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Original Research Article

Evaluation of Haemoglobin, Total White Blood Cell and Differential Counts in Patients Suffering from Infectious Mononucleosis in Imo State

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Abstract: Infectious mononucleosis (IM) or Mononucleosis syndrome is caused by an acute infection of Epstein-Barr virus (EBV). This study was aimed at determining the levels of haemoglobin, total white blood cell (TWBC) count, neutrophils, lymphocytes, monocytes and eosinophils in patients infected with infectious mononucleosis at Federal Teaching Hospital, Owerri. A total of sixty subjects (30 patients and 30 controls) were enrolled in the study after giving their informed consent and completing questionnaires. The procedure was carried out at Federal Teaching Hospital, Owerri. Five millilitres of venous blood sample was collected at the ante-cubital vein aseptically and was dispensed into ethylenediaminetetraacetic acid (EDTA) containers. The EDTA containers were properly labeled with the subject's name, sample number and date of collection. Haemoglobin was determined using the cyanmethaemoglobin method, TWBC was determined using the improved Neubauer counting chamber, while the differential count was determined using Romanowsky staining method. Data generated were analyzed using SPSS version 27, and mean, standard deviation, t-test, correlation and p-value were determined. The mean values of haemoglobin (8.9±1.44)g/dl and neutrophils (28.53±12.77)%, were significantly reduced in patients with infectious mononucleosis when compared to the controls (12.83±1.34)g/dl and (54.27±10.20 ((p=0.000 and p=0.001)) The mean values of TWBC (17.66±8.54)%, lymphocytes (59.87±13.14)% and monocytes (10.30±6.68)%)% were significantly increased in patients with infectious mononucleosis when compared to the controls (6.17±2.53)%, (49.23±13.57)% and (5.93±2.91)%) respectively (p=0.000, p=0.003 and p=0.002). There was no significant difference in the mean value of eosinophil count in infectious mononucleosis (1.30±1.56)% (p=0.784) when compared to the controls (1.20±1.24)%. There were no significant differences in the mean values of haemoglobin, TWBC, neutrophil, lymphocyte, monocyte and eosinophil counts in male patients with infectious mononucleosis (9.14±1.52)g/dl, (19.16±9.36)x10^9/L, (27.69±11.18)%, (59.44±11.17), (10.13±6.12)% and (1.44±1.89)% when compared to the female patients (8.82±1.38)g/dl, (15.94±7.46)x10^9/L, (29.50±14.38)%, (60.36±15.51)%, (10.50±7.50)% and (1.14±1.09)% (p=0.568, p=0.311, p=0.705, p=0.852, p=0.881 and p=0.614). There was a non-significant positive correlation of haemoglobin with TWBC, neutrophils, lymphocytes, monocytes and eosinophils in infectious mononucleosis patients (r=0.17, p=0.357; r=0.15, p=0.421, r=0.07, p=0.730, r=0.11, p=0.563 and r=0.06, p=0.751). In conclusion, the data in the present study showed that infectious mononucleosis is characterized by increase in lymphocytes and monocytes with decreased levels of haemoglobin and neutrophils. Haemoglobin concentration does not have any relationship with white blood cells in patients with infectious mononucleosis. In the management and treatment of patients with infectious mononucleosis, complete blood count should be incorporated as a routine test, so as to aid in the diagnosis.

Keywords: Haemoglobin, Total White Blood Cell, Differential White Cell Counts, Infectious Mononucleosis.

INTRODUCTION

Infectious mononucleosis (IM) results from primary infection by the Epstein-Barr virus (EBV). EBV is a double-stranded DNA gamma herpesvirus that was first isolated in 1964 from Burkitt lymphoma tissue (Balfour, 2015). Humans are the only source of EBV and the virus has a worldwide distribution, with seropositivity rates of 90% among adults.

In most non-industrialized communities, primary EBV infection is usually asymptomatic and

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occurs within the first three years of life (Fica, 2013, characterized by fever, exudative pharyngitis, lymphadenopathy, hepatosplenomegaly and atypical lymphocytosis. Complications may occur, resulting in a spectrum of clinical entities manifested by specific organ dysfunction syndromes (eg, hepatitis), and hematological and biochemical abnormalities in individuals with presumably normal immune systems. An understanding of the spectrum and frequencies of EBV complications and markers of illness severity in these subjects will inform management of patients with EBV-related illnesses (Grotto, 2013).

