International Journal of Celiac Disease, 2020, Vol. 8, No. 3, 110-116
Available online at http://pubs.sciepub.com/ijcd/8/3/8
Published by Science and Education Publishing
DOI:10.12691/ijcd-8-3-8

A Systematic Review on Use of Liver Function Tests to Assess Association between Liver Injury and COVID 19 Disease

Richard Chinaza IKEAGWULONU[1], Nkereuwem Sunday ETUKUDOH[2], Mark Uchejeso OBETA[3,*], Henry Chukwuemeka URO-CHUKWU[4], ImohEtim IBANGA[5]

[1]Department of Chemical Pathology, Alex Ekwueme Federal University Teaching Hospital, Abakaliki-Nigeria
[2]Department of Haematology, Federal School of Medical Laboratory Science, Jos, Nigeria
[3]Department of Medical Laboratory Management, Federal School of Medical Laboratory Science, Jos, Nigeria
[4]Department of Community Medicine, College of Health Science, Ebonyi State University, Abakaliki, Ebonyi State, Nigeria
[5]Department of Chemical Pathology, Federal School of Medical Laboratory Science, Jos, Nigeria
*Corresponding author: uchejesoobeta@gmail.com

Received July 10, 2020; Revised July 24, 2020; Accepted August 02, 2020

Abstract **BACKGROUND**: As at 27th of June 2020, the COVID 19 pandemic had affected 9,653,048 people across the world including 491,128 deaths. We reviewed different studies on liver function tests in COVID 19 patients to better understand how the liver injury is associated with COVID 19 disease. **METHODS**: A review of the literature was carried out between18th May and 10thJune 2020 on the studies that investigated liver function tests in COVID 19 patients as a marker of liver injury in the patients. The databases used were Pubmed/Medline, Google Scholar and JSTOR and the search protocol involves a combination of words like laboratory diagnosis, liver function tests and COVID 19, SARS-COV-2 and coronavirus. **RESULT**: Twelve relevant articles were identified out of a total of 212 articles that were initially identified after duplicates were removed. The twelve articles reviewed comprise of 1,926 COVID 19 infected patients representing 1,003(52.1%) males and 923(47.9%) females. Comparing mild to severe cases of COVID 19, the most prevalent laboratory findings were increased AST (100%), ALT (91.7%) and total bilirubin (71.4%), as well as 100%, decreased serum level of albumin. **CONCLUSION**: Liver injury is associated with COVID 19 as evident with observed changes in serum levels of liver enzymes, bilirubin and albumin in these individuals.

Keywords: *SARS-CoV-2, COVID-19, medical laboratory diagnosis, liver function tests*

Cite This Article: Richard Chinaza IKEAGWULONU, Nkereuwem Sunday ETUKUDOH, Mark Uchejeso OBETA, Henry Chukwuemeka URO-CHUKWU, and ImohEtim IBANGA, "A Systematic Review on Use of Liver Function Tests to Assess Association between Liver Injury and COVID 19 Disease." *International Journal of Celiac Disease*, vol. 8, no. 3 (2020): 110-116. doi: 10.12691/ijcd-8-3-8.

1. Introduction

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus [1]. The novel coronavirus has not been previously identified in humans and it was first identified in Wuhan, Hubei Province of China in December 2019 (WHO 2020 2). Before the advent of COVID 19, other forms of coronaviruses like Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) exist and just like COVID 19 cause illness which ranged from the common cold to severe diseases [2]. The main target of COVID 19 is the respiratory system with an unexplainable case fatality rate such that as at 27 June, 2020, there were about 9,653,048 confirmed cases including 491,128 deaths worldwide [3]. COVID 19 cases in America, Europe and Africa as at June 27 2020 stood at 4816794, 2638903 and 268102 respectively [3] while in Nigeria confirmed cases were 23,298 with 554 deaths [4]. Severe pneumonia, acute cardiac injury, combined with the incidence of ground-glass opacities have been identified as the main pathogenesis of COVID 19 infection [5]. Unfortunately, up till now, there are no vaccines or targeted drugs used in the management of COVID 19, though in many countries, some drugs and vaccines are currently reported to be undergoing clinical trials.

