Original Research Article

Characteristics of Haematological Indices in Hospitalized Covid 19 Positive Patients at Centre for Communicable Disease Control and Research (CCDCR), Federal Medical Centre, Asaba, Delta State, Nigeria.

ABSTRACT

Aims: To assess some haematological indices of hospitalized COVID-19 infected patients treated during the first wave of the pandemic in the Centre for Communicable Disease Control and Research (CCDCR) Federal Medical Centre Asaba, Delta State, Nigeria.

Study design: Retrospective observational study.

Place and Duration of Study: Centre for Communicable Disease Control and Research, Federal Medical Centre, Asaba, Delta State, Nigeria., between May and September, 2020.

Methodology: Descriptive data was collected from the records of 52 patients who were hospitalized and treated at the CCDCR FMC Asaba, within the months of March to September, 2020 and 40 non Covid-19 subjects as control subjects. The patient samples that were previously collected and analyzed for haematological parameters (lymphocytes, neutrophil, eosinophil, basophil, monocytes, platlets count, mean cell volume (MCV), mean cell haemoglobin (MCH) and mean cell haemoglobin concentration (MCHC), using an automated hematology analyzer. Data collected was analyzed using SPSS version 25 and P values less than *.05* were considered statistically significant.

Results: The outcome of statistical analysis showed that the mean levels of lymphocytes, MCH and MCHC were significantly lower (*P<.05*) in COVID-19 positive subjects when compared with that of COVID-19 negative control group. Also, the mean level of total white cell count was significantly higher (*P<.05*) in COVID-19 positive subjects when compared with that of the control group. There was no significant difference (*P<.05*) in PCV, neutrophil, eosinophil, basophil, monocytes, platelet and MCV in the case study when compared with the control group. No correlation was observed between severity and PCV, total WBC, eosinophil, monocyte, platelet count, MCV and MCHC. Whereas, a weak negative correlation (*r = -.284, P=.041*) was observed between severity and neutrophil. On the other hand, a weak positive correlation between severity and MCH (*r=.303, P=.029*) as well as between severity and lymphocytes (*r=.0305, P=.029*) was observed. No significant difference (*P>.05*) was observed in the outcome of haematological indices of COVID-19 positive subjects who are below fifty (50) years and those more than fifty (50) years of age. Also, no correlation was observed between haematological indices of the case subjects and their age. There is a significant difference in PCV (*P<.05*) based on gender. However, other haematological indices did not differ based on gender.

Conclusion: Assessing the outcome of haematological indices in COVID 19 positive patients provides insight into the physiological state of these subjects which in turn aids management, treatment monitoring and prognostication. Further observational and experimental studies using larger sample size is hence recommended as this will give a more promising outlook of these indices in COVID 19 subjects.

Keywords: Haematological Indices, Hospitalized Covid 19 Positive Patients, Centre for Communicable Disease Control and Research (CCDCR), Federal Medical Centre, Asaba, Delta State, Nigeria.

1. INTRODUCTION

The global pandemic of Coronavirus disease 2019 (COVID-19) first reported in Wuhan, China in December, 2019 has constituted an absolutely challenging healthcare concern all around the world causing varied degree of morbidity, the need for hospitalization, in some cases provision of intensive care and even death to inconceivable number of patients.

Coronaviruses are mRNA viruses that belong to the Coronaviridae family in the Nidovirales order. Corona is derived from the Latin word "*Corona"* meaning "crown or halo" which refers to the characteristic appearance of the virus. The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 and the disease as COVID-19 [1,2]. The virus is petal shaped with spikes surrounding the virus on its outer surface resembling the "solar corona" hence the name; coronavirus [3]. These glycoprotein spikes on the outer surface of coronaviruses are responsible for the attachment and entry of the virus to host cells. SARS-coronavirus require angiotensin-converting enzyme 2 (ACE2) as a key receptor [4,5]. The life cycle of SARS-CoV-2 in host cells begins when S protein binds to the cellular ACE 2 receptor. This could be a possible reason for the report of more males being hospitalized with greater severity of the disease than females since males have higher activity of ACE 2 [6]. Following viremia, SARS-CoV-2 primarily affects the tissues expressing high levels of Angiotensin Converting Enzyme-2 including the lungs, heart, gastrointestinal tract and blood cells especially the lymphocytes [7]. The entire mechanism of pathogenicity of SARS-CoV-2, from attachment to replication follows this order.

