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Original Research Article

CORRELATION OF CHOLESTEROL & CRP WITH Ig-G & Ig-M POSITIVE TYPHOID PATIENTS FROM ITTEFAQ HOSPITAL, LAHORE, PAKISTAN

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ABSTRACT

Almost 21.6 million people are infected and 200,000 people killed by typhoid fever each year. This study was intended to evaluate the importance of serum levels of C-reactive protein and cholesterol to determine their correlation with typhoid disorder. In a prospective study, 50 patients were clinically diagnosed as typhoid patients by ELISA method and evaluated as per criteria for serum levels of cholesterol, CRP, Immunoglobulin G and Immunoglobulin M. These patients were compared with 20 healthy controls. The data was analyzed for finding the significance of serum cholesterol and CRP in typhoid. All parameters were found to be highly significant with typhoid and showed high degrees of variations with controlled population. P- Values were less than 0.05 for all parameters. Highest correlation was seen between Immunoglobulin M and CRP. So, in light of our findings, CRP and cholesterol have a strong impact of typhoid disease and appear as disturbed markers in worsening condition of typhoid. Consequently, patients coming with typhoid disorders must also be examined for any commotion in these two markers so that the culprit cause may be removed and patients could effectively be treated against secondary threatening ailments.

Keywords: *Salmonella typhi*, C - reactive protein, Serum cholesterol, Immunoglobulin G, M

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INTRODUCTION

Typhoid fever is a severe multi-systemic illness characterized by the classic prolonged fever, sustained bacteremia without endothelial involvement, and bacterial invasion and multiplication within the mononuclear phagocytic cell of the liver, spleen and lymph nodes (Dutta et al., 2006), (Abro et al., 2009). Carriers are treated with prolonged antibiotics that reduce the case-fatality rate to approximately 1% and death occurs in between 10% & 30% of untreated cases. Liver involvement in typhoid patients is perpetually seen after 1st week of infection and closed relationship of this disease has also been observed with spleen, gallbladder and intestine. In infected individuals; *Salmonella enteric* subspecies *Entericaserovartyphi* colonies the gall bladder & remains after long time invading inside the body which affects gallbladder severely. Splenic rupture and multiple liver metastases have been pathologically confirmed owing to brutal circumstances of typhoid (Al-Khuwaitiret al., 2009).

During the course of typhoid fever, the usual histologic finding of the liver is non-specific reactive hepatitis. In previous studies incidences of granulomas of bone marrow, spleen and liver were

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recorded secondarily due to typhoid (Feasey et al., 2010). The endemicity and the outbreaks of the disorder in the region are highly associated with the chronic carrier of typhoid. Patients with biliary diseases, gastrointestinal disorders and other related diseases are highly susceptible for typhoid (Kelly et al, 2007).

Since episodes of secondary diseases due to typhoid are clear, likewise there are wider chances of interruption in various biomarkers in presence of typhoid. Different typhoid patients belonging to different age groups & both sexes along with an equal number of matched patients with fever due to non-enteric causes were studied with regard to variations in lipid profile. It was observed that HDL-cholesterol level decreases & an increase in LDL-cholesterol in patients with enteric fever at the peak of fever observed, but, the values returned to normal after recovery & convalescence. This study indicates the complexity of lipid variation during typhoid (Khosla SN et al., 1991).

A study was done by Crum in 2003 to show the complexity of lipid variation during *Salmonella typhi*. Blood samples were collected after subjects had fasted for 12 hours overnight. Total cholesterol concentrations were lower in typhoid patients than in control subjects, whereas, the LDL-cholesterol concentrations were higher. Concentrations of total cholesterol were characterized by increasing LDL-cholesterol with insignificant variation of HDL-cholesterol. The patients had abnormal lipoprotein status characterized by lesser concentration of total cholesterol with high concentration of LDL-cholesterol while, triglyceride & HDL-cholesterol had no significant value in typhoid fever patients. The conclusion of their results indicates that abnormalities occur in the concentration of serum lipids of patients with typhoid fever (Crum, 2003).

