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ENZYME ACTIVITIES OF AKP, CPK, SGOT & LDH IN BLOOD SERUM OF MALARIA PATIENTS

Purohit Chitra*[1], Jain Suman[1]

[1]Dept. of Biochemistry, Geetanjali Medical College & Hospital, Udaipur (Rajasthan) India.

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***Correspondence for Author**
Dr. Chitra Purohit
Dept. of Biochemistry, Geetanjali Medical College & Hospital, Udaipur (Rajasthan) India..

ABSTRACT

Malaria is one of the most serious tropical diseases in the world. It becomes a severe health problem in country like India due to poor hygienic conditions; malnutrition borne non-defensive immunity system. Enzyme activity plays vital roles in metabolic pathways & are disturbed in malarial patients. In present study, blood serum Creatine phosphokinase (CPK), Lactate Dehydrogenase (LDH), Alkaline Phosphatase (AKP) & Glutamate Oxalo-transaminase (SGOT) activity was evaluated in 30 malarial patients & in the same number of normal control subjects using kit method. The enzyme activity of AKP, LDH & SGOT increases significantly, whereas the activity of CPK decreases in malarial patients as compared to control subjects.

KEY WORDS: malaria, creatine phosphokinase, lactate dehydrogenase, Liver enzymes, alkaline phosphatase.

INTRODUCTION

Malaria is a major public health problem in India and one which contributes significantly to the overall burden in south-east Asia. The National Vector Borne Disease control programme of India reported ~1.6 million cases & ~1100 malaria deaths in 2009 (8). Recently, it has been suggested that the malaria incidence is between 9 and 50 times greater than reported(15) with a 13 fold under-estimation of malaria-related mortality(10). The disease is caused by protozoan parasite of the genus Plasmodium. Five species of the parasites can infect humans. P.falciparum is the most common cause accounting for 80% of all malaria cases. It is also responsible for 90% of death arising from malaria(19). Epidemiological factors that make malaria endemic in the tropics include; climatic conditions (Relative humidity, altitudes, rainfall level, mean temperature between 18-29ºC) and socio-economic factors. All these

have effects on the availability of vectors which maintain the transmission of malaria (5). Malaria can be transmitted by three known ways; vector transmission (2), blood transfusion (22) and congenital transmission (12).The vector for malaria parasite is the female Anopheles mosquito (7). The malaria parasite interferes with 3 major organs in the body, namely: the brain, kidney and liver (11). A mosquito infects a person with sporozoites in the process of taking a blood meal. The sporozoites then enter the bloodstream and migrate to the liver. In the liver, they multiply into merozoites which infect and rupture the liver cells in an attempt to escape back into the bloodstream where infection continues. The invasion of liver cells by the sporozoite form of the malarial parasites can cause organ congestion, sinusoidal blockage and cellular inflammation(16). These changes in hepatocytes can lead to the leakage of parenchymal (transaminases) and membraneous (alkaline phosphatase) enzymes of the liver into the circulatory system (4). The hepatic (liver) stage of the parasite's life cycle in its human host is accompanied by significant perturbation in the hepatocyte's parenchyma and membrane, leading to leakage of the liver enzymes into the general circulation (20). Since the pathogenesis of this disease involves both the liver and red blood cells, this study aimed at assaying the serum levels of SGOT, AKP, LDH & CPK with the aim of assessing the effect of acute P. falciparum malaria infection on the serum activity of these enzymes, considering their high concentration in both the liver and RBC.

MATERIALS & METHODS

Patient Selection

The study was performed on 30 patients, comprising both males and females, of age 16 – 62 years, during the month of July - August, when mean daily temperature is 24°C - 26°C & a humidity of 67%. During this period, malaria endemecity is at its peak due to high average rainfall. Patient selection & prequalification were done by simple random sampling of individuals attending medicine OPD at Geetanjali Medical College & Hospital, Udaipur. Clinical malaria was suspected in patients with short history of high grade fever, chills with or without hepatosplenomegaly, after ruling out URI, UTI & other diseases with similar conditions, who were confirmed to be infected with the Plasmodium falciparum malaria parasite by microscopical examination of Giemsa - stained thin blood slides (PBS) & were considered smear positive if examination revealed any stage of malarial parasite - ring form, trophozoite, schizont or gametocyte. Same number of age and sex-matched apparently healthy subjects were included as control group.

Exclusion Criterion

Patient who presented with AIDS, Anaemia (chronic anaemia due to hypoproliferative , haemolytic or other known haemolytic disorder), kidney disorder, alcoholism, liver cirrhosis, patient on anti-malarial drugs , malignancy were excluded from the study .

Sample Collection

Venous samples were drawn from antecubital vein and were collected in double distilled washed plain vial. Serum was separated by centrifugation of blood sample. The serum thus separated was used for the determination of the enzyme activity (SGOT, AKP, LDH, CPK) by kit method using Roche (Hitachi) 902 autoanalyzer. The data obtained was analysed statistically using student's "t" test.