COVID 19 infection has been associated with organ damage especially in its severe form [6,7]. Studies that highlighted the importance of substances like Vitamin D in preventing multiple organ damage induced by COVID 19 infection [8,9] also buttress to the fact that some level of organ damage does occur in infected patients. Laboratory studies have also shown an increase in pro-inflammatory markers [5,10] and hematological parameters [11] in COVID 19 infected patients. Varying

degrees of liver Impairment occasioned by changes in liver function tests have equally been reported [7].

Furthermore, research is still evolving to fully understand how laboratory parameters can best be used to predict severity and prognosis of COVID 19 and in this study, the effort is made to systematically review and summarize findings from studies that investigated the association between liver injury and severity of COVID 19 infection.

2. Method

From May 18 to June 10, 2020, a literature search was conducted in Pubmed/Medline, Google Scholar and JSTOR for publications relating COVID 19 to changes in liver function tests. In this review liver function tests, also referred to as a hepatic panel, are groups of blood tests that provide information about the state of a patient's liver and includes tests like ALT, AST, ALP, GGT, Total bilirubin and albumin and globulin. The search protocol involves a combination of words like laboratory diagnosis, liver function tests and COVID 19, SARS-COV-2 and coronavirus. Reference lists of selected articles were also searched to identify missed studies. Time of publications was not restricted, however, only studies published in English were included. Studies were also included if they were primary research articles, assessed the association between serum levels of liver biochemical outcome from COVID 19 infection and reported in mean (SD) or median (IQR). Review articles, expert opinions, books, newsletters, commentaries, theses, editorials were all excluded. Patients were grouped as mild or severe cases. All patients in an intensive care unit (ICU) and non-survival cases were classified as severe cases whereas patients who are not in ICU and those that are survivors as seen in some studies were grouped as mild cases. All publications were retrieved online while data extraction was carried out for each paper highlighting the following: name of first author and year of publication, study design, study location, laboratory parameter, serum levels of the analytes, sample size, age, gender, and disease severity criteria. The search strategy and results are provided in Figure 1.

