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# EVALUATION OF SERUM LACTATE DEHYDROGENASE LEVELS IN TYPHOID FEVER.

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## ABSTRACT

Typhoid fever is a systemic life-threatening infection caused by the bacterium *Salmonella enterica* serotype Typhi occurring more frequently in underdeveloped regions of the world due to overcrowding and poor sanitation. Initiation of appropriate therapy decreases severity and clinical outcome of the disease which requires early and accurate diagnosis. Pathogenesis due to typhoid leads to various biochemical alterations. Present study was undertaken to investigate serum LDH activities in typhoid fever and to assess its clinical utility as a biochemical marker in typhoid fever. Comparison of LDH levels were also done in other fevers and healthy controls. Other parameters were also investigated viz, serum urea, serum creatinine, serum sodium and serum potassium. In the present study we observed a statistically significant increase in concentrations of LDH in typhoid fever patients when compared with other fever patients and in healthy controls. Other parameters did not exhibit any statistical significance.

**KEYWORDS: Typhoid fever, Lactate dehydrogenase, Serum urea, Serum creatinine, Serum sodium, Serum potassium.**

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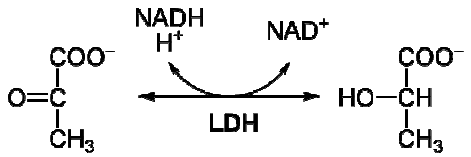
# INTRODUCTION

Typhoid fever is endemic in India[1]. In some areas the annual incidence is as high as 198 cases per 1, 00,000 [2] and, the disease causes considerable morbidity in children [3].A limited study in an urban slum in India showed 1% of children up to 17 years of age suffer from typhoid fever every year[4]. The highly adapted, human-specific bacterium *Salmonella enterica* serotype typhi that causes typhoid is usually acquired through ingestion of water or food contaminated by the urine or feces of infected and that of carriers. 10% case-fatality rate of typhoid fever can be reduced to 1% with appropriate antibiotic treatment [4].Hence for decreasing morbidity and mortality due to typhoid infection early diagnosis and initiation of therapy are important. LDH is widespread in distribution in the body. LDH is an intracellular cytoplasmic enzyme that catalyzes the oxidation of L-lactate to pyruvate with $NAD^+$ as the hydrogen acceptor, the final step in the metabolic chain of anaerobic glycolysis. This reaction is reversible and the reaction equilibrium favors the reverse reaction namely reduction of pyruvate to lactate.




Very clear and conclusive reports are not available on serum LDH levels in patients of typhoid fever. Hence in view of above mentioned facts, the present study was designed to evaluate the serum LDH activity in patients of typhoid and it has been compared with LDH activity in other febrile illness patients and in controls. Other parameters Urea, Creatinine, sodium and potassium in serum were also evaluated in this study.

# MATERIALS AND METHODS

The subjects included in the present study were 100 patients suffering from fever>102$^o$F of less than 7 days duration, attending the OPD of department of Medicine. A group of 50 normal healthy individuals, age and gender matched served as controls and were grouped as Group A. Blood culture was conducted on samples from fever patients. Culture positive patients were grouped under Group B and culture negative patients were lined up under Group C. We have excluded cases with a history of AIDS, Collagen Vascular Disease, Diabetes Mellitus and Liver Disorders.

These 150 subjects were divided into 3 groups:

- GROUP A comprised of 50 normal healthy individuals both males and females of all ages from the general population who volunteered for getting included in the present study.
- GROUP B comprised of 50 patients suffering from typhoid both males and females of all ages whose blood samples showed positive for the culture of typhoid bacilli.
- GROUP C comprised of 50 patients suffering from fever other than typhoid both males and females of all ages whose blood samples turned negative for the culture of typhoid bacilli.