It is speculated that the virus is zoonotic affecting animals and humans who consume affected animal products [3]. Apparently, Coronavirus is spread primarily by person to person. The reservoir though unclear and still being researched is thought to be the pangolins, bats. Coronavirus can be spread by asymptomatic carriers. Droplets and close contact are the most common routes of transmission of SARS-CoV-2, and aerosol transmission may be another route where viral particles enter lungs via droplets [8]. Additionally, researchers have detected SARS-CoV-2 in samples of saliva, urine, stool and gastrointestinal tissue raising the question of viral gastrointestinal infection and a fecal-oral transmission route [8]. Based on bioinformatics, evidence has indicated that the digestive tract may be a route of SARS-CoV-2 infection [9]. Moreover, SARS-CoV-2 was detected in the tears and conjunctival secretions of patients with COVID-19 [8].

Essentially, widely varied clinical spectrum of the disease has been noted, ranging from minor unspecific symptoms like pyrexia, dry cough and diarrhoea, sometimes alongside mild pneumonia and mild dyspnoea, to severe pneumonia with dyspnoea, tachypnoea and disturbed gas exchange, leading approximately 5% of the patients to severe lung dysfunction, a need for ventilation, shock or multiple organ failure [10]. Approximately 7 to 14 days from the onset of the initial symptoms, there is a surge in the clinical manifestations of the disease with a pronounced systemic increase of inflammatory mediators and cytokines, which may even be characterized as a "cytokine storm" [11]. One key point to note is that the disease severity also correlates with pro-inflammatory cytokines including IL-2, IL6, IL-7, G-CSF and TNF-α. Nevertheless, the cause of such cytokine storm is still unclear [12]. Medical laboratory investigations are essential to confirm diagnosis of coronavirus disease using real time reverse transcriptase polymerase chain reaction (rRT – PCR) and monitor the health status of infected subjects by carrying out both biochemical and haematological tests [13]. Haematological parameters provide valuable information on the immune status of individuals and these parameters may vary depending on age, gender, race, environmental and genetic background [14,15,16]. These changes are of value in assessing response to various physiological situations [17,18]. The haematological parameters widely studied to aid the management and monitoring of COVID 19 treatment include; total leucocyte count with adult reference range of 4,000–10,000cells/mm^3 (Adults of African origin 2,600 – 8,300cells/mm3, differential white blood cell count consisting of neutrophils (40–75%), basophils (<1%), eosinophils (1 – 6%), lymphocytes (20 -45%) and monocytes (2 – 10%) as well as

erythrocyte sedimentation rate (ESR) [19]. The haemostatic indices including the Prothrombin Time (10 – 14secs) test, Activated Partial Thromboplastin Time test (32 – 42secs), D – dimer assay (220 - 500ng/ml) and Fibrinogen level (1.4 – 4.0g/L) [19], are assessed to monitor the effects of the virus on the patient's haemostatic mechanism. It is however important to point out that, among the numerous clinical and biochemical parameters linked with poor prognosis, elevated D-dimer levels have gained particular attention as a predictor of the development of acute respiratory distress syndrome (ARDS), the need for admission into an ICU or even death [20,21,22].

According to Li et al. [11], SARS- CoV-2 has an important effect on both haematopoietic system and haemostasis. Patients infected with COVID-19 showed higher leukocyte numbers, increased neutrophils, decreased eosinophils, decreased lymphocytes, and increased levels of plasma pro-inflammatory cytokines [10]. Also, high erythrocyte sedimentation rate (ESR) and D-dimer levels were observed in these patients [23]. At present, there are many reports on the outcome of haemostatic and other haematological parameters in hospitalized COVID 19 infected individuals from several countries of the world, nonetheless, there are few reports on how the infection affects these indices in patients of Nigerian descent and none on patients treated in Delta State. The aim of this study is to assess some haematological indices of hospitalized COVID 19 infected patients treated during the first wave of the pandemic in the Centre for Communicable Disease Control and Research (CCDCR), Federal Medical Centre Asaba, Delta State. Additionally, we explored the relationship between these indices and severity, gender as well as age.