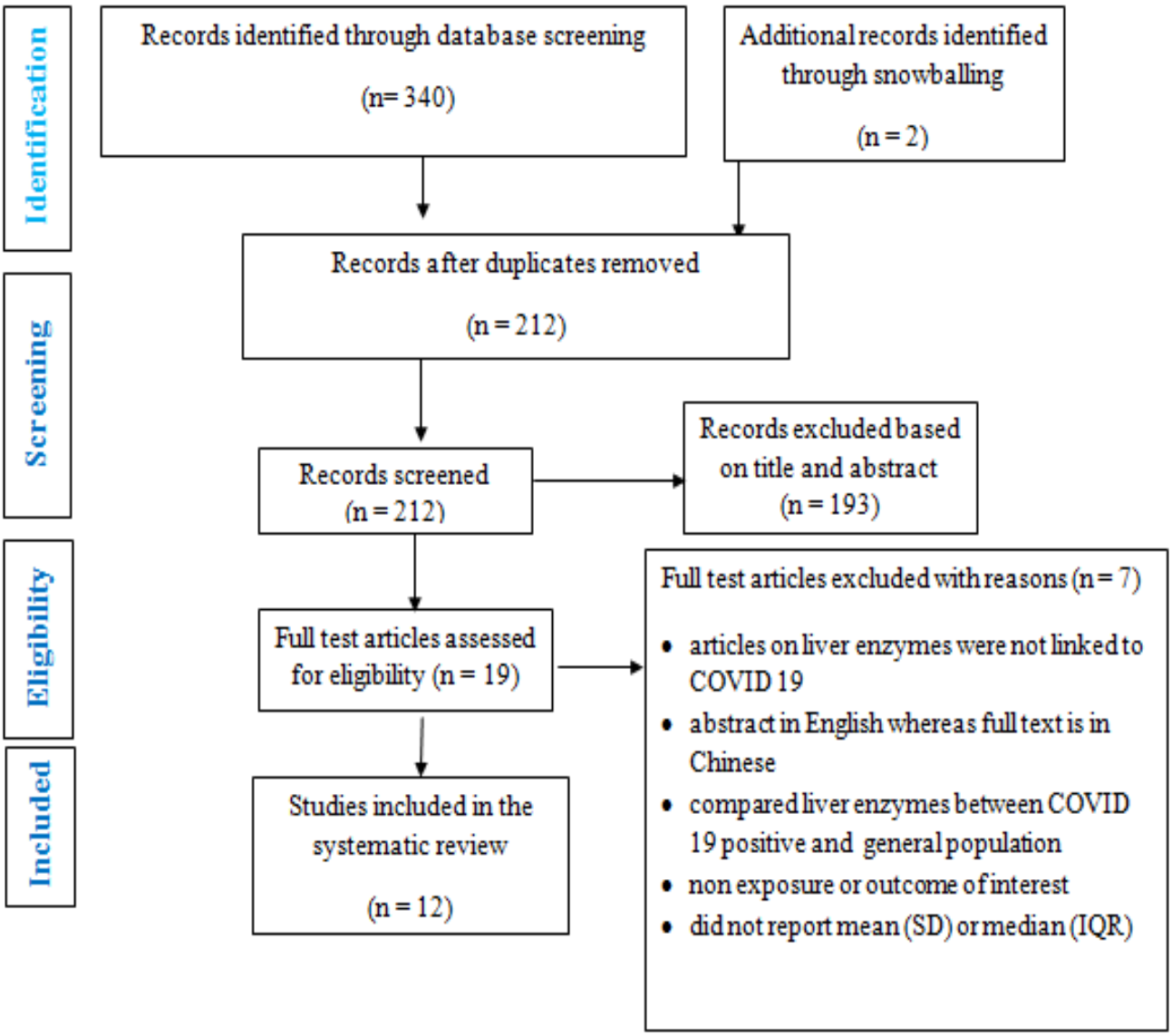

Figure 1. PRISMA Flow diagram for the selection of studies based on study inclusion and exclusion

3. Results

342 articles were found after the initial search of literature which was reduced to 212 articles following the removal of duplicates. Further evaluation of the titles, abstracts and full texts of the 212 articles applying the study inclusion and exclusion criteria aforementioned yielded a total of 12 articles which met the study criteria and were systematically reviewed in this study. All the reviewed studies (12-23) were retrospective in design and conducted in China except one done in Denmark. The twelve articles reviewed comprise of 1,926 COVID 19 infected patients representing 1,003(52.1%) males and 923(47.9%) females. The included articles characteristics are presented in Table 1. In all the studies, COVID 19 infection was identified using real-time reverse transcriptase-polymerase chain reaction (RT-PCR).

Table 1. General characteristics of reviewed articles

Author	Study design	Study location	Sample population	Age (mean /median years[a])	Gender	Year of publication
12	Retrospective	China	155	54(42-66)	Males: 86 (55.5%) Females: 69(44.5%)	2020
13	Retrospective	China	78	38 (33-57)	Males: 39(50%) Females:39(50%)	2020
14	Retrospective	Beijing China	63	47(3-85)	Males : 37(58.7%) Females: 26(41.3%)	2020
15	Retrospective	Wuhan China	69	42(35-62)	Males:32(46.4%) Female: 37(53.6%)	2020
16	Retrospective	Shenzhen, China	298	47 (33-61)	Males: 145 (48.7%) Females:153(51.3%)	2020
17	Retrospective	Wuhan China	28	68.6(53 - 82)	Males: 21 (75%) Females: 7(25%)	2020
18	Retrospective cohort	Hubei China	299	53.4 ± 16.7	Males:160 (53.5%) Females:139(46.5%)	2020
19	Retrospective	China	21	56.0 (50.0-65.0)	Males: 17(81.0%) Females: 4(19.0)	2020
20	Retrospective	Zhejiang province China	645	46.65 ± 13.82	Males:328(50.9%) Females:317(49.1%)	2020
21	Retrospective	China	76	44.5	Males: 42(55.3%) Females:34(44.7%)	2020
22	Retrospective	Denmark	175	71	Males =85(48.6%) Females= 90(51.4%)	2020
23	Retrospective	Wuhan, China	19	73 (38-91)	Male: 11(57.9%) Female: 8(42.1%)	2020

[a]Age data presented as median (IQR) or mean (SD), IQR=inter quartile range.NA=not available, SD=standard deviation.

