

Observation of Deviations and Comparisons of Liver Function Test in Different Stages of Kala-Azar

Sujit Kumar¹, Rashmi Singh²

¹(Tutor, Department of Physiology, Nalanda Medical College, Patna, Bihar, India)

²(Tutor, Department of Community Medicine, Patna Medical College, Patna, Bihar, India)

*Corresponding Author: Sujit Kumar

Abstract: Kala-azar is a protozoal disease characterised by fever of alternating, remittent or intermittent type. The problem of kala-azar assumes considerable importance today in view of epidemic outbreak in our country India. Liver is vital organ of the body and it is invariably affected in Kala-azar. The main aim of this work is to assess the severity of damage of liver in Kala-azar by means of various liver function tests. A Study on 100 diagnosed cases of kala-azar in NMCH & RMRIMS, Patna and 25 healthy individuals was done. Predefined questionnaire was used. Appropriate statistical tests were used whenever necessary. In the present study, the different types of liver function tests were performed and analysed. The mean value of different parameters of liver function test were deranged in comparison to mean value of control group. As the disease advances, these values were found abnormal. It was concluded from all the biochemical tests of liver function and observed tests finding that there was a definite degree of hepatic damage in Kala-azar cases and hepatic damage was proportionally related to the advancement of the disease

Keywords: Kala-azar, Liver Function test, Hepatic damage.

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I. Introduction

The problem of kala-azar assumes considerable importance today in view of epidemic outbreak in our country India. This disease has made abode in the plains of Ganges and Brahmaputra. It has been known to occur epidemically and endemically in well defined areas in the eastern sector of the country viz., Assam, West Bengal, Bihar, eastern districts of Uttar Pradesh, foothills of Sikkim and to a lesser extent in Tamil Nadu and Orissa¹.

As a result of the massive insecticide spraying campaign for malaria eradication between 1958 and 1964, Kala-azar declined to a point of extremely low endemicity. After its resurgence in Bihar in early seventies, the disease spread from the four northern districts to adjoining areas. Currently about 33 districts of Bihar, 10 districts of West Bengal and 2 districts of Uttar Pradesh are affected by kala-azar. The increasing trend of the disease is evident from the fact, that the total no. of cases which were 17,806 with 72 deaths in 1986 rose to total of 77,102 cases with 1419 deaths in 1992. Also, there were 33,234 cases with 146 deaths in 2008 and 20,478 cases in Nov. 2009 with 70 deaths in India¹. For a better observation and clear study, the kala-azar cases have been classified into below mentioned 3 stages (based on worldwide accepted classification of N.K. Chakravarty and P.C. Gupta, with duration of illness being the main criteria for classification²).

- Early stage : duration of illness below 3 months
- Mid stage : duration of illness between 3-5 months
- Advanced stage: duration of illness above 5 months.

In affected districts, patient presents with almost proportionate enlargement of the liver & spleen in kala-azar. It has been shown that in most of the cases of kala-azar, there was evidence of altered plasma protein secondary to liver involvement. Also, it has been observed clearly that there is a definite variation in the values of different plasma protein in above mentioned stages of kala-azar cases.

The main aim of this work was to assess the severity of damage of liver in Kala-azar by means of various liver function tests like total serum protein, serum albumin, serum globulin, serum albumin-globulin ratio, serum bilirubin, serum alkaline phosphatase, serum SGPT and serum SGOT in different stages of illness and to provide information related to prognosis in kala-azar regarding to liver.

II. Material And Methods

In the present study one hundred patients of kala-azar were selected from Medical Indoor of RMRIMS, Patna and NMCH, Patna. For the convenience, the kala-azar cases were classified in three stages on the basis of classification made by N.K. Chakarvarty and P.C. Gupta, on the basis of duration of illness.

1. Early stage –Duration of illness below 3 months.
2. Mid stage –Duration of illness between 3 to 5 months.
3. Advanced stage – Duration of illness above 5 months.

In the present study of one hundred cases of kala-azar, it was noted that the hepatic enlargement in most of the cases depend upon the duration of illness.

Study Location: This study was carried out among Kala-azar patients admitted for treatment in Rajendra Memorial Research Institute of Medical Sciences, Patna and Nalanda Medical College & Hospital, Patna

Study Duration: October 2012 to September 2013

Subjects & selection method: 100 cases of kala-azar admitted for treatment. 25 cases of normal healthy persons were also selected among medical students, staff and other volunteers as control.

