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Some Haematological and Biochemical Profiles of Typhoid Fever in IGBOS of Nigeria.

KEYWORDS: Typhoid fever, Heamatological profile, Biochemical profile, Igbos.

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ABSTRACT *This work is aimed at investigating the biochemical and haematological effects of typhoid fever in a Nigerian population. Blood samples were collected from two hundred typhoid fever patients attending University of Nigeria Teaching Hospital Enugu. Haemoglobin concentration (Hb) packed cell volume (PCV) total/differential white blood cell count (wbc T&D) reticulocytes, platelet count, glucose, ascorbic acid, total and differential proteins were estimated. Students "t" tests was used to compare the mean values. There were significant reductions in PCV, Hb, Total wbc, lymphocytes, neutrophils, ascorbic acid, albumin and platelets ($P < 0.05$), in the typhoid fever patients). The blood film showed moderate toxic granules in neutrophils and rouleaux formation in the red blood cells. Conclusively, typhoid fever causes significant depression of erythropoeisis, myelopoesis and thrombopoesis. These changes may be a potent cause of pancytopoenia that may complicate management of typhoid fever and rouleaux formation and thrombocytopaenia can precipitate to disseminated intravascular coagulation.*

INTRODUCTION

Typhoid fever is a widespread and potentially lethal infection which follows ingestion of salmonella typhus. It is endemic in the tropics and sub tropics. Over 1000 species of salmonellae have now been described. Salmonella typhi B are distributed throughout the world. S. paratyphi C is the rarest of the enteric fever pathogens being confined to the far East, West Africa, Central and South America and certain countries in Eastern Europe (Geddes 1981). The salmonella causing typhoid and paratyphoid fevers are only pathogenic to man and the source of infection is therefore always human.

Typhoid fever is usually acquired from a drink or food but the primary source of infection is almost invariably a human carrier, symptom-free but excreting the organism in stool or urine and failing to observe basic hygiene principles. Most commonly, the disease occurs sporadically but epidemics may result from contamination of drinking water, less commonly of food. Following ingestion, the organisms pass into the stomach. If only small numbers are present, they may be killed by gastric acid. When the innoculum is large or if there is reduction in gastric acid for example after gastrectomy, S. typhi passes into the upper small bowel and invades the mucus membrane and Peyers patches of lymphatic tissue from where it enters the blood and is disseminated throughout the reticuloendothelial system where multiplication occurs. After a latent period of one or two weeks, bacteraemia recurs and the signs and symptoms of typhoid fever appear. Any organ or system in the body may be invaded which result into varied clinical picture.

The serological test (widal test) is well known as an indirect test to detect the shadows or foot prints of salmonella groups. However, the gold standard is the isolation of the organism from stool or blood culture. Hamze et al (1999) evaluated the use of widal test in Lebanon and concluded that the test is still a valuable tool for typhoid fever control. During the course of typhoid fever, the patient develops a high titre of agglutinins. The detection and estimation of these agglutinins by widal reaction is done routinely in many countries. It is most useful in patients not normally resident in typhoid - endemic areas and who have not been immunized against the disease as previous salmonella infection and also TAB immunization can cause problems in interpretation. A negative widal reaction does not exclude typhoid fever. Elevation of 0 antigen titres is suggestive of active infection while the other antigens reflect previous or TAB immunization (Abraham et al 1981).

Biochemical and haematological changes have been associated with typhoid fever. Olubuyide et al (1989) reported an increase in C – reactive proteins and suggested that the increase could be used as a diagnostic parameter for typhoid fever. Also Singh et al (1999) documented increases in levels of cytokines (IL - 1, IL - 2, IFN-gamma and IL - 4) while Ohinish and Kimura (1998) reported elevated plasma level of thrombomodulin (TM) in febrile patients with typhoid fever. In earlier studies a fall in serum iron was reported in bacteria! infection[7]. These changes are involved variously in the pathophysiology of typhoid fever and its complications. Igbo tribe is one of the major ethnic groups in Nigeria and constitute the majority of persons in the South East geopolitical zone with Enugu as its political centre and University of Nigeria Teaching Hospital as the apex medical institution. There appears to be paucity of data with regard to haematological and biochemical profiles in typhoid fever in Nigeria. Since, the disease is common in Nigeria, it is therefore necessary to address this problem starting with the Igbos of South East Nigeria. The data furnished by the study may be useful in the clinical and laboratory management of the infection.