Table 2. Major findings from the reviewed studies

AUTHOR	Covid-19 DETECTION	DISEASE SEVERITY CLASSIFICATION	LABORATORY PARAMETER	SERUM LEVELS IN MILD CASES MEAN ± SD	SERUM LEVELS IN SEVERE CASES MEAN ± SD	P VALUE	DISEASE SEVERITY CRITERIA
12	real-time RT-PCR	Severe cases: 85 Mild cases: 70	Alanine aminotransferase	20 (15-33)	28 (17-42)	0.545	The diagnosis of pneumonia was based on clinical characteristics and chest imaging
			Aspartate aminotransferase	32 (23-38)	37 (25-65)	0.004	
			Albumin	39 (36-42)	36 (32-40)	0.001	
			Globulin	29 (26-32)	28 (26-31)	0.766	
13	real-time RT-PCR	Mild cases: 67 Severe cases: 11	Alanine aminotransferase	18.5(12.5-27.7)	17.4(13.9-43.9)	0.776	The guidelines for diagnosis and management of COVID-19 (4th edition, in Chinese) by the National Health Commission of China
			Aspartate aminotransferase	20.0(13.9-30.9)	21.6(12.0-45.6)	0.788	
			Albumin	41.27±4.55	36.62±6.60	0.006	
14	real-time RT-PCR	8 mild cases (12.7%), 36 moderate cases (57.1%), 10 severe cases (15.9%) and9 criticallyill(14.3%)	Alanine aminotransferase	29.88±20.7	83.11±140.4	0.100	The guidelines for diagnosis and management of COVID-19 (4th edition, in Chinese) by the National Health Commission of China
			Aspartate aminotransferase	31.00±17.00	67±153.65	0.034	
			ALP	97.50±53.3	73.00±35.	0.436	
			GGT	23.25±13.83	54.89±29.3	0.061	
			Total bilirubin	12.14±9.98	10.83±5.5	0.965	
			Albumin	43.62±3.20	32.77±5.1	0.000	
			Globulin	28.63±2.39	28.00±4.	0.919	