Procedure methodology

1. Selection of Cases:

- Study group: One hundred diagnosed cases of kala-azar were selected from RMRIMS, Patna and NMCH, Patna. The blood samples were taken within the first week of their admission.
- Control groups: Twenty five healthy individuals were selected as control from medical students, staffs and other volunteers. The control groups were non-alcoholic, non-smoker and had no past history of jaundice, Tb, altered sensorium, hematemesis, melena, blood transfusion, drug addiction or tobacco chewer and prior hospitalization for any disease.
- The study of the cases was recorded in following headings:
 - Name
 - Age
 - Sex
 - Religion
 - History of duration of Illness.

2. Investigations in cases of Kala-azar patients:

- Routine hematological investigations in cases of kala-azar are as follows :-
 - Total and differential count of WBC (i.e. TC & DC of WBC)
 - Total RBC
 - Platelet count
 - Hemoglobin percentage (Hb %)

3. Diagnosis:

- Diagnosis was based on:
 - Splenic aspirate examination for L.D. bodies, or
 - Bone marrow aspiration examination for L.D. bodies

➤ Liver Function Tests:

These are widely accepted liver function tests which were the basis of observation in this study.

They were as follows:

- Serum protein: a. Total Protein
- b. Albumin
- c. Globulin
- d. AG ratio
- Serum Bilirubin
- Serum Alkaline Phosphatase
- SGPT (Serum Glutamic Pyruvic Transaminase)
- SGOT (Serum Glutamic Oxaloacetic Transaminase)

4. Collection of Specimen:

About 10 ml of blood was collected in a clean dry test tube using a dry sterilized disposable syringe and was allowed to clot. The serum was separated and centrifuged in a Kahn's test tube. Finally the clear serum was collected in a dry test tube. That test tube was used for the estimation of various liver function tests.

5. Bone Marrow Smear Examination for L.D. Bodies:

This is used for diagnosis purposes in suspected cases of Kala-azar particularly in early cases where the spleen is not sufficiently enlarged as to be punctured. In comparison to the splenic puncture it is a safer procedure. In this case risk of haemorrhage is greatly minimized, but it is more painful. Disadvantage regarding this test is that, when the parasites are scanty, the examination can give a negative result. Nearly 60-70% of bone marrow aspirations show L.D. bodies.

6. Splenic Aspirate Smear Examination:

When the spleen is markedly enlarged, it is one of the most valuable methods of establishing the diagnosis. The amastigote forms are found in stained films. The only risk in splenic puncture is that bleeding might continue from the puncture wound in the soft and enlarged spleen, resulting in death. The risk of such haemorrhage can be avoided if blood is previously examined to exclude hemorrhagic diathesis and leukaemia. Splenic puncture is usually the most valuable method of obtaining material for diagnosis. About 90% of kala-azar cases, parasites are found in the smears from the first splenic puncture.

7. Liver Function Test:

➤ Serum Protein Estimation:

This includes total protein, albumin and globulin estimation. Total protein and albumin estimation was done by Biurette method. We used gm% as its unit.

Globulin = Total Protein – Albumin

➤ Serum Bilirubin Estimation:

For this estimation, the technique used in present series of work was that of Jandreck & Crof. We used mg% as its unit.

➤ Serum Alkaline Phosphatase Estimation:

The technique used in present series of work was based on the UV Kinetic (at 37 °C) method. We used unit/l as its unit.

➤ Serum SGPT Estimation:

The technique used for estimation of SGPT in present series of work was UV Kinetic (at 37°C) method. We used unit/l as its unit.

➤ Serum SGOT Estimation:

The technique used for estimation of SGOT in present series of work was UV Kinetic (at 37°C) method. We used unit/l as its unit.

Statistical analysis

Data was analyzed using SPSS version 16. Mean value, Standard Deviation (S.D.), Standard Error of Mean (SEM) and comparison of two means were analyzed statistically.

III. Result

Different types of observations were obtained during the course of study which are reflected in following tables.

