Total serum lactate dehydrogenase activity in acute Plasmodium falciparum malaria infection
I H Garba, G A Ubom

ABSTRACT

Introduction: Lactate dehydrogenase (LDH) activity was assayed in the sera of 76 adult male and 76 adult female patients within the age group of 18 - 40 years presenting with acute, uncomplicated Plasmodium falciparum malaria infection and a control group of 80 healthy adults within the same age group.

Methods: Patient selection and pre-qualification were done by simple random sampling of individuals presenting at the Bauchi Specialist Hospital Outpatient Department with a history of fever and malaise within a period of one to eight days, and who were confirmed to be infected with the P. falciparum malaria parasite by microscopical examination of Giemsa-stained thin blood slides.

Results: The mean serum LDH activity in male patients was found to be 789.4 ± 35.0 IU. This activity is significantly higher than the control LDH activity of 247.10 ± 19.0 IU (p-value is less than 0.05). The mean serum LDH activity among female patients was 634.0 ± 35.0 IU, which is a relatively higher activity compared to the control LDH activity of 247.10 ± 19.0 IU (p-value is less than 0.05).

Conclusion: The combination of acute hepatocellular injury and red cell haemolysis induced by the invading merozoites may account for the increase in serum LDH activity during this infection. Therefore serum LDH activity is a potentially valuable enzymatic marker of acute, uncomplicated P. falciparum malaria infection, especially in the absence of other complicating diseases known to be associated with the above normal serum LDH activities.

Keywords: lactate dehydrogenase, malaria, Plasmodium falciparum, serum enzymatic marker

INTRODUCTION

Lactate dehydrogenase (LDH) is an intracellular enzyme, which catalyses the readily reversible reaction involving the oxidation of lactate to pyruvate with nicotinamide adenine dinucleotide (NAD) serving as coenzyme. Five theoretically possible forms of this enzyme are found in human tissues, their concentrations differing in various organs. LDH is an example of the enzyme, which is classified as a true intracellular enzyme because of its high degree of tissue specificity where overall tissue concentrations are some 500-fold greater than serum levels under normal circumstances. Generally, high concentrations of LDH are found in the liver, heart, erythrocytes, skeletal muscles and kidneys.

Consequently, diseases affecting those organs, such as renal infarction, myocardial infarction and haemolysis, have been reported to be associated with significant elevations in total serum LDH activity. Such elevations have been widely applied as diagnostic indices for kidney, liver, heart and red blood cell dysfunction. Additionally, high serum LDH activity has also been reported in a variety of cancers, e.g. small cell carcinoma of the lung, nephroblastoma, neuroblastoma and metabolic neuroendocrine tumour. Serum LDH is also increased in patients with measles and cervical lymphadenitis. Furthermore, in monitoring the progress of diseases, LDH has been found to be relevant in establishing the survival duration and rate in Hodgkin’s disease and non-Hodgkin’s lymphoma, and in the follow-up of ovarian dysgerminoma. LDH plays an important role in predicting response to therapy and prospects of remission in leukaemia and colon cancer, and as an important clue to the diagnosis of reactive haemophagocytic syndrome (RHPS) in febrile cytopaenic patients with immunodeficiency.

Plasmodium falciparum malaria infection is a febrile illness accounting for 300-500 million clinical cases annually, with 90% of such cases occurring in Africa. It is the commonest type of malaria in Africa, where its hyperendemicity has been estimated to cost about 1.8 billion US dollars in direct costs of prevention and care, and in indirect costs such as lost productivity, time costs and other indirect costs and losses. The life cycle of this parasite in the human host includes the developmental cycle in...
This study aimed at assaying the serum level of LDH with the objective of assessing the effect of acute P. falciparum malaria infection on the serum activity of this key intracellular enzyme, considering its high concentration in both the liver and red blood cells.

**METHODS**

The southern and northern limits of Bauchi State where the study was conducted are demarcated by latitudes 9°30’ North and 10°30’ North, respectively. Its western and eastern limits are bounded by longitudes 8°45’ East and 11°0’ East, respectively. Two-thirds of the land area is in the south of latitude 11°15’.

