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Original Article

Electrolyte Disturbance and the Type of Malarial Infection

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Abstract

Background: Electrolytes play an important role in the normal functioning of human body. Electrolyte imbalance and mineral disturbances is the common clinical manifestation in several infectious diseases including malaria. Malaria is a mosquito borne serious infectious disease of the world. *Plasmodium vivax and P. falciparum* are the main agents responsible for malaria in Pakistan. Electrolyte imbalance in malarial infection may lead towards the severity of disease.

Methods: The present study analyzed the electrolytes levels (Na, K, Ca and Mg) in malarial patients and healthy individuals. Patients were categorized into two groups, *P. falciparum* and *P. vivax,* based on causative species of *Plasmodium.* Study consisted of 173 individuals, out of which 73 were malarial patients and 100 were normal healthy individuals.

Results: Concentrations of Na, K, and Ca were low in the blood of malarial patients as compared to healthy individuals ($P<0.05$). No significant difference for these electrolytes exists between *P. falciparum* and *P. vivax* infected groups ($P>0.05$). The concentration of Mg was changed based on exposure to the type of parasite. In *P. falciparum* infection, the level of Mg was lower than healthy individuals was ($P<0.05$). Discordantly, in case of *P. vivax*infection, Mg level was higher than healthy individuals were ($P<0.05$). No variation was noticed in electrolytes levels due to gender differences ($P>0.05$).

Conclusion: Variation in Mg levels occurs due to exposure of *Plasmodium* depending on its type. The levels of Na, K and Ca are also changed due to *Plasmodium,* regardless of its type.

Keywords: Malaria, Electrolytes, *Plasmodium falciparum, Plasmodium vivax*

Introduction

Malaria is one of the most widespread infectious diseases among humans. People from more than 100 countries suffer from the havoc caused by malaria. World Health Organization (WHO) estimated 198 million cases and 5, 84,000 deaths due to malaria in 2013(1). Malaria is endemic in tropical and subtropical regions with highest prevalence in Africa and Southeast Asia. Pakistan, being a subtropical country, provides good habitat to mosquitoes and bears strong malarial burden. WHO declares Pakistan among one of the six countries with the highest malaria transmission in 2013 (1). Five species of *Plasmodium* are known to infect humans; these include *P. falciparum, P. malariae, P. ovale, P. vivax and P. knowlesi. P. vivax and P. falciparum* were recognized as the main agents responsible for malaria in Pakistan. Prevalence of malaria due to *P.* vivax is high in Pakistan (1,2).

Electrolytes are minerals present in blood and other body fluids. There optimum range is essential for proper physiological activities (3). Electrolyte imbalances and mineral disturbances were known to be common clinical manifestations in several infectious diseases including malaria. Hyponatraemia, hyperkalaemia, hypocalcaemia and hypomagnesaemia usually develops because of infection with *Plasmodium* (4).

Sodium (Na) is known as the major cation of exracellular fluid. It regulates the normal distribution of water and osmotic pressure in various

body fluids. Various health problems occur due to Na^+ ion disturbance (5). Hyponatraemia, the decline in the Na concentration, is considered as an important clinical manifestation of malaria. Decreased level of Na exaggerates the disease symptoms and results in severe malaria (6). Potassium (K) is identified as a crucial electrolyte for accurate functioning of all body cells, tissues and organs. It maintains blood pH and water levels in the body. It is particularly important in skeletal and smooth muscle contraction. Hypokalaemia is a common complication of severe malaria. Decreased level of K is an obvious correction of acidosis in malaria (7). Calcium (Ca) is considered as an essential nutrient for human body. It provides strength to bones and teeth. It plays an important role in the maintenance of health and nutritional qualities (8). Low level of Ca is a common observation during malaria infection. Decline in calcium occurs due to clinical symptoms associated with malaria like fever, high pulse rate, sweating and shivering (9). Magnesium (Mg) is known as an important element that acts as a cofactor of more than 300 enzymes. It regulates protein synthesis, blood glucose, blood pressure, neuromuscular function and several other biochemical reactions (10). Its levels usually drop because of malaria mostly in case of *P. falciparum* (11).

Prevalence of malaria is very high in Pakistan. *P. vivax*and *P. falciparum* impart heavy health burdens on the local population of Pakistan. Electrolyte imbalance appears because of malaria and may lead towards the severity of disease.

The present study aimed to find out the levels of Na, K, Ca and Mg in malarial patients suffering from both *P. vivax* and *P. falciparum*.

Materials and Methods

Sample collection

All procedures complied with the declaration of Helsinki. The Advance Research and Study Board, University of Sargodha approved the protocol of present study. Prior permission was also taken from the Ethical Committee of the University of Sargodha.