This study was approved by an institutional review board and informed consent was obtained from all subjects involved in the study. It was a case control study. Participants were in the supine position for 5 to 10 minutes before venipuncture and 5 ml venous blood was collected in plain bottle and allowed to clot to separate serum. The following methodology was applied to the samples to obtain the required parameters. Serum was separated within one hour after sample collection. Care

was taken to avoid hemolysis. Serum from all 150 subjects was analyzed for the following parameters: Serum Lactate dehydrogenase by the Spectrophotometric method of Wroblewski and La Due (1955).

1) Serum Urea by Di Acetyl Monoxime method
2) Serum Creatinine by Jaffe's method
3) Serum Sodium by Flame Photometry method.
4) Serum Potassium by Flame photometry method.

### *STATISTICAL ANALYSIS*

Results were represented as tables and bar diagrams. Statistical analysis was carried out by using SPSS (Statistical Package for social science) software version 15.0.

The data was expressed using Mean, Standard deviation of all parameters in different groups. Multiple comparison ANOVA test was used to assess the significance of difference of means between Group A, Group B and Group C. 'p' value was used to assess the significance of difference of means between the cases and controls. $P < 0.05$ was considered significant. Specificity and sensitivity of parameters in diagnosing typhoid fever were computed by using ROC curves with the "graph pad prism" software.

**TABLE 1**
***Mean and SD values of studied parameters in controls, other fever patients and typhoid patients.***

| Parameters | GROUP A (n=50) | | Group B (n=50) | | Group C (n=50) | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD |
| Serum LDH (IU/L) | 92.10 | 21.900 | 193.00 | 20.250 | 95.32 | 15.856 |
| Serum Urea (mg/dL) | 28.36 | 7.018 | 27.62 | 6.830 | 28.80 | 6.490 |
| Serum Creatinine (mg/dL) | 0.880 | 0.1917 | 0.896 | 0.2000 | 0.840 | 0.1852 |
| Serum Sodium (meq/L) | 141.46 | 4.900 | 141.40 | 4.611 | 141.36 | 3.874 |
| Serum Potassium (meq/L) | 4.130 | 0.4432 | 4.234 | 0.4231 | 4.082 | 0.6397 |

**Figure 1**
***Mean ± SD chart for serum LDH***

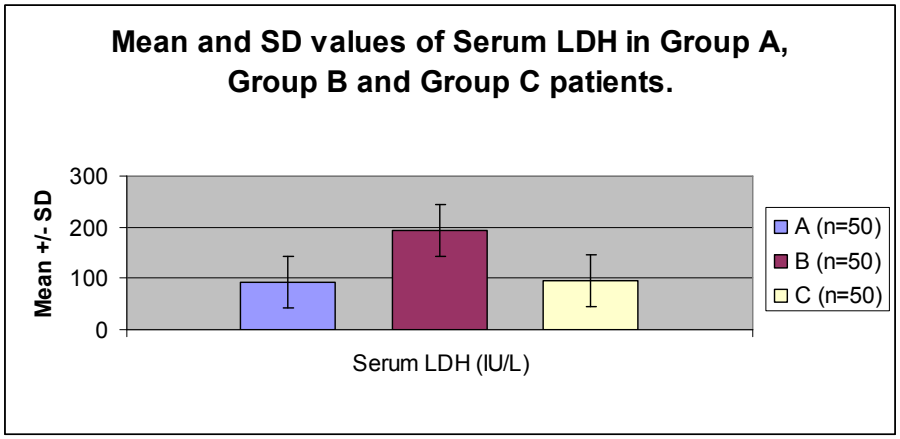


**Table 2**
***Anova Multiple Comparision of significance***

| Parameter | Significance in between Groups |
|---|---|
| LDH | .000 |
| Urea | .680 |
| Creatinine | .328 |
| Sodium | .994 |
| Potassium | .318 |

From tables 1&2 the mean values for serum LDH were significantly higher in typhoid fever group when compared to other fever group and control group as shown in the table
'p' values in between groups are < 0.05 for LDH . So, post hoc tests were done for this parameter.

