



Research article

Changes in some haematological parameters in typhoid fever patients attending Landmark University Medical Center, Omuaran-Nigeria

James A. Ndako^{a,*}, Victor T. Dojumo^b, Jeremiah A. Akinwumi^b, Victor O. Fajobi^b, Akinyomade O. Owolabi^a, Oludolapo Olatinsu^a^a Department of Microbiology, Landmark University, Omu-Aran, Nigeria^b Department of Medical Laboratory Services, Landmark University Medical Center, Omu-Aran, Nigeria

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ABSTRACT

Background: Typhoid or enteric fever is caused by *Salmonella typhi*. It is largely a disease of developing nations due to poor standard of hygiene and unavailability of potable water. The most prominent feature of the infection is fever which gradually rises to a high plateau. The prevalence of typhoid fever has been on the increase which is associated with several hematological parameters.

Objectives: This study was carried out to determine the changes in various hematological parameters in our study subjects.

Method: Four Hundred- (400) samples were obtained from volunteer subjects visiting the outpatient department of the Landmark University Medical Center. 200 typhoid positive samples were collected from subjects while 200 typhoid negative blood samples served as controls (From both male and female subjects each). Widal test was carried out as a confirmatory test for typhoid fever and evaluation of the hematological parameters were performed. The hematological parameters considered includes Packed Cell Volume (PCV), White Blood Cell count (WBC), Platelet count (PLT), Lymphocyte (LYMP) their implications on both male and female typhoid fever patients were also determined.

Results: The result showed a significant reduction in the values for PCV, WBC, ESR and HAE concentration in typhoid positive males in comparison to typhoid negative males. In females, a significant decrease was observed in values for PCV, ESR, HAE concentration and PLT in typhoid positive females when compared to typhoid negative females. These parameters when compared showed a significant decrease recorded in PCV, ESR and HAE concentration of the typhoid positive male patients in comparison to typhoid positive female patients.

Conclusion: This study implies that anemia, bone marrow suppression and hemaphagocytosis are likely resulting factors of typhoid fever due to the changes in the hematological parameters. Therefore, these parameters have to be further studied to allow for efficient management of this illness.

1. Introduction

The incidence of typhoid fever annually and its role in the increasing mortality and morbidity rate is of a great concern as the World Health Organization (WHO) has reported over 25 million typhoid fever cases yearly. Typhoid fever is a systemic illness and its causative agent is *Salmonella enterica/typhi* [1]. This strain of *Salmonella* affects only humans and can be asymptomatic in most cases.

The most common means of infection is from drinking or eating already-contaminated food and food products as the causative agent is passed out in urine or fecal matter of infected persons [2]. This connotes

that untreated water sources are also major means of contracting and spreading typhoid fever. Typhoid fever is associated with symptoms such as constipation, body aches, diarrhea and these symptoms, if the infection remains untreated, can become severe after a period of days. This illness is a global health issue as it is responsible for approximately 200,000 deaths annually [3].

Although, reports obtained over time shows that increasing morbidity and decreasing mortality rates have been observed over a few years now. Vaccines are available to aid the prevention of the illness; about 40–90% of typhoid fever cases are preventable for a period of two years using the vaccine, however these data include patients aged 3–44 years which

* Corresponding author.

E-mail address: ndako.james@lmu.edu.ng (J.A. Ndako).

makes it unsuitable for children under 2 years, [4]. Data from various studies carried out revealed that majority of the reported cases of typhoid fever evolve from the Indian subcontinent such as in places like Asia. Diagnosis of typhoid fever is by Widal test for the production of antibody and this is commonly employed in Asia, Africa. Specific detection of IgA in order to diagnose typhoid fever by ELISA method has proven to be a new and more reliable method for diagnosis, [5].

Typhoid fever causes significant hematological changes which could be helpful in diagnosis. Thrombocytopenia is common in typhoid but this association is not well recognized. Awareness of this associate on could be useful in diagnosis of typhoid fever more so in under resourced endemic regions in developing countries, [1, 2]. The study was aimed at ascertaining the differences in various hematological parameters in both male and female typhoid fever patients and also to compare the results obtained from both male and female patients.

