Advances in Biomedical Sciences
2016; 1(1): 10-13
http://www.openscienceonline.com/journal/abs

Open Science

Plasma Proteins in Enterica Serovar Typhi Patients in Merowe Locality Northern Sudan

Nagah A. A. Mohamed[1], Mohammed Amanullah[2], Mohieldin Omer[3]

[1]Department of Biochemistry Faculty of Medicine, Ondokuz Mayis University, Samsun, Turkey

[2]Department of Clinical Biochemistry, College of Medicine, King Khalid University, Abha, Saudi Arabia

[3]Faculty of Medical Laboratory Sciences, Sudan University of Science and Technology, Khartoum, Sudan

Email address

amanullahmohammed@yahoo.com (M. Amanullah)

To cite this article

Nagah A. A. Mohamed, Mohammed Amanullah, Mohieldin Omer. Plasma Proteins in Enterica Serovar Typhi Patients in Merowe Locality Northern Sudan. *Advances in Biomedical Sciences.* Vol. 1, No. 1, 2016, pp. 10-13.

Received: May 15, 2016; **Accepted**: June 16, 2016; **Published**: June 25, 2016

Abstract

The study entailed a quantitative assessment of serum total protein, albumin, globulin, and albumin: globulin ratio in individuals who diagnosed positively with typhoid fever and detection any alteration in plasma protein in receptiveness to typhoid titers. One hundred positively diagnosed with typhoid infection mean age (41.5 ± 2.1) years on zero day treatments. In addition to healthy one hundred individuals mean age (42.9 ± 1.9) years were recruited in this study. There were significant difference P. value = 0.000 in total protein, serum albumin, serum globulin and A/G ratio for typhoid positive and negative, mean (8.4±0.01,6.8±0.06), (3.5±0.01, 4.1±0.03), (4.9±0.01, 2.8±0.06), (0.7 ± 0.003, 1.5 ± 0.02) respectively No significant difference, P. value was 0.632, 0.832 and 0.760 serum total protein (7.5 ± 0.92, 7.6 ± 0.79) serum albumin (3.8 ± 0.38, 3.8 ± 0.37) and serum globulin (3.8 ± 0.16, 3.9 ± 0.16) for males and females respectively. Also no significant difference, P. value was 0.11, 0.60, and 0.06 serum total protein (8.4 ± 0.01, 8.4± 0.02) serum albumin (3.5 ± 0.01, 3.5 ± 0.01) and serum globulin (5.0 ± 0.01, 4.9 ± 0.01) for titer 1/160 and titer 1/320. Low albumin level and hypoglycemia should be surveillant when anti typhoid pharmaceutical commenced.

Keywords

Typhoid, Salmonella Titre, Serum Total Proteins, Albumin, Globulin

1. Introduction

Salmonella enterica serovar Typhi (serovar Typhi) is the cause of typhoid fever, an illness that affects over 20,000,000 individuals worldwide each year, killing over 200,000. The largest burden of typhoid fever is borne by impoverished individuals in resource-poor areas of the world. Serovar Typhi is a human-restricted invasive enteric pathogen which, after ingestion, crosses the intestinal mucosa, is taken up by gut-associated lymphoreticular tissues, and enters the systemic circulation. Both mucosal and systemic host immune responses are stimulated after infection. Serovar Typhi is an intracellular pathogen, and antibody and cell-mediated immune responses occur after infection or immunization with live oral attenuated typhoid vaccines.

Salmonellae are rod-shaped pathogens that infect a broad array of hosts, causing significant morbidity and mortality in impoverished and developed nations worldwide. Members of this genus have been preeminent research models in laboratories for over a century and belong to the family Enterobacteraciae, a large group of clinically relevant gram-negative, facultative anaerobic commensal and invasive bacilli. Salmonella has minimal nutritional requirements, does not ferment lactose, resists the caustic nature of bile salts, and, as such, can be differentiated on selective growth media that take advantage of these traits.

Typhoid fever caused by Salmonella enterica serovar Typhi is endemic in developing countries [1]. In industrialized countries, non-typhoid salmonella are a frequent cause of bacterial gastroenteritis [2] and such patients are subjected to extra-intestinal complications [3, 4]. It is potentially lethal and systemic infection and can be fetal if left untreated [5, 6]. Typhoid fever causes high incidence

of biochemical changes [7]. It causes significant decrease in serum albumin, while an increase in total protein and globulin. These increments are consistent with humeral immune response and inflammatory conditions [7, 8]. However, the low albumin concentration may be a suggestive of increased loss through renal tubules due to possible damage or disproportionate increase in globulin fraction of total protein [8]. The total protein test measures the total amount of two kind of protein in the body. Albumin and globulin are used as a part of the routine health checkup. It may also be used if the patient is experiencing unexpected weighed loss, fatigue, or have symptoms of kidney or liver disease [9].