After taking proper consent and completion of ethical criteria, blood samples of 173 individuals were collected and stored at -20°Cuntil further processing. Blood samples of 73 malarial patients were collected from different hospitals in district Sargodha, Punjab, Pakistan from March 2013 to February 2014.Patients were categorized into two groups, *P. falciparum* and *P. vivax,* on the basis of causative species of *Plasmodium* for malaria. Forty samples were placed in *P. falciparum* group and 33 in *P. vivax* group. Data related to patients like age, gender and *Plasmodium* species responsible for malaria was collected from laboratories of hospitals. Blood samples of 100 age matched healthy volunteers were also collected. Three ml blood was taken from each sample and anticoagulant was added to prevent it from clotting.

The patients were between 1-45 yr in age. *Plasmodium* parasite resides in the red blood cells resulting in their lysis. If the electrolyte level variation happens due to the presence of pathogen, it may be detected through the comparison of whole blood electrolyte levels in blood of patients and healthy individuals. Whole blood was used for electrolyte determination in the present study. The determination of electrolytes in whole blood was performed using wet acid digestion method followed by atomic absorption spectrophotometry.

Estimation of electrolytes

From each sample, 1ml of whole blood was shifted into beaker and 0.5ml of distilled water was added in it followed by the addition of 1ml of Hydrogen peroxide ($H_2O_{2)}$ and 4ml of Nitric acid (HNO_3) for wet acid digestion. The beaker was covered and left overnight. Next day, samples were heated on hot plate and H_2O_2 was added drop wise until solution became clear. After filtration, de-ionized water was added to make volume up to50ml and was stored in Teflon tubes (12).

After wet acid digestion, the blood samples were analyzed for determination of Na, K, Ca and Mg through Atomic absorption spectrophotometer (AA 6600 Shimadzu). Standards were used for the standard curve formation and estimation of electrolyte levels in the samples.

Statistical Analysis

Data was processed using SPSS 13.One way ANOVA was performed to depict statistical differences. The results were presented as Mean ± Standard deviation (SD) and a *P*-value of <0.05 was considered as significant.

Results

Table 1 shows the results for comparison of electrolytes levels in the blood samples (µg/l) of malarial patients (*P. falciparum* group, *P. vivax* group) and healthy individuals. Na, K and Ca levels significantly differ between malaria infected and healthy individual groups (*P*< 0.05).

The results suggest that hyponatraemia, hypokalaemia and hypocalcemia were more common in malaria-infected individuals as compared to healthy individuals. The difference of electrolytes levels was not significant between *P. falciparum* group and *P. vivax* group.

Table 1: Comparison of electrolytes level in different groups

Electrolytes	*Plasmodium falciparum* (n=40)	*Plasmodium vivax* (n=33)	Healthy individuals (n=100)
Na	3.9925±1.40701***	3.1318±1.46990***	7.1750±0.12275***
K	0.1208±0.02795***	0.1209±0.08494***	0.2262±0.02605***
Ca	65.2250±10.98831***	60.7273±13.29068***	90.4400±4.48188***
Mg	9.6750±3.50375***	34.6667±8.73451***	19.5895±2.26279***

*= Significant, **= highly significant, ***= very highly significant, NS=Non significant

Mg level significantly differ between *P. falciparum* and *P. vivax* group (*P*<0.05). Mg levels were high in *P. vivax* group as compared to *P. falciparum* group. Table 2 represents the comparison of electrolytes levels in males and females suffering from malaria (*P. falciparum, P. vivax*) and healthy individuals. Electrolytes level did not differ between males and female.

Table 2: Gender wise distribution of electrolytes in different groups

Gender	Electrolytes	*P. falciparum*	*P. vivax*	Healthy individuals
Male	Na	3.9032±1.40154^{NS}	3.2231±1.51481^{NS}	7.1884±0.11786^{NS}
	K	0.1168±0.02891^{NS}	0.1281±0.09282^{NS}	0.2270±0.02628^{NS}
	Ca	65.4839±10.54789^{NS}	59.3462±12.94277^{NS}	89.9600±4.61126^{NS}
	Mg	9.5484±3.65001^{NS}	34.3462±7.93444^{NS}	19.6000±2.19461^{NS}
Female	Na	4.3000±1.46544^{NS}	2.7929±1.33866^{NS}	7.1616±0.12722^{NS}
	K	0.1344±0.02007^{NS}	0.0943±0.03910^{NS}	0.2254±0.02605^{NS}
	Ca	64.3333±13.04799^{NS}	65.8571±14.32281^{NS}	90.9200±4.34173^{NS}
	Mg	10.1111±3.10018^{NS}	35.8571±11.93634^{NS}	19.5790±2.35125^{NS}

*= Significant, **= highly significant, ***= very highly significant, NS=Non-significant

Discussion

Malaria is a common parasitic disease of tropical and subtropical regions of the world. Approximately 500 million individuals become the victim of malaria each year. It is a highly devastating parasitic disease caused by intra-erythrocytic protozoa of genus *Plasmodium*. Two species of *Plasmodium*, *P. falciparum* and *P. vivax* are widespread and responsible for majority of deaths. Among these, infections resulting from *P. falciparum* if left untreated might cause kidney and brain complications and even death (13, 14).