**Table 3**
***Post hoc tests.***

| Dependent Variable | (I) GROUP | (J) GROUP | Mean Difference (I-J) | Sig. |
|---|---|---|---|---|
| LDH (IU/L) | 1.00 A | 2.00 C | -3.220 | .410 |
| | | 3.00 B | -100.900(*) | .000 |
| | 2.00 C | 1.00 A | 3.220 | .410 |
| | | 3.00 B | -97.680(*) | .000 |
| | 3.00 B | 1.00 A | 100.900(*) | .000 |
| | | 2.00 C | 97.680(*) | .000 |

The mean difference is significant at the .05 level. From table 3 rises in serum LDH values are statistically significant when compared with those of control group and other fever group. From the above data LDH has shown the maximum significance. Hence in order to assess the maximum sensitivity and specificity of LDH in identifying abnormality the best cut off values are calculated using ROC analyses. Best cut off values are established by selecting a point closer to top left hand curve that provides greatest sum of sensitivity and specificity.

**Table-4**
***Sensitivity specificity at best cut off values in between 3 groups***

| | Best cutoff value | Sensitivity | Specificity |
|---|---|---|---|
| Group A Vs. Group B | 142.50 | 100% | 100% |
| Group B Vs. Group C | 136.5 | 100% | 100% |
| Group A Vs. Group C | 83.5 | 74% | 44% |

**Table-5**
***Table comparing AUC, 95% CI and p value among the 3 groups***

| PARAMETERS | AUC | 95% CI | p value |
|---|---|---|---|
| A&B AUC | 1.000 | 1.000 to 1.000 | < 0.0001 |
| B&C AUC | 1.000 | 1.000 to 1.000 | < 0.0001 |
| A&C AUC | 0.5548 | 0.4399 to 0.6697 | 0.3450 |

**Figure 2**
***ROC curve for LDH in Group A vs Group B***

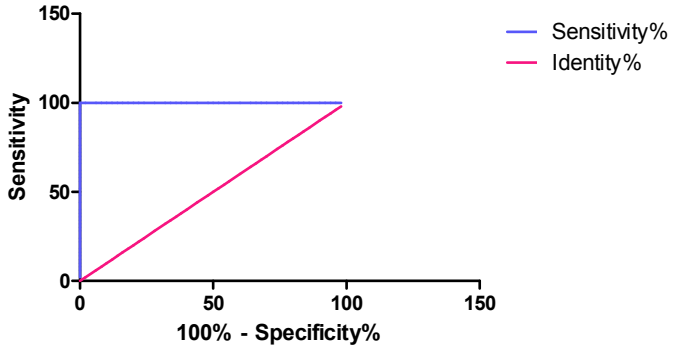



**Figure 3**
***ROC curve for LDH in Group B vs Group C***

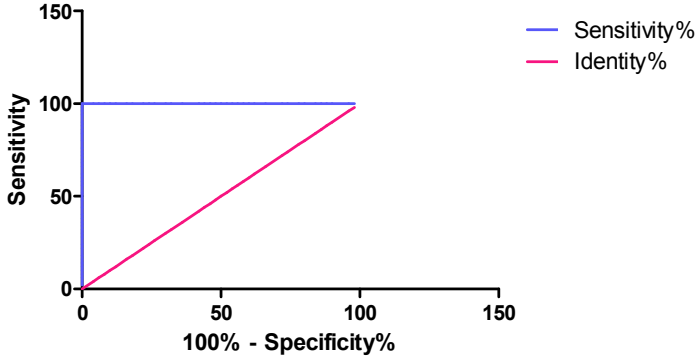
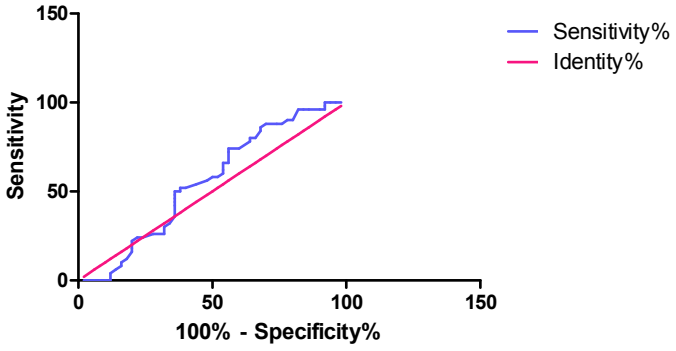



