Nigerian Journal of Paediatrics 1986; **13(1)**: 27–31

Total Fasting Serum Bile Acids in the Diagnosis of Obstructive Liver Diseases in Children — A Preliminary Study

AM YAKUBU*, SS ANGO† AND EA IROKO**

Summary

Yakubu AM, Ango SS and Iroko EA. Total Fasting Serum Bile Acids in the Diagnosis of Obstructive Liver Diseases in Children - A Preliminary Study. *Nigerian Journal of Paediatrics* **1986; 13:27.** In order to evaluate the diagnostic value of serum bile acids in obstructive liver diseases, fasting serum bile acids in five children with schistosomal hepatic fibrosis and five infants with biliary atresia were estimated by 3-hydroxysteroid dehydrogenase assay. The total fasting serum bile acids in biliary atresia ranged from 2.1 to 8.4 ug/dl (mean 4.86±2.60) compared to a level of 2.2 to 3.7 ug/dl (mean 2.80± 0.69) in healthy infants ($p > 0.1$) while in schistosomal hepatic fibrosis, it ranged between 2.0 and 6.0 ug/dl (mean 4.8±1.64) as against levels of 1.0 to 11.0 ug/dl (mean 4.83±2.58) in controls ($p > 0.5$). Determination of total fasting serum bile acid levels as carried out in this study, would thus appear not to provide much useful information in the evaluation of children with obstructive liver diseases.

Introduction

THE estimation of total serum bile acids as a sensitive test of the excretory function of the liver has been a subject of extensive research and conflicting reports.[1–4] Because of the unique role of the liver in the synthesis and metabolism of bile acids, it has been logically believed that the estimation of total serum bile acids would be of important diagnostic value in the differential diagnosis of intrahepatic cholestasis and biliary atresia, as a non-invasive method of assessing disease activity and monitoring treatment, especially in chronic hepatitis. Several workers have reported elevated values of total serum bile acids in hepatobiliary disorders,[5–7] while some authors consider the estimation of serum bile acids very important in the diagnosis of cholestasis such as occurs in Gilbert's syndrome[8]. The purpose of this study was to evaluate the diagnostic value of fasting total serum bile acids in obstructive liver diseases namely: biliary atresia and hepatic schistosomiasis, in infancy and childhood.

Ahmadu Bello University Teaching Hospital, Zaria

Department of Paediatrics
* Senior Lecturer
† Registrar

Department of Chemical Pathology
** Chief Technologist

† Present Address: Ashaka Cement Company, Bauchi State
Correspondence: Dr AM Yakubu

Materials and Methods

Two groups of subjects were studied. Group I consisted of 5 infants (4 males and 1 female) aged 3-8 months (mean 5.3 months) with conjugated hyperbilirubinemia due to extrahepatic biliary atresia. All the 5 presented with jaundice dating from birth and all had hepatomegaly greater than 3cm below the costal margin. The diagnosis of biliary atresia was confirmed at laparotomy and histologic examinations of sections of liver specimens obtained at open biopsy. Group II was made up of 5 children (3 males, 2 females) aged between 5 and 8 years (mean 6.3 years). They had hepatic schistosomal fibrosis confirmed by liver biopsy. They had presented with painful abdominal swelling (2 cases), loss of weight and joint pain (1 case), bloody stool (1 case) and painless abdominal swelling (1 case). Three of the 5 had firm hepatosplenomegaly while the remaining 2 had only hepatomegaly.

The controls were apparently healthy infants and children who had no clinical or biochemical evidence of liver disease and had not been taking any drug for at least, a week prior to the time of blood sampling. For the Group I subjects, the controls comprised 7 infants (5 males, 2 females) aged 2 months to 9 months (mean, 5.0 months) while 22 children (9 males and 13 females) aged between 1 and 10 years (mean 4.7 years) constituted the controls for the subjects in Group II.

