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Autor: Osifo, 'Bola O.A. / Adeyokunnu, A.
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Departments of Chemical Pathology and Paediatrics, College of Medicine,
University College Hospital, Ibadan, Nigeria

Serum aminotransferase activities in sickle cell children during crises

'BOLA O. A. OSIFO, A. ADEYOKUNNU

Summary

A total of 78 children with diagnosis of sickle cell disease (HbSS) aged 1–12 years were involved in this study; while 60 normal children (HbAA) of the same age range served as controls. Serum levels of alanine aminotransferase (EC 2.6.1.2), aspartate aminotransferase (EC 2.6.1.1), total protein and albumin were assayed in all the sickle cell children both in crises and steady state and in all the normal children. During crises, most of the sickle cell children had significantly raised levels of serum aminotransferases together with reduced levels of serum total protein and albumin. When these levels are compared with the ones observed during the steady state, the differences are highly significant. On the other hand, when the results obtained during the steady state are compared with those of the control group, the differences are not significant. These results are discussed in relation to the hepatic degenerative changes observed in sickle cell crises. It is clear from this study that the more clinical painful crises the children experience, the hepatic cells would be exposed to persistent injury which may eventually result in cell death.

Key words: ALAT; ASAT; total protein albumin.

Introduction

Reports have shown that there are hepatic abnormalities in sickle cell disease (SCD) (Murphy and Shapiro, 1945; Konotey-Ahulu, 1969; Lagundoye, 1970; Diggs, 1973; Hendrickse, 1960; Song, 1957). The liver is frequently enlarged and it is the seat of pathologic changes (Murphy and Shapiro, 1945; Konotey-Ahulu, 1969; Langundoye, 1970; Diggs, 1973). Most of these reports have been based on the macroscopic and microscopic appearances of the liver.

Correspondence: Dr. 'Bola O. A. Osifo, Department of Chemical Pathology, College of Medicine, University College Hospital, Ibadan, Nigeria

Biochemical studies on hepatic function by several workers (Green et al., 1953; Bogoch et al., 1955; Rosenblate et al., 1970; Holkovitz and Jacobson, 1961; Ferguson and Scott, 1959; Isichei, 1980) clearly showed that there is impaired liver metabolism in SCD. Very few workers (Rosenblate et al., 1970; Holkovitz and Jacobson, 1961; Ferguson and Scott, 1959; Isichei, 1980) have studied the levels of alanine and aspartate aminotransferases in SCD. In fact the known work on both enzymes in SCD were reported by Rosenblate et al. (1970) and Holkovitz and Jacobson (1961). They observed that the levels of these aminotransferases were within the normal range among their paediatric patients but these levels were raised among their adult patients. The other workers reported on only one of the enzymes in SCD and except for Isichei (1980) they all reported on ASAT levels. Moreover, most of these observations were in adult patients and they were mostly in a crisis free state. On the basis of their studies, it appears that the hepatic dysfunction was more marked among adult patients.

Since evidence has shown that serum activities of both ALAT and ASAT become elevated whenever disease processes affect liver cell integrity and due to lack of information on the levels of both enzymes in sickle cell children during crises; this project was set up to investigate the activities of serum ALAT and ASAT in sickle cell children both in the asymptomatic period and in crises. By so doing, it is hoped that each sickle cell child will act as his own reference point in the interpretation of the results.

Materials and Methods

A total of 78 children of both sexes aged 6 months to 12 years with diagnosis of sickle cell anemia (HbSS) and sixty normal children of both sexes of the same age range serving as double controls were involved in this study. Informed parental consent was obtained in each case.

All subjects used for control underwent physical examination to exclude those with acute illnesses such as fever, vomiting and diarrhoea; and those with chronic illnesses like anaemia, enlarged liver and spleen or any evidence of other systemic diseases. All the sickle cell patients were selected from among those coming to the anaemia clinic for routine checkup. Their haemoglobin genotypes were confirmed by electrophoreses. When they were in crises they were admitted into the hospital.