AUTHOR	Covid-19 DETECTION	DISEASE SEVERITY CLASSIFICATION	LABORATORY PARAMETER	SERUM LEVELS IN MILD CASES MEAN ± SD	SERUM LEVELS IN SEVERE CASES MEAN ± SD	P VALUE	DISEASE SEVERITY CRITERIA
15	real-time PCR.	Mild cases ($SpO_2 \geq 90\%$ group): 55 Severe cases ($SpO_2 \geq 90\%$ group): 14	Alanine aminotransferase	24.00 (16.00-40.00)	31.50 (23.00-52.00)	0.119	All patients with COVID-19 enrolled in this study were diagnosed and admitted in accordance with the guideline of the national health commission of China
			Aspartate aminotransferase	26.00 (21.00-39.00)	40.50 (24.00-62.00)	0.03	
16	real-time PCR.	Mild cases: 240(80.5%) Severe cases: 58(19.5%)	Alanine aminotransferase	20 (13-28.25)	26.85 (20-40.8)	.003	The diagnosis of COVID-19 was based on the World Health Organization's interim guidance And diagnostic criteria were based on the recommendations by the National Centers for Disease Control and Prevention (CDC) of China
			Aspartate aminotransferase	26 (21-34)	36 (28-48.3)	<.001	
			ALP	61 (50-74)	58 (46-63)	.032	
			GGT	21 (14.5-31.85)	35.25 (23-53.4)	<.001	
			Total bilirubin	10.9 (8-15.5)	11.25 (8.4-18.3)	.133	
17	real-time PCR.	Mild cases (14 patients in isolation) Severe cases (14 patients in ICU)	Alanine aminotransferase	17.5 (10.8, 26.0)	21 (15.5, 40.5)	.2317	Coronavirus Pneumonia Prevention and Control Program (fifth edition) published by the National Health Commission of China
			Aspartate aminotransferase	22.2 ± 7.2	44.8 ± 20.8	.0058	
			Total bilirubin	9.1 ± 3.6	15.8 ± 6.8	.0082	
			Albumin	35.8 (30.7- 38.5)	31.6 (27.1- 32.7)	.0108	
18	real-time PCR.	Mild cases (survivors): 283 Severe cases (non survivors): 16	Alanine aminotransferase	27.5 ± 21.2	29.4 ± 28.5	.800	diagnostic criteria was as set out by World Health Organization for COVID-19
			Aspartate aminotransferase	25.5 ± 18.2	35.4 ± 16.8	.037	
			Total bilirubin	11.0 ± 6.7	11.0 ± 4.6	.993	
			Albumin	92 (32.5)	14 (87.5)	<.001	
19	real-time RT-PCR	severe cases ($\leq 93\%$ SpO_2): 11 mild cases (> 93%): 10	Alanine aminotransferase	16.0 (13.3-21.8)	42.0 (32.5-50.0)	0.000	The guidelines for diagnosis and management of COVID-19 (6th edition, in Chinese) by the National Health Commission of China
			Aspartate aminotransferase	24.0 (21.5-26.5)	47.0 (28.0-74.5)	0.014	
			Total bilirubin	7.8 (6.4-9.5)	8.8 (7.9-10.5)	0.24	
			Albumin	37.2 (35.8-38.8)	29.6 (28.6-33.0)	0.013	
20	real-time RT-PCR	Severe cases: 573 Mild cases: 72	Alanine aminotransferase	25.53 ± 19	29.37 ± 25.71	0.222	The diagnosis of novel COVID-19 was based on WHO interim guidance (World Health Organization, 2020); subtype definition of COVID-19 was according to the diagnosis and treatment scheme for SARS-CoV-2 of China (5th edition) (National Administration of Traditional Chinese Medicine, 2020)
			Aspartate aminotransferase	25.67 ± 15.52	30.08 ± 20.37	0.077	
			Total bilirubin	9.11 ±4.86	11.26 ± 8.04	0.027	
			Albumin	42.53 ± 4.70	41.02 ±4.47	0.007	
21	real-time RT-PCR	Mild cases (CRP 1: C-reactive protein<20.44 g/L)= 48 Severe cases(CRP 2: C-reactive protein≥20.44 g/L)= 28	Alanine aminotransferase	27.08 ± 26.47	35.21 ± 23.34	0.182	Diagnostic criteria for COVID-19 severity is based on the CDCP (China) Diagnosis and Treatment of COVID-19
			Aspartate aminotransferase	28.00 ± 17.94	40.50 ± 25.66	0.015	
			Total bilirubin	14.68 ± 8.18	15.12 ± 8.98	0.826	
			Globulin	28.70 ± 4.46	31.50 ± 5.24	0.016	
			Total protein	70.88 ± 5.31	71.13 ± 6.55	0.854	

AUTHOR	Covid-19 DETECTION	DISEASE SEVERITY CLASSIFICATION	LABORATORY PARAMETER	SERUM LEVELS IN MILD CASES MEAN ± SD	SERUM LEVELS IN SEVERE CASES MEAN ± SD	P VALUE	DISEASE SEVERITY CRITERIA
22	real-time RT-PCR	Mild cases(Adults treated on a general ward or intermediate care unit)= 148 Severe cases(Adults treated in the intensive care unit) =27	Alanine aminotransferase	29(19-45)	36(25-75)	0.03	The diagnosis of novel COVID-19 was based on WHO interim guidance (World Health Organization, 2020); subtype definition of COVID-19 was according to the diagnosis and treatment scheme for SARS-CoV-2 of China (5th edition) (National Administration of Traditional Chinese Medicine, 2020)
23	real-time RT-PCR	Mild case 11(Survivors): Severe cases (Non-survivors): 8)	Aminotransferase Albumin	39.5 (26.4-77.5) 36 (31.8-37.3)	50.9 (43.2-71.2) 33.65 (29.2-34.7)	NA NA	NA