2. Materials and methods

2.1. Study design/geographical location

This research was carried out at Landmark University Omuran-A city located in North Central Nigeria, with an Average relative humidity (%) (at 15:00 LST). Omuaran is Located in Kwara –South Senatorial zone of Nigeria. The Landmark University Medical Laboratory was used for sample collection and assay. Four hundred patients were recruited for the study after oral consent was given. They comprised of 200 men and 200 women (100 Typhoid positive females, 100 Typhoid negative females, 100 Typhoid positive males and 100 Typhoid negative males). Information of subjects recruited for the study was obtained by a well-structured questionnaire format.

2.2. Study area and population

The study was conducted at the Medical Laboratory department of the Landmark University Health Center, Omuaran. The study population comprised of volunteer subjects and patients attending the outpatient department of the Health Facility. The age range of test and control groups was 18–60 years.

2.3. Sample size formulae

Mode of Sample size determination for the Prevalence of typhoid fever in this research was:

$$n = \left[z^2 \times \frac{p \times q}{d^2} \right]$$

where,

- n = sample size
- z = linked to 95% confidence interval.
- p = previous prevalence.
- q = 1 – p (previous non-prevalence).
- d = relative desired precision.

With the minimum sample size as n above, the sample size of 400 used in the study was to ensure wider coverage of the population, hence increase in precision.

2.4. Ethics approval and consent to participate

Oral consents were made to the subjects prior to the sample collection. Ethical clearance and approval was obtained from the appropriate ethical committee of the Landmark University Medical Center, with the ethical approval reference: LMC/2019/02/30.

2.5. Collection of blood sample

Samples of blood were obtained from the individuals using standard procedures. Collected samples were placed into EDTA universal containers. After coagulation occurred, the serum sample was used for Widal test while samples of blood (plasma) were employed for use in determining the full blood count [6]. After the tests were carried out, patients who tested positive for typhoid fever were recruited for the study.

The data obtained from the questionnaire distributed was analyzed for central tendencies with the use of descriptive statistics, mean standard deviation of the parameters were obtained from the research. Least Significant Difference (LSD) and analysis of variance were used for testing the significant differences amidst the treatment. The analysis employed in this study was carried out using SPSS for Windows statistical software package version 20. The results were represented as tables. The analysis of the study can be seen in two parts. The first one focuses on the comparison of the haematological properties of the patients based on gender (male and female separately) – here, the independent t-test statistical method was employed. The second one focuses on the difference between the combined genders which can be seen in the light of four treatments – here the analysis of variance method was used, that is, the f statistic model for clarity and ease of inference.

3. Results

3.1. Hematological differences in male typhoid fever patients

From the results obtained, the PCV value was (44.19 ± 2.96) in the Typhoid negative males as compared to (40.70 ± 4.36) in Typhoid positive males and this denotes a statistically significant difference at (p < 0.01) and this was shown in Table 1. The WBC also showed an increase from (5.65 ± 1.81) to (6.47 ± 2.52) while NEUT, MONO and PLT showed a decrease from (65.27 ± 16.69) to (63.11 ± 15.32), (7.69 ± 3.52) to (7.67 ± 2.07) and (10.09 ± 7.04) to (4.97 ± 5.27) respectively LYMP showed an increase from (27.07 ± 15.67) to (28.94 ± 13.85) as the difference was observed to be statistically insignificant. However, a statistically significant difference was recorded in ESR and HAE concentration as the values increased from (193.09 ± 64.25) to (246.37 ± 53.92) and (13.37 ± 1.48) to (14.62 ± 1.16) respectively (Table 1).

