

Serum enzymes activities in *Plasmodium falciparum* infection in Southern Pakistan

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Abstract

Objective: Serum levels of lactate dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) were assessed to determine the liver functions of patients infected with *Plasmodium falciparum*. The enzyme activities were assessed in 60 malarial patients and a control group of 44 people.

Materials and Methods: The data for the study was collected from the survey conducted from Liaquat University of medical and health sciences Hospital, Hyderabad, Pakaistan. Sample of 60 patients aged between 20 and 50 years were collected. A control group of 44 healthy individual adults was also assessed for comparative purposes. All the malaria patients who visited the OPD during the study period enrolled in the study.

Results: The LDH activity in male patients was found to be 674.89 ± 33.354 IU/L. This is above the control LDH activity of 296.59 ± 14.476 IU/L. Similarly, in female patients, the serum LDH activity of 580.25 ± 24.507 IU/L is over twice the control female serum LDH activity of 302.18 ± 18.082 IU/L. Further one-way anova test was performed to find any significance in infected and control male and female.

Conclusion: Hepatic dysfunction was found to be associated to *P. falciparum* malaria infection.

Key words:

Malaria, *P. falciparum*, hepatic dysfunction

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Introduction

Malaria is caused by Plasmodium protozoan parasite. The most common forms of this parasite are Plasmodium (P)

falciparum, *Plasmodium vivax*, *Plasmodium malariae* and *Plasmodium ovale*. Among these strains *P. falciparum* is considered to be the most lethal. Malaria accounts for 500 million cases a year and causes 2.7 million deaths per year. *P. falciparum* has also developed multidrug resistance in Southeast Asia [1-2]. Eradication programmes were carried out in Pakistan from 1961–1967, however a resurgence was later observed between 1972–73 [3].

P. falciparum is known to cause acute illness with severe complications and is also the only plasmodium species that can infiltrate the RBCs. Infections of *P. falciparum* are increasing and are also reappearing in previously eradicated areas [4]. Malaria can also cause the inhibition of certain liver functions and can cause liver damage in case of long continued malarial infection [5].

Lactate dehydrogenase (LDH) is an enzyme that facilitates the conversion of lactate to pyruvate. LDH is found in various organs in varying degrees of proportion. Higher proportions of LDH are usually found in the liver, heart, erythrocytes, skeletal muscles and kidneys. Increased levels of LDH are known to be associated with *P. falciparum* infection [6].

Alanine aminotransferase (ALT) also referred to as glutamate pyruvate transaminase (GPT). It is found in heart, kidney and is mainly concentrated in the liver and catalyses the transfer of aminogroups between L-alanine and glutamate. Aspartate amino-transferes (AST) also known as glutamate oxaloacetate transaminase (GOT) is present in heart, kidney, brain, and liver. The concentration of AST in the blood is proportional to tissue or organ damage (liver), both ALT and AST are reported to be elevated in malarial infection [5, 7-8].

Alkaline phosphatase catalyses the transfer of a phosphate group to an acceptor molecule. ALP is found in the liver, intestine, kidney, bone and platelets. Raised levels of ALP obstructive liver diseases and elevated levels of ALP have been reported in acute *P. falciparum* infection [9].

The activities of these enzymes in *falciparum* malaria infection are previously known [5-6]. In this study we report the levels of these enzymes associated with the liver in patients with *falciparum* malaria, in Southern Sindh, Pakistan.

Materials and Methods

Samples were collected from 60 patients, aged between 20 and 50 years, attending at the Outpatient Department of Liaquat University of medical and health sciences Hospital, Hyderabad, Pakistan. Patients with confirmed *P. falciparum* malaria infection were examined by thin blood slides stained with Giemsa and were selected for this study. Patients with other liver complications associated with LDH, ALT, AST and ALP elevations were removed from the study. A control group of 44 healthy individual adults was also assessed for comparative purposes.

Patients were initially weighed and examined than venous blood (5ml) was drawn from their antecubital vein. The blood was immediately centrifuged at 2500 rpm to obtain the sera. The enzyme assay was carried out with 12 hours of collection, ALP, ALT, AST and LDH levels of the sera were determined using a Microlab 300 and the activity is reported U/L.

Data was analysed using the SPSS ver. 16 statistical software. Results are expressed as mean values with \pm standard error of the mean. The difference between the mean serum LDH, AST, ALT and ALP activity in healthy and infected male and female *P. falciparum* malaria patients was analysed using the one-way analysis of variance test (one-way ANOVA). P-value of less than 0.05 ($p < 0.05$) was considered significant.