3.1. Alanine Aminotransferase

A total of twelve studies [12-23] investigated ALT levels in COVID 19 infected patients out of which 11 (91.7%) studies [12,14-22] reported increase in ALT. Of the eleven studies, the ALT increase in 3 (27.3%) studies were significant ($P < 0.05$) as against seven studies [12,14,15,17,18,20,21] were the increase was reported to be non-significant ($P \geq 0.05$). ALT level decreased in one study [13].

3.2. Aspartate Aminotransaminase

Ten studies [12-21] reported AST changes in COVID 19 infected patients and according to their findings, all the studies (100%) reported that AST levels were increased. The increase in AST was significant in eight studies [12,14-19,21] and non-significant in two studies [13,20].

3.3. Alkaline Phosphatase

ALP was investigated in two studies [14,16] and in the two studies, the serum level of ALP decreased in COVID 19 infected patients. The decrease was significant in one study [16] and non-significant in the other [14].

3.4. Gamma Glutaryl Transferase

Two studies [14,16] investigated GGT and reported an increase in serum GGT level in COVID 19 infected patients. The increase was significant in one study [16] and non-significant in the other [14].

3.5. Total Bilirubin

Total bilirubin was identified in seven studies [14,16-21]. Five of the seven studies [16,17,19,20,21] reported an increase in total bilirubin levels in COVID 19 infected patients. The increase was significant in three [16,17,21] of the five studies and non-significant in two studies [19,21]. An decrease in total bilirubin was reported in one study [14] whereas in another study [18] there is no change in serum level of total bilirubin.

3.6. Albumin

Albumin level was investigated in eight studies [12,13,14,17,18,19,20,23] and in all of them (100%), serum level of albumin significantly decreased in COVID 19 infected patients.

3.7. Globulin

A total of three studies [12,14,21] investigated globulin level in COVID 19 infected patients. According to two of the studies [12,14], serum level of globulin decreased non-significantly in the infected patient whereas a significant increase was seen in one study [21].

4. Discussion

The purpose of the present review was to figure out the laboratory characteristics of liver function tests of patients with COVID 19 and from this study, it is evident that COVID 19 is associated with liver damage. Any damage to the liver is associated with changes in liver enzymes and other substances that are either produced in the liver or are excreted through the liver. The level of these substances in the blood depends on the severity of the damage to the liver. The most prevalent laboratory findings in the present study were increased AST (100%), ALT (91.7%) and total bilirubin (71.4%), as well as 100%, decreased serum level of albumin. This result links severe cases of COVID 19 to liver damage. A similar systematic review and meta-analysis equally reported similar findings [24]. Also, a previous study that analyzed a cohort of patients who died of severe COVID 19 reported elevated levels of AST (79%), ALT (14%) and GGT (36%) in these patients [25]. Interestingly, studies have associated other forms of coronaviruses with liver damage [26,27]. The use of liver function tests (LFT) in the predicting severity of the liver injury is well documented in the work

of [28] and AST is significant for stage 3 and 4 fibrosis [29]. The elevation of GGT shows the involvement of the biliary epithelial cells whereas the decreased in albumin is a pointer that the synthetic function of the liver is also impaired.

Medical laboratory science should not be neglected in the fight against COVID 19 [30,31,32], as the containment of the pandemic has a lot to do with such medical laboratory diagnosis and management of the severity among the patients.

5. Conclusion

Liver injury is associated with COVID 19 infection especially in its severe form and earlier detection and reversal of these effects can positively affect patient's prognosis and survival.

Conflict of Interest

None.

Financial Assistance

None.

References

[1] World health organization 2020. WHO Coronavirus disease (COVID 19) outbreak. 2020. Available from https://www.who.int/health topics/coronavirus#tab=tab_1.