Ten millilitres of venous blood were obtained from each subject and control, following an overnight fast. Half of the serum obtained from the blood in each case was used for the analysis of liver function tests namely, serum aspartate aminotransferase (serum glutamic oxalo-acetic transaminase, SGOT), alanine aminotransferase (serum glutamic pyruvic transaminase, SGPT), alkaline phosphatase and bilirubin. The rest of the serum was frozen and kept at -20°C until it was used for the analysis of total serum bile acids.

Liver function tests were carried out according to standard methods. Total serum bile acid concentrations were measured by 3-hydroxysteroid dehydrogenase assay based on the principle that the 3-hydroxyl group common to most bile acids is oxidised to 3-oxo-group by the enzyme 3-hydroxysteroid dehydrogenase in the presence of nicotinamide adenine dinucleotide (NAD+) as co-enzyme; using hydrazine to combine with the 3-oxo-group to ensure the reaction goes to completion[9]. The activity of nicotinamide adenine dehydrogenase (NADH) was measured at 340nm. The students' t test was used to evaluate the significance of the differences between means.

Results

The mean levels of the serum bile acids in both subjects and controls are shown in Table I while individual values are shown in the Figure. The total fasting serum bile acids in infants with biliary atresia ranged between 2.1 and 8.4 ug/dl (mean 4.86 ± 2.60) compared to levels in normal healthy infants of 2.2 and 3.7ug/dl (mean 3.8 ± 0.69) ($p > 0.1$), while in children with schistosomal hepatic fibrosis, the total fasting serum bile acid levels ranged from 2.0 to 6.0 ug/dl (mean 4.8 ± 1.64) as opposed to levels of 1.0 to 11.00 ug/dl (mean 4.80 ± 2.58) in the controls ($p > 0.5$). There was a wide scatter of fasting serum bile acids in both groups with overlap in health and disease (Fig).

Liver function tests were normal in all the controls. The SGOT was elevated in only one patient with schistosomal hepatic fibrosis (Table II). All the five patients with biliary atresia had elevated serum bilirubin and liver enzymes: SGOT and SGPT ranged from 60 to 135 (mean 74) and 47 to 173 IU/L (mean 73) respectively. There was no correlation between the total fasting serum bile acids and any index of the liver function tests in both groups of subjects (Table II).

TABLE I

Total Fasting Serum Bile Acid Levels in Subjects and Controls

	No of Cases	*Mean SBA (ug/dl)*	*Standard Deviation*	*Range (ug/dl)*	*P*
Group I					
Subjects	5	4.86	2.60	2.1-8.4	
					>0.1
Controls	7	3.80	0.69	2.2-3.7	
Group II					
Subjects	5	4.80	1.64	2.0-6.0	
					>0.5
Controls	22	4.80	2.58	1.0-11.0	

SBA = Serum bile acid
Group I consists of cases with biliary atresia
Group II consists of cases with hepatic schistosomal fibrosis

TABLE II

Relationship between Serum Bile Acid Levels and Liver Function Test Values in the Subjects

	Group I Subjects (n = 5)			*Group II Subjects (n = 5)*		
	Mean	*Range*	*r*	*Mean*	*Range*	*r*
SBA (ug/dl)	4.86	2.1 - 8.4	-	4.8	2.0 - 6.0	-
SGOT (IU/L)	74	55 - 135	0.25	21.4	3 - 52	0.07
SGPT (IU/L)	74	47 - 173	0.15	13.8	7 - 30	0.05
Conjugated Bilirubin (umol/L)	118	65 - 185	0.25	<17.0*	-	-

Group I consisted of cases with biliary atresia
Group II consisted of cases with hepatic schistosomal fibrosis
SBA = Serum bile acid
SGOT = Serum glutamic oxalo-acetic transaminase (serum aspartate aminotransferase)
SGPT = Serum glutamic pyruvic transaminase (serum alanine aminotransferase)
* Serum conjugated bilirubin was <17 umol/L in each of the 5 subjects

