ORIGINAL ARTICLE

Characteristics of Malaysian Infants with Biliary Atresia and Neonatal Hepatitis

S Karnameedi, MRCP, CT Lim, FRCP, Department of Paediatrics, Faculty of Medicine, University Malaya, 50603 Kuala Lumpur

Summary

Cholestatic disorders of infancy (viz neonatal hepatitis and biliary atresia) have not been well studied in Malaysia. In a retrospective study in the Department of Paediatrics, University Hospital, Kuala Lumpur from January 1982 through December 1991, a total of ninety-three infants with such conditions were identified: 35 (38%) had biliary atresia, 58 (62%) neonatal hepatitis. There was a statistically significant male preponderance in the neonatal hepatitis group (P=0.020). There was no significant difference in the racial distribution and in the proportions of low birthweight infants between the two groups of disorders. When the biliary atresia group was compared with the neonatal hepatitis group, significant differences were observed in the age of presentation (mean ± SD) 9.8 ± 6.8 VS 20 ± 17.3 weeks (P < 0.001), proportion of infants with prolonged jaundice (> seven weeks) 28/35 (80%) VS 20/58 (34.5%) (P < 0.00001), occurrence of acholic stools 26/35 (74.3%) VS 27/58 (46.6%) (P=0.020), liver size (mean ± SD) : 4.3 (1.6cm VS 3.3 ± 1.8cm (P < 0.01) and splenic size : 2.5 (1.8cm VS 1.4 (1.2cm (P < 0.001). There was however considerable overlap between the two groups in these features at presentation, making clinical differentiation between the two conditions difficult.

Infants with cholestasis tended to present late, compromising the chance of survival. In order to improve the medical care of these patients, these conditions must be emphasised during the training of medical practitioners, and efforts to increase public awareness of these conditions must be created.

Key Words: Neonatal Hepatitis, Biliary Atresia, Cholestatic Disorders, Malaysian

Introduction

Cholestatic disorders of infancy, in particularly biliary atresia and neonatal hepatitis are important and common clinical conditions in Malaysia. Very few studies have been carried out locally. In a significant proportion of these infants the disease is relentlessly progressive resulting in death by the age of 1 year.

Neonatal hepatitis (NH) is regarded as a clinical condition in which persistent cholestatic jaundice is present in early infancy associated with abnormal liver function and when biliary atresia is excluded.

On the other hand biliary atresia (BA) is seen in infants who have obstuctive jaundice and in whom the diagnosis is proved either at laparotomy or with liver biopsy.

Materials and method

This is a retrospective cohort study of cases of neonatal hepatitis and biliary atresia, over a 10 - year period : January 1982 to December 1991 inclusive. Cases admitted for the investigation of neonatal hepatitis, biliary atresia, prolonged neonatal jaundice or cholestatic jaundice, "TORCHES" infection, and metabolic disorders such as alpha - one antitrypsin deficiency, galactosaemia, were identified from the admission records of all the wards in the Department

of Pediatrics, University Hospital, Kuala Lumpur. Their medical records were recalled and reviewed. Those whose final diagnoses were neonatal hepatitis or biliary atresia were further studied in detail with respect to demographic profiles and clinical manifestations.

Chi - square tests with Yates correction where appropriate were used to calculate the difference between proportions and student's t- test was used to calculate differences between means. A p value of less than 0.05 was considered significant.

Results

Between January 1982 and December 1991 inclusive, a total of 93 patients were studied. Thirty - five of these patients (37.6%) had BA and 58 patients (62.4%) had NH. The population incidence could not be derived as the University Hospital was a tertiary referral centre.

In general there was a male preponderance (figure I) in cholestatic disorders of infancy (M:F = 1.7:1), although it was not statistically significant ($p > 0.05$) when compared with the male female ratio in the age group of 0 - 4 years in Malaysia. This is the youngest age group available (Department of Statistics, Malaysia).

In the BA group there was a slightly higher incidence of females ; M:F = 16:19 but the results were statistically not significant when compared to the male female ration in the age group 0 - 4 years of the population in Malaysia. However, in NH males were more commonly affected than females - M:F = 2.6:1. This was statistically significant ($p < 0.02$), when similarly compared. A comparison of various characteristics in the two groups of infants studied were summarized in Table I.

