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Liver Function Tests During The Perinatal Period

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SUMMARY

Onwuameze IC. Liver Function Tests During the Perinatal Period. *Nigerian Journal of Paediatrics* 1990; 17: 43. Serum iso-citrate dehydrogenase (ICD), aspartate transaminase (AST), alkaline phosphatase (ALP) gamma-glutamyl transferase (GGT), total bilirubin, total protein and albumin were determined and compared in 68 paired maternal and corresponding cord blood and in 70 age-matched non-pregnant females. The subjects were without previous history or physical findings of liver disease. The data show that the levels of AST, ALP, GGT and total bilirubin were significantly higher in cord blood ($p<0.001$) than in either maternal or non-pregnant female blood. Serum total protein and albumin were however significantly lower in cord blood ($p<0.001$) than in either maternal or non-prenant female blood. The significance of the finding especially in the interpretation of liver function tests in the neonate is discussed.

INTRODUCTION

IN many African countries especially in the sub-Sahara region there is a higher incidence of liver disease than in the temparate countries[1–5]. The higher incidence of liver disease has been attributed to several factors such as genetics, diet, the environment, parasites (malaria, amoebic liver diseases, liver flukes) mycotoxins and malnutrition[5–7]. Hepatomegaly and fatty infiltrations of the liver, increased susceptibility to infections and decreased immune response affecting all organs especially the liver are common characteristics of malnutrition which may contribute to the increased incidence of liver disease.

The human foetal liver undergoes extensive biochemical and physiological development as well as differentiation during the perinatal period. Most of the bilirubin in foetal or neonatal bile occur as bilirubin monoglucuronide. Little is known about foetal liver enzymes (alkaline phosphatase, transminases and isocitrate dehydrogenase) in circulation.

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Perinatal liver damage in the foetus has however been shown to occur following certain infections[8] or as a result of metabolic defects.[9]

This communication reports on liver function tests during the perinatal period.

MATERIALS AND METHODS

The subjects studied comprised healthy non-pregnant females, normally delivered mothers and their foetuses. The majority of the selected subjects were either civil servants or petty traders living in the city. Healthy full term normally delivered babies with normal birth weight (i.e. above 2500 g) and their respective mothers were selected for this study. To qualify for selection the subjects showed no evidence of jaundice, liver diseases, no history of post-partum haemorrhage, infection or inflammatory disease three months before the test. Patients who were treated with phenorbarbitone or other drugs to reduce hyperbilirubinaemia during the last few days of pregnancy were excluded from the investigation. The subjects were generally in good health during the period of this study. Sixty-eight maternal and cord blood (foetal blood) were eventually selected and compared with 70 healthy non-pregnant females.

Blood specimens were obtained from the antecubital fossa vein without any occlusion from the pregnant females, usually about an hour before or after delivery. Foetal blood (cord blood) was obtained by ligaturing the umblical cord and the foetal blood was obtained from the foetal end.

The blood specimen was allowed to clot in a vacutainer glass tube for 2 hours and the serum obtained by centrifugation. The sera obtained were stored at $-20^{\circ}C$ pending analysis, which was generally carried out in batches twice weekly. Haemolysed and jaundiced specimens were discarded.

Serum bilirubin was determined using the Powell method as described by Varley[10] Aspartate transaminase (AST) was determined using AST monotest kit obtained from Boehringer Mannheim GmbH. Isocitrate dehydrogenase (ICD) was assayed using the method of Bell and Baron.[11] Alkaline phosphatase (ALP) was determined using the method of Kind and King[12] while serum gamma-glutamyl transferase (GGT) was assayed using the Scandinavian recommended method.[13] Serum total proteins and albumin were determined using a modified Reinhold-biuret method as described by Varley.[14] The serum total globulins were obtained by the difference between the serum total protein and the serum albumin.

Colorimetric determinations were performed on a 4010 photometer obtained from Boehringer Mannheim GmbH since this permits the use of micro-methods.

Statistical analysis:

The significance of the difference between the means of the groups were evaluated by the Student's paired t-test.

RESULTS

Table I shows the serum levels of ICD, AST, ALP, GGT, total bilirubin, total proteins, albumin and total globulins healthy non-pregnant females compared with age-matched full term mothers. The data show no significant differences in the levels of serum ICD and total bilirubin. Serum total protein, albumin and globulins were significantly lower in full-term maternal subjects than in healthy non-pregnant females ($p<0.001$). Serum GGT, ALP and AST levels were however significantly higher in full-term maternal subjects than in non-pregnant females ($p<0.001$).

There was no correlation between foetal birth weight and cord blood enzymes.

TABLE I

Serum Liver Function Tests in Healthy Non-Pregnant Females Compared with Age-Matched Full Term Maternal Subjects.