2. MATERIALS AND METHODS

2.1 Study Area

The research was conducted at the CCDCR**,** Federal Medical Centre, Asaba, Delta State, Nigeria, as a single-center study, which is one of the three COVID-19 treatment centers located in Delta State. The treatment center is completely upheld by the management of Federal Medical Centre, Asaba in conjunction with the Delta State government. The centre has an exceptional laboratory and groups of qualified clinical staff who are competent in the management of patients with COVID-19 virus.

2.2 Study Design and Population

A retrospective descriptive cross-sectional study was conducted following ethical approval and permission from the Federal Medical Center Asaba ethical committee. Information was gathered from patients' records as they were successively conceded into CCDCR Federal Medical Center in light of the rules for affirmed instances of COVID-19 by the Nigeria Center for Disease Control (NCDC). The haematological parameters of all the COVID 19 positive patients hospitalized in CCDCR, FMC Asaba in the first wave of the pandemic were analyzed in the study.

2.3 Data Collection and Analysis

2.3.1 Data Collection

Data of 52 patients admitted into the CCDCR Federal Medical Center Asaba, Delta State in the months of May-September, 2020 was collected and those of 40 non-Covid-19 subjects were also collected. Data collected included; demographic profile, and laboratory findings of their haematological indices.

2.3.2 Sample Analysis

2.3.1.1 Estimation of Full Blood Count Red Cell Indices and Platelet Count using BC – 5000 auto haematology analyzer model manufactured by Shenzhen Mindray Bio – medical Electronics Co. Ltd

Full blood count of all participants in this study was carried out using the Mindray BC – 5000 5-part differential Auto haematology analyzer. The measurement methods used in this analyzer are; the Electrical Impedance method for determining the Red blood Cell (RBC) and Platelet (PLT) data, the colorimetric method for determining the haemoglobin, flow Cytometry by laser for determining the white blood cell data. Other parameter results including the Red blood Cell indices (MCV, MCH, MCHC, RDW) were obtained through automated calculation.

2.4 Statistical Analysis

The Statistical Package for Social Sciences Software (SPSS) version 25 was used to analyze the data. Continuous variables are shown as mean and standard deviation, whereas categorical variables are displayed as frequencies and percentages in tables and ANOVA was used to analyze differences in continuous variables between multiple groups. P – value less than *.05* was considered statistically significant. Spearman's correlation method was applied in determining relationship.

3. RESULTS AND DISCUSSION

Table1: Basic characteristics of patients and mean values of Hematological in COVID-19 positive subjects

Variables	Freq. n= 52	Percentage (%)
Sex		
Male	32	61.5
Female	20	38.5
Age group		
<50years	30	57.7
>50years	22	42.3
Age (mean ±S.D)	48.87 ± 16.9	

Parameter	Mean value (Control)	Mean Value (COVID 19 positive subjects)	P-value
PCV (%)	39.85 ± 5.85	37.70 ± 5.42	0.462
WBC (cells/cub)	6487.56 ± 3831.86	7300 ± 3498.94	0.029
Neutrophil (%)	53, 20 ± 15. 37	59.15 ± 14.27	0.067
Lymphocyte (%)	45.20 ± 15.39	25. 67 ± 13. 72	0.026
Eosinophil (%)	2.16 ± 2.73	1. 75 ± 1.20	0.412
Monocytes (%)	2.00 ± 0.63	4.69 ± 1.22	1.00
Platelets (cells/l)	256675 ± 45.5	283077.50 ± 97834.49	0.591
MCH (Pg)	36.17 ± 45.52	28.79 ± 2.92	0.000
MCHC (g/l)	343.53 ± 30.92	243.55 ± 35 .21	0.000
MCV (Fl)	85.00 ± 6.61	82. 69 ± 11.120.	0.251

Spo2	96.1

Table:2 Relationship between the Haematological indices and severity of COVID-19 infection

Parameter	Correlation	Spo2
PCV (%)	R	-0.097
	P-value	0.503
WBC (cells/cub)	R	-0.267
	P-value	0.056
Neutrophi (%)	R	-0.284
	P-value	0.041
Lymphocytes (%)	R	0.305
	P-value	0.029
Monocytes (%)	R	0.146
	P-value	0.306
Platelet (cells/l)	R	-0.146
	P-value	0.482
MCH (Pg)	R	0.303
	P-value	0.029
MCHC (g/l)	R	0.233
	P-value	0.097
MCV (Fl)	R	0.226
	P-value	0.107