An escalation in serum C reactive protein level is well recognized as a non-specific reaction to a number of tissue injuries. C reactive protein can be estimated in two sequential measurements that can be useful in identifying inflammatory complications such as thrombosis and postoperative sepsis but in complex inflammatory diseases earlier prediction of disease by CRP estimation might not reveal any helpful picture (Olubuyide et al., 1989).

In order to investigate the level of serum C-reactive protein (CRP) in typhoid patients 227 febrile Malaysian children hospitalized during 12-month period were studied. Some children were culture-positive for *Salmonella typhi* but some were culture negative with few features of typhoid fever. Those children having culture-positive for *Salmonella typhi* were appeared with high C-reactive protein (CRP) concentration. This study show that the serum CRP is raised in culture-positive children having typhoid fever and reflects the immune response to the infection (Ridker et al., 2002).

The value of C-reactive protein (CRP) is seen in the diagnosis of intestinal perforation during typhoid fever. For this serum CRP level were measured in 28 Nigerian typhoid patients who were hospitalized. Five of the 28 were observed as suffering from ileal perforation. These five patients had high concentration of C-reactive protein (CRP) than those without perforation (Olubuyide et al, 1989).

As we discussed complications of typhoid as well as its association with other diseases, so the current study was based with the objective to determine association of typhoid disease with C-reactive protein levels of Pakistani typhoid patients, further we were also aimed to find any relation of hypercholesterolemia with typhoid.

MATERIAL AND METHODS

In a prospective case controlled study, a total of 50 patients from Ittefaq Hospital, Lahore were clinically diagnosed as typhoid patients by Enzyme Linked Immunosorbent Assay (ELISA) and evaluated as per criteria for serum Immunoglobulin G (IgG) and Immunoglobulin M (IgM) antibodies.

Serum levels of cholesterol and C- reactive protein (CRP) were estimated through spectrophotometry by using reagents of Human Company (Max-Planck-Ring, Wiesbaden, Germany). Before conducting analyses, informed consents were taken by patients. These patients were compared with 20 healthy subjects. The data was analyzed for finding the implication of serum cholesterol, C- reactive protein, IgG and IgM levels in the diagnosis of Typhoid fever. Results were analyzed statistically by applying analysis of variance (ANOVA) test for checking of significance or insignificance. Confidence interval was 0.95 and p-value less than 0.05 were deemed as significant while values greater than 0.05 were taken as non-significant. Two-tailed Pearson correlation test was applied for comparing parameters with each other.

RESULTS

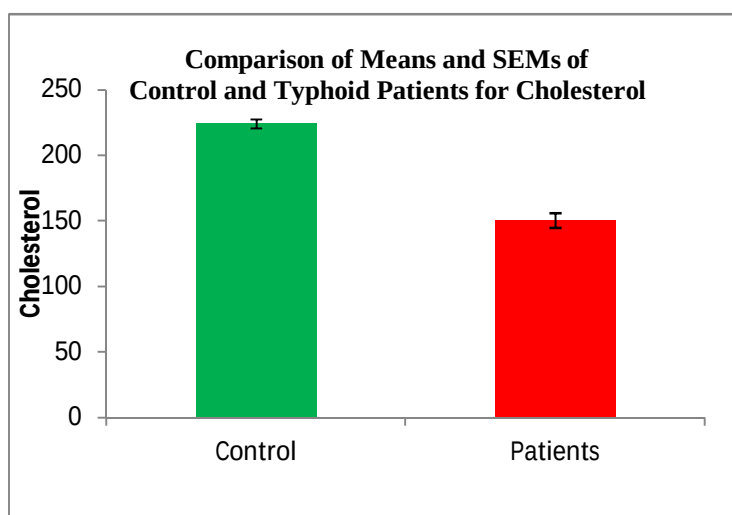
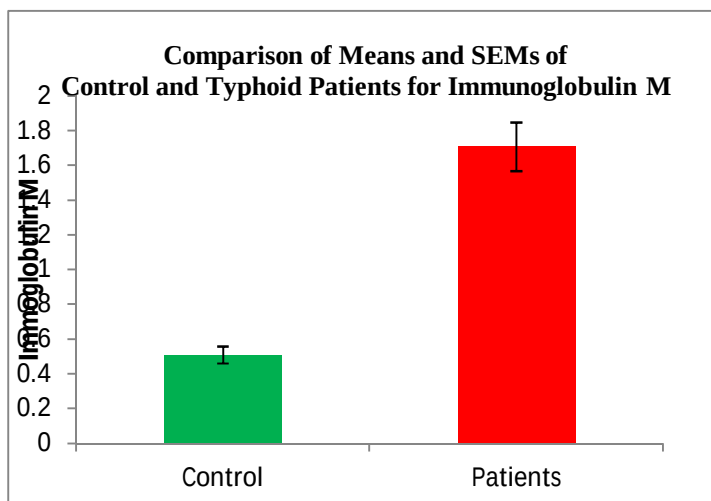
Table 1.Means, Standard Deviations (SD) Standard Error of Means (SEMS) and P-values of Study Parameters