As a member of the Herpesviridae family, EBV possesses the ability to establish a latent infection with the possibility of later reactivation, which may be clinically manifested as recurrent parotitis, uveitis or interstitial pneumonia (Kutok and Wang, 2016). EBV also leads to an aetiological relation-ship with some carcinomas such as nasopharyngeal carcinoma, Burkitt's tumour, Hodgkin's disease and B-cell lym-phoma in HIV-infected patients. EBV has a specific affinity for B-lymphocytes and epi-thelial cells in the oropharynx that bind to the CD21 receptor. Infection is most often transmitted by the saliva. The antigenic structure of EBV is quite complex. It possesses capsid antigen (EBV-VCA), nuclear antigen (EBV-NA), early antigen (EBV-EA) and lymphocyte-determined membrane antigens (LYDMA) (Fica, 2013).

The natural infection by EBV occurs only in humans and the result is a life-long infection. In industrialized countries, there is greater possibility of developing mononucleosis if EBV infection occurs in the second decade of life. Sero-epidemiological studies have shown that about 91% of all adults worldwide have had first-time infection by EBV. In developing countries, first-time infection by EBV is more frequent in the first decade of life. The incidence of infectious mononucleosis varies in each country in such a way that in U.S.A., 500 cases per 100,000 inhabitants are reported every year with a higher incidence in the age group from 15 to 24 years. Ebell, (2014) reported a higher incidence of infectious mononucleosis in people from 10 to 19 years old (6 to 8 cases per 1,000 people per year), and a lower incidence in children less than 10 years old (1 case per 1,000 people per year) and a milder clinical manifestations which is frequently underdiagnosed (Crawford, 2016).

Elevated white blood cell count (WBC) is a classical inflammatory marker and is associated with several disease risk factors (Akinlaja, 2016). In the last decades, platelet counts were introduced as potential markers to determine inflammation in prostate disorders. It is routinely requested by physicians in clinical practice as part of the complete blood count and is currently mainly used as an index in the differential diagnosis of anemia and other disease condition. Several studies have it that haematological analysis is a characteristic test for diagnosing IM with leukocytosis and lymphocytosis (more than 10% atypical lymphocytes) (Andersson, 2016). From the differential blood count is typical lympho-monocytosis of over 50-60% and atypical lymphocytes of over 10% which are CD8 and CD4 T lymphocytes. Morphologic heterogenity of the lymphoid population – normal lymphocytes and monocytes and atypical lymphoplasmotic cells with wide cytoplasm, peripheral basophilia and eccentrically positioned nuclear are observed. A blood chemistry test may reveal abnormalities in liver function (Andersson, 2016).

Hematological complications have been reported in 25% to 50% of the cases. Such complications include hemolytic anemia, thrombocytopenia, aplastic anemia, thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, and disseminated intravascular coagulation (Ebell, 2014). Neurologic complications are seen in 1% to 5% of the cases, and include such complications as Guillain-Barre syndrome, facial paralysis, meningoencephalitis, aseptic meningitis, transversal myelitis, peripheral neuritis, cerebellitis and optical neuritis (Luzuriaga and Sullivan, 2020). A potentially fatal complication is splenic rupture, which has been reported in 0.5% to 1% of the cases as well as air way obstruction (1% of the cases) provoked by lymphoid hyperplasia and mucosal edema (Andersson, 2016). It is calculated that this problem is seen in approximately 1 of every 800,000 According to Luzuriaga and Sullivan, (2020), haematologic abnormalities include a peripheral blood lymphocytosis, more than 10 % of the leucocytes in blood consist of atypical lymphocytes but the authenticity of the data has not been confirmed.

In Nigeria, there is little information pertaining to the clinical manifestations and complications of this disease. Hence, this study was aimed at determining the effect of infectious mononucleosis on some haematological parameters in the affected patients. The result from this study will enlighten the physicians on the how to manage and treat patients suffering from infectious mononucleosis.