Table 3: Haematological indices in Male and Female subjects

Variable	Male (32)	Female (20)	P-value
PCV (%)	39.1 ±6.6	34.7 ± 6.5	0.025
WBC (cells/cub)	7977.31 ± 6621.6	7559 ± 4320.1	0.739
Neutrophils (%)	64.1 ±12.5	56.7 ± 16.1	0.06
Lymphocytes (%)	29.4 ±11.5	36.8 ± 15.5	0.067
Monocytes (%)	4.8 ± 1.2	5.2 ± 2.4	0.435
Platelet (cells/l)	297636.4 ± 180076.8	282736.7± 9492.9	0.701
MCH (Pg)	29.3 ± 2.3	28.5 ± 3.4	0.334
MCHC (g/l)	350.8 ± 44.2	338.6 ± 16.9	0.174
MCV (Fl)	84 ± 7.1	82.4 ± 12.3	0.586

Table 4. Comparison between the haematological indices based on the age of the subjects.

Variable	<50 years (30, 57.7%)	>50 years (22, 42.3%)	Students t-test (p value)
PCV (%)	36.40±7.40	36.50±5.91	0.003(P=0.960)
WBC (cells/cub)	6995.67±3833.80	8745.45±4900.70	2.039(P=0.160)
Neutrophils (%)	57.73±15.11	63.32±14.82	1.762(P=0.190)
Lymphocytes (%)	36.00±14.05	30.36±14.31	1.983(P=0.165)
Eosinophils (%)	1.96±1.27	1.86±1.61	0.046(P=0.831)
Monocytes (%)	4.86±2.39	5.23±1.15	0.436(P=0.512)
Platelet (cells/l)	291,703.33±147,243.38	285,409.09±122648.81	0.027(P=0.871)
MCH (g/l)	29.26±3.31	28.36±2.39	1.188(P=0.281)

MCHC (g/l)	347.43±40.07	308.82±13.53	0.834(P=0.338)
MCV (Fl)	83.69±12.21	82.24±7.24	0.246(P=0.622)

Coronavirus disease is a major cause of concern worldwide causing significant morbidity and mortality. The major objective of this study was to assess the characteristics of haematological indices in hospitalized COVID 19 positive patients treated at Federal Medical Center Asaba, Delta State in the months of March-September 2020. In addition, the study aimed to investigate the relationship between haematological indices and severity, gender as well as age in these subjects.

Currently, there are many reports showing that SARS- CoV 2 has an important effect on both haemostatic and haematological parameters [11]. Varying results have been obtained depending on the stage of the infection. Our result from this study revealed that the mean levels of lymphocytes, MCH and MCHC was significantly lower (*P<.05*) in COVID-19 positive subjects when compared with that of COVID-19 negative control group. Also, the mean level of total white cell count was significantly higher (*P<.05*) in COVID-19 positive subjects when compared with that of the control group. There was no significant difference (*P<.05*) in PCV, neutrophil, eosinophil, basophil, monocytes, platelet and MCV in the case study when compared with the control group. This could possibly be due to the stage of the disease and quick emergency response by medical experts upon hospitalization of positive COVID-19 patients in CCDCR Federal Medical Centre Asaba. Related to these arguments is the critique that a small sample size could pose a contributing factor to the result obtained in this study. Research have shown that many haematological abnormalities occur in viral infections possibly due to cell distortions that occur following inflammation caused by viral invasion which may likely result to alterations in iron metabolism, aberrant production of haematological precursor cells as well as defect in red blood cell morphology [24,25].