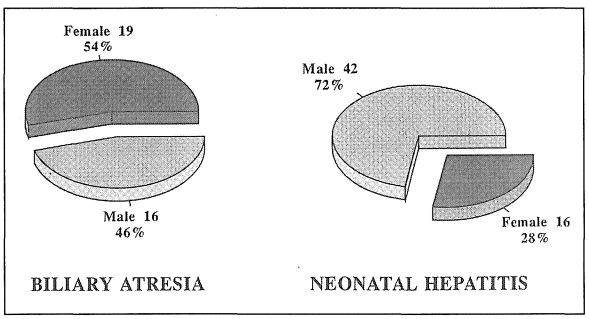

Fig. 1: Biliary atresia and neonatal hepatitis by sex

Ethnic Distribution

In this study there were no significant differences in the ethnic composition of the NH and BA groups

Relationship with Birthweight

The study showed the number of patients with low birth weight (<2.5 kg) with BA was 8 (22.8%) as compared to 14 (24.1%) with NH. Hence there was a slight difference which was not statistically significant. ($p > 0.05$)

Age of Presentation

This was defined as the age when the parents first noticed the presence of jaundice or pale stools and

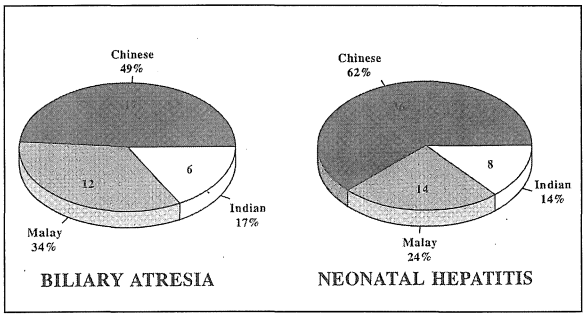

Fig. 2: Biliary atresia and neonatal hepatitis by ethnic groups

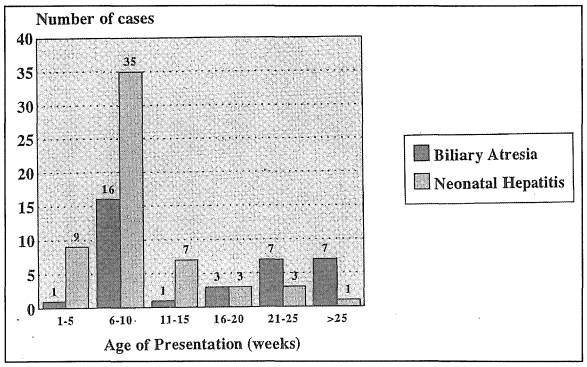

Fig. 3: Biliary atresia and neonatal hepatitis: by age of presentation

Table I
Comparison of the various characteristics in the two groups; biliary atresia (BA) and neonatal hepatitis (NH)

Characteristics	BA (n = 35)	NH (n = 58)	p values
Ethnic distribution			
Malay (no)	17	14	> 0.2 (ns)
Chinese (no)	17	36	> 0.2 (ns)
Indian (no)	6	8	> 0.2 (ns)
Age at presentation (weeks) (mean ± SD)	20.0 ± 17.3	9.8 ± 6.8	< 0.001
Birth weight < 2500 g (no.)	8	14	> 0.05 (ns)
Duration of jaundice > 7 weeks (no.)	28	20	< 0.01
Presence of acholic stools (no.)	26	27	< 0.02
Presence of tea-coloured (no.)	25	33	> 0.05 (ns)
Liver size, cm (mean ± SD)	4.3 ± 1.6	3.3 ± 1.8	< 0.01
Spleen size, cm (mean ± SD)	2.5 ± 1.8	1.4 ± 1.2	< 0.001

sought medical advice. The mean age (ISD) of presentation of BA was 20 ± 17.3 weeks. The mean age (SD) of presentation of NH was 9.8 ± 6.8 weeks. This diffference was statistically significant ($p < 0.001$). The mode of the age at presentation for both groups was 8 weeks.

Jaundice

In the NH group all the 58 patients at presentation had jaundice whereas in the BA group all except 1 of the 35 cases had jaundice at presentation.