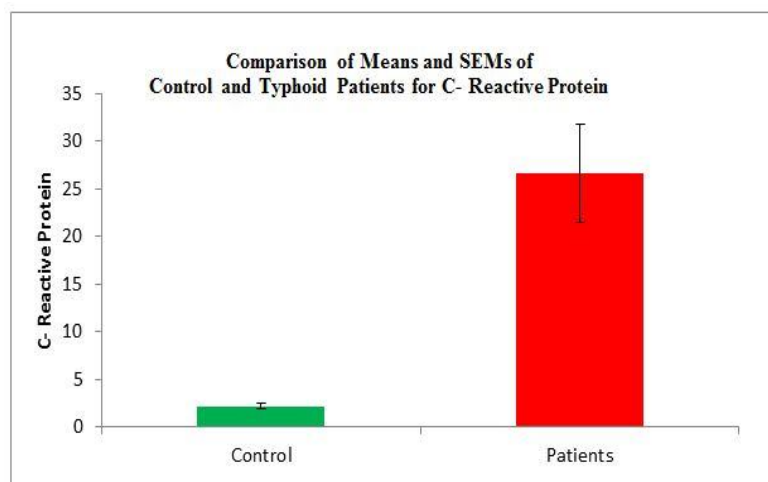
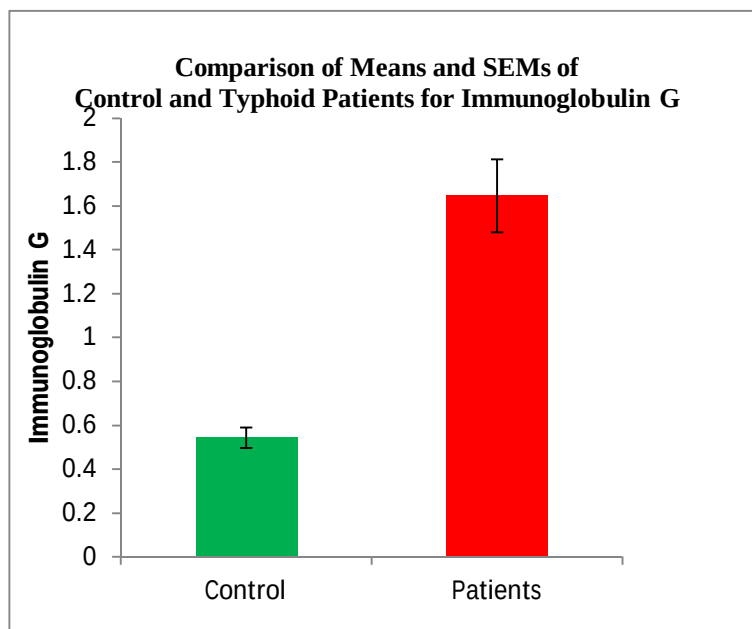
No	Parameters	Controlled Population N=20 M $\pm$ SEM	Typhoid Population N=50 M $\pm$ SEM	P-Values
1.	Immunoglobulin M	0.5100 $\pm$ 0.04861	1.7080 $\pm$ 0.14014	0.02
2.	Immunoglobulin G	0.5450 $\pm$ 0.04615	1.6480 $\pm$ 0.16656	0.00
3.	Cholesterol	224.0000 $\pm$ 3.37015	150.2060 $\pm$ 5.62201	0.02
4.	C- Reactive Protein	2.2100 $\pm$ 0.32806	26.5800 $\pm$ 5.12841	0.04