Interestingly, our result is in line with several reports revealing lymphocytopaenia in COVID-19 positive subjects. Several factors have been linked to this phenomenon. It is not unreasonable to postulate that lymphocytopaenia in COVID-19 positive subjects is due to high expression of ACE2 by lymphocytes [9]. Thus, SARS-CoV-2 may directly infect these cells and ultimately lead to their lysis. Mention should also be made of the fact that, markedly increased levels of interleukins and tumor necrosis factor (TNF)-alpha reported among COVID-19 positive subjects may promote lymphocyte apoptosis thereby resulting to lymphocytopenia. Also, substantial cytokine activation may be associated with atrophy of lymphoid organs, including the spleen, and further impairs lymphocyte turnover [26,27]. Researches have shown that during the incubation period, usually ranging from 1 to 14 days, and during the early phase of the disease, when non-specific symptoms are present, total peripheral blood leukocyte and lymphocyte counts are normal or slightly reduced. It is noteworthy that some studies have tendered contrasting submissions as their results for patients infected with COVID-19 showed higher leukocyte numbers, increased neutrophils, decreased eosinophils, decreased lymphocytes, and increased levels of plasma pro-inflammatory cytokines [10]. Although the eosinophil count in this study appeared normal, various researchers have reported decreased eosinophil in COVID 19 positive subjects. This decreased eosinophil count seen in these subjects has been attributed to the fact that two eosinophil granule proteins namely, eosinophil cationic protein (ECP) and eosinophil – derived neurotoxin (EDN) function as a neutralizer to destroy most viruses [28]. It is speculated that the decreasing eosinophil in COVID–19 patients may be as a result of the SARS- CoV-2 virus attacking ECP and EDN. Besides, basophils and eosinophils produce IL–4 which plays a crucial role in stimulating the proliferation of activated B and T lymphocytes. Hence, reduction in eosinophil and basophil count in COVID–19 patients may further result to reduction in lymphocyte count [11]. Also, high erythrocyte sedimentation rate (ESR) and D-dimer levels were observed in these patients [23].

Disease severity was considered based on Peripheral saturation of Oxygen (SPO_2) level of hospitalized COVID-19 positive patients in our centre. SPO_2 greater than 94% saturation

were grouped as mild to moderate while SPO2 less than 94% were considered as severe. No correlation was observed between severity and PCV, total WBC, eosinophil, monocyte, platelet count, MCV and MCHC. Whereas a weak negative correlation (*r = -.284, P=.041*) was observed between severity and neutrophil. On the other hand, a weak positive correlation between severity and MCH (*r = .303, P=.029*) as well as between severity and lymphocytes (*r =.0305, P=.029)* was observed. Previous studies have reported association between lymphopenia and acute respiratory distress syndrome (ARDS), disease severity and the need of Intensive Care Unit (ICU) admission was widely highlighted [29]. Similarly, elevated D – dimer levels being one of many clinical and biochemical indices associated with poor prognosis have gained currency in predicting the onset of ARDS, the need for admission into ICU or even death.

In this study thirty-two (32) males and twenty (20) females were admitted within the period under review showing that more males were hospitalized than females. This observation is similar to a report by Dan-Jumbo et. al. [6] who reported same occurrence in their study of a single centre in Rivers State where more male COVID 19 patients were admitted than their female counterparts as was also the case in independent studies carried out in China by Meng et. al. [30] and in Bangladesh by Chowdhury et. al. [31]. This could be attributed to the fact that males have higher activity of Angiotensin Converting Enzyme-2 (ACE2) as they express this enzyme more compared to females [6]. Additionally, our result shows that there was no significant difference (*P>.05*) in Total WBC count, Neutrophils, Lymphocytes, Eosinophils, Monocytes, Platelet count, MCH, MCHC, MCV based on gender. Nonetheless, there was a significant difference in PCV based on gender (*P>.05*). This could be attributed to the fact that females naturally have lower PCV values than males.

An epidemiological investigation report showed that elderly people are most susceptible to SARS-CoV-2 (median age at death 75 years), and most of the patients who died had comorbidities particularly hypertension and diabetes or a history of surgery before admission [5]. In this study, no significant difference (*P>.05*) was observed in the outcome of haematological indices of COVID 19 positive subjects who are below than fifty (50) years and those more than fifty (50) years. Also, no correlation was observed between haematological indices of the case subjects and their age. The susceptibility of elderly people to COVID 19 can be alluded to the physiological fact that immunity to infection decreases with age. In addition, the aforementioned co-morbidities usually prove fatal and commonly associated with the later part of adulthood. However, in the general management of COVID – 19 infected subjects, the monitoring of laboratory parameters including haemostatic and other haematological values will give an insight in the severity of the disease and also in predicting prognosis.