**Figure 4**
***ROC curve for LDH in Group A vs Group C***




From tables 4 & 5 and figures 2, 3 &4 the parameter lactate dehydrogenase has shown highest sensitivity and specificity in discriminating patients suffering from typhoid fever from those suffering from other fevers and healthy controls. Hence Serum LDH is best discriminatory marker when compared with other selected parameters.

# DISCUSSION

Typhoid fever presents with continuous fever, abdominal pain, constipation as symptoms and rose spots and relative bradycardia as signs usually, but sometimes it may present with variations in clinical findings such as diarrhea[5]

Several stages are seen in the patho-physiology of typhoid fever which is a complex process[6]. As the symptoms of typhoid fever are often nonspecific, they result in frequent diagnostic confusion with malaria, dengue fever, influenza or other febrile illnesses. Confirmed diagnosis requires isolating S. typhi in the laboratory through blood cultures during first seven days of illness. These tests are not usually conducted for the majority of patients in developing countries, especially those treated in non-hospital settings[7]. In the present study evaluation of lactate dehydrogenase was done for the purpose of selecting marker with high sensitivity and specificity. This parameter was also studied in patients suffering from fever>102 $^{O}$F due to reasons other than typhoid and also in age and sex matched healthy controls. Other parameters like serum urea, serum creatinine, serum sodium and serum potassium were also measured in all the subjects but after subjecting the data to statistical procedures none of them showed significance. Inter-conversion of lactate and pyruvate is mediated by the enzyme LDH. This enzyme has a wide tissue distribution and is abundantly present in the myocardium, skeletal muscle, kidney and liver. Necrosis, degeneration, or inflammation results in an increased rate of release of the enzyme from the cells and a rise of its level in the serum[8,9].

There is a unique relationship between *S. typhi* and macrophages in the liver, spleen, intestinal lymphoid follicles, and mesenteric lymph nodes which could be responsible for the pathogenesis. Functionally active cytokines (TNF alpha, IL-1, interferon alpha and beta) are synthesized by macrophage cells and are an important source of arachidonate metabolites and reactive oxygen intermediates. These products can lead to cellular necrosis, other inflammatory cells recruitment, immune system stimulation, vascular instability, initiation of the clotting mechanism, and other abnormalities associated with typhoid fever [10]. Reports state that elevated serum enzyme levels related to hepatic damage are seen in 50-100% of typhoid patients[11,12]. Hepatic involvement is one of the earliest reported complications in the course of typhoid fever [13]. Increases in reports on myopathy during the course of typhoid are also found[14]. Both these entities are responsible for release of the enzyme LDH. Typhoid fever is thus associated with cellular necrosis and has increased values of serum LDH.

# CONCLUSION

Typhoid fever remains a public health problem in developing countries like India where the sanitary conditions are poor. Initiation of early treatment through early diagnosis can considerably decrease the morbidity and mortality caused by typhoid. Blood culture is the gold standard diagnostic method available for detecting typhoid but the disadvantages with it are its high throughput time and lack of availability of blood culture techniques in rural areas of underdeveloped countries. WIDAL test is another popularly done test for diagnosing typhoid which lacks sensitivity in determining typhoid. Therefore the hallmark of the present study is to identify non culture parameters with high sensitivity and specificity. Among all studied parameters in the present study we observed a significant increase in serum LDH values in typhoid patients compared to controls. This significance of increase was also found when typhoid patient's LDH values were compared with those in non-typhoid fevers. There is no significant increase in the values of serum Urea, Creatinine, Sodium and Potassium compared to controls. The increase in LDH in typhoid patients is because of the necrosis taking place in the lymphoid tissue of a typhoid patient. Urea, Creatinine, Sodium and Potassium levels are not significantly altered in