METHODS

Study Design

Two hundred typhoid patients (120 males and 80 females) with widal titre of 1/160 and above were included in the study after informed consent. They were all seen in the Medi-

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cal Clinic of University of Nigeria Teaching Hospital Enugu in 2006. The control group consisted of one hundred apparently healthy persons (50 males and 50 females) with a widal titre of 1/20 to 1/40. The age range of test and control groups was 20 - 60 years. 5mls of blood was collected from the test and control groups. A portion (2mls) was anticoagulated with EDTA and used for the haematological profiles while the remaining was allowed to clot and serum used for biochemical profiles. Haematological profiles were determined by the method of Bain (1997). The glucose was determined by glucose oxidase method of Trinder 1969 while the methods of Kway (1975) and Kingsley (1942) were used, for ascorbic acid and protein profiles respectively. The mean results of tests and controls were analysed using students "t" test. The results based on sex and titres (1/160 and 1/320) were compared. The major results are presented in Tables 1 and 2.

RESULTS

When the mean results of test and control subjects were compared, there were significant decreases in PCV, haemoglobin, total white blood cell count, lymphocytes, neutrophils, ascorbic acid and albumin (P<0.05). In the comparison between 1/160 (the minimum inclusion titre in Nigeria) and 1/320 (the highest titre obtained), there was significant difference (P<0.05) in platelets while others were not significant (P > 0.05). The only abnormal feature observed in the blood film was moderate to marked rouleaux formation. Comparison on the basis of sex maintained the same pattern.

TABLES:

TABLE 1: MEAN RESULTS IN TEST AND CONTROL SUBJECTS

Parameters	Test Subjects	Controls	P-Values
	n=200	n=100	
PCV (L/L)	0.30±0.41	0.40±0.03	P < 0.05
Hb (g/dL)	9.9±0.95	13.45±0.81	P < 0.05
WbcTxTo^/L)	3.0±1.00	5.78±1.68	P < 0.05
Neutrophils (%)	40.7±8.89	62.22±4.69	P < 0.05
Lymphocytes (%)	60.08±9.60	35.96±4.06	P < 0.05
Monocytes (%)	0.28±0.54	0.30±0.55	P < 0.05
Basophils (%)	0.1±0.30	0.14±0.40	P < 0.05
Eosinophils (%)	1.4±1.37	1.4±1.20	P < 0.05
Platelets (xlO^L)	100.40±50.06	282.20±71.24	P < 0.05
Reticulocytes (%)	08.0±0.05	2.1±0.03	P < 0.05
Glucose (mmol/L)	4.76±0.96	5.83±1.07	P < 0.05
Ascorbic Acid (mg/dl)	0.56+0.96	1.50±0.42	P < 0.05
Total protein (g/dl)	9.20±3.01	16.62±0.92	P < 0.05
Albumin (g/dl)	3.57±1.44	4.5±0.70	P < 0.05
Globulin (g/dl)	5.54±2.0	2.12±0.51	P < 0.05

TABLE 2: A COMPARISON OF MEAN RESULTS IN TITRES OF 1/150 AND 1/320

Parameters	1/160 n= 130	n =1/320	P - Values
	n= 130	n=70	
PCV (L/L)	0.28±0.02	0.30±0.02	P > 0.05
Hb (g/dL)	9.92±0.97	10.1±1.0	P > 0.05
WbctxIO^L)	2.8±0.29	3.10±0.90	P > 0.05
Neutrophils (%)	40.30±9.03	37.90±10.10	P > 0.05
Lymphocytes (%)	57.80±1.63	60.40±2.03	P > 0.05
Monocytes (%)	0.25±0.2	0.29±0.15	P > 0.05
Basophils (%)	0.17±0.40	0.13±0.61	P > 0.05
Eosinophils (%)	1.42±1.30	1.20+0.50	P > 0.05
Platelets (xlO^9/!.)	151.16±4350	90.00±78.50	(P < 0.05)
Reticulocytes (%)	1.0±0.03	092±0.01	(P > 0.05)
Glucose (mmol/L)	5.0±0.45	46±0.55	(P > 0.05)
Ascorbic Acid (mg/dl)	0.60±0.10	0.55±0.30	(P > 0.05)
Total protein (g/dl)	9.90±1.0	9.52±1.30	(P > 0.05)
Albumin (g/dl)	3.0±1.3	3.50±1.50	(P > 0.05)
Globulin (g/dl)	5.77±1.5	6.02±1.2	(P>0.05)

