



## EVALUATION OF SERUM LIPIDS IN ENTERIC FEVER

## Biochemistry

**Dr. Abhaykumar S. Sardeshmukh**

Professor & Head, Dept. of Biochemistry, RSCM Govt. Medical College, Kolhapur

**Dr. Nitin R. Gurav\***

Associate Professor, Dept. of Biochemistry, RSCM Govt. Medical College, Kolhapur  
\*Corresponding Author

**Dr. Atul A. Patil**

Assistant Professor, Dept. of Biochemistry, RSCM Govt. Medical College, Kolhapur

**Dr. Sujata R. Namey**

Associate Professor, Dept. of Biochemistry, RSCM Govt. Medical College, Kolhapur

## ABSTRACT

Enteric fever is characterized by sepsis & endotoxemia affecting lipid metabolism. Present study included quantitation of serum lipids in 50 patients of enteric fever at the time of admission, during follow up after 6 weeks, 3 months and 50 age, sex matched healthy control subjects. Enteric fever patients showed significantly increased levels of serum triglycerides, total cholesterol, LDL cholesterol, VLDL cholesterol, total cholesterol/HDL cholesterol ratio and decreased levels of HDL cholesterol in comparison with control subjects. Maximum alterations in above biochemical parameters were seen in enteric fever patients after 3 weeks follow up ( $p < 0.05$ ). Elevated total cholesterol / HDL cholesterol ratio in typhoid patients warns about possible atherosclerotic involvement.

## KEYWORDS

Enteric fever, lipids, S. typhi

## INTRODUCTION

Enteric fever is a major public health problem in underdeveloped & developing countries of the world with an estimated annual incidence of 540 per 100,000 individuals and is endemic & more severe in infants & the elderly.<sup>1,2,3</sup> It is one of the most common infectious diseases in tropical countries & a source of extensive morbidity & mortality.<sup>4</sup> Organism causing typhoid fever namely *Salmonella typhi* can cause endotoxemia. Lipid metabolism is affected by different ways during infection depending on causative agent. The most profound effect occurs with gram negative bacteria infection associated with endotoxemia & sepsis. Extensive work on the pathogenesis of enteric fever is available with the singular exception of metabolic derangements.<sup>5</sup> Efforts have been made to correlate lipid response with the severity, stage & nature of infection.<sup>6,7</sup>

There are few reports of lipid profile abnormalities in enteric fever. Khosla et al<sup>8</sup> observed severe & profound hypertriglyceridemia, increase in total cholesterol, low density lipoprotein cholesterol (LDL cholesterol) & decrease in high density lipoprotein cholesterol (HDL cholesterol) values in 20 typhoid patients at the peak of fever. An increase in LDL cholesterol remained steady during follow up study. Gallin et al<sup>7</sup> observed that in infection due to gram negative bacilli there was a noticeable rise in the levels of triglycerides & pre beta lipoproteins. Fischer et al<sup>9</sup> found increased levels of triglycerides, prebeta & alpha lipoproteins & decreased levels of phospholipids, cholesterol & beta lipoproteins in plasma of monkeys artificially infected with salmonella typhi. Segura et al<sup>10</sup> noticed elevated triglycerides & normal cholesterol levels in 19 patients of acute typhoid fever. Triglyceride levels returned to normal after resolution of typhoid fever. Foldvari & Kertai<sup>11</sup> found that in rabbits infected with s. typhi endotoxin serum cholesterol levels were increased in cholesterol fed rabbits & decreased in controls. Enteric fever affects the intestine which is also the site of lipid absorption. Hence C. Ikegwonu Ifeoma et al<sup>12</sup> carried out a study and found that the lipid profile of all the patients showed non significant difference ( $p > 0.05$ ) when compared with the controls. Zulfiqar - Ul - Hassan et al<sup>13</sup> found elevation in the levels of TG & decline in the levels of HDL, LDL & TC in typhoid patients as compared to controls. However these studies are mostly on experimental animals & effect of salmonella typhi infection on serum lipids in humans is still not adequately studied. Further hardly any report is available regarding very low density lipoprotein cholesterol (VLDL cholesterol) in enteric fever patients. The reports available are conflicting & controversial & that prompted us to investigate serum lipids in enteric fever.

