Research Article

Second Wave of Covid-19

Check for updates

Impact of Covid-19 Second Wave Among Various Age Groups in South-Chennai

Dr.V.S.Kalai Selvi,[1]* iD Dr.Jainulavudeen Mohamed Rabeek[2], Dr. B. Shanthi[3], and Dr. Mary Chandrika. A[4]

[1]*Professor, Department of Biochemistry, Sree Balaji Medical College and Hospital.*
[2]*Post Graduate, Dept of Biochemistry, Sree Balaji Medical College and Hospital.*
[3]*Professor, Department of Biochemistry, Sree Balaji Medical College and Hospital.*
[4]*Assistant Professor, Department of Biochemistry, Sree Balaji Medical College and Hospital*

Abstract: India is under the second wave of the coronavirus disease (COVID-19). It seems that the second wave has created more impact than the first wave with an increased mortality rate. The mortality rate among young age group below 17 years is 0.05% with an increase of 16.6% above 17 years. Various studies have revealed that COVID-19 positive individuals show altered levels of both biochemical and hematological parameters with increased severity. To the best of our knowledge, no studies have investigated the altered levels with different age group. Hence, the study's primary goal is to assess biochemical and haematological parameters in COVID-19 positive individuals and compare the levels in different age groups of the South Indian population in the second wave of COVID-19. The subjects were divided into 3 groups based on their age as between 19-40 years, 41-60 years, and 61-80 years. The biochemical parameters measured included liver and renal function tests, electrolytes, inflammatory markers, and blood glucose. ESR and haematological parameters were measured. Under biochemical parameters, serum urea, uric acid, and creatinine increased significantly with increasing age group, whereas serum albumin decreased significantly with increasing age group. With ferritin and CRP, there was statistical significance among different age groups. It was found that diabetic patients with high HbA1C levels with increase age are more prone to COVID-19 infection. On hematological investigation significant decrease in the eosinophil count and increased basophil count were observed among different age group. The study concludes that compared to younger age groups, older ones with COVID-19 showed increase in immune and inflammatory markers, Markers of the adaptive immune response also increased with age. Hence, continuous monitoring and additional care must be given the older ones to reduce the effects of severity of COVID-19 among south Indian population.

Keywords: COVID-19, Ferritin, CRP, HbA1C, LDH, ESR, renal function test.

*Corresponding Author

V.S.Kalai Selvi , Professor, Department of Biochemistry, Sree Balaji Medical College and Hospital.

1.   INTRODUCTION

In the recent past coronavirus disease 2019 (COVID-19) has spread all over the world was found to be the most dreaded disease. In March 2020 India started to experience a significant increase in the number of COVID-19-positive cases.[1] At present, India is under the   second wave of COVID-19. This second wave started to rise since second week of April. It seems that the second wave has created more impact than the first wave. The worst part is, the virus is mutated in the second wave, which even affects the younger once more exponentially.[2]The mortality rate in the second wave of COVID-19 is 0.05% among young age group below 17 years, with an increase in the mortality rate to 16.6% above 17 years.[3]The clinical features of COVID-19 can range from asymptomatic infection to mild and severe forms. Recent studies on COVID-19 positive subjects have shown that various biochemical, hematological and inflammatory parameters are altered in these patients and is useful as diagnostic markers to assess the severity, progression of disease and classify patients presenting with severe or fatal clinical conditions.[4] Several studies from COVID-19 positive individuals show alteration in hematological and biochemical laboratory parameters associated with the condition of a COVID-19 patients.[5] The role of laboratory parameters in screening of COVID-19 cases has been established. This alteration in the parameters is due to the involvement and injury of major organs induced by COVID-19 patients.[6] The measurement of inflammatory parameters could help the physicians to rapidly identify severe COVID-19 patients, hence facilitating the early initiation of effective treatment. The level of LDH, CRP, ALT and NEU can be used to predict the result of COVID-19 test. They can help in detection of COVID-19.[7]Previous studies were on the assessment of clinical parameters on non-severe, severe and critical COVID-19 patients and found an increase in various markers associated with the immune response and markers of tissue and organs damage.[8]Studies have also shown that severe COVID-19 were also found to have dysregulated inflammation and coagulation activation and therefore, it is biologically reasonable that the hematological parameters included in the prediction model have clinical significance. These routine clinical hematology parameters can identify the patients at risk of developing severe COVID-19 disease.[9] Clinical evaluation will be paramount at every step and biomarkers will need to be meaningfully integrated bedside decision making. Biomarker panels rather than single biomarkers may provide more reliable information.[10]Though studies on COVID-19 positive subjects shows that with the increase in severity there is alteration in biochemical and hematological markers and parameters, to the best our knowledge, no studies have investigated the effect and association of different age group with the altered levels of biochemical and hematological parameter, which may gives us more predictive outcomes among COVID-19 positive subjects. Hence, the aim of the study is to assess the biochemical and hematological parameters of COVID-19 positive individuals of different age groups among South Indian population in the pandemic condition during the second wave in India and this information can contribute to patient care are questions which currently lack convincing answers.