Salmonella enterica is a leading cause of community-acquired bloodstream infection in Africa [10]. The contribution of typhoidal and non typhoidal Salmonella serovars to invasive disease varies considerably in place and time, even within the same country. Nonetheless, many African countries are now thought to experience typhoid fever incidence >100 per 100,000 per year with approximately 1% of patients dying [11].

Diagnostic tests for typhoid fever often lack sensitivity and/or specificity, especially in areas of the world that are endemic for typhoid fever, where clinically distinguishing typhoid fever from other febrile illnesses is difficult. Microbiologic culturing of blood is approximately 30 to 70% sensitive, with the highest sensitivity being associated with an absence of prior use of antibiotics and the culturing of larger volumes of blood, features that complicate this mode of diagnosis in young children. Microbiologic culturing of bone marrow aspirates is more sensitive than blood but often clinically impractical. Serum Widal assay titers are often nonspecific in endemic settings and are of limited value unless titers are markedly elevated or are analyzed for changes from acute to convalescent phases of illness. Molecular diagnostic assays including PCR are promising, but issues of practicality, contamination, and quality control have limited their use in many resource-poor areas of the world.

Enteric fever is a serious systemic disease caused by the bacterium *Salmonella enterica*serovar Typhi (*S. typhi*) and other *S. enterica* serovars, including *Salmonella enterica* Paratyphi A, B, and C. 1 These organisms are facultative intracellular pathogens and cause systemic infections following ingestion of the organism, colonization of the small intestine, invasion of the gastrointestinal mucosal surface, and dissemination throughout the body in the reticuloendothelial system including the liver, spleen, and bone marrow. The complete pathogenesis of enteric fever is unknown, and complications of the disease become more severe when it is harbored in the gall bladder, resulting in a chronic carrier state through which the bacteria are disseminated via frequent shedding. The disease is prevalent in underdeveloped countries, where clean drinking water is lacking and hygiene standards are compromised. In developed countries, the incidence is lower and the disease is mainly associated with travel to endemic locations. The long-term persistence of *S. typhi* in carriers explains why typhoid fever remains endemic in regions of the world with poor quality drinking water and defective sewage disposal.

Proteomics-based methods are currently being employed to increase our understanding of the pathogenesis of enteric fever and to explore the peripheral signatures of enteric fever. The molecular signature can be of host or bacterial origin, or a combination of both, produced during the process of infection. Biomarkers for intracellular pathogens, such as tuberculosis, have been developed using proteomics and mass spectrometry. The severe acute respiratory syndrome (SARS) protein biomarker has been identified using surface-enhanced laser desorption/ionization time-of-flight (SELDI-TOF).

To the best of our knowledge there is lack of information regarding serum proteins profile in patients diagnosed positively with Typhoid fever in Merowe locality, northern Sudan. This study entailed a quantitative assessment of serum total protein, albumin, globulin, and albumin: globulin ratio in individuals diagnosed positively with typhoid fever on zero day treatment compared to healthy ones, detection of any variations in estimated biochemical parameters between different genders in positive typhoid patients. In addition to, detect any alteration in plasma protein in receptiveness to typhoid titers.

2. Materials and Methods

This is descriptive analytical case control study. The study was done in El-Bar-Omdarag, Gelass, El-Brsa, Karema and Merowe (Merowe locality), northern Sudan. Data collection was done during the period from April to June 2014. Two hundred adult Sudanese individuals were volunteered to play a role in this study. One hundred positively diagnosed with typhoid infection (50 males and 50 females) with mean age (41.5 ± 2.1) on zero day treatments were the cases for this study. While, one hundred individuals (50 males and 50 females) with mean age (42.9 ± 1.9) negative for typhoid and apparently healthy, as obtained by physical examination and disease history were defined as control in this study.

2.1. Sampling

Five milliliter of venous blood was collected from each volunteer. Serum total proteins, Albumin were evaluated by using ELISA. Globulin was calculated by subtracting serum albumin from total protein.

Serum globulin = total protein-Serum albumin (g/dl)

2.2. Ethical Consideration

An informed consent, aims and benefits of this study were explained to the participants**.** Authors declare that there is no conflict of interest

2.3. Data Analysis

The data was analyzed using Statistical Package for Social

Sciences (SPSS), Windows version 8 x, 1997 SPSS, Inc, Chicago, IL, and USA. Mean, SD, Independent T test, were calculated

3. Results

This study showed highly significant differences in all estimated biochemical parameters with mean ± S.D. (8.4±0.01,6.8±0.06), (3.5±0.01, 4.1±0.03), (4.9±0.01, 2.8±0.06), (0.7 ± 0.003, 1.5 ± 0.02) for serum total protein, serum albumin, serum globulin and A/G ratio for typhoid positive and negative, respectively (P > 0.001) Table 2.