3.2. Hematological differences in female typhoid fever patients

In the female typhoid fever patients, hematological changes observed showed PCV values to increase from (35.47 ± 4.25) in positive female patients to (38.14 ± 2.72) in negative female patients that served as control. This difference was statistically significant at (p < 0.01). An increase in the values for WBC, LYMP and MONO were observed from (6.42 ± 2.29) to (7.01 ± 2.82), (31.92 ± 13.99) to (32.33 ± 14.91) and (7.41 ± 2.49) to (7.62 ± 2.20) respectively. Reverse was the case in NEUT as there was a recorded decrease in the value from (60.48 ± 15.10)

Table 1. Haematological changes in typhoid fever patients (male).

Parameters	Positive Male	Control Male
PCV	40.70 ± 4.36 ^a	44.19 ± 2.96 ^b
WBC	5.65 ± 1.81 ^a	6.47 ± 2.52 ^b
NEUT	65.27 ± 16.69 ^a	63.11 ± 15.32 ^a
LYMP	27.07 ± 15.67 ^a	28.94 ± 13.85 ^a
MONO	7.69 ± 3.52 ^a	7.67 ± 2.07 ^a
ESR	193.09 ± 64.25 ^a	246.37 ± 53.92 ^b
HAE Conc.	13.37 ± 1.48 ^a	14.62 ± 1.16 ^b
PLT	10.09 ± 7.04 ^a	4.97 ± 5.27 ^a

Key: mean ± standard deviation.

Mean values with the different superscripts differ significantly (p < 0.01).

Table 2. Hematological changes in typhoid fever patients (female).

Parameters	Positive Female	Control Female
PCV	35.47 ± 4.25 ^a	38.14 ± 2.72 ^b
WBC	6.42 ± 2.29 ^a	7.01 ± 2.82 ^a
NEUT	60.48 ± 15.10 ^a	60.12 ± 15.84 ^a
LYMP	31.92 ± 13.99 ^a	32.33 ± 14.91 ^a
MONO	7.41 ± 2.49 ^a	7.62 ± 2.20 ^a
ESR	225.67 ± 92.66 ^a	270.64 ± 51.06 ^b
HAE Conc.	11.78 ± 1.46 ^a	12.68 ± 0.91 ^b
PLT	12.35 ± 6.58 ^a	6.30 ± 7.96 ^b

Key: mean ± standard deviation.

Mean values with the different superscripts differ significantly (p < 0.01).

to (60.12 ± 15.84) but the difference was statistically insignificant. ESR and HAE concentration showed increase in the values from (225.67 ± 92.66) to (270.64 ± 51.06) and (11.78 ± 1.46) to (12.68 ± 0.91) as the difference was statistically significant at (p < 0.01). PLT decreased from (12.35 ± 6.58) to (6.30 ± 7.96) and the difference was statistically significant (Table 2).

3.3. Comparison of hematological changes in relation to male and female typhoid fever patients

3.3.1. Packed cell volume (PCV)

PCV values associated with the male and female typhoid fever patients of the individuals recruited involving the (Typhoid positive females, Typhoid negative females which served as control, Typhoid positive males and Typhoid negative males also serving as control) showed that Typhoid negative male had a PCV of (44.19 ± 2.96) which is higher when compared to PCV of Typhoid positive male (40.70 ± 4.36) and Typhoid positive female (35.47 ± 4.25) and the differences were both statistically significant at (p < 0.01). Also, PCV of TPM (40.70 ± 4.36) was higher in comparison to PCV of TPF (35.47 ± 4.25) and TNF (38.14 ± 2.72) and the differences were statistically significant at (p < 0.01). TPF (35.47 ± 4.25) showed a lower value for PCV than TNF (38.14 ± 2.72) and the difference was statistically significant at (p < 0.01). Finally, PCV of TNF (38.14 ± 2.72) was lower than PCV of TNM (44.19 ± 2.96) and TPM (40.70 ± 4.36) and the differences were statistically significant at (p < 0.01) (Table 3).