Table 1 shows that majority of cases of kala-azar belongs to the age group less than 10yrs, constitute 23% of the total cases. 21% of the patients of kala-azar belongs to the age group of 10-19yrs and 19% belongs to age group of 20-29yrs. 18% cases belongs to age group of 30-39yrs and 19% cases above the group of 40yrs. Out of 100 cases of kala-azar 64% patients are males and 36% are females.

Table No.1 Showing the age and sex Distribution of the Kala-azar and normal control subjects.

Age group (in years)	No. of Kala-azar cases			No. of control subjects		
	Male	Female	Total	Male	Female	Total
0 – 10	12	11	23	4	2	6
10 – 19	14	7	21	5	6	11
20 – 29	11	8	19	1	1	2
30 – 39	11	7	18	4	1	5
40 – 49	9	1	10	1	0	1
50 – 59	4	1	5	0	0	0
60-69	3	1	4	0	0	0
Total	64	36	100	15	10	25

Histogram Showing Incidence Of Age And Sex In Kala-Azar Cases (Table-1)

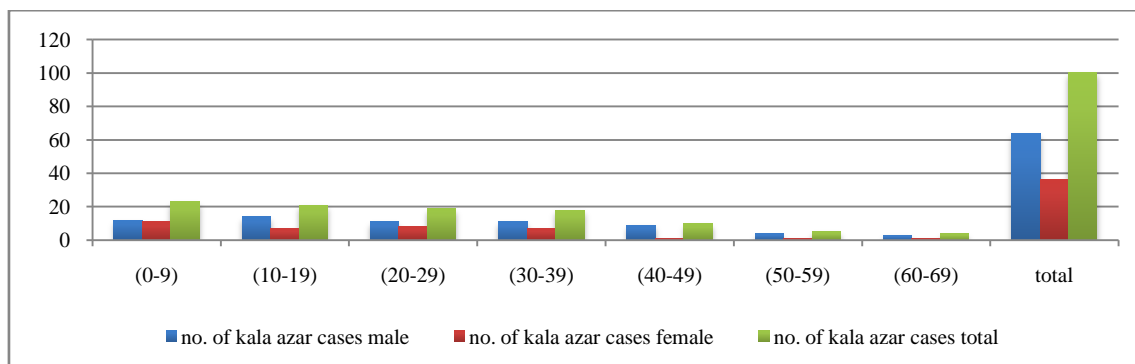


Table no 2 Showing Different Stages Of Kala-Azar With Different Duration Of Illness

Stages	No. of Kala-azar cases	Duration of Illness
Early Type	34	Below 3 Months
Mid Type	47	Between 3-5 Months
Advanced Type	19	Above 5 months

The above table shows that early stages of Kala-azar, the duration of illness is below three months. In Mid-type, duration of illness is between 3 to 5 months and in advance type, the duration illness above 5 months.

Table no3: Showing Comparative Mean Value Of Total Protein In Normal Control And Kala-Azar Cases

Types of cases	No. of cases	Total Protein in Gm%						Remarks
		Range	Mean	S.D.	SEM	t	P	
Control-groups	25	6.3-8.4	7.24	0.57	0.11	7.56	<0.001	Significant
Kala-azar	100	4.0-8.0	6.01	0.76	0.077			

The above table shows that the mean serum protein in kala-azar cases and control group is 6.01 and 7.24 gm% respectively. The above table shows that the serum protein in Kala-azar cases is lower than control group. t & p values were calculated and found to be 7.56 and <0.001 which indicates that protein was significantly lower in Kala-azar cases than control group

Table no 4 Showing Comparative Mean Value Of Serum Albumin In Normal Control And Kala-Azar Cases

Types of cases	No. of cases	Serum Albumin in Gm%						Remarks
		Range	Mean	S.D.	SEM	t	P	
Control Group	25	4.0-5.4	4.84	0.37	0.069	15.89	<0.001	Significant
Kala-azar	100	1.0-4.4	2.41	0.74	0.074			

The above table shows that the mean serum albumin in kala-azar cases and control group is 2.41 gm% and 4.84 gm% respectively. The above table shows that the serum albumin in Kala-azar cases is lower than control group, t & p values were calculated and found to be 15.89 and <0.001 respectively which shows that serum albumin was significantly lower in Kala-azar cases than control group.