No significant difference, P. value was 0.632, 0.832 and 0.760 with mean ± S.D. serum total protein (7.5 ± 0.92, 7.6 ± 0.79) serum albumin (3.8 ± 0.38, 3.8 ± 0.37) and serum globulin (3.8 ± 0.16, 3.9 ± 0.16) for males and females respectively Table 3. Also no significant difference, P. value was 0.11, 0.60, and 0.06 with mean ± SD serum total protein (8.4 ± 0.01, 8.4± 0.02) serum albumin (3.5 ± 0.01, 3.5 ± 0.01) and serum globulin (5.0 ± 0.01, 4.9 ± 0.01) for titer 1/160 and titer 1/320 Table 4.

Table 1. *Base line characteristic of study participants.*

Parameter	Typhoid positive N = (100)	Typhoid negative N = (100)
Male: Female	1: 1	1: 1
Mean age (years)	41.5 ± 2.1	42.2 ±1.9
Titer of typhoid bacteria	1/160, 1/320	1/40, 1/80

Table 2. *Comparison of estimated biochemical parameters between studied participants.*

Variables	Typhoid positive Mean ± SD	Typhoid negative Mean ± SD	P. value
Serum total protein(mg/dl)	8.4 ±0.01	6.8 ±0.06	0.000
Serum albumin(mg/dl)	3.5 ±0.01	4.1± 0.03	0.000
Serum globulin(mg/dl)	4.9± 0.01	2.8 ±0.06	0.000
Albumin: globulin ratio	0.7	1.5	0.000
Glucose(mmol/L)	8.38 ± 0.07	17.56 ± 7.5	0.001

Table 3. *Biochemical parameters between genders in Typhoid positive participants.*

Variables	Male group Mean ± SD	Female group Mean ± SD	P. value
Serum total protein(mg/dl)	7.5± 0.92	7.6± 0.79	0.632
Serum albumin(mg/dl)	3.8± 0.38	3.8± 0.37	0.832
Serum globulin(mg/dl)	3.8± 0.16	3.9± 0.16	0.760
Glucose(mmol/L)	4.76±0.96	5.83±1.07	0.05

Table 4. *Comparison study of estimated parameters regarding typhoid titers.*

Variables	Titer=1/160 Mean ± SD	Titer=1/320 Mean± SD	P. value
Serum total protein(mg/dl)	8.4± 0.01	8.4 ± 0.02	0.11
Serum albumin(mg/dl)	3.5± 0.01	3.5± 0.01	0.60
Serum globulin(mg/dl)	5.0 ± 0.01	4.9± 0.01	0.06
Glucose(mmol/L)	5.0±0.45	4.6±0.55	0.05

4. Discussion

In patients with typhoid fever there was significantly increase in total serum protein and serum globulin while a decrease in serum albumin and albumin: globulin ratio as compared to healthy, irrespective of gender. This elevation of globulin is due to pathogen induced humeral immunity. Also low albumin level may amenable to the pharmaceutical treatment and the prognosis of the disease. This in consistency with the results of Bernardi, et al., 2014 [12] who reported that serum globulin concentration was higher in typhoid patients as compared to that of normal individuals which is in further confirmation with the reports of Emenuga, *et. al.*, 2014 [8] and Reinoso, 1998 [13]. The increases in total protein and globulin were in agreement with previous reports and these are consistent with humeral immune response Amen, et al., (2012) [7]. However, the low albumin concentration may suggest increased loss through renal tubules due to possible damage. It is possible that it may be due to disproportionate increase in globulin fraction of total protein [14].

When comparing serum proteins between infected male and female this study showed no differences between the two genders. This indicates that both the sexes respond in the same way to the pathogen. The findings are contrary to the reports of Emenuga, *et. al.*, 2014 [8] and Bernardi, et al., 2014 [12]. Mean total serum proteins were significantly higher in female child as compared to male child. Mean serum albumin did differ significantly between age and age x gender interaction; however, serum albumin concentration was low in young female as compared to that of young male. Serum albumin concentration was reported to be lower during infection.

A study revealed there was no variation in serum protein in receptiveness to infection titer. The result was supported by Abro, *et. al.*, 2009 [14] and Amen Shamim . *et. al.*, 2012 [7]. Correlations between the titers and serum total protein, albumin and globulin were negative.

Typhoid fever can cause anemia by a variety of mechanisms. In acute infection or hepatic dysfunction, there is usually very little change in serum albumin levels, because albumin has a long biological half-life. The level of albumin was upregulated in chronic typhoid cases in our study, and this might be due to an increase in free radicals during Salmonella infection; the release of hydroxyl radicals and nitric oxide in cases of Salmonella has already been reported. The increase in albumin found mainly in chronic typhoid carriers in the current study might occur in order to counteract the generation of free radicals, because albumin is known to have antioxidant properties during free radical generation in the case of infection.