Parameter and Units Measurement	Non-Pregnant Females (n = 70)	Full-Term Maternal Subjects (n = 68),	P	Level of Significance
ICD u/L	5.6 ± 2.5	6.1 ± 2.6	> 0.1	NS
AST u/L	21.4 ± 4.6	30.2 ± 8.6	< 0.001	Significant
ALP KA Units/dl	5.8 ± 2.6	18.5 ± 3.7	< 0.001	Significant
GGT u/L	12.6 ± 2.9	27.3 ± 4.1	< 0.001	Significant
Total Bilirubin mg/dl	0.5 ± 0.2	0.6 ± 0.2	> 0.1	NS
Total Protein g/l	73.7 ± 6.0	66.4 ± 6.2	< 0.001	Significant
Albumin g/l	41.5 ± 5.2	38.1 ± 6.0	< 0.01	Significant
Total globulin g/l	31.8 ± 5.2	28.3 ± 6.5	< 0.001	Significant

(Figures are expreseed as mean ± SD)
n = Number of Subjects studied
p = Probability ratio
NS = Not significant

TABLE II

Serum Liver Function Tests In Paired Maternal and Foetal Blood

Parameter With Unit of Measurement	Full Term Maternal Subjects n = 68	Foetal Cord Blood Full Term n = 68	P	Level of Significance
ICD u/l	6.1 ± 2.6	6.7 ± 3.4	> 0.1	NS
AST u/l	30.2 ± 8.6	42.7 ± 8.2	< 0.001	Significant
ALP KA Units/dl	18.5 ± 3.7	10.2 ± 2.5	< 0.001	Significant
GGT u/l	27.3 ± 4.1	66.2 ± 10.8	< 0.001	Significant
Total bilirubin mg/dl	0.6 ± 0.2	1.1 ± 0.3	< 0.001	Significant
Total Protein g/l	66.4 ± 6.2	62.9 ± 8.7	< 0.001	Significant
Albumin g/l	38.1 ± 6.0	34.7 ± 6.6	< 0.001	Significant
Total Globulins g/l	28.3 ± 6.5	28.8 ± 6.2	> 0.1	NS

(Figures are expressed as mean ± SD)
n = Number of subjects
p = Probability ratio
NS = Not Significant

TABLE III

Serum Liver Function Tests in Healthy Non-Pregnant Females Compared With Neonates (Foetal Blood)

Parameter and Units of Measurement	Non-Pregnant Females (n = 70)	Foetal Cord Blood, Full Term (n = 68)	P	Level of Significance
ICD u/l	5.66 ± 2.5	6.7 ± 3.4	> 0.001	Significant
AST u/l	21.4 ± 4.6	42.7 ± 8.2	> 0.001	Significant
ALP KA Units/dl	5.8 ± 2.6	10.2 ± 2.5	> 0.001	Significant
GGT u/l	12.6 ± 2.9	66.2 ± 10.8	> 0.001	Significant
Total Bilirubin mg/dl	0.5 ± 0.2	1.1 ± 0.3	> 0.001	Significant
Total Protein g/l	73.7 ± 6.0	62.9 ± 8.7	< 0.001	Significant
Albumin g/l	41.5 ± 5.2	34.7 ± 6.6	< 0.001	Significant
Total globulin g/l	31.8 ± 5.2	28.8 ± 6.2	> 0.001	Significant

(Figures are expressed as mean ± SD)

n = Number of subjects

p = Probability ratio

The levels of serum liver enzymes as well as proteins in full-term maternal subjects paired with their foetal blood (cord blood) are shown in Table II. The serum level of ICD and total globulins in both full-term maternal subjects and their paired foetus were not significantly different. Serum AST, GGT and total bilirubin were significantly higher in foetal blood than in maternal blood, while serum ALP, total protein and albumin were significantly lower in foetal blood ($p<0.001$).

Table III shows a comparison of the serum liver function tests in adult blood and foetal (cord) blood. Serum liver enzymes in foetal cord blood were significantly higher while serum proteins especially albumin were significnatly lower in cord blood.

DISCUSSION

There has been a changing spectrum relating to the infective disorders of liver, and in children, liver disease has a widely differing spectrum depending on the part of the world under discussion.[3] The neonatal period is usually characterised by anatomical and physiological changes which are reflected in the biochemical values found in the body fluids. In the neonate, the extent of liver damage is a reflection of previous intra-uterine environment, adaptations and the assaults on the foetal liver.

Our results are similar to those reported elsewhere on neonates, pregnant females at term and non-pregnant females.[16–20] The cord plasma bilirubin is usually under 2 mg per dl because (provided placental function is good) foetal blirubin is readily disposed of by the maternal liver. The bilirubin levels in the neonate during the first days of life depend on whether the baby is born at term or prematurely. The levels of the serum liver enzyme (AST, ICD and GGT) and bilirubin obtained in this study were signifi-

cantly higher in the foetus than in maternal circulation (pregnant and non-pregnant) although serum proteins were lower in foetal circulation. However, alkaline phosphatase level in the foetus is lower than in maternal circulation. The elevated GGT activity observed in foetal blood in this study may be due to preferential release of GGT from the placenta into the foetal circulation. The elevated GGT and bilirubin in foetal blood and their correlation excludes microsomal enzyme induction of GGT but does not exclude minor insults to the microsomal enzyme system during labour. The lower serum protein in foetal (cord) blood especially albumin observed in this study is in agreement with previous reports[20] and this has been attributed to the role of protein in favouring the dialytic transfer and clearance of bilirubin and its metabolite from foetal circulation.[21] The differences in the level of alkaline phosphatase may be due to the effect of pregnancy since the placenta is known to secrete alkaline phosphatase[22–24] and this may cross the placenta into the foetal circulation.

Although we were unable, because of ethical reasons, to obtain blood from healthy neonates for the determination reference values, the data obtained from foetal (cord) blood in this study is a reliable reflection of normal values in the neonate especially during the first week of life.

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