Table no 5 Showing Comparative Mean Value Of Serum Globulin In Normal Control And Kala-Azar Cases

Types of cases	No. of cases	Serum globulin (in gm%)						Remarks
		Range	Mean	S.D.	SEM	t	p	
Control group	25	1.8-3.4	2.40	0.35	0.068	12.04	<0.001	Significant
Kala-azar cases	100	2.6-5.2	3.61	0.47	0.047			

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The table no 5 shows that the mean serum globulin in Kala-azar cases are higher than the control group is 3.61 gm% and 2.40 gm% respectively. Table shows that the serum globulin in kala azar cases is higher than in control group. t and p value were calculated and found to be 12.04 and <0.001 respectively which shows that serum globulin was significantly higher in Kala-azar cases than control group.

Table no 6 Showing Comparative Mean Value Of Albumin, Globulin Ratio (A: G Ratio)

Types of cases	No. of cases	Albumin-Globulin (A:G) Ratio						Remarks
		Range	Mean	S.D.	SEM	t	P	
Control group	25	1.4-2.8	1.98	0.29	0.058	13.2	<0.001	Significant
Kala- azar cases	100	0.25-1.69	0.68	0.47	0.047			

The table no.6 shows that A:G ratio is lower in kala azar cases in comparison to control group. t& P values were calculated and found to be 13.2 and <0.001 respectively which indicates that A : G ratio is significantly lower in kala azar in comparison to control group.

Table no 7 Showing Comparative Mean Value Of Serum Bilirubin Level In Control Group And Kala Azar Cases.

Types of cases	No. of cases	Serum Bilirubin in mg%						Remarks
		Range	Mean	S.D.	SEM	t	P	
Control group	25	0.1-0.6	0.30	0.14	0.028	7.5	<0.001	Significant
Kala-azar cases	100	0.2-3.1	1.07	0.54	0.054			

The above table shows that Serum bilirubin level in kala azar cases is higher in comparison to control group. t and P values were calculated and found to be 7.5 and < 0.001 respectively which shows that Serum bilirubin is significantly higher in kala azar cases than in control group.

Table no 8. Showing Comparative Mean Value Of Serum Bilirubin

Types of cases	No. of cases	Serum bilirubin in mg%						Remarks
		Range	Mean	S.D.	SEM	t	P	
Early stage	34	0.2-1.4	0.71	0.29	0.049	6.52	<0.001	Significant
Mid stage	47	0.3-2.4	1.11	0.41	0.060	9.56	<0.001	Significant
Advanced stage	19	0.3-3.1	1.62	0.68	0.156	9.48	<0.001	Significant
Control group	25	0.1-0.6	0.3	0.14	0.020			

The above table shows that the serum bilirubin level in different stages of kala-azar cases is significantly higher than control group and it also shows that level of serum bilirubin increases as the disease advances.

Table no 9. Showing Comparative Mean Value Of Serum Alkaline Phosphatase Level

Types of Cases	No. of Cases	Serum Alkaline Phosphatase Level (u/l)						Remarks
		Range	Mean	S.D.	SEM	t	P	
Early stage	34	148-355	249.76	61.08	10.48	10.56	<0.001	significant
Mid stage	47	160-485	265.04	75.74	11.05	9.53	<0.001	significant
Advanced stage	19	162-490	280.11	89.44	20.52	8.91	<0.001	significant
Control group	25	100-140	120.0	9.87	1.98			

The above table shows that the level of serum alkaline phosphatase in different stages of Kala-azar is significantly higher in comparison to control group and it also shows that the level of serum alkaline phosphatase level increases as the disease advances.

Table no 10 Showing Comparative Mean Value Of SGOT

Types of cases	No. of cases	SGOT in U/L						Remarks
		Range	Mean	S.D	SEM	t	p	
Early stage	34	22-73	39.09	12.19	2.08	9.01	<0.001	significant
Mid stage	47	22-91	40.55	14.10	2.06	8.46	<0.001	significant
Advanced stage	19	32-95	43.15	14.95	3.43	8.59	<0.001	significant
Control group	25	9-27	15.92	4.71	0.94			

The above table shows that the level of SGOT in different stages of Kala azar is significantly higher in comparison to control group and it shows that the level of SGOT increases as the disease advances.