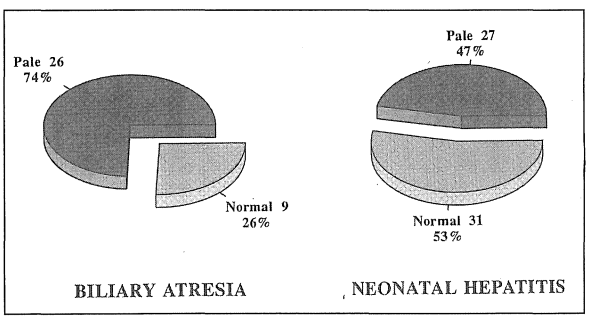

Fig. 4: Biliary atresia and neonatal hepatitis by stool colour

Duration of Jaundice

This is taken as the duration (in weeks) of jaundice prior to seeking treatment. A greater proportion of cases of BA 28/35 (80%) presented with a duration of jaundice of 7 weeks or more. In the NH group only 20/58 (34.5%) presented with duration of jaundice of 7 weeks or more, ($p = 0.00001$). However there was considerable overlap in the duration of jaundice between the two groups.

Stool Colour

Of the 35 patients with BA 26 / 35 (74.3%) had pale stools whilst only 27 / 58 (46.6%) patients with NH had pale stools, ($p < 0.02$).

Tea Coloured Urine

This was present in 25 / 35 (71.4%) of patients with BA and in 33 / 58 (56.9%) with NH. This difference was not statistically significant. ($p > 0.05$)

Hepatomegaly

The liver was not palpable in all the patients studied

in both the groups. The distribution of the liver sizes are depicted in figure 5. The mean size ± SD of the liver at the time of presentation in the BA and NH groups were 4.3 ± 1.6 cm and 3.3 ± 1.8 cm respectively ($p < 0.01$). The liver size was measured in cm below the right costal margin along the mid - clavicular line.

Splenomegaly

The spleen was not palpable in 4 / 35 (11%) of BA patients and in 17/58 (29%) of NH patients. Figure 6 shows the distribution of the spleen size of the patients. The mean size ± SD of the spleen was 2.5 ± 1.8 cm in the BA group and 1.4 ± 1.2 cm in the NH group ; ($p < 0.001$). This however was not documented in this group of patients studied.

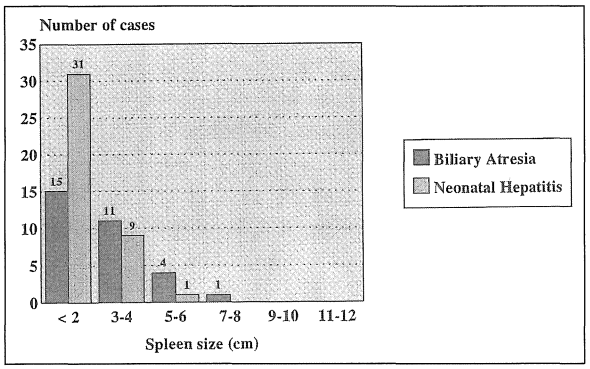

Fig. 5: Biliary atresia and neonatal hepatitis by spleen size

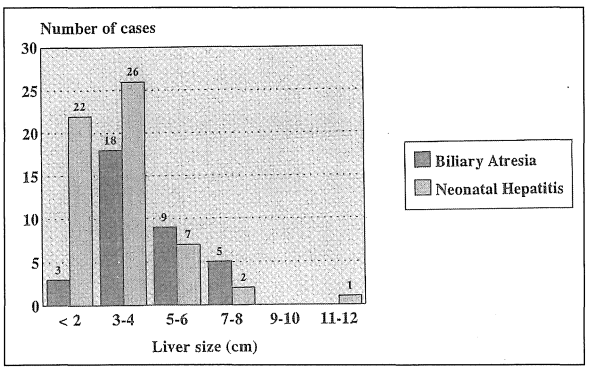

Fig. 6: Biliary atresia and neonatal hepatitis by liver size

Ascites

Ascites was found in 6/35 (17.3%) patients with BA whereas it was found only in 1/58 (1.7%) of patients with NH.

Rickets

Only 2 patients had BA with clinical, biochemical and radiological evidence of rickets at presentation.

Discussion

Biliary atresia and neonatal hepatitis are the most common causes of prolonged neonatal cholestasis. Although the clinical presentation may be similar there are some albeit minor differences.

In general the incidence of BA ranges from 1 in 18,000 to 1 in 25,000 livebirths[1,2]. The incidence could not be derived in this study because this data was based only on the admission to an institution and not population based.

A slight male preponderance was observed in the study. Similar results were also observed by other authors[3,4].