Results

The mean serum LDH activity in male patients was found to be 674.89 ± 33.354 IU/L. This is over approximately three times above the control LDH activity of 296.59 ± 14.476 IU/L. Similarly, in female patients, the serum LDH activity of 580.25 ± 24.507 IU/L is over twice the control female serum LDH activity of 302.18 ± 18.082 IU/L. Table 1 shows the serum LDH activity in both male and female patients and their significance differences with their control groups. Among the patients, males and females were found to have no significant difference serum LDH activity relative to their male and female healthy counterparts, ($p < 0.05$). Table 2 shows the serum ALP activity in both male and female patients and their significance differences with their control groups.

Table 1: Total LDH activity in infected and adult *falciparum* malaria patients.

Subjects U/L	Mean LDH activity (U/L)
Infected Males	$674.89 \pm 33.354^*$ (n=28)
Infected Females	$580.25 \pm 24.507^*$ (n=32)

*No significance difference with healthy male and female at $p=0.05$

The mean serum ALP activity in male patients was found to be 142.18 ± 15.094 IU/L. This is to some extent was found above the control ALP activity of 132.50 ± 12.860 IU/L. Similarly, in female patients, the serum ALP activity of 129.16 ± 11.460 IU/L is slightly over the control female serum ALP activity of 127.27 ± 10.088 IU/L. Among the patients, male were found to

have significant difference serum ALP activity relative to healthy male, ($p < 0.05$).

Table 2: Total ALP activity in infected and adult *falciparum* malaria patients.

Subjects U/L	Mean Serum alkaline phosphatase activity (U/L)
Infected Males	$142.18 \pm 15.094^{**}$ (n=28)
Infected Females	$129.16 \pm 11.460^*$ (n=32)

*No significance difference with healthy female at $p=0.05$

**Significance difference with healthy male at $p=0.05$

Table 3 shows the serum AST and ALT activity in both male and female patients and their significance differences with their control groups.

Table 3: Total AST and ALT activity in infected and adult *falciparum* malaria patients.

Subjects U/L	Mean activity (U/L)	
AST	Infected Males	$43.14 \pm 4.819^{**}$ (n=28)
	Infected Females	$39.09 \pm 3.676^*$ (n=32)
ALT	Infected Males	$29.11 \pm 4.249^{**}$ (n=28)
	Infected Females	$23.44 \pm 3.023^*$ (n=32)

*No significance difference with healthy female at $p=0.05$

**Significance difference with healthy male at $p=0.05$

The mean serum AST activity in male patients was found to be 43.14 ± 4.819 IU/L. This was found twice above the control AST activity of 18.50 ± 1.071 IU/L. Similarly, in female patients, the serum AST activity of 39.09 ± 3.676 IU/L was also found above the control female serum AST activity of 18.95 ± 1.56 IU/L. Among the patients, male were found to have significant difference serum AST activity relative to healthy male, ($p < 0.05$). At the same time the mean values of ALT in male patients was found 29.11 ± 4.249 IU/L also found above 19.32 ± 1.643 in control group. Female value was found 23.44 ± 3.023 which was slightly above control group 20.45 ± 1.558 . Male were found to have significant difference serum ALT activity relative to healthy male, ($p < 0.05$). However in both AST and ALT no significant difference was found in females.

Discussion

It is reported that hepatic failure is associated with *P. falciparum* which causes local circulatory failure and centrilobular cellular damage. Since these enzymes (LDH, AST, ALT and ALP) are known to be associated to the liver and the red blood cells. The destruction of the liver and red blood cells triggers the release of these enzymes into circulation. The elevation of these enzymes indicates rupture of the hepatocytes and RBC membranes leading to hepatic dysfunction and hyperbilirubinaemia [10-11]. Since *P. falciparum* malaria is reported to be associated with erythrocytes sequestration thus it is consistent with the elevation of LDH enzyme [12]. Moreover complicated malaria is associated with multi-organ dysfunction rather than marked elevation of liver enzymes (ALT and AST) [13]. The levels of AST and LDH in the infected patients were observed to be thrice the upper limit of normal. While the other enzymes were also found to be elevated, thus suggesting possible hepatic dysfunction in the patients. In conclusion elevation in the levels of serum enzymes and temporary hepatic complications are common features of *P. falciparum* malaria.

Conclusion

It is concluded that hepatic dysfunction and increased levels of serum enzymes is a common characteristic of *P. falciparum* malaria infection in Southern Pakistan.

Limitations

In this study we have focused on *P. falciparum* infection, however it would be interesting to evaluate the serum enzyme levels in infections of other *Plasmodium* strains in the area.

Recommendations

It would be valuable to assess the serum enzyme levels in mixed infections of malaria with other diseases associated with hepatic dysfunction in the area. It would also be interesting to evaluate variations in the concentrations of certain metals in a malaria infection in the area.

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