## MATERIALS AND METHODS

Present study was carried out in the Dept. of Biochemistry, Dr. V. M. Govt. Medical College & S.C.S.M. General Hospital, Solapur. This study included fifty patients of enteric fever & age, sex matched fifty healthy control subjects. All healthy control subjects & enteric fever patients were in the age group of 18 – 47 years. Patients selected for the study were non diabetic, normotensive. Their hepatic functions & renal functions were normal & nutritional & socio – economic status were matching well with those of control subjects. Diagnosis of the patients of enteric fever was done by clinical examination & relevant laboratory investigations.

Informed consent was taken from all subjects included in study. Ethical clearance was obtained from Institutional Ethics Committee. Approximately 5 to 7ml. of venous blood samples were collected in the morning after an overnight fast & non hemolysed sera were used for all biochemical assays without further storage.

Serum triglycerides were estimated by the method of Frankel et al.<sup>14</sup> Estimations of serum lipid phosphorous and phospholipids were carried out by the method of Fiske & Subbarow.<sup>15</sup> Separation of HDL cholesterol was done by the method of Sckett.<sup>16</sup> Quantitation of LDL cholesterol & VLDL cholesterol were done by using Friedwald's method.<sup>17</sup> During follow-up above biochemical assays were carried out again on enteric fever patients after 06 weeks & 03 months. Students 't' test was used for assessment of statistical significance. Values were expressed as mean  $\pm$  S.D.

## RESULTS:

**Table No 1: Serum triglycerides, phospholipids & total cholesterol values in control subjects & enteric fever patients.**

Sr. No	Groups studied	No. of Subjects	S. Triglycerides mg %	S. Phospholipids mg %	S. Total cholesterol mg%
1	Control Subjects	50	90.00 $\pm$ 18.2	226 $\pm$ 21.4	178 $\pm$ 14.4
2	<b>Enteric fever patients:</b>				
a)	at the time of admission	50	127.00 $\pm$ 15.2*	218 $\pm$ 18.2 <sup>o</sup>	196 $\pm$ 22.1 <sup>o</sup>
b)	After 6 weeks	50	145.00 $\pm$ 20.5*	229 $\pm$ 12.6 <sup>o</sup>	216 $\pm$ 10.1*
c)	After 3 months	50	158.00 $\pm$ 26.3*	220 $\pm$ 17.5 <sup>o</sup>	233 $\pm$ 15.3*

<sup>o</sup> -  $p > 0.05$       \* -  $p < 0.05$

Table 1 shows levels of serum triglycerides, phospholipids & total cholesterol in control subjects & enteric fever patients at different stages. Serum triglycerides & total cholesterol values were

significantly increased in enteric fever patients as compared to control subjects whereas serum phospholipids levels showed no statistical difference between typhoid patients & control subjects. ( $p < 0.05$ )

**Table No. 2: Serum HDL – cholesterol, VLDL – cholesterol & LDL – cholesterol levels in control subjects & enteric fever patients.**

Sr. No	Groups studied	No. of subjects	S. HDL Cholesterol mg %	S. VLDL Cholesterol mg %	S. LDL Cholesterol mg%
1	Control Subjects	50	44.4 ± 5.8	18.0 ± 3.64	115.6 ± 12.3
2	Enteric fever patients:				
a)	at the time of admission	50	43.0 ± 4.1 <sup>0</sup>	25.4 ± 3.04 *	127.6 ± 10.6 <sup>0</sup>
b)	After 6 weeks	50	36.2 ± 3.6 *	29.0 ± 4.10*	15.8 ± 17.3*
c)	After 3 months	50	34.3 ± 4.5 *	31.6 ± 5.26*	167.1 ± 18.4*

<sup>0</sup> -  $p > 0.05$  \* -  $p < 0.05$

Table 2 indicates serum HDL cholesterol, VLDL cholesterol & LDL cholesterol levels in control subjects & enteric fever patients. Serum HDL cholesterol concentrations were depleted & serum VLDL cholesterol & LDL cholesterol concentrations were elevated in enteric fever patients in comparison with control subjects. ( $p < 0.05$ )

**Table No. 3: Serum Total cholesterol / HDL cholesterol ratio in control subjects & enteric fever patients.**

Sr. No	Groups studied	No. of subjects	Total Cholesterol : HDL Ratio
1	Control Subjects	50	4.00
2	Enteric Fever patients:		
a	at the time of admission	50	4.56 <sup>0</sup>
b	After 6 weeks	50	5.97 *
c	After 3 months	50	6.79 *

<sup>0</sup> -  $p > 0.05$  \* -  $p < 0.05$

Table 3 depicts serum total cholesterol / HDL cholesterol Ratio in controls & typhoid patients. This ratio was found to be increased in enteric fever patients as compared to control subjects ( $p < 0.05$ ).

