

Significance of Biochemical Parameters of Kala-azar Patients for the Treatment and Prognosis of the Disease in Bangladesh

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ABSTRACT

Introduction: Kala-azar or Visceral Leishmaniasis (VL) is a protozoal disease caused by the parasite *Leishmania donovani* and is transmitted by the biting of certain species of female phlebotomine sand-fly. This study was carried out to determine the changes of biochemical parameters in Kala-azar patients those are very much significant for the diagnosis of disease. **Methods:** This cross-sectional study was done among 56 Kala-azar patients and 30 healthy persons in 'Surjokan to Kala-azar Research Center' (SKRC) in Mymensingh under supervision of Mymensingh Medical College Hospital from July, 2015 to June, 2016. All biochemical parameters were measured according to different recommended methods. **Results:** This study revealed the changes in SGPT, SGOT, ALP, Serum total protein level, Albumin level, Globulin level and A/G ratio level. The changes of all those parameters were statistically significant ($p < 0.001$). **Conclusion:** According to the study findings, it could be recommended that the changes of biochemical parameters are very important for diagnosis and management of Kala-azar patients. So, the routine biochemical investigation should be done in suspected Kala-azar patients.

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INTRODUCTION

Leishmaniasis is a group of vector borne diseases which have three main types: visceral, cutaneous and mucocutaneous.¹

Visceral Leishmaniasis (VL) or Kala-azar is a systemic infection of the reticuloendothelial

system caused by protozoa *Leishmania donovani* (LD) of the genus *Leishmania*. Genus *Leishmania* was created by Ross in 1903.² Sir William Leishman discovered the parasite in spleen smears simultaneously with Charles Donovan identifying the same parasite in spleen biopsy.

The parasite has two forms: aflagellate or amastigote and flagellate or promastigote form. These two forms complete within man and sandfly respectively. The amastigote exists and proliferates in the mononuclear phagocytic system (MPS), especially spleen, liver and bone marrow. This causes hyperplasia of the MPS in phagocyte bearing organs, producing hematological and biochemical manifestations.³

Kala-azar or VL is endemic in more than 60 countries worldwide.⁴ In every year about 0.2-0.4 million new cases of VL have been reported globally and more than 90% of the new cases of VL occurred in Bangladesh, India, Brazil, Ethiopia, Sudan, and South Sudan. Twenty four lacs (2.4 millions) disability-adjusted life-years (DALYs) are lost each year due to Kala-azar and the South-East Asia region accounts for the loss of about 0.4 million DALYs. Kala-azar is the disease of poverty and mostly distresses the socially downgraded and deprived communities of the rural population and is recognized as the neglected tropical disease (NTD).⁴

Kala-azar is one of the major public health problems in Bangladesh. In this country 45 districts are endemic for VL and 20 million people (around 18% of the total population), are considered to be at risk for VL. The genetic factors, malnutrition, migration, poor housing and sanitary conditions and the presence of infected animals in the environment are major factors responsible for the high prevalence of this disease.⁵

The clinical feature of VL is characterized by fever, weight loss, splenomegaly, hepatomegaly, skin darkening and anemia which is known as Kala-azar ("black fever" in Hindi).⁶ It carries a high mortality ranging from 80% to 100% in untreated cases. Even with treatment, case fatality rates in excess of 10% are common.⁷

Some biochemical parameter changes indicate the occurrence of Kala-azar. Alterations in these parameters occur due to pathophysiological changes of the patient. Biochemical and immunological parameters such as serum bilirubin, serum creatinine, serum glutamic pyruvic transaminase (SGPT), serum glutamic oxaloacetic transaminase (SGOT), alkaline phosphatase (ALP), serum total protein, albumin,

globulin, albumin-globulin (A/G) ratio and IgG are important.^{8,9}

The aim of this study was to determine the changes in biochemical parameters of Kala-azar patients and compare them with the healthy persons to know the alterations of which parameters are significant to the disease.