Blood samples: Venous blood specimens were taken from all the sickle cell children during crises and in the steady state, and from the normal children for the following determinations: serum alanine aminotransferase (ALAT) serum aspartate aminotransferase (ASAT), total serum protein and albumin. Other haematological indices PCV and leucocyte counts were done. Blood samples were usually taken 2–3 weeks after any crisis as experience has shown reversion of hepatic architecture to normal 4–5 days after an acute episode of crisis (Holkovitz and Jacobson, 1961). All samples were sent to the diagnostic laboratory for assay.

Serum enzymes: Both serum alanine and aspartate, aminotransferases' activities were assayed according to the method described by Mohun and Cooke (1957). The units of this method are Cabaud units, same as spectrophotometric units per litre by multiplying the results by factor 0.483 (Varley, 1968).

Serum proteins: Serum proteins were estimated by the Biuret method described by Reiner (1953).

Statistics: Non-parametric statistics was used. Tests of significance were analyzed with the Student's t test.

Results

Details of all biochemical parameters are shown in Tables 1 and 2. For biochemical recording, the children were divided into two groups (aged 1–5 years and 6–12 years) during crises. Figs. 1 and 2 show the distribution of ALAT and ASAT activities among the sickle cell children.

Alanine aminotransferase (ALAT): The mean activity of this enzyme (35.3 i.u./l) among the sickle cell children during crises was higher than during the steady state (mean 19 i.u./l) and this difference was significant ($p < 0.001$). The difference between the mean value during the steady state and the mean value in the normal children (14.0 i.u./l) was significant ($p < 0.001$). The distribution of this enzyme among all the children during various phases (Fig. 1) showed

Table 1. Mean serum levels of alanine aminotransferase, total protein and albumin of sickle cell and normal children (\pm S.D.)

Biochemical parameters	Sickle cell* in crises	Sickle cell* steady state	Normal group (n = 60)
Alanine aminotransferase	35.3 \pm 27.8	19 \pm 9.5	14.0 \pm 3.8
i.u./l (range)	(7.4–190)	(5–50)	(6–19)
Aspartate aminotransferase	35.8 \pm 30.2	22 \pm 14.2	17.7 \pm 4.4
i.u./l (range)	(7.5–230)	(8–63)	(5.2–22.7)
Total protein g/l	73 \pm 9	78 \pm 9	76 \pm 6
(range)	(55–90)	(64–92)	(64–84)
Albumin g/l	34 \pm 5.8	44 \pm 7	44 \pm 4
(range)	(19–44)	(35–55)	(37–53)
A/G ratio	0.905	1.29	1.38

* No of sickle cell children is 78.

Table 2. Comparison of biochemical changes in the blood of sickle cell children of various age groups during crises (\pm S.D.)

Biochemical parameters	1–5 years (n = 35)	6–12 years (n = 43)	P value
Alanine aminotransferase	43.31 \pm 37	27.6 \pm 25.7	0.001
i.u./l (range)	(8.7–190)	(7.4–107)	
Aspartate aminotransferase	47.1 \pm 46.5	25.85 \pm 20.5	0.005
i.u./l (range)	(7.5–230)	(7.5–97)	
Total protein g/l	73 \pm 9	73 \pm 9	0.2
(range)	(58–90)	(59–89)	
Albumin g/l	35 \pm 6.5	34 \pm 7	0.001
(range)	(22–43)	(20–46)	