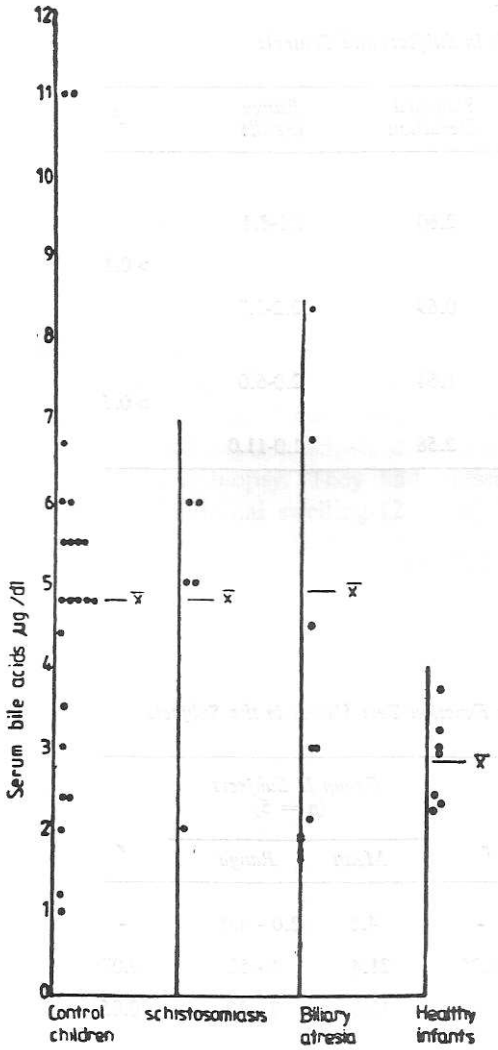

Fig Serum bile acid levels in patients with obstructive liver diseases and in controls.

Discussion

The method used for the measurement of serum bile acids described in this study was based on procedures previously described by Murphy, Billing and Baron.[9] The results however, compare favourably with those obtained by Angelin and Bjorken[10] who used gas chromatographic mass spectrometric technique. The method used in the present study did not measure sulphated bile acids as was done by Stiehl[11] and Makino *et al*,[12] who reported an elevated value of sulphated serum bile acids in cholestasis. However, the measurement of sulphated bile acids is too cumbersome and therefore, unpracticable for routine evaluation of patients with hepatobiliary disease. Sulphated serum bile acids are elevated only for a short period in acute hepatobiliary disease and are rapidly excreted in the urine as a protective mechanism, since they are hepatotoxic[12-14].

In the present study, the mean total fasting serum bile acids was found not to be significantly elevated in the infants with biliary atresia as compared to controls. This is in contrast with the findings of Rudman and Kendall[15] who reported significantly elevated values in children with biliary atresia. It has recently been suggested that the measurement of total serum bile acids in the postprandial state is superior to the conventional liver function test in the detection of hepatobiliary disease[16]. It has also been shown that the measurement of individual serum bile acids such as cholic: chenodeoxycholic acid ratio is even better than the estimation of total fasting serum bile acids in detecting biliary atresia[17 18].

There was no correlation between total fasting serum bile acids and any of the indices of liver function tests in the groups of patients with liver diseases that were studied in the present series. This finding is at variance with those of others who have reported serum bile acid concentrations to be of diagnostic value in liver diseases.[19 20] From the present study which admittedly, involved only a few cases, the measurement of total fasting serum bile acids by the 3-hydroxysteroid dehydrogenase method would appear not to add much useful information to the conventional liver function tests in the evaluation of hepatic disorders.

There are some claims that the measurement of serum bile acids by radioimmunoassay is more sensitive than and superior to the conventional liver function tests in the evaluation of patients with hepatobiliary disorders.[21] Using radioimmunoassay technique, Bolarinwa and Andy[22] have shown

that conjugated cholic acid and chenodeoxycholic acid are reliable and sensitive indicators of tropical liver diseases in adults. There would therefore, appear to be a need to evaluate the diagnostic value of such a radioimmunoassay technique in childhood liver diseases.

