
5	Motala etal	52%	48%
6	AIIMS Study	70%	30%
Comparasionof sex incidence among the 6 studies			

The female preponderance in biliary atresia agrees well with the figures reported in standard text books.

CONCLUSION: The study was conducted on 58 cases of cholestasis jaundice between age groups of 0-12 years: This study also utilized the newly developed "AIIMS clinical scoring index" to differentiate the two main groups of cholestasis disorder's, i.e., Biliary atresia and hepatitis and compared the score with the scan patterns of HIDA scan patterns. Finally the present study was analysed and the results compared with the results of other similar studies reported in literature.

Etiological analysis revealed that out of 58 cases of cholestasis jaundice, 39.6% were diagnosed as biliary atresia using HIDA scan as end point. This figure compares well with other studies which reported 24% Filiz Ticker[2] et al, 24% A Abdel Moniem Degadhy[7] et al, 19% John Matthai[8] et al, 65% AI IMS study, 24% IN Mussa[6] et al, and 32% in Motala et al[5].

1. 41.37% of the cases were diagnosed to be hepatitis.
2. 1 case of intra hepatic bile duct atresia were identified.

The age incidence showed that vast majority of the cases belonged to the age groups 0-4 years (62.06%).The mean age at presentation was 0-1 year.

The sex incidence showed increased female preponderance in the whole group since increasing prevalence of other factors including social factors like Gender discrimination increasing usage of abortifacients to terminate the pregnancy by unethical, unlawful revealing of sex, and hepatitis groups. Whereas equal sex incidence was noted in the biliary atresia group. The sex incidence in other studies showed a female preponderance in biliary atresia group.

Significant and abnormal maternal and antenatal histories obtained with significant P- value of 0.013. This underscores the importance of adverse antenatal and perinatal factors in the etiopathogenesis of cholestatic disorders. Positive familiar incidence was noted in 40% of all cases of hepatitis group while no such history was forth coming in any case of biliary atresia. This confirms the familial nature of hepatitis presenting as cholestasis. The most common presenting features were jaundice, PEM, refusal of feeds and hepatosplenomegaly.

Of the routine investigations visual stool examination was found to be nearly equal in reliability to radio HIDA scanning with insignificant the P-value 0.499, this might be lab error. AIIMS clinical scoring index 5 was found to be a highly reliable and simplest bed side test to differentiate Biliary atresia from Hepatitis. Majority are either Low or middle income groups indicating that malnutrition, overcrowding increased infections, poor antenatal care all contribute to increased incidence of cholestatic jaundice especially hepatitis group.

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