4. CONCLUSION

In conclusion, we observed reduced levels of lymphocytes, MCH and MCMC in hospitalized COVID 19 subjects, while other parameters were not affected. A weak positive correlation was observed between severity and both lymphocytes and MCH and no age - based difference in haematological parameters of patients with COVID-19 was also observed. We therefore recommend further research in this area as this will give better insight in this regard.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFERENCES

1. Cui, J., Li, F., Shi, Z.L. Origin and evolution of pathogenic coronaviruses. *Nature Rev*iews *Microbiology*, 2019; 17(3): 181–92.
2. Lai, C. C., Shih, T. P., Ko, W. C., Tang, H. J., Hsueh, P. R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges. *International Journal of Antimicrobial Agents*, 2020; 55(3): 10592-4.
3. Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*, 2020; 395(10224): 565–74.
4. Raj, V.S., Mou, H., Smits, S.L., Dekkers, D.H., Müller, M.A., Dijkman, R. Dipeptidylpeptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature*, 2013; 495(7440): 251–4.
5. Wang, N., Shi, X., Jiang, L., Zhang, S., Wang, D., Tong, P. Structure of MERS-CoV spike receptor-binding domain complexes with human receptor DPP4. *Cellular Respiration,* 2013; 23(8): 986-9.
6. Dan – Jumbo, A., Uzosike, C. T., Okuku, M. O. Clinical Symptoms and Haematological Characteristics among Male and Female COVID – 19 Patients in Rivers State: A Single – center Case Asian Journal of Research in Infectious Diseases, 2021; 6(1): 8 –16.
7. Bourgonje, A. R., Abdulle, A. E., Timens, W., Hillebrands, J. L., Navis, G. J., Gordijn, S. J., Bolling, M. C., Dijkstra, G., Voors, A. A., Osterhaus, A. D., Van der Voort, P.H., Mulder, D.J., & Van Goor, H. Angiotensin-converting enzyme 2 (ACE2),

SARS-CoV-2 and the pathophysiology of coronavirus disease 2019 (COVID-19). *The Journal of pathology*, 2020; 251(3): 228-48.
8. Xiao, F., Tang, M., Zheng, X., Liu, Y., Li, X., Shan, H. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology*, 2020; 158(6): 1831-3.
9. Xu, X., Chen, P., Wang, J., Feng, J., Zhou, H., Li, X. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Science China Life Sciences,* 2020; 63(3): 457–60.
10. Marietta, M, Ageno, W, Artoni, A, Candia, E., Gresele, P., Marchetti, M., Marcucci, R. & Tripodi, A. COVID-19 and Haemostasis: a position paper from Italian Society on Thrombosis and Haemostasis (SISET). *Blood Transfusion*, 2020; 18(3):167-9.
11. Li, T., Wang, L., Wang, H., Gao, Y., Hu, X., Li, X., Zhang, S., Xu, Y & Wei, W. Characteristics of laboratory indexes in COVID-19 patients with non-severe symptoms in Hefei City, China: diagnostic value in organ injuries, *European Journal of Clinical Microbiology & Infectious diseases,* 2020; 7(20): 3967–9.
12. Sarzi-Puttini P, Giorgi V, Sirotti S, Marotto, D., Ardizzone, S., Rizzardini, G., Antinori, S. & Galli, M. COVID-19, cytokines and immunosuppression: what can we learn from severe acute respiratory syndrome? *Clinical Experimental Rheumatol*ogy, 2020; 202(38): 337–42.
13. Dan – Jumbo, A., Uzosike, C. T., Okuku, M. O. Clinical Symptoms and Haematological Characteristics among Male and Female COVID–19 Patients in Rivers State: A Single – center Case Asian Journal of Research in Infectious Diseases, 2021; 6(1): 8 –16.
14. Dosoo, D.K., Kayan, K., Adu-Gyasi, D., Kwara, E., Ocran, J. Haematological and Biochemical Reference Values for Healthy Adults in the Middle Belt of Ghana. *Ghana Medical Journal,* 2012; 4: 56-9.
15. Onwurah, O.W., Onyenekwe, C.C., Ifeanyichukwu, M., Ezeugwunne, I.P., Odiegwu, N.C.). Haematological Values for Children, Adults and Geriatrics in Nnewi and Environs, Anambra State, Nigeria. *Journal of Hematology and Thromboembolic Diseases*, 2018; 6: 286-9.
16. Gudbjartsson D.F., Bjornsdottir U.S., Halapi E., Helgadottir A., Sulem P. Sequence variants affecting eosinophil numbers associate with asthma and myocardial infarction. *Nature Genetics*, 2009; 41: 342–7
17. Khan, T. A., Zafar, F. Haematological Study in Response to Varying Doses of Estrogen in Broiler Chicken. *International Journal of Poultry Science*, 2005; 4(10): 748-51.
18. Afolabi, K.D. Akinsoyinu, A.O. Olajide, R. and Akinleye, S.B. Haematological parameters of the Nigerian local grower chickens fed varying dietary levels of palm kernel cake. Proceedings of 35th Annual Conference of Nigerian Society for Animal Production. (p.247). *Arch Blood Transfus Discord,* 2010; 1(2): 506–10.
19. Moore, G., Knight, G., Blann, A. *Fundamentals of Haematology*. Oxford: Oxford University Press. Pp 48 – 60, 2010.
20. Tang, N., Li, D., Wang, X., Sun, Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *Journal on Thrombotic Haemostasis*, 2020; 18(4)**:** 844-7.
21. Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, *Lancet,* 2020; 395(20): 30183-5.
22. Han, H., Yang, L., Liu, R. Prominent changes in blood coagulation of patients with SARS-CoV-2 infection. *Clinical Chemistry Laboratory Medicine*, 2020; 7: 15-9.
23. Lei, J., Li, J., Li, X., Qi, X. CT imaging of the 2019 novel coronavirus (2019-nCoV) pneumonia. *Radiology*, 2020; 295(1): 18-28.