The effect of haptoglobin on endotoxin-induced cytokine release is not yet known. However, it is evident from past research that haptoglobin enters monocytes and neutrophils and interrupts the intracellular function triggered by intracellular LPS. The role of haptoglobin in the modulation of proinflammatory cytokines and anti-inflammatory

cytokines is debatable and needs further investigation.

Glucose level was higher among typhoid negative; females have elevated level of glucose. While, increased typhoid titer showed low glucose level. Invasion of typhoid pathogen to small intestine induced inflammation that influence nutrients absorption efficiency so typhoid positive patients have low level of glucose consequently other nutrients. This study showed despite female did not differ from infected male in their response to pathogen but their physiological function differs as female glucose absorption didn't affected as male did. So this indicated that females are more tolerant to pathogen induced intestinal inflammation. Lend supportive result by Emenuga, *et. al.*, (2014) [8]. Blood glucose concentration was significantly lower in typhoid fever patients. This indicates compromised energy metabolism as a result of increased demand. This suggests that hypoglycaemia may be one of the biochemical complications of severe typhoid fever which may be considered in planning management regime.

5. Conclusion

Typhoid fever increased serum total protein and globulin while decreased albumin and albumin: globulin ratio, irrespective of genders. Typhoid positive females had higher serum glucose level compared to their counterpart males. Typhoid titers did not affect serum proteins concentrations.

Recommendations

Low albumin level and hypoglycemia should be surveillant when anti typhoid pharmaceutical are commenced

References

[1] World health organization (2000). WHO position paper. *Wkly Epidomol Rec.* 75; 25–64.

[2] Falkenhorst G, Ceper T. H, Strid M. A, Mølbak K, Krogfelt K. A. (2013). Serological follow-up after non-typhoid salmonella infection in humans using a mixed lipopolysaccharide ELISA. *Int J Med Microbiol.* 303(8): 533-8.

[3] Năşcuţiu AM. (2014). Role of Salmonella serology a Century after the Widal era. Roum Arch Microbiol Immunol. 73(3-4): 105-17.

[4] Jagadish K, Patwari A. K., Sarin S. K., Prakash C., Srivastava D. K., Anand V. K. (1994). Hepatic manifestations in typhoid fever. Indian Pediatr. 31(7): 807-11.

[5] Igbal, S. M. J., Serfraz, M. M. and Khan, M. N. (2004). Clinical spectrum of Typhoid fever in children. *Pakistan journal of medical of Health Sciences.* 10 (4): 366-367.

[6] Ozen, H. G.; Sec meer, G.; Kanra, Z.; Ecevit, M.; Ceyhan, A. and Dursun, Y. A., (1995). Typhoid fever with very high transaminase Levels. *Turky, Pediatre*, 37 (2), 169-171.

[7] Amen Shamim, Ayesha, Bilal Hussain. (2012). Study of Biochemical Changes and Elevated Levels of Enzymes in *Salmonella typhi* Infected Patients in Pakistani Population. *Int. J. Bio Automation.* 16(1): 33-42.

[8] Emenuga V. N., Ureme S. O., Ohanu M. E., Ejezie F. E. and Nnabuchi C. I. (2014). Some Hematological and Biochemical Profiles of Typhoid Fever in IGBOS of Nigeria. *Indian journal of applied research.* 3(4): 330-332.

[9] Janice, T. Busher, (1990). Clinical Methods; The history, physical and laboratory examination. 3rd edition chapter 101. Boston; Butler Worths; Gerogia.

[10] Crump J. A, Luby S. P. and Mintz E. D. (2004). The Global burden of typhoid Fever. *Bull world Health organ.* 38: 346-353.

[11] Crump J. A, Heyderman R. S. (2015). A Perspective on Invasive Salmonella Disease in Africa. Clin Infect Dis. 1; 61 Suppl 4:S235-40.

[12] Bernardi M, Ricci CS, Zaccherini G. (2014). Role of human albumin in the management of complications of liver cirrhosis. J Clin Exp Hepatol. 4(4):302-11.

[13] Reinoso, M. A. C.; Whitly, J. J. and Schwarzenberg, S. J. (1998). Lysinuric Protein Intolerance Masquerading as Celiac Disease; Acase Report. J Pediatr. 132(1): 153-155.

[14] Abro A. H., Abdou, J. L., Gangwani A. M., Ustadi N, J., Younis, H. S., Hussaini S. (2009). Hematological and Biochemical change in typhoid fever. *Pak J Med Sci.* 25(2): 166-171.