DISCUSSION

Typhoid fever caused by salmonella typhi has been associated with some physiological changes in affected persons. It is a common disease in most of Africa, Asia and Central and South America. These changes form part of the pathophysiology of the infection irrespective of geographical location. The haematological profiles obtained in this study showed that erythropoesis and myelopoesis were depressed as indicated by packed cell volume, haemoglobin, total and differential white blood cell counts respectively. The lower values obtained in the measured erythropoetic series suggested that typhoid fever, could be a potent cause of anaemia in Igbos of Nigeria. Ohaeri and Ohaeri (2002) reported similar results in Jos Nigeria. The value of the total white blood cells though within normal range was significantly lower in typhoid fever patients compared with controls. It may be due to possible bacteria metabolism and its toxins on the bone marrow, the major site of myelopoesis

Neutropaenia recorded in this study is worthy of anxiety since these phagocytic cells are crucial in cellular immune response to bacterial infection: Earlier, Cartwright and Lee 1971 reported that in many chronic disorders, the activities of the bone marrow may be suppressed leading to a non- progressive mild to moderate anaemia characterized by reduced plasma and erythroblast iron or increased reticuloendothelial iron stores. This can constitute potent problems in rural communities where good nutrition is hardly within reach of the indigenes (Ohnishi and Kimura 1998). Although, empirical data with regard to epidemiology of anaemia among the Igbos of Nigeria do not appear to have been documented, it is likely that typhoid fever which is endemic in Nigeria and other African countries may be a factor in anaemia surveillance and management. Leucopaenia and neutropaenia which were observed in this study agreed with previous reports of pathophysiology of typhoid fever. This could be as a result of increased demand of cellular immune responses to the infection. Neutrophils are particularly crucial in oxygen - dependent toxicity against invading bacteria. A study has stated that one of the most severe complications of typhoid fever in Ghana is perforation of ileum and post-operative wound infection (Olubuyide,1992). This may be related to poor neutrophil function and number. It had earlier been reported that there was reversed immature neutrophils to total neutrophil count ratio (1/T ratio) in neonatal sepsis in Rawalpindi (Olubuyide,1992) Salmonella species being intravascular organisms invade the white cells and are consequently transported to organs and tissue where it vegetates to cause metabolic derangements.

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Blood glucose concentration was significantly lower in typhoid fever patients studied. This indicates compromised energy metabolism as a result of increased demand. Glucose is the major substrate for ATP production in animal tissues. It also serves as a fuel molecule for bacterial metabolism. This suggests that hypoglycaemia may be one of the biochemical complications of severe typhoid fever which may be considered in planning management regime. Similarly ascorbic acid was consistently lower in almost all cases. It is not very clear if the vitamin is required for bacterial metabolism. It is likely that the reduced value was due to its antioxidant role in attenuating the deleterious effects of oxygen free radicals and reactive oxygen species. It has long been documented that bacteria utilizes oxygen in its phagocytic activities and therefore contribute to oxygen free radical burden of human and animal tissues. Various workers have documented low ascorbic acid concentrations in some diseases (Trinder, 1969). Drugs and chemicals have been reported to affect this metabolite (Ureme et al 2002). It is also possible that the low value may be due to increased erythropoesis due to the observed anaemia since ascorbic acid is an erythropoetic factor. The increases in total protein and globulin were in agreement with pervious reports and these are consistent with humoural immune response. 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. The mild to moderate rouleaux formation in the peripheral blood film is supportive of the opinion.

The comparison of mean values of haematological and biochemical profiles of 1/160 and 1/320 titers yielded rather curious result. The two titres when compared showed no significant differences in all measured profiles except platelets. The inference could be that as soon as the critical titre clinically accepted for diagnosis is attained, further increases may not elicit increased derangement of erythropoesis and myelopoesis. This may be because of metabolic resilience of the biosynthetic pathways of energy metabolism which are associated with these cells. Although, nutritional assessment of the test subjects was not done, it is possible that this could have affected the results. The thrombocytopenia observed in the comparison may suggest that platelets' activation could be a major factor when antibody level rises. Platelets have been reported to be activated by some particulate factors like bacteria and soluble chemicals like toxins. Once activated, it undergoes viscous metamorphosis that leads to intravascular thrombus formation which is a prelude to disseminated intravascular coagulation (DIC).

Conclusively, the results of the study suggest that typhoid fever may be a cause of pancytopaenia and disseminated intravascular coagulation. Also, the results suggest that although erythropoesis, myelopoesis, thrombopoesis, glucose homeostasis and ascorbic acid metabolism may be suppressed in typhoid fever, further increases of agglutination titre may not adversely affect homeostatic balance but can cause qualitative and quantitative platelet abnormality.

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