Table no 11. Showing Comparative Mean Value Of SGPT

Types of cases	No. of Cases	SGPT in U/L						Remarks
		Range	Mean	S.D.	SEM	t	p	
Early stage	34	10-80	34.71	18.57	3.18	4.38	<0.001	significant
Mid stage	47	13-94	35.62	19.95	2.91	4.36	<0.001	significant
Advanced cases	19	18-95	36.42	17.82	4.09	4.95	<0.001	significant
Control group	25	10-30	17.88	5.09	1.017			

The above table shows that the level of SGPT in different stages of Kala azar is significantly higher in comparison to control group and it shows that the level of SGPT increases as the disease advances.

IV. Discussion

For the convenience of discussion, the kala-azar cases were classified in three stages on the basis of classification made by N.K. Chakarvarty and P.C. Gupta, on the basis of duration of illness

1. Early stage –Duration of illness below 3 months.
2. Mid stage –Duration of illness between 3 to 5 months.
3. Advanced stage – Duration of illness above 5 months

In one hundred cases of kala-azar majority of patients belonged to the age group below 10 yrs, constitute 23% of the total cases, 21% of the kala azar belongs to the age group of 10–19 yrs, 19% patients belonged to age group 20-29 yrs, 18% belonged to age group of 30-39 yrs and 19% belonged to above 40yrs.64% of patients were males and 36% females were affected in present study .This indicates prevalence of disease among males. These findings were also observed by Plarde and C.P. Thakur, K.P. Sinha, A.K. Gupta and S.C. Kumar^{3,4}.

The mean value of total serum protein and serum albumin was significantly low in kala-azar cases in comparison to control group. The mean level in serum globulin was significantly high in kala-azar cases in comparison to control group.

The albumin-globulin ratio was altered in kala-azar cases in comparison to control group and it was found to be low in kala-azar cases in comparison to control group. These findings are in close conformity with the work of P.C. Sen Gupta and Chatterjee⁵.

S.R. Naik, P.N.Rao, D.V.Datta, S.K.Mehta, R.C. Mahajan have reported serum albumin less than 2.50 gm%, serum globulin greater than 3.0gm% in their study on kala-azar, which compares well with the findings of the present observation⁶.

It was evident from the observations that the total serum protein was decreasing with the progress of the disease. The serum albumin levels were also decreased proportionally with the progression of the disease. The serum globulin showed increasing trend with the advancement of the disease process and the albumin-globulin ratio were also altered with the advancement of the disease.The above observations were also close with the work of Sen Gupta and Chatterjee⁵.

In the early stage of kala-azar, serum bilirubin level ranged between 0.2-1.4 mg% with the mean value of 0.71±0.29, whereas in mid stage of kala-azar the serum bilirubin level ranged between 0.3-2.4mg% with mean value of 1.11 ±0.41 while in advanced stage of kala-azar the serum bilirubin level ranged between 0.3-3.1 mg% with the mean value of 1.62±0.68mg% (Table no.8).Similar findings were observed by Chakarvarty et al, Bhattacharya have reported hyperbilirubinemia in 10 to 30% cases of kala-azar cases⁷. Manson Bahr has same reports about hyperbilirubinemia in kala-azar cases⁸.

It was very clear from the above observations that the level of serum alkaline phosphatase increased significantly with the advancement of the disease.According to Dutta et al , Sen Gupta et al , serum alkaline phosphatase level was higher in kala-azar⁹.

In early stage, SGOT ranged 22-73u/l with mean value of 39.09 ± 12.19 u/l. In mid stage, it ranged 22-91unit with mean value of 40.55 ± 14.10 u/l. In advanced stage, it ranged 32-95unit with mean value of 43.15 ± 14.95 unit (Table-10). Again it was also evident that level of SGPT shows a rising trend with the increase in severity of disease. The above findings of this observation compares with the findings of S.R.Naik, P.N. Rao, D.V.Dutta, S.K. Mehta et al⁶.

V. Conclusion

The mean value of total serum protein, albumin and globulin ratio were low in comparison to mean value of control group. The mean value of serum bilirubin, serum alkaline phosphatase, SGPT and SGOT were high in comparison to the mean value of control group. As the disease advances these value were much lowered. It was concluded from all these biochemical tests and observed tests finding that there was a definite degree of hepatic damage in kala-azar cases and hepatic damage was proportionally related to the advancement of the disease. It was concluded that liver function test can give guideline to know the prognosis of the disease as well as it may also help in treatment plan.

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