RESULTS

The results obtained are shown in Table 1 and Table 2. Activity of SGOT, AKP, LDH, CPK in control subjects is depicted in Table 1. The activity of all enzymes in normal subjects fall within normal range. Table 2 shows the activity of enzymes in malaria infected cases. The activity of SGOT, AKP, LDH showed significant increase ($p<0.05$, $p<0.05$, $p<0.001$) respectively and CPK significantly decreased ($p<0.05$) in malaria patients when compared to controls.

Table 1 : Activity of SGOT, AKP, LDH, CPK in Controls.

ENZYME ACTIVITY	NO. OF CASES	NORMAL CASES
SGOT	30	16.24 ± 1.18 U/L
AKP	30	119.45 ± 14.25 U/L
LDH	30	256.23 ± 13.84 U/L
CPK	30	88.23 ± 9.40 U/L

Values are Mean ± S.D.

Table 2 : Activity of SGOT, AKP, LDH, CPK in Malaria cases.

ENZYME ACTIVITY	NO. OF CASES	MALARIA CASES
SGOT	30	40.08 ± 7.32 U/L*
AKP	30	174.34 ± 24.78 U/L*
LDH	30	523.08 ± 43.62 U/L**
CPK	30	76.22 ± 8.76 U/L*

Values are Mean ± S.D, * denotes $p<0.05$, ** denotes $p<0.001$

DISCUSSION

As evidenced from the present work, enzyme activity of SGOT, ALP, LDH, CPK were determined in the blood serum levels of malarial patients and control subjects. It is observed that the activity of the enzymes SGOT, ALP, LDH increases significantly indicative of hepatic compromise during malarial infection. The enzyme SGOT is associated with liver parenchymal cells and is also present in red blood cells and cardiac muscles. It is raised in acute liver damage which is true in malaria if other causes are ruled out. Alkaline phosphatase (AKP) is known to be phosphate removing agent, found in liver, bile duct, kidneys, bones and placenta. Its decreased levels could increase the phosphate levels in the cells which could harsh the entire body with toxicity, leading to other complications and fatal for the patient with low immunity (3). The factors involved in hepatic dysfunction in acute Plasmodium falciparum malaria infection involve a synergy between local circulatory failure and centrilobular cellular damage i.e. the hepatic activity of the invading sporozoites leads to centrilobular liver damage and destruction of the host red blood cells consequent to erythrocytic merogony (18). Pre-erythrocytic shizogony with hepatic parenchymal damage is part & parcel of natural history of malaria. Signs of liver damage & derangement of liver function tests of varying degrees of severity have been reported in all four naturally acquired human malarial infections (21).The increase in liver enzymes (AST, ALT and ALP) have been observed among malarial infected patients (18). Onyesom (20) also demonstrated that the various liver enzyme (AST, ALT and ALP) activities in serum increased with increase in malarial parasite density and confirmed that the hepatic (liver) stage of the parasite's life cycle in its human host is accompanied by significant perturbation in the hepatocyte's parenchyma and membrane, leading to leakage of the liver enzymes into the general circulation. Increase in aminotransferases, although generally regarded as reflecting liver cell changes in acute malaria could be contributed to varying extent, by enzymes released from lysed erythrocytes and other tissues (1, 9). LDH is present abundantly in tissues (liver, RBC) which get infected by malarial parasite during completion of asexual cycle. So, raised LDH level may be considered as an evidence for P. falciparum infection. Being rich sources of LDH, the acute liver injury and red blood cell destruction will be followed by the release of LDH 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 Plasmodium falciparum malaria infection (17), particularly when all other possible causes of increased serum LDH levels have been eliminated (13). The variations in the relative magnitudes of serum LDH activities place the P. falciparum-induced increase in

serum LDH in between the value reported in patients with AIDS or acute viral hepatitis A & B, ischemic hepatitis and acetaminophen-induced injury (6,14) which are associated with increase of up to five times the upper limit of normal LDH activity. This is a reflection of the differences in the aetiology and pathogenesis of these varied conditions. Our study showed decrease in CPK activity in malarial patients as compared to normal subjects. There is no clear role of CPK in malaria but its level may be decreased due to the decrease in the ATP content of the body. CPK is used for the rapid buffering & regeneration of ATP from ADP and serves as an energy reservoir as well as used for intracellular energy transportation. The decreased levels of this enzyme could lead to low energy and immunity in the body. The variation in serum enzyme activity of patients with malaria shows the severity of disease (3).

CONCLUSION

Although, diagnosis of malaria rest on the demonstration of asexual forms of the parasite in stained peripheral blood smear. Sometimes no parasites can be found in PBS from patients with malaria, even in severe infections. This may be explained by partial antimalarial treatment or by sequestration of parasitized cells in deep vascular beds (17). So, indirect evidences for diagnosis of malaria becomes only the reason to start or to justify anti-malarial treatment. Thus it is concluded that these enzymes can be used as markers in malaria patients.

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