MATERIALS AND METHODS

Study Area

The study was conducted at the Federal Teaching Hospital, Owerri, Imo state, a government tertiary institution.

Study Design

A cross-sectional study was carried out from the month of January to March, 2024 and all subjects who gave their informed consent and completed the questionnaire were enrolled in the study. The study population consisted of 30 patients infected with infectious mononucleosis and an equivalent number of age-matched apparently healthy subjects (30) served as the controls. The procedure was carried out at Federal

Teaching Hospital, Owerri, and the results of the tests were analyzed using SPSS version 27.

Sample Collection

Five millilitres of venous blood sample was collected at the antecubital vein aseptically and was dispensed into ethylenediaminetetraacetic acid container, which were properly labeled with the subjects' name, sample number and date of collection. The blood was stored in a refrigerator at 4^0C prior to use.

Ethical Consideration

This study was approved by the research and ethics committee of the Federal University Teaching Hospital, Owerri, and subjects who gave their informed consent were enrolled in the study.

Selection Criteria

Inclusion Criteria

1. Infectious Mononucleosis patients from 18 years and above.
2. Those without any other infection such as HIV, HBsAg, HCV, Syphilis etc.
3. Infectious mononucleosis patients who gave their informed consent.
4. Age-matched non-infectious mononucleosis subjects.

Exclusion Criteria

1. Infectious mononucleosis patients below 18 years of age.
2. Infectious mononucleosis patients whose informed consent could not be obtained because they were skeptical about the research.
3. Those with other infections such as HIV, HCV, HBsAg and syphilis.

Laboratory Analysis

Haemoglobin concentration was determined using Cyanmethaemoglobin method. Determination of the total white blood cell and the differential white cell counts were done manually using neubaeur counting chamber and thin blood films respectively.

Statistical Analysis

Statistical analysis was performed using SPSS version 27. Mean, standard deviation, t-test and Pearson correlation were determined. The level of significance was set at $p < 0.05$.

RESULTS

Table 1 shows the mean values of haemoglobin, total white blood cell count, neutrophils, lymphocytes, monocytes and eosinophils in Patients with Infectious ononucleosis and healthy Subjects.

The mean values of haemoglobin (8.9±1.44)g/dl and neutrophils (28.53±12.77)%, were significantly reduced in Infectious mononucleosis patients when compared to the controls (12.83±1.34)g/dl and (54.27±10.20)% (t = 10.68, p=0.000 and t = 8.62, p=0.001) respectively.

The mean values of TWBC (17.66±8.54)x10^9/L, lymphocytes (59.87±13.14)% and monocytes (10.30±6.68)%)% was significantly increased in infectious mononucleosis patients when compared to the controls (6.17±2.53)%, (49.23±13.57)% and (5.93±2.91)% (p=0.000, p=0.003 and p=0.002) respectively.

There was no significant difference in the mean values of eosinophil count in infectious mononucleosis patients (1.30±1.56)% when compared to the controls (1.20±1.24)% (p=0.784).

Table 1: Mean Values of Haemoglobin, Total White Blood Cell Count, Neutrophils, Lymphocytes, Monocytes and Eosinophils in Patients with Infectious Mononucleosis versus Controls (mean±SD)

Parameter	Test	Control	[t-value	p-value
Hb (g/dl)	8.9±1.44	12.83±1.34	10.68	0.001*
TWBC (X10^9/L)	17.66±8.54	6.17±2.53	7.06	0.000*
Neutrophils (%)	28.53±12.77	54.27±10.20	8.62	0.000*
Lymphocytes (%)	59.87±13.14	49.23±13.57	3.08	0.003*
Monocytes (%)	10.30±6.68	5.93±2.91	3.28	0.002*
Eosinophils (%)	1.30±1.56	1.20±1.24	0.28	0.784

Key:
Hb: Haemoglobin
TWBC: Total White Blood Cell
*: Significant p-value
SD: Standard Deviation

Table 2: Mean Values of Haemoglobin, TWBC, Neutrophils, Lymphocytes, Monocytes and Eosinophils in Male and Female Patients with Infectious Mononucleosis.