these patients. The reason could be that the patients selected for the study are suffering from fever of a duration less than 7 days which shows that the cases are non-complicated and thus the serum levels of these parameters are not altered significantly. In conclusion, evaluation of LDH level in patients with typhoid could represent an additional and useful parameter in determining the clinical and prognostic aspect of the disease.

## REFERENCES


1. Gopal Muthu, Arumugam Suresh, Gnadesikan Sumathy And Ramesh Srivani; Studies On Antimicrobial Susceptibility Pattern Of Salmonella Isolates From Chennai, India International Journal of Pharma and Bio Sciences vol2/ issue 2/ apr- june 2011
2. Lin FY, Vo AH, Phan VB, Nguyen TT, Bryla D, Tran CT, et al. The epidemiology of typhoid fever in the Dong Thap Province, Mekong Delta region of Vietnam. Am J Trop Med Hyg 2000; 62:644-8
3. Sinha A, Sazawal S, Kumar R, Sood S, Reddaiah VP, Singh B, et al. Typhoid fever in children aged less than 5 years. Lancet 1999;354:734-7.
4. Typhoid fever [fact sheet N149]. Geneva: World Health Organization; 1997. Available: www.who.int/inf-fs/en/fact149.html (accessed 2003 June 23)
5. Hoffman TA, Ruiz CY, Counts GW, Sachs JM, Nitzkin JL. Water borne typhoid fever in Dade county Florida: Clinical and therapeutic evaluation of 105 bacteremic patients. Am J Med 1975; 59:481-6.
6. Abro AH, Abdou AMS, Gangwani JL, Ustadi AM, Younis NJ, Hussaini HS. Ischemia modified albumin a potent marker in acute myocardial infarction in normolipidaemic. Pak J Med Sci 2009;25(2): 166-171
7. WHO: Weekly epidemiological record (http://www.who.int/wer). 8 FEBRUARY 2008, 83rd YEAR, No. 6, 2008, 83, 49–60.
8. Gamal E. Megahed and Ahmed M. Yassin; Serum Lactic Dehydrogenase Level as a Diagnostic Test for Carditis in Rheumatic Fever Circulation published by the American Heart Association. 1965;32:925-931
9. Chandrakanth Kh, Nagaraj, Jayaprakash Murthy Ds,Satishkumar D and Anand Pyati. Study Of Serum Levels of Gamma-Glutamyl Transferase, Lactate Dehydrogenase, Malondialdehyde And Vitamin-E In Breast Cancer. International Journal of Pharma and Bio Sciences vol 2/issue 4/ oct- dec 2011.
10. A. Murinello, a. Morbey, j. Figueira coelho, p. Mendonça, a. C. Pires, v. Magalhães ramalho, n. Carrilho ribeiro, a. Lázaro, h. Peres, j. Netta; Typhoid Fever – Clinical And Endoscopic Aspects; GE - J Port Gastrenterol 2008; 15: 76-82
11. Ozen H, Secmeer G, Kanra G, Ecevit Z, Ceyhan M, Dursun A, et al. Typhoid fever with very high transaminase levels. Turk J Pediatr 1995; 37 :169-71.
12. Morgenstern R, Hayes PC. The liver in typhoid fever: Always affected, not just a complication. Am J Gastroenterol 1991; 86 :1235-9.
13. Ramachandran S, Godfrey JJ, Perera MV. Typhoid hepatitis. JAMA 1974; 230 :236-40.
14. Mody GM, Gathiram V, Abdulla EA. Severe reversible myopathy due to typhoid. J Trop Med Hyg 1989; 92 :102-3.