24. Eze, M. E. and Buseri, F. I. Effects of hepatitis B infection on haematological parameters in Pregnancy in Port Harcourt, Nigeria. *Research Journal of Medical Sciences,* 2009; 3(6): 194–7.
25. Ali, S. J. A correlative study between haematological and biochemical parameters in hepatitis B. *Ibn Al Haitham Journal for Pure and Applied Science,* 2019; 32 (2): 21-9.
26. Chan, J.F., Zhang, A.J., Yuan, S. Simulation of the clinical and pathological manifestations of Coronavirus Disease 2019 (COVID-19) in golden Syrian hamster model: implications for disease pathogenesis and transmissibility. *Clinicals of Infectious Diseases*, 2020; 71(9): 2428-46.
27. Singh, S., Sharma, A., Arora, S.K. High producer haplotype (CAG) of -863C/A, -308G/A and -238G/A polymorphisms in the promoter region of TNF-alpha gene associate with enhanced apoptosis of lymphocytes in HIV-1 subtype C infected individuals from North India. *PLoS One*, 2014; 9(5): 98020-2.
28. Hamann K, J., Ten, R. M., Loegering, D. A., Jenkins, P. B., Heise, M. T., Schad, C. R., Pease, L. R., Gleich, G. J., Barker, R. L. Structure and chromosome localization of the human eosinophil-derived neurotoxin and eosinophil cationic protein genes: evidence for intronless coding sequences in the ribonuclease gene superfamily. *Genomics,* 1990; 7(4): 535–46.
29. Wang, W., Tang, J., Wei, F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China, *Journal on Medical Virology*, 2020; 92 (4): 441–7.
30. Meng, Y., Wu, P., Lu, W., Liu, K., Ma, K., Huang, L., Cai, J., Zhang, H., Qin, Y., Sun, H. and Ding, W. Sex-specific clinical characteristics and prognosis of coronavirus disease-19 infection in Wuhan, China: A retrospective study of 168 severe patients. *PLoS pathogens,* 2020; 16(4): 1008520-3.
31. Chowdhury, A. T., Karim, M. R., Mehedi H. H., Shahbaz M., Chowdhury M. W., Dan, G., He, S. Analysis of the primary presenting symptoms and hematological findings of COVID-19 patients in Bangladesh, *The Journal of Infection in Developing Countries*, 2021; 15(2): 214-23.