METHODS

This cross-sectional type of descriptive study was carried out in the Institute of Biological Sciences (IBSc), Rajshahi University, Rajshahi Bangladesh, during the period of July, 2015 to June, 2016. Kala-azar patients were selected from "Surjokanto Kala-azar Research Center" (SKRC), Mymensingh which is under supervision of Mymensingh Medical College Hospital. There were 56 Kala-azar patients (35 males and 21 females) aged up to 60 years and 30 control groups (18 males and 12 females) were selected from the same socio-demographic background for this study. The patients were free from comorbidity diseases such as malaria, enteric fever, chronic liver disease, thalassemia, lymphoma, leukemia, diabetes mellitus and hypertension etc. All study subjects were informed about the procedure and their informed written consent were taken before collection of sample. The ethical consent was taken from the authority of SKRC. Socio-demographic data were collected by using structured questionnaires and interviews. Data related to biochemical parameters were collected from the blood sample of the patients. The patients were diagnosed by clinically and rK39 test. With all aseptic precautions two (2) ml of venous blood was collected from the study subjects and the blood samples were immediately transferred to the anticoagulant e.g. Ethylenediaminetetraacetic acid (EDTA) containing labeled test tube. Serum bilirubin, serum creatinine, SGPT, SGOT, ALP, serum total protein, albumin, globulin, A/G ratio was measured according to different current methods.

All statistical analysis was done by using Statistical Package for Social Science (SPSS), version-20. Results were expressed as Mean±Standard Deviation (SD). Statistical significance of reference between two groups was evaluated by using independent student's 't' test and *p* value <0.05 was considered statistically significant.

RESULTS

In this study, age ranges of study subjects were from 5 to 60 years.

Majority (25, 44.60%) of the patients were of 18-40 years age group (Table I).

Table I: Distribution of the study subjects by age group

Age (in years)	Patients (n-56)		Control group (n-30)	
	Frequency	Percentage (%)	Frequency	Percentage (%)
<18	10	17.90	7	23.34
18-40	25	44.60	17	56.66
40-60	21	37.50	6	20.00

Among the patients, 35 (62.5%) were male and 21 (37.5%) were female with M: F ratio of 1.67:1 and the control group 18 (60%) were male and 12

(40%) were female with M: F ratio of 1.5:1 (Figure 1).

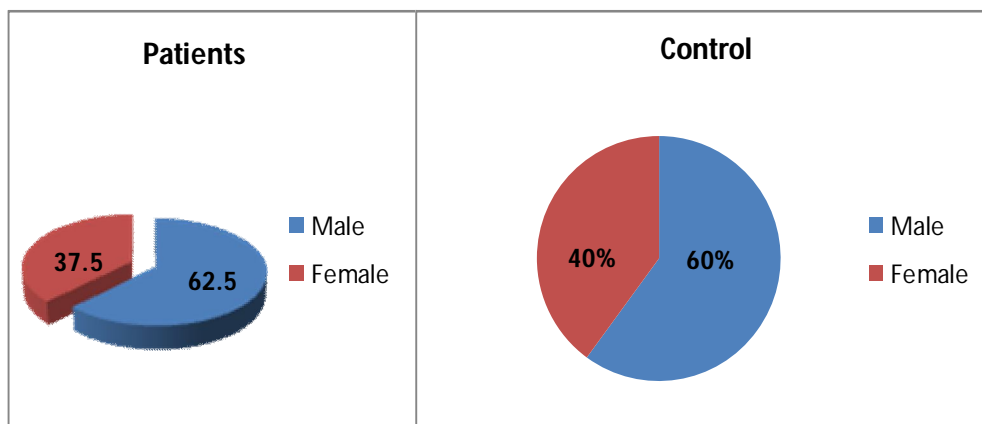


Figure 1: Sex distribution in Kala-azar patients and control group

In this study, almost all (56, 100%) patients complained of fever, 76.8% suffered from weight loss. Darkening of skin and gum bleeding occurred in 60.7% and 37.5% of patients respectively. Most common clinical signs of the patients was splenomegaly (75%) followed by anemia (50%) and hepatomegaly (19.6%) (Table II).

Table II: Symptoms and signs in Kala-azar patients (n-56)

Traits	No. of patients	Percentage (%)
Symptoms		
Fever	56	100
Weight loss	43	76.8
Darkening of skin	34	60.7
Gum bleeding	21	37.5
Signs		
Anemia	23	50
Splenomegaly	42	75
Hepatomegaly	11	19.6
Hepatosplenomegaly	7	12.5
Lymphadenopathy	5	8.9

*Multiple responses

Serum ALP (178.9±21.1 U/L), total protein (98.38 ± 2.3 g/L), globulin (65.22 ± 2.8 g/L) and A/G ratio (0.63 ± 0.06) were significantly increased in Kala-azar patients in comparison to control group. Serum creatinine was normal (1.01 ± 0.05 mg/dl), but serum bilirubin was slightly increased (0.97± 0.05 mg/dl) (Table III).