3.3.2. White Blood Cell Count (WBC)

White Blood Cell Count of TPM (5.65 ± 1.81) was lower in comparison to WBC of TNM (6.47 ± 2.52) and this difference was statistically significant at (p < 0.01). Also, WBC of TNF (7.01 ± 2.82) was higher than WBC of TPF (6.42 ± 2.29) and TNM (6.47 ± 2.52) and the difference was statistically insignificant at (p < 0.01). WBC of TPM (5.65 ± 1.81) was

lower when compared to that of TPF (6.42 ± 2.29) and TNF (7.01 ± 2.82) and both differences were statistically significant at (p < 0.01). The WBC of TNM (6.47 ± 2.52) was higher than that of TPF (6.42 ± 2.29) and the difference was statistically insignificant at (p < 0.01) (Table 3).

3.3.3. Neutrophil level

NEUT of TPM (65.27 ± 16.69) was higher than that of TNM (63.11 ± 15.32) and TPF (60.48 ± 15.10) and both differences were statistically insignificant at (p < 0.01). Furthermore, NEUT of TNM (63.11 ± 15.32) was higher than that of TNF (60.12 ± 15.84) and TPF (60.48 ± 15.10) and the differences were recorded to be statistically insignificant at (p < 0.01). NEUT of TNF (60.12 ± 15.84) was lower than NEUT of TNM (63.11 ± 15.32) and TPM (65.27 ± 16.69) and the differences were statistically insignificant at (p < 0.01) (Table 3).

3.3.4. Lymphocytes

In comparison of the hematological changes of male and female typhoid fever patients, it was observed that the lymphocytes level of TPM (27.07 ± 15.67) was lower than the LYMP of TNM (28.94 ± 13.85), the LYMP of TPF (31.92 ± 13.99) was lower than LYMP of TNF (32.33 ± 14.91) and the differences were statistically insignificant at (p < 0.01). Furthermore, the LYMP of TNF (32.33 ± 14.91) was lower than that of TPM (27.07 ± 15.67) and TNM (28.94 ± 13.85), and the differences were statistically significant at (p < 0.01). LYMP of TPF (31.92 ± 13.99) was higher than that of TNM (28.94 ± 13.85) and TPM (27.07 ± 15.67) and the differences were statistically significant at (p < 0.01) (Table 3).

3.3.5. Monocytes

The comparative hematological changes in male and female typhoid fever patients as it relates to monocytes was observed to be higher in TPM (7.69 ± 3.52) when compared to TNM (7.67 ± 2.07) and MONO of TPF (7.41 ± 2.49) was lower than TNF (7.62 ± 2.20) and the difference were statistically insignificant at (p < 0.01). Also, the MONO of TNM (7.67 ± 2.07) was higher than that of TPF (7.41 ± 2.49) and TNF, the MONO of TNF (7.62 ± 2.20) was higher than that of TPF (7.41 ± 2.49) and all the differences were statistically insignificant at (p < 0.01) (Table 3).

3.3.6. Erythrocyte Sedimentation Rate

In comparing the hematological differences in male and female typhoid fever patients, it was observed in relation to erythrocyte sedimentation rate that the ESR of TPM (193.09 ± 64.25) was lower than that of TNM (246.37 ± 53.92) and that of TPF (225.67 ± 92.66) and both differences were statistically significant at (p < 0.01). Also, the ESR of TNF (270.64 ± 51.06) was higher than that of TPF (225.67 ± 92.66) and TNM (270.64 ± 51.06) and the differences were statistically significant at (p < 0.01). Furthermore, the ESR of TNM (246.37 ± 53.92) was lower than that of TPF (225.67 ± 92.66) and TNF (270.64 ± 51.06) and the ESR of TPF (225.67 ± 92.66) was higher than ESR of TNM (246.37 ± 53.92)

Table 3. Comparison of haematological changes in male and female typhoid fever patients.