[2] WHO Emerging respiratory viruses, including COVID-19: methods for detection, prevention, response and control. Available from https://openwho.org/courses/introduction-to-ncov . Accessed 28th June 2020.

[3] WHO Coronavirus Disease (COVID-19) Dashboard. Available from https://covid19.who.int/?gclid=Cj0KCQjw3N.v3BRC8ARIsAPh8hgLgwA6Dip5mUrQHwoAs3eeyCyex9FqAFQai05STszLr26QSfwTVL. pkaAj54EALw_wcB. Accessed 27 June 2020.

[4] Nigerian Center for Disease Control (NCDC) 2020. COVID-19 Nigeria. Available at https://covid19.ncdc.gov.ng/. Accessed 27June 2020.

[5] Huang Y, Wang X, Li L, Ren J, Zhao Y, Hu, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395 (10223) (2020): 497-506.

[6] Ronco C.and Reis T. Kidney involvement in COVID-19 and rationale for extracorporeal therapies. Nat Rev Nephrol. 2020: 1-3.

[7] Feng G,Zheng K.I,Yan Q.Q, Rios R.S,Targher G, Byrne C.D, Poucke S.V, Wen-Yue Liu W.Y, and Zheng M.H.COVID-19 and Liver Dysfunction: Current Insights and Emergent Therapeutic Strategies.J ClinTranslHepatol. 2020 Mar 28; 8(1): 18-24.

[8] Aygun H. Vitamin D Can Prevent COVID-19 Infection-Induced Multiple Organ Damage. NaunynSchmiedebergs Arch Pharmacol 2020; 393(7): 1157-1160.

[9] Ikeagwulonu R.C, Etukudoh N.S, Obeta M.U, Mgbecheta C.U. Does Vitamin D Serum Levels Affect The Risk of Covid 19 and its Clinical Outcomes? A Review of Literature. EAS J Med Surg 2020; 2(6).

[10] Zeng F, Huang Y, Guo Y, Chen X, Xiao L, Deng G. Association of inflammatory markers with the severity of COVID-19: A meta-analysis. *International Journal of Infectious Diseases.* 2020; 96: 467-474.

[11] Rothan H.A, Byrareddy S.N. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. Journal of Autoimmunity 2020; 109.

[12] Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, Xiong Y, Cheng Z, Gao S, Liang K, Luo M, Chen T, Song S, Ma Z, Chen X, Zheng R, Cao Q, Wang F, Zhang Y. Clinical characteristics of refractory COVID-*19 pneumonia in Wuhan, China .Clinical Infectious Diseases.*

[13] Liu W; Tao Z.W, Wang L, Yuan M.L, Liu K, Zhou L, Wei S, Deng Yan, Liu J, Liu H.G, Yang M, Hu Y.Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. Chinese Medical Journal; 2020 (133(9): 1032-1038.

[14] Sun Y, Dong Y, Wang L,Xie H, Li B,Chang C, Wang F. Characteristics and prognostic factors of disease severity in patients with COVID-19: The Beijing experience. *Journal of Autoimmunity*.

[15] Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. Clin Infect Dis. 2020; 272.

[16] Cai Q, Huang D, Ou P, Yu H, Zhu Z, Xia Z, Su Y, Ma Z, Zhang Y, Li Z, He Q, Liu L, Fu Y, Chen J. COVID-19 in a designated infectious diseases hospital outside Hubei Province, China. Allergy; 2020; 00: 1-11.

[17] Wang F, Yang Y, Dong K, Yan Y, Zhang S, Ren H, Yu X, Shi X. Clinical characteristics of 28 patients with diabetes and covid-19 in wuhan, china.Endocr Pract.2020; 26.

[18] Huang J, Cheng A, Kumar R, Fang Y, Chen G, Zhu Y, Lin S. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. Journal of Medical Virology; 2020.