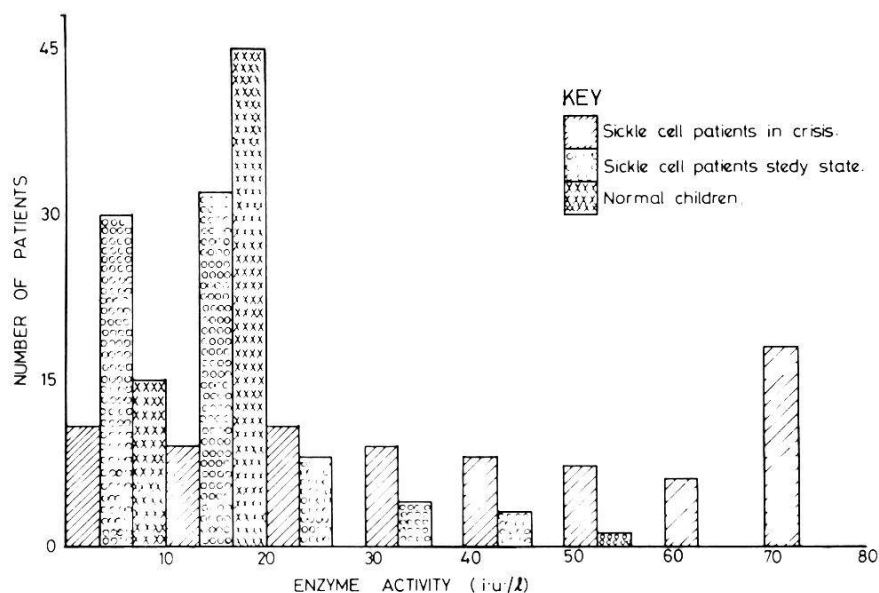


Fig. 1. Serum alanine aminotransferase activity of sickle cell and normal children.

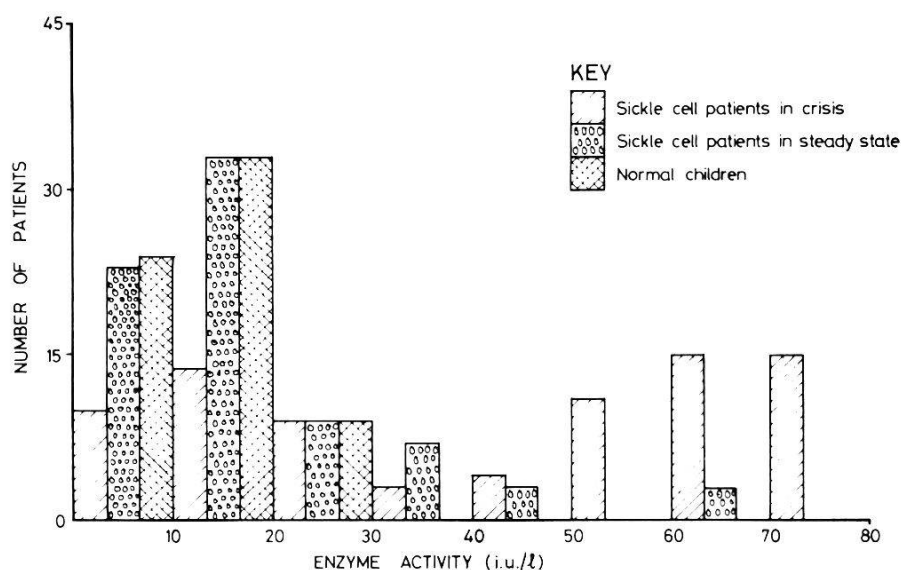


Fig. 2. Serum aspartate aminotransferase activity of sickle cell and normal children.

that 58 of the children in crises had raised enzyme levels compared with 15 in steady state. The highest values were recorded among the younger sicklers during crises (mean 43.31 i.u./l).

Aspartate aminotransferase (ASAT): During crisis, the mean activity of this enzyme was 35.8 i.u./l; while the mean during the steady state was 22 i.u./l. More than half of the children during crises had ASAT values above 50 i.u./l as shown in Fig. 2 while only six of the children in the steady state had values above 50 i.u./l. The difference between the means of this enzyme during the two phases is highly significant ($p < 0.005$). These differences were also significant when compared with the mean value of 17.7.