In this study, there was no significant difference in the proportion of NH and BA among the various major ethnic groups. A large scale study by Tan[3] in Singapore also failed to show any difference in the ethnic distribution of NH and BA. However Hays and Kimura[5], did find racial predilection among Chinese infants for BA.

In the present study, no significant difference was observed between the proportions of low birthweight infants in NH and BA groups. This contrasts with the findings of Alagille[6] who found a significantly higher proportion of low birthweight infants in NH and BA groups.

The results of this study show that the most consistent feature of biliary atresia and neonatal hepatitis is the presence of jaundice at presentation. All biliary atresia patients had persistent cholestatic jaundice until death or the obstruction was relieved by surgery. The jaundice in infants with neonatal hepatitis usually shows signs of resolution but if it persists for a long

period (>4 weeks) then diagnostic problems arise. In both groups the severity of jaundice may be variable during the course of the disease process. Acholic stools are more common and appear earlier in BA group of patients. Persistent acholic stools too are more indicative of the diagnosis of BA. This is of major clinical importance (Alagille, 1978)[7], although it too may be present in neonatal hepatitis as cholestasis may be present albeit transietly during the course of severe neonatal hepatitis. Tea-coloured urine is less specific and need not be present at presentation in either condition.

Hepatomegaly is the other consistent feature of both biliary atresia and neonatal hepatitis as in the present study. There is however a great variation in liver sizes and there is considerable overlap in all patients with both the disorders and hence hepatomegaly is not a very useful clinical sign to differentiate NH from BA. In general however it can be said that patients with biliary atresia tend to have bigger and firmer livers than those with neonatal hepatitis. Splenomegaly is less consistently present in both the disorders than hepatomegaly. Considerable overlap in splenic size is observed in the disorders but generally infants with biliary atresia tend to have bigger spleens than those with neonatal hepatitis. There is an increased incidence of polyspenia syndrome and intra-abdominal vascular anomalies in patients with BA[7]. This however was not documented in the present series.

Infants with biliary atresia hence tend to have distended abdomen as a result of the gross hepatosplenomegaly and increased incidence of ascites. Ascites as an early feature is rare. Some degree of failure to thrive is present in both the disorders but as a result of inadequate documentation, definitive conclusion cannot be derived. The same holds true for the presence of rickets and anomalies of other organ systems.

The age of presentation at the hospital (age when first seen) was very much delayed and is disappointing, especially so with the group with biliary atresia. It is shocking to know that the age (mean ± S.D.) of presentation for biliary atresia was 20 (± 1 7.3) weeks. Infants operated on before 2 months of age have a 90% chance of eventual satisfactory bile drainage. Beyond this age the success rate with surgery rapidly falls and is nil by 5 months. Two weeks are needed for the pre-operative investigations and infants must therefore be referred before the age of 6 weeks.

Conclusion

Neonatal hepatitis and biliary atresia are common causes of cholestatic disorders of infancy in Malaysia. In the two groups, there is considerable overlap in the duration of jaundice, occurrence of acholic stools and tea-coloured urine, as well as the splenic size. In general, however, longer duration of jaundice, the presence of acholic stools, splenomegaly and ascites favour the diagnosis of BA.

Infants with cholestasis tended to present late. In order to improve the medical care of there patients, the conditions must be emphasised during training of medical practitioners and public awareness of these conditions and their need for early investigation and treatment must be created.

References

1. Henriksen NT, Drablos PA, Aagenaes O : Cholestatic jaundice in infancy. The importance of familial and genetic factors in aetiology and prognosis. Arch Dis Child 1981;56 : 622-7.

2. Mathis RK, Andres JM, Walker WA : Liver disease in infants. Part II : Hepatic disease states. J Pediatr 1980;90 : 864-80.

3. Tan SG : Obstructive Jaundice Syndrome in Infants, M D Thesis. University Singapore, 1976.

4. Danks DM : Prolonged neonatal obstructive jaundice. Clin Pediatr 1965;4 : 499-510.

5. Hays DM, Kimura K : Biliary Atresia, The Japanese Experience, Hays DM, Kimura K (Eds), Harvard University Press, Cambridge, 1980.

6. Alagille D : Clinical aspects of neonatal hepatitis. Am J Dis Child 1972;123 : 287-91.

7. Alagille D, Odievre M : Liver and Biliary Tract Diseases in Children. Wiley J, New York, 1978.