References

1. Josephson B. The elimination of cholic acid IV. In patients with liver diseases. *J Clin Invest* 1939; **18:** 343–50.
2. Kitazma K and Shibata S. Determination of serum bile acids and its use as a hepatic function test. *Kawasaki Med J* 1975; **1:** 55–67.
3. Sherlock S and Walshe V. Blood cholates in normal subjects and in liver disease. *Clin Sci* 1948; **6:** 223–34.
4. Karjo M, Holtzapple PG and Lubin BH. Differential diagnosis of neonatal hepatitis and biliary atresia by the measurement of serum and intraluminal duodenal bile acid concentration. *Pediat Res* 1973; **7:** 337.
5. Murphy GM and Singer E. Bile acid metabolism in infants and children. *Gut* 1974; **15:** 151–63.
6. Pennington GR, Rose PE and Bouchier AD. Serum bile acids in the diagnosis of hepatobiliary disease. *Gut* 1977; **18:** 903–8.
7. Makino I, Nakagawa S and Mashimo K. Conjugated and unconjugated serum bile acid levels in patients with hepatobiliary disease. *Gastroenterology* 1969; **56:** 1033–9.
8. Javitt NB. Diagnostic value of serum bile acids. *Clin Gastroenterol* 1977; **6:** 219–26.
9. Murphy GM, Billing BH and Baron DN. A fluorimetric and enzymatic method for the estimation of serum total bile acids. *Clin Pathol* 1970; **23:** 594–8.
10. Angelin B and Bjorkhen J. Postprandial serum bile acids in healthy men. *Gut* 1977; **19:** 606–9.
11. Steihl A. Bile sulphates in cholestasis. *Euro J Clin Invest* 1974; **4:** 59–67.
12. Makino I, Hashimoto H, Shinozaki K, Yoshino K and Nakagawas S. Sulphated and non-sulphated bile acids in urine and serum of patients with hepatobiliary disease. *Gastroenterology* 1975; **68:** 545–53.
13. Javitt G. Bile acid excretion, the alternate pathway in the hamster. *J Clin Invest* 1977; **60:** 693–701.
14. Kaplowitz N. Bile acid sulphates: First you see them, then you don't. *Gastroenterology* 1978; **74:** 795.
15. Rudman D and Kendall FE. Bile acid content of human serum I. Serum bile acids in patients with hepatic disease. *J Clin Invest* 1957; **36:** 530–7.
16. Kaplowitz N, Kok E and Javitt NB. Postprandial serum bile acid for the detection of hepatobiliary disease. *JAMA* 1973; **225:** 292–3.
17. Bloomer JR, Allen RM and Klatskin G. Serum bile acids in primary biliary cirrhosis. *Arch Int Med* 1976; **136:** 57–61.
18. Javitt NB, Mirrossey KP, Siegel E, Goldberg H, Garther LM, Hollander M and Kok E. Cholestatic syndromes in infancy: diagnostic value of serum bile acid pattern and cholestyramine administration. *Pediat Res* 1973; **7:** 119–25.
19. Barnes S, Gallo GA, Trash DB and Marris JS. The diagnostic value of serum bile acid estimations in liver disease. *J Clin Pathol* 1975; **28:** 506–9.
20. Fausa O and Gjone E. Serum bile acid concentrations in patients with liver disease. *Scand J Gastroenterol* 1976; **11:** 537–43.
21. Editorial. Serum bile acids in hepatobiliary disease. *Br Med J* 1978; **1:** 392.
22. Bolarinwa DM and Andy JJ. Radioimmunoassay of conjugated cholic acid and chenodeoxycholic acid in the serum of Nigerian patients with liver abscess and other liver diseases. *W Afr J Med* 1985; **4:** 69–74.

Accepted 30 August, 1985