Total protein: The mean concentration of the serum total protein fell during crises (73 g/l) when compared with its level during the steady state (mean 78 g/l). This difference is significant ($p < 0.01$).

Albumin: The mean concentration of this protein fell significantly during crises (34 g/l) when compared to its level during the steady state (mean 44 g/l). This difference is significant ($p < 0.0001$). On the other hand, no significant changes occurred between the mean albumin concentrations during the steady state and the control group. The low serum albumin during crises affects the albumin/globulin ratio which is below 1.

Discussion

The hepatic enzymes studied showed marked increases in their activities during crises. About 70% of all the sickle cell children had elevated enzyme activities during crises. The levels of these enzymes (ALAT and ASAT) seen during crises showed adequate evidence of some liver cell damage as a result of the disease. Serum activities of these enzymes are elevated whenever disease processes affect liver cell integrity.

ASAT is present in both mitochondria and cytoplasm whereas ALAT is found only in the cytoplasm. With mild cellular damage, serum ALAT levels are higher than those of serum ASAT, whereas the latter predominates in cases with more severe cellular damage, e.g. necrosis. Evidence has also been shown that in any form of liver disease associated with hepatic necrosis, serum levels of both enzymes would be elevated even before the clinical symptoms of the disease appear.

From our present data, both ALAT and ASAT levels are equally raised during crises and these results support the view that there is some hepatic necrosis during crises in SCD.

Several workers (Song, 1957; Green et al., 1953; Bogoch et al., 1955; Rosenblatt et al., 1970; Owen et al., 1965) have described necrosis in the central and paracentral zones of the liver lobule of sickle cell adults. They observed that the necrotic areas contained increased amounts of connective tissue. If these crises occur often, the liver becomes intermittently but more chronically exposed to hypoxia, undergoes focal intermittent reversible cellular changes of injury and occasionally of cell death.

It is also interesting to note that the younger children had highly significantly raised serum ALAT and ASAT activities when compared with their older counterparts during crises. In fact, the serum ASAT level of the younger children during crises was slightly higher than the ALAT level but this difference is not significant. In the older group, the ALAT level is slightly higher than that of the ASAT and this difference is not significant either. The lower aminotransferases' activities among the older children can be explained on the basis that which recurrent painful crises, the liver in sickle cell disease undergoes persis-

tent fibrosis which may proceed to chronic hepatocellular damage. Since evidence has shown that as liver damage progresses, plasma aminotransferases' activities are increased less often. Thus, the lower enzyme activities observed among the older children may be an indication of progress towards chronic hepatocellular damage. This observation supports the work by Holkovitz and Jacobson (1961) which showed that liver disease may become worse with advancing age and may terminate in cirrhosis with hepatic failure, the more the damage to the liver cells.

There was a significant reduction in both the serum proteins and albumin fraction during crises. This fall in both serum albumin and proteins during crises lead support to the view that there is some hepatocellular damage during crises. Though, it has been shown by Edozien (1957) that the serum of African contains less albumin and more globulin yet our albumin results, during crises are significantly lower than those obtained during the steady state. In fact, the levels of both serum proteins and albumin during the steady state are the same as that of normal healthy children. This supports the view that during the steady state, there is no significant hepatocellular damage to cause a disturbance in protein synthesis as it is seen during crises. During crises, the albumin/globulin ratio is less than 1 whereas during the steady state, it is 1.29. Our findings agree with the observation of Diggs (1965) who similarly reported decreased serum albumin and elevated globulin fractions among sickle cell children in crises. The results of both serum proteins and albumin among the children during the steady state support the work of Isichei (1979) who found no difference among the sicklers during steady state when compared with normal healthy children.

From our results, we can recommend that a routine assay of these serum aminotransferases should always be done in all sickle cell children in crises along with the serum albumin to reveal the extent of the hepatocellular damage before major clinical symptoms are observed.

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