Table III. Comparison of biochemical parameters

Parameters	Kala-azar patients	Controls	p-value	Inferences
Bilirubin (mg/dl)	0.97± 0.05	0.95 ± 0.09	0.877	n.s
S. Creatinine (mg/dl)	1.01 ± 0.05	0.85 ± 0.03	0.063	n.s
ALP (U/l)	178.9±21.1	83.36 ± 4.21	0.0001	*
SGOT (U/l)	20.17 ± 1.2	14.59 ± 0.62	0.002	*
SGPT (U/l)	52.13±1.99	31.33 ± 3.42	0.003	*
Total protein (g/L)	98.38 ± 2.3	76.92 ± 1.2	0.0001	*
Albumin (g/L)	33.10 ± 1.2	41.10 ± 0.77	0.0001	*
Globulin (g/L)	65.22 ± 2.8	35.8 ± 1.05	0.0001	*
A/G ratio	0.63 ± 0.06	1.17 ± 0.04	0.0001	*

^{n,s}Non-significant, *Significant

DISCUSSION

This study was carried out to determine the changes in biochemical parameters of Kala-azar patients and to compare with the healthy person. These biochemical changes are useful for the diagnosis and treatment of the patients to evaluate the prognosis of the disease.

In this study, out of 56 Kala-azar patients, male was 62.5% and female was 37.5%. Bhowmick et al.¹⁰ found that the prevalence of Kala-azar was higher in male (51.22%) than female (36.96%). Boggiatto et al.¹¹ showed that male patients (40,56.3%) were higher than female patients (31,43.7%). Another study conducted by Singh et al.¹² established that infection of VL had higher in males than females in India. These results were consistent to our findings due to occupational variation.

Fever and weight loss were the common symptoms in Kala-azar patients due to infection and anorexia. Gum bleeding and darkening of the skin were also present possibly due to thrombocytopenia. Regarding the signs, anemia was common in the patients. The presence of anemia in Kala-azar patients would suggest haemolysis, hypoplasia of bone marrow and intravascular volume contraction.¹³ In our study, splenomegaly (75%) was the most marked signs in Kala-azar patients as a result of haemolysis in spleen. In a study conducted by Islam et al.,¹⁴ splenomegaly was reported to be present in 100% patients, but it may be absent in

immunocompromised patients, such as those who are HIV positive, renal transplant recipients, hematological malignancies and are on long-term steroid therapy. Several studies^{15,16} revealed that splenomegaly may be absent in acute cases, or in the early stages of the disease. Besides, hepatomegaly, hepatosplenomegaly and lymphadenopathy were less frequent in those patients.

In our study, serum bilirubin was not significantly increased in Kala-azar patients. This finding is similar with other study conducted in Kala-azar endemic areas of Malda District, West Bengal, India. It established the early stage of infection.¹⁷ Serum creatinine level was found normal (1.01±0.05 mg/dl of blood) in both patients and control group of our study. Ganguly et al.¹⁷ and Caldas et al.¹⁸ showed that serum creatinine level was 0.66 and 1.21±1.24 mg/dl of blood respectively. These findings revealed that Kala-azar does not hamper the renal function.

In this study serum SGPT, SGOT and ALP level were significantly increased than the control group due to functional disturbance of liver. This finding is almost similar to other study conducted in Etheopia by Tesfanchal et al.¹⁹

Changes in serum albumin and globulin level were significant in Kala-azar patients. Caldas et al.¹⁸ reported same change in their study. Gatto et al.⁹ showed that patients had lower albumin (hypoalbuminemia) levels compared to the control group. Hypoalbuminemia in Kala-azar

patients would suggest intravascular volume contraction, malnutrition, infections etc.

Study limitations were short study period, small sample size, and localized study area. Further study may be done on hematological and immunological parameters of Kala-azar patients on large sample size including the region of Jamalpur, Tangail and Sirajganj district of Bangladesh.

CONCLUSION

In this study, we found that serum SGPT, SGOT, ALP, globulin level was significantly increased and serum albumin level significantly decreased in Kala-azar patients than the control group. So, these changes of biochemical parameters are very much helpful for diagnosis and treatment of Kala-azar.

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Conflict of Interest: The authors declare no conflict of interest.

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