Table 2.Correlation of Typhoid parameters among each other

	Immunoglobulin M	Immunoglobulin G	Cholesterol	CRP
IgM				
Pearson Correlation	1	-.022	-.163	.427**
Sig. (2-tailed)		.880	.258	.002
N	50	50	50	50
IgG				
Pearson Correlation	-.022	1	0.01	-.039
Sig. (2-tailed)	0.880		0.932	0.788
N	50	50	50	50
Cholesterol				
Pearson Correlation	-.163	0.012	1	0.163
Sig. (2-tailed)	0.258	0.932		0.259
N	50	50	50	50
CRP				
Pearson Correlation	0.427**	-.039	0.163	1
Sig. (2-tailed)	0.002	0.788	0.259	
N	50	50	50	50

Graphical representation of Means and Standard Error of Means of Control and Typhoid Patients for Study Parameters





DISCUSSION

Typhoid fever is one of the most important infectious diseases in developing countries including Pakistan. This disease is present especially in areas where healthcare facilities are limited and peoples are illiterate, living in unhygienic environment, and drinking raw-water from tube-wells and not habitual of hand-washing after toilet by soap. If typhoid disease is left untreated then it may hail several other secondary diseases which are always terrifying for patients as well as for other community. Typhoid patients exhibit condition of disturbed cholesterol levels along with signs of acute inflammation, as a complication if they are not medicated appropriately. Furthermore, it also has been seen that C - reactive protein also gets increased in response to a number of tissue injuries (Wu et al., 2009).

In present study 50 patients of typhoid were selected and their immunological assay was done. Immunoglobulin G and immunoglobulin M were analyzed. The levels of C-reactive protein and

cholesterol were estimated of all patients to check degree of complication of typhoid in Pakistani population. All data of patients was compared statistically with levels of healthy population.

The means and standard error of means (SEM) for immunoglobulin M (IgM) levels in control and typhoid population were $0.5100, \pm 0.04861$ and $1.7080, \pm 0.14014$ respectively. For immunoglobulin (IgG) levels, means and standard error of means of control and typhoid population were $0.5450, \pm 0.04615$ and $1.6480, \pm 0.16656$ respectively. Means and standard error of means of control and patient populations for cholesterol were $224.4444, \pm 3.37015$ and $150.2060, \pm 5.62201$ respectively, whereas, for c-reactive protein means and standard error of means were $2.2100, \pm 0.32806$ and $26.5800, \pm 5.12841$ respectively (Jesudason et al., 2002).

Higher significances were found between all parameters of control and typhoid populations as showed by p-values for all parameters i.e., IgM, IgG, C-reactive protein and cholesterol. P-values were as follow 0.00, 0.00, 0.00 and 0.00 respectively when compared with control showing that these parameters have high chances of discrepancy in patients of typhoid.

It has been observed that the levels of C-reactive protein (CRP) become high in patients of typhoid fever more aggressively. A strong correlation was found between augmentations in C - reactive protein due to rise in immunoglobulin M. Both markers i.e., IgM and CRP are 43% related to each other as demonstrated by statistical correlation analysis (Olubuyide et al., 1989, Wahid R et al., 2012).

Percentages of patients with high, low and normal values of cholesterol were 14, 82 and 4, respectively. 68 % of total typhoid population exhibited high values of C- reactive protein. A total of 70 % of population appeared with high value of IgM, and, for IgG this percentage was 68%.

CONCLUSION

Typhoid patients develop irregular concentrations of cholesterol as well as C- reactive protein. These disturbed levels of cholesterol render typhoid patients more vulnerable to secondary ailments such as hyperthyroidism, adrenal insufficiency or other possible liver disease. Furthermore, chances of acute inflammation are always present for typhoid patients so quick and rationale remedies should be employed for typhoid patients in order to hamper likelihood of these intruding secondary ailments.

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