Parameters	Positive Male	Control Male	Positive Female	Control Female
PCV	40.70 ± 4.36 ^a	44.19 ± 2.96 ^b	35.47 ± 4.25 ^c	38.14 ± 2.72 ^d
WBC	5.65 ± 1.81 ^a	6.47 ± 2.52 ^b	6.42 ± 2.29 ^b	7.01 ± 2.82 ^b
NEUT	65.27 ± 16.69 ^a	63.11 ± 15.32 ^a	60.48 ± 15.10 ^a	60.12 ± 15.84 ^a
LYMP	27.07 ± 15.67 ^a	28.94 ± 13.85 ^{ab}	31.92 ± 13.99 ^b	32.33 ± 14.91 ^b
MONO	7.69 ± 3.52 ^a	7.67 ± 2.07 ^a	7.41 ± 2.49 ^a	7.62 ± 2.20 ^a
ESR	193.09 ± 64.25 ^a	246.37 ± 53.92 ^b	225.67 ± 92.66 ^c	270.64 ± 51.06 ^d
HAE Conc.	13.37 ± 1.48 ^a	14.62 ± 1.16 ^b	11.78 ± 1.46 ^c	12.68 ± 0.91 ^d
PLT	10.09 ± 7.04 ^a	4.97 ± 5.27 ^a	12.35 ± 6.58 ^b	6.30 ± 7.96 ^c

Key: mean ± standard deviation.

Mean values with the different superscripts differ significantly (p < 0.01).

PCV- Packed Cell Volume; WBC- White Blood Cell; NEUT- Neutrophil; LYMP- Lymphocytes; MONO- Monocytes; ESR- Erythrocyte Sedimentation Rate; HAE Conc.- Haemoglobin concentration; PLT- Platelet count.

and TPM (193.09 ± 64.25) and also, the ESR of TPF (225.67 ± 92.66) was lower than that of TNF (270.64 ± 51.06) and all the differences were statistically significant at ($p < 0.01$) (Table 3).

3.3.7. HAE concentration

The comparative hematological changes in relation to male and female typhoid fever patients in HAE Concentration shows that the HAE Conc. of TNM (14.62 ± 1.16) was higher than that of TPM (13.37 ± 1.48) and TNF (12.68 ± 0.91) and the differences were both statistically significant at ($p < 0.01$). Also, the HAE Conc. of TPM (13.37 ± 1.48) was lower than that of TNM (14.62 ± 1.16) and the HAE Conc. of TPF (11.78 ± 1.46) was lower than that of TNF (12.68 ± 0.91) and TPM (13.37 ± 1.48) and both differences were statistically significant at ($p < 0.01$). Finally, the HAE Conc. of TNF (12.68 ± 0.91) was higher than that of TPF (11.78 ± 1.46) and that of TNM (14.62 ± 1.16) was higher than TPM (13.37 ± 1.48) and TPF (11.78 ± 1.46) and all the differences were statistically significant at ($p < 0.01$) (Table 3).

3.3.8. Platelet count

In comparing the hematological changes of male and female typhoid fever patients as regards to Platelet count, PLT of TPF (12.35 ± 6.58) was higher than that of TPM (10.09 ± 7.04) and TNF (6.30 ± 7.96) and the differences were statistically significant at ($p < 0.01$). Also, the PLT of TNM (4.97 ± 5.27) was lower than that of TPF (12.35 ± 6.58) and TNF (6.30 ± 7.96) and both differences were statistically significant at ($p < 0.01$). Although, the PLT of TNM (4.97 ± 5.27) was lower than that of TPM (10.09 ± 7.04) but the difference was statistically insignificant at ($p < 0.01$). Finally, the PLT of TNF (6.30 ± 7.96) was higher than that of TNM (4.97 ± 5.27) and the difference was statistically significant at ($p < 0.01$) (Table 3).

From the tables above, there was a significant decrease in the Packed cell volume, White blood cell count, Erythrocyte Sedimentation rate and HAE Concentration in the typhoid positive male patients in comparison with that of the typhoid negative male patients but reverse was the case in the Neutrophils, Lymphocytes, Monocytes and Platelet Count of the recruited persons.