There was no significant difference in the mean values of haemoglobin(9.14±1.52)g/dl, TWBC (19.16±9.36)x109/L, neutrophils (27.6 +11.18) %, lymphocytes (59.44+11.17)%, monocytes (10.13+6.13)% and eosinophils (%)1.44±1.89 in male patients with infectious mononucleosis when compared

to the females (8.82±1.38)g/dl, (15.94±7.46)x10^9/L, (29.50±14.38)%, (60.36+15.5)%, (10.50±7.50) % and (1.14±1.09)% (p=0.568, p=0.311, p=0.705, p=0.852, p=0.881 and p=0.614).

Table 2: Mean Values of Haemoglobin, TWBC, Neutrophils, Lymphocytes, Monocytes and Eosinophils in Male Versus Female Patients with Infectious Mononucleosis (mean±SD)

Parameter	Male	Female	t-value	p-value
Hb (g/dl)	9.14±1.52	8.82±1.38	0.58	0.568
TWBC (X10^9/L)	19.16±9.36	15.94±7.46	1.03	0.311
Neutrophils (%)	27.69±11.18	29.50±14.38	0.38	0.705
Lymphocytes (%)	59.44±11.17	60.36±15.51	0.19	0.852
Monocytes (%)	10.13±6.12	10.50±7.50	0.15	0.881
Eosinophils (%)	1.44±1.89	1.14±1.09	0.51	0.614

Key:
Hb: Haemoglobin
TWBC: Total White Blood Cell
SD: Standard Deviation

Table 3 shows the comparison of the mean values of haemoglobin, TWBC, neutrophils, lymphocytes, monocytes and eosinophils in patients with infectious mononucleosis in relation to Age.

Among ages 15-30 years, there were no significant differences in the mean values of haemoglobin (8.88±1.40)g/dl, (19.15±8.48)x10^9/L, neutrophils (27.88±13.82)%, lymphocytes (61.84±12.40)%, monocytes (10.32±6.93)% and eosinophils (1.32±1.65)% in patients with infectious mononucleosis when compared to ages(>30 years) (9.68±1.91)g/dl, (14.99±7.11)x10^9/L, (32.25±4.38)% (51.36±15.37)%, (8.27±4.62)% and (1.50±1.05)% respectively (p=0.321, p=0.081, p=0.542 p=0.135 p=0.572 and p=0.835).

Table 3: Comparison of the Mean Values of Haemoglobin, TWBC, Neutrophils, Lymphocytes, Monocytes and Eosinophils in Patients with Infectious Mononucleosis in Relation to Age (Mean±SD)

Parameter	(15-30)yrs	>30 yrs	t-value	p-value
Hb (g/dl)	8.88±1.40	9.68±1.91	1.01	0.321
TWBC (X10^9/L)	19.15±8.48	14.99±7.11	1.81	0.081
Neutrophils (%)	27.88±13.82	32.25±4.38	0.11	0.542
Lymphocytes (%)	61.84±12.40	51.36±15.37	1.54	0.135
Monocytes (%)	10.32±6.93	8.27±4.62	0.57	0.572
Eosinophil (%)	1.32±1.65	1.50±1.05	0.21	0.835

Key:
Hb: Haemoglobin
TWBC: Total White Blood Cell
SD: Standard Deviation

Table 4.4 Shows the Correlation of Haemoglobin with TWBC, Neutrophils, Lymphocytes, Monocytes and Eosinophils in Infectious Mononucleosis.

There was a non - significant positive correlation of haemoglobin with TWBC, neutrophils, lymphocytes, monocytes and eosinophils in infectious mononucleosis patients (r=0.17, p=0.357; r=0.15, p=0.421, r=0.07, p=0.730, r=0.11, p=0.563 and r=0.06, p=0.751).