Electrolytes are important for the normal physiology of life. These are the ionized salts (minerals) present in human body fluids and the blood

stream. The whole body actually acts like a bioelectric organism and electrolytes are both the switch and the energy source for our body (15). Electrolyte disturbance is known to be the common complication in severe malaria. Hyponatraemia and hypokalaemia has long been considered as a common complication in severe malaria. Electrolyte disturbance acts as an indicator for the severity of disease, because they are usually associated with the severe *P. falciparum* and *P. vivax*malaria (16). In the present study, blood samples were used for the evaluation of electrolytes in malaria patients and healthy individuals.

Na is one of the most important mineral in human body. Na is necessary for the fluid distribution, blood pressure, cellular work and electrical activity of the body. Alterations in Na level can cause several health problems (17). Present study indicates that malarial infection led to reduction in the levels of Na i.e., hyponatraemia. The pathophysiology of hyponatraemia in malaria remains unclear, but several studies have reported that an increased secretion of vasopressin (ADH), either appropriately or inappropriately, plays an important role in the low level of sodium in malaria because sodium may enter into the infected cells and result in loss of blood (18). Hyponatraemiahas been identified as a common outcome of malaria (16, 19). Ikekpeazu et al. also observed reduction in the Na level of malaria patients (20). Hyponatraemia has been reported to occur frequently in patients suffering from *P. falciparum* malaria than in *P.vivax* malaria (16, 21).However, we observed no such difference. Potassium (K) is an important electrolyte in human body. It is also known as mineral of the heart because it directly affects the heart muscle cells. It is essential for the normal functioning of nervous system and heart muscle activity. Minor changes in potassium level can cause weakness, fatigue and rapid heartbeat. Therefore, its balance is very important for the normal physiology of human body (22). The present findings showed the decline in K level due to *Plasmodium* infection. Decline in the level of K has been reported in various studies (19, 20). Enhanced urinary removal of K and hypokalemia has been reported as common outcomes of malaria (12). *Plasmodium* presence may lower the K levels and aggravates the complications associated with malaria disease. *P. falciparum* infected individuals were frequently observed with hypokalaemia as compared to *P. vivax* infected individuals (16). No significant variation in the levels of K was found in our study among *P. falciparum* infected and *P. vivax* infected cases. However Maitland et al. observed no change in the level of Na and K in patients suffering from malaria as compared to healthy individuals (23).

Ca is the most abundant mineral present in the human body. Bones are the main reservoir of calcium. It is an important mineral for teeth and bones. Other than bones and teeth, the level of ionized calcium in the blood must be maintained within a narrow range to perform calcium's regulatory functions. Alterations in Ca level can cause several changes in the body like muscle cramps, osteoporosis, etc.(24). Hypocalcaemia in the blood samples of malaria patients was noticed as compared to the healthy individuals. Various studies reveal reduction in the level of Ca in malarial patients (25-27).Trophozoites concentrate calcium in their internal compartment for metabolism (28). Losses in calcium can also be caused by losses during digestive and renal problems following malaria (28).

Plasmodium infection may change the cell permeability for Ca (29). Infected cells increased Ca permeability, which led to reduction of Ca in blood that is observed in malarial patients. Another possible cause of hypocalcaemia is that parasites may adhere in the glomerular capillaries causing renal insufficiency. This might result in increased urinary excretion of minerals e.g. Ca causing hypocalcemia (28).

Magnesium (Mg) is the fourth most abundant cation in the human body. It is a cofactor involved in more than 300 enzyme systems regulating the different biochemical reactions in human body. It is involved in the muscle and nerve functions, blood glucose control and regulation of blood pressure (30, 10). Its balance is very important for the normal functioning of body. Its deficiency results in vomiting, fatigue, weakness, muscle contraction and cramps (10). The present study observed the

variation in level of Mg depending on the type of parasite exposed to the patients. The reduced Mg level was noticed in patients suffering from *P. falciparum* infection. Discordantly, the increased Mg level was observed in patients suffering from *P. vivax* infection. Controversial reports were available about variations in Mg level between different Plasmodium species. Baloch et al. reported decrease in level of magnesium in patients suffering from *P. vivax* malaria (31). Increase in magnesium has been reported in patients suffering from *P. falciparum* malaria. Mg level increases due to hemolysis resulted from RBCs merogny by the parasite. Magnesium deficiency is associated with reduced number of RBCs (32-34). Electrolytes levels under observation did not vary due to gender effects. Jasani et al. also reported the similar information (16). It may be because *Plasmodium* affects electrolytes levels without gender discrimination.

Conclusion

Levels of Na, K, Ca and Mg are influenced by the presence of both *P. falcipaum* and *P. vivax* malaria. There is a need to manage the electrolyte derangements for overall management of malaria. It can be concluded that mineral supplementation may help to prevent disease severity.

Ethical Considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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