[19] Chen G,Wu D, Guo W, Cao Y, Huang D, Wang H, Wang T, Zhang X, Chen H, Yu H, Zhang X, Zhang M, Wu S, Song J, Chen T, Han M,Li S, Luo X, Zhao J, and Ning Q. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest*. 2020; 130(5): 2620-2629.

[20] Zhang X, Cai H, Hu J, Lian J, Gu J, Zhang S, Ye C, Lu Y, Jin C, Yu G, Jia H, Zhang Y, Sheng J, Li L, Yang Y. Epidemiological, clinical characteristics of cases of SARS-CoV-2 infection with abnormal imaging findings. *International Journal of Infectious Diseases, 2020;* 94: 81-87.

[21] Chen W, Zheng K.I,Liu S,Yan Z, Xu C, and Qiao Z. Plasma CRP level is positively associated with the severity of COVID-19. Ann ClinMicrobiolAntimicrob 2020; 19: 18.

[22] Israelsen S.B, Kristiansen K.T, Hindsberger B, Ulrik C.S, Andersen O, Jensen M, Andersen S, Rasmussen C, Jørgensen H.L, Østergaard C, Lindhardt B. Ø, Kronborg G, & Benfield T.Characteristics of patients with COVID-19 pneumonia at Hvidovre Hospital, March-April 2020. *Dan Med J 2020*; 67(6): A05200313.

[23] Zhang J, Liu P, Wang M, Wang J, Chen J, Yuan W, Li M, Xie Z, Dong W, Li H, Zhao Y, Wan L, Chu T, Wang L, Zhang H, Tao T, Ma J. The clinical data from 19 critically ill patients with coronavirus disease 2019: a single-centered, retrospective, observational study. *Journal of Public Health (Berl.): From Theory to Practice.*

[24] Parohan M, Yaghoubi S, and Sera A. Liver injury is associated with severe coronavirus disease2019 (COVID-19) infection: A systematic review and meta-analysis of retrospective studies. Hepatology Research 2020.

[25] Tian S, Liu H, Liao M, Wu Y, Yang C, Cai Y, Peng Z, and Xiao S.Y. Analysis of Mortality in Patients With COVID-19: Clinical and Laboratory Parameters.Open Forum Infect Dis. 2020; 7(5): 152.

[26] Saad M, Omrani AS, Baig K et al. Clinical aspects and out-comes of 70 patients with Middle East respiratory syndromecoronavirus infection: a single-center experience in SaudiArabia.Int J Infect Dis2014; 29: 301-6.35

[27] Al-Hameed F, Wahla AS, Siddiqui S et al. Characteristics andoutcomes of Middle East respiratory syndrome coronaviruspatients admitted to an intensive care unit in Jeddah, SaudiArabia.J Intensive Care Med. 2016; 31: 344-8.

[28] McLernon DJ, Donnan PT, Sullivan FM, *et al.* Prediction of liver disease in patients whose liver function tests have been checked in primary care: model development and validation using population-based observational cohorts. *BMJ Open* 2014; 4: e004837.

[29] Ahmed Z, Ahmed U, Walayat S, Ren J, Martin D.K, Moole H, Koppe S, Yong S, and Dhillon S. Liver function tests in identifying patients with liver disease.ClinExpGastroenterol. 2018; 11: 301-307.

[30] Vishal Sanklecha, Novel Coronavirus COVID-19 and Its Diagnosis and Treatments.International Journal of Celiac Disease, vol. 8, no. 1 (2020): 39-43.

[31] Etukudoh NS, Ejinaka RO, Olowu FA, Obeta MU, Adebowale OM, Udoudoh M P. Coronavirus (COVID-19); Review from ANigerian Perspective. 2020-9(1). AJBSR.MS.ID.001347.

[32] Obeta M. Uchejeso, Ejinaka R. Obiorah, Ofor I. Bassey, Ikeagwulonu R. Chinaza, AgboEjiofor C., and AbaraUkeme S, "Nigerian COVID-19 (Coronavirus) Patients Update, the Realities with MedicalLaboratory Diagnostic Sites." American Journal of Epidemiology and Infectious Disease, vol. 8, no. 1 (2020): 13-15.