Maximum induction in the levels of serum triglycerides, total cholesterol, LDL cholesterol, VLDL cholesterol and total cholesterol / HDL cholesterol ratio and maximum depletion in the levels of HDL cholesterol were observed in enteric fever patients during follow – up studies after 3 months in comparison to control subjects ( $p < 0.05$ ) (Table 1,2,3).

## DISCUSSION

This study has shown certain significant findings. Increased triglyceride levels in typhoid patients in the present study are in accordance with the results of Fischer et al,<sup>7</sup>

Khosla et al,<sup>8</sup> Gallin et al,<sup>9</sup> Segura et al.<sup>10</sup> *Salmonella typhi* causes a more severe & protracted hypertriglyceridemia than other bacterial infections & these changes persist for longer duration. Changes in levels of triglycerides could be due to i) defective lipid disposal mechanisms, ii) effect of salmonella typhi infection on lipoprotein lipase activity or iii) defect in the release of hormones like epinephrine & corticotrophins. The relationship between serum lipids & sepsis remains undefined.<sup>18</sup>

In our study elevated levels of serum total cholesterol in enteric fever patients are similar to reports of Khosla et al<sup>8</sup> & Foldvari & Kertai<sup>11</sup> and differ from those of Fischer et al<sup>7</sup> & Segura et al.<sup>10</sup> Alterations noticed in our study could reflect an overall metabolic status during infection, it may be hypothesized that catabolism may be found primarily during severe endotoxemia or may be due to elevated cholesterol turnover. In contrast to the reports of Fischer et al<sup>7</sup> a significant rise in serum LDL cholesterol was noted in the present study that remained unaltered during follow up. This might be because the endotoxemia in enteric fever may block the clearing factor activity through an increased secretion of ACTH & cortisone.<sup>19</sup> This blocking effect is enhanced by the thrombocytes damaged in enteric fever. The endotoxemia of enteric fever may also enhance the synthesis or out flux of LDL from the liver<sup>11</sup>. Also a decrease in post heparin lipolytic activity in Salmonellosis could explain the severity of lipid defects

observed<sup>6</sup>. Finally a defective hormone balance in gram negative sepsis might be responsible for these lipid alterations<sup>20,21,22</sup>.

We also observed a decrease in HDL cholesterol & an increase in VLDL cholesterol values in enteric fever patients. There is hardly any report documented about quantification of serum VLDL cholesterol in typhoid patients. The causes behind these alterations are not clear. It has been postulated that albumin may share a common pathway with HDL cholesterol. The increased capillary permeability in sepsis may lead to escape of albumin in to the extravascular space.<sup>5</sup>

Present study also showed significantly elevated total cholesterol / HDL cholesterol ratio in enteric fever patients & maximum rise was seen in follow up after 3 months. This increased total cholesterol / HDL Cholesterol ratio is important as it cautions about possible atherosclerotic and subsequent cardiovascular and cerebrovascular involvement in enteric fever patients. This possibility can be ascertained by a further study.

No alterations found in serum phospholipids levels in the present study may be because of the fact that phospholipids are stable lipids in comparison with other lipids such as triglycerides & cholesterol.

Results of this study should serve to caution interpretation of the lipid profile in a subject who has faced a recent *S. Typhi* infection.

## SUMMARY

Present study included assays of serum triglycerides, phospholipids, total cholesterol, HDL cholesterol, VLDL cholesterol, LDL cholesterol and total cholesterol / HDL cholesterol ratio in 50 healthy control subjects & 50 age, sex matched enteric fever patients at the time of admission & during follow up after 6 weeks & 3 months. Enteric fever patients showed significantly increased levels of serum triglycerides, total cholesterol, VLDL cholesterol, LDL cholesterol, total cholesterol / HDL cholesterol ratio and decreased levels of HDL cholesterol in comparison with control subjects. Maximum induction in the values of serum triglycerides, total cholesterol, VLDL cholesterol, LDL cholesterol, total cholesterol / HDL cholesterol ratio & maximum depletion in the levels of HDL cholesterol were noticed in enteric fever patients after 3 weeks follow up ( $p < 0.05$ ). Increased total cholesterol / HDL cholesterol ratio in typhoid patients cautions about possible atherosclerotic & subsequent cardiovascular & cerebrovascular involvement.

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