Venous blood (5ml) was obtained from each patient by venepuncture of the antecubital vein using a sterile needle and syringe between eight and ten o’clock in the morning. The blood samples were then transferred into clean, sterile centrifuge tubes and allowed to clot. Each clotted sample was centrifuged (Griffith and George Centrifuge, Griffith and George Ltd, England) at 3,000g for ten minutes to obtain the sera. Enzyme assay was carried out within 24 hours of collection. Serum LDH activity was assayed according to the method described in Stroeve and Makarova. This involved incubating the serum sample with nicotinamide adenine dinucleotide (3 µg/ml) and DL-lactic acid (0.45M) with sodium pyrophosphate buffer, pH 8.8. This assay condition eliminates the contribution of parasite LDH, which has a different pH and substrate optima for activity. All the reagents used in the work were of AnalaR grade. LDH activity is reported in International Units (IU).

Data was analysed using the Minitab-10 statistical software (Minitab Inc, Quality Plaza, Pennsylvania, USA). Results are expressed as mean ± standard error of the mean. The difference between the mean serum LDH activity in healthy and infected male and female P. falciparum malaria patients was analysed using the one-way analysis of variance test. The Dunnett’s multiple range test was used to test for significant difference between means of the three groups. P-values of less than 0.05 were considered significant.

This work was conducted in accordance with the following ethical declarations: World Medical Association’s Declaration of Helsinki, American Psychological Association’s Ethical Principles in the Conduct of Research with Human Participants, World Medical Association’s Declaration on the Rights of the Patient, and Council for International Organisations of Medical Sciences/World Health Organisation (CIOMS/WHO): International Ethical Guidelines for Biomedical Research Involving Human Subjects.

**RESULTS**

Table I shows the serum LDH activity in both categories of patients and the control group. The mean serum LDH activity in male patients was found to be 789.40 ± 35.0 IU. This is over twice the control serum LDH activity of 247.10 ± 19.0 IU. Among the patients, the males were found to be significantly different from the females (p<0.05).

**DISCUSSION**

**P . falciparum malaria infection** involves a synergy between local circulatory failure and centrilobular cellular damage. Since LDH is found in clinically-significant amounts in...
both the liver and red blood cells, the observed increase in serum LDH activity during acute P. falciparum malaria infection in this study can be accounted for by a synergy between the two pathophysiological processes usually associated with acute P. falciparum malaria infections, i.e., the hepatic injury of the invading sporozoites leading to centrilobular liver damage and the destruction of the host red blood cells consequent to erythrocytic merogony\(^{20}\). Being rich sources of LDH, the acute liver injury and red blood cell destruction will be followed by the release of LDH into the circulation. This finding has important implications because it highlights the potential of using serum LDH activity as an index in the monitoring of acute P. falciparum malaria infection, particularly when all other possible causes of increased serum LDH levels have been eliminated.

Grover et al\(^{26}\) reported a serum LDH level of 432 IU in hospitalised acquired immunity deficiency syndrome (AIDS) patients with Pneumocystis carinii pneumonia. Similarly, Cassidy and Reynolds\(^{27}\) showed that patients with acute viral hepatitis A and B, ischaemic hepatitis and acetaminophen-induced injury are all associated with increases of up to five times the upper limit of normal LDH activity. These variations in the relative magnitudes of serum LDH activities place the P. falciparum-induced increase in serum LDH in between the values reported in the studies by Grover et al\(^{26}\) and Cassidy and Reynolds\(^{27}\). This is a reflection of the differences in the aetiology and pathogenesis of these varied conditions.

Ischaemic hepatitis, viral hepatitis and acetaminophen-induced injury are much more severe manifestations of a progressive and irreversible liver damage, sometimes involving other organs like the kidney and brain as seen in viral hepatitis\(^{28}\), while the picture in AIDS is a consequence of the onset of a multisystem disease whose progression has been slowed down by anti-retroviral drug therapy\(^{29}\). In addition, the magnitude of changes in serum LDH activity during acute P. falciparum malaria infection and other diseases/conditions like Pneumocystis carinii pneumonia, hepatitis and drug-induced liver injury can also potentially be used in distinguishing the aetiology and pathogenic outcomes of these conditions.

### Table I. Serum LDH activity in adult male and female P. falciparum malaria patients and controls

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Serum LDH activity (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male patients</td>
<td>789.40 ± 35.0(^{26})</td>
</tr>
<tr>
<td>Female patients</td>
<td>634.00 ± 35.0(^{26})</td>
</tr>
<tr>
<td>Controls</td>
<td>247.10 ± 19.0(^{26})</td>
</tr>
</tbody>
</table>

Values with the same superscript differ at p<0.05.

\(^{a}\): One-way ANOVA; \(^{b}\): Duncan’s multiple range test.

### References