4. Discussion

Based on previous studies, the changes observed can be as a result of a decline in the bone marrow activity and this can be due to hemophagocytosis as these are the major means of evasion by the causative agent, *Salmonella typhi* patients infected with typhoid fever [7]. There was an observed decrease in PCV, ESR, HAE Concentration and PLT in female typhoid fever patients.

Reduction in the levels of PCV and WBC can be as a result of metabolic process in *Salmonella* which is common in most bacteria and this causes the release of toxins on the bone marrow which serves as the main site of myelopoiesis. The invasion of organs affected during hematopoiesis such as lymph nodes, bone marrow, spleen, tonsils can be the main reason for the reduction in the hematological parameters and this drastically lowers the rate of hematopoiesis [8].

In most Patients, Hemoglobin is normal in the initial stages but drops with progressing illness. Kakaria et al. [9], reported Anemia in 42.9% in their prospective study, Similarly, Shilpa et al [10] observed anemia in 34% of their enteric fever patients. Our results of anemia were comparable to these studies. Severe anemia is unusual in typhoid fever which may result in suspected case of intestinal haemorrhage or hemolysis or even an alternative diagnosis such as malaria, [11].

The result obtained in this study for anemia was comparable to these studies but they were statistically not significant. It may have been attributed to the maturational arrest of the cell lines in salmonella infection in the bone marrow, [12]. The hematological changes observed in male and female typhoid fever patients shows that lymphocytosis and neutropenia was suppressed as there was no

significant difference observed in the values of lymphocytes and neutrophils in typhoid fever patients and non-typhoid fever patients [13].

However, platelet count (PLT) was higher in females than in males and typhoid fever has been clearly seen to have an effect on hematological parameters. A significant decrease was observed in erythrocyte sedimentation rate (ESR) and haemoglobin concentration and this was observed in both male and female typhoid fever patients. This state of the patients may lead to anemia.

However, it has been discovered that platelet count (PLT) is higher in females than in males and this is in concordance with the studies by Ozougwu et al. [7]. This may be related to menstrual blood loss and the associated compensatory mechanisms, [16]. A significant decrease in mean platelet levels observed in male patients compared to normal individuals 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 [15]. Basophils were not observed in this study and this concurs with the study of Unaiza et al. [14].

However, the observed changes in typhoid fever were anemia, bone marrow suppression, and hemophagocytosis. These factors are major mechanisms in the production of hematological changes. Some hematological parameters have been affected due to typhoid fever as this illness affects several body systems including the bone marrow and this can be the cause of lowered neutrophil levels, packed cell volume and platelet count [15].

The result obtained in this work is in agreement with those of [17] and [18] in which haematological alterations due to typhoid fever were evaluated. These changes may be attributed to suppression of bone marrow activity and haemophagocytosis which are the major attacking mechanism of *Salmonella typhi* in typhoid patients.

Therefore, Typhoid fever has significant effect on some haematological parameters studied. These changes could be useful in the diagnosis of typhoid fever. Therefore, Full Blood Count Tests should be ordered early by the clinicians for effective and prompt diagnosis of typhoid infection and proper treatment of the patients **and** while these haematological parameters have to be monitored closely.

5. Conclusion

The result obtained from this study shows that typhoid fever may likely lead to thrombocytopenia and anemia due to the increased platelet counts but the chances of developing neutropenia are very low. Generally, based on several studies, typhoid fever has been recorded to be more prevalent among females than males and this can be attributed to the fact that a higher level of predisposing factors that cause typhoid fever, occurs more among the male subjects, probably as a result of their occupational and social practices, this tends to provides a greater immunity to this infection to the male subjects than in women. Typhoid fever has been clearly seen to have an effect on hematological parameters and therefore, these parameters have to be further studied and observed to allow for efficient management of this illness.

Declarations

Author contribution statement

J. Ndako: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

V. Fajobi: Performed the experiments.

J. Akinwumi and O. Olatinsu: Analyzed and interpreted the data.

V. Dojumo: Contributed reagents, materials, analysis tools or data.

A. Owolabi: Performed the experiments; Wrote the paper.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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