Table 4: Correlation of Haemoglobin with TWBC, Neutrophil, Lymphocytes, Monocytes and Eosinophil in Infectious Mononucleosis

Variable	N	R	p-value
TWBC	30	0.17	0.357
Neutrophils	30	0.15	0.421
Lymphocytes	30	0.07	0.730
Monocytes	30	0.11	0.563
Eosinophils	30	0.06	0.751

Key: TWBC: Total White Blood Cell

DISCUSSION

Infectious mononucleosis is a disease in children and young adults. It is common mainly in countries with temperate and cold climate. Patients usually present with fever, sore throat, lymphadenopathy, often hepatosplenomegaly (David and Dale, 2018)

In the present study, the mean value of haemoglobin was significantly reduced in infectious mononucleosis patients when compared to the controls. Red cell agglutinins are infrequently seen in infectious mononucleosis (~1% of cases) and have been ascribed to polyclonal IgG/IgM cold agglutinins specific for the antigen on the red cells (Canović *et al*., 2015). The weakly positive DAT using anti-C3d and the negative DAT using anti-IgG are characteristic for infectious mononucleosis, indicative of complement-mediated intravascular hemolysis that can occur 1 to 2 weeks after infection which according to several studies is the main cause of low haemoglobin in patients with Infectious mononucleosis. The result of this study is consistent with the study carried out by Ernest and Girish, (2016), who stated a similar reason.

From the result of the present study the mean value of neutrophils was significantly reduced in infectious mononucleosis patients when compared to the controls. According to several reports, infectious mononucleosis is associated with antineutrophilic antibodies which destroys the neutrophils thereby leading to decreased level of neutrophils in patients with infectious mononucleosis (Downey and McKinlay, 2023). The occurrence of mild decreases in granulocyte counts early in infectious mononucleosis was first documented in the classic monograph by Downey and McKinlay (2023). Later studies supported the occurrence of this phenomenon, showing that a fall in total circulating granulocyte numbers regularly occurred in up to 40 percent of cases during the first and second weeks of illness (Carter, 2016). Although several case reports have suggested that severe, life-threatening granulocytopenia may occur with infectious mononucleosis, David and Dale, (2018), whose report was also in support of this study stated that the onset of severe neutropenia occurs from 14 to 40 days after symptoms begin, generally later than the previously noted mild granulocytopenia. Third, the time course of the neutropenia is extraordinarily predictable: in eight of the nine patients who recovered, the granulocyte count exceeded 500 per day within 3 to 7 days, and in the two patients who died the supervening fatal bacterial infections.

The current study revealed that the mean values of TWBC, lymphocytes and monocytes were significantly increased in infectious mononucleosis patients when compared to the controls. The increase in total white blood cell count might be mainly as the result of an increase in the level of lymphocyte count which has been proven by several studies to be associated with infectious mononucleosis. The lymphocytes in infectious mononucleosis are activated (as connoted by HLA-DR expression) and are composed of a mixture of CD8+ cytotoxic-suppressor T-cells, NK cells, and CD4+ helper T-cells. The dominant population by far is the CD8+ T cells, which have a role in the suppression of viral replication and have cytotoxic activity against virally infected B cells (Cantow and Kostinas, 2016). Increased numbers of CD8+ cytotoxic-suppressor T-cells also have been seen in other viremias, including HIV and cytomegalovirus infection, as well as in hepatitis C. According to Claveaux *et al*., (2023), increase in monocyte was noted in 61% of patients, while Jamal *et al*., (2021) noted monocytosis in 86.1% of children who had infectious mononucleosis (Claveaux *et al*., 2023). Furthermore, increase in monocyte with lymphocytosis occurred in 51% of patients, which is similar to the results of Tomkinson *et al*., (2017) who investigated the same aged population.

There was no significant decrease in the mean value of eosinophil count in patients with infectious mononucleosis when compared to the controls. This is in agreement with the study carried out by Claveaux *et al*., (2023), who showed a similar finding.

The haemoglobin, TWBC, neutrophil, lymphocyte, monocyte and eosinophil counts were not affected by age and gender in patients with infectious mononucleosis. This is similar to the study by Knowles, (2018), who found out that age and sex were not a predisposing factors in the determination of complete blood count in patients with infectious mononucleosis.

There was a non-significant positive correlation of haemoglobin with TWBC, neutrophils, lymphocytes, monocytes and eosinophils in infectious mononucleosis patients. The result of this study is similar to the study carried out by Knowles, (2018).

CONCLUSION

The data in the present study showed that infectious mononucleosis is characterized by increase in lymphocytes and monocytes with decreased levels of haemoglobin and neutrophils. Haemoglobin concentration does not have a relationship with white blood cells in patients with infectious mononucleosis.

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