2.   MATERIALS AND METHODS

This cross-sectional study was conducted with 195 COVID-19 positive individuals. The participants were divided into 3 groups based on different age groups as GROUP A, GROUP B, and GROUP C. In which 19-40 years were in GROUP A, 41-60 years were in GROUP B and 61-80 years were in GROUP C.

Inclusion Criteria

COVID-19 positive patients between the ages of 18 and 80.

Exclusion Criteria

 Age less than 18 years and more than 80 years were excluded.

All patients registered in the study were explained about the study. Under aseptic precautions, a 3 ml venous blood sample was collected from the ante   cubital vein from all the subjects in appropriate vacutainer tubes. Serum Bilirubin by DPD method, AST and ALT by UV KINETIC method, ALP by -NP AMP KINETIC method, GGT by KINETIC method, Total protein by Biuret method, Albumin by BCG using BS 480 analyzer, and Globulin by calculation are the biochemical parameters of liver function tests. The renal function tests include urea by Urease-GLDH method, Creatinine by Jaffe's KINETIC method and Uric acid by Uricase method using BS 480 analyzer. Electrolytes such as sodium, potassium, and chloride were measured using the DIRECT-ISE method, inflammatory markers such as LDH were measured using the UV kinetic method in the BS 480 analyzer, ferritin was measured using the CLIA method in the SIEMENS ADVIA CENTAUR CP Analyzer, and CRP was measured using the Latex agglutination test, RBS (random blood glucose) was measured using the GOD-POD method in the The electrical impedance method was used to analyse haematological parameters such as total cell count, neutrophil, lymphocytes, eosinophil, basophils, monocytes haemoglobin, RBC, MCV, MCH, and MCHC and ESR by Westergren method using automated VESMATIC CUBE 30 analyser.

3.   STATISTICAL ANALYSIS

Data were analyzed using the Statistical Package of Social Service (SPSS 22.0). Normally distributed data with continuous variables were presented as Mean ± SD and the categorical variables were expressed as percentages. To compare the difference between the mean levels of parameters between the three groups, one way ANOVA was used. To indicate a significant difference, a p value <0.05 was taken, for all statistical tests.

4.   RESULTS

A total of 195 COVID-19 positive individuals between the ages of 18 and 80 years were studied, 52 subjects between the age group of s were taken as GROUP A, 94 subjects between the age group of 41-60 years were taken as GROUP B and 49 subjects between the age group of 60-80 years were taken as GROUP C. The mean ages of GROUP A, GROUP B and GROUP C were 33.9 ± 3.22years,50.21 ± 5.36years and 66.22 ± 5.36 years respectively. Among 195 subjects about 69%, GROUP A, 61% GROUP B and 67%GROUP C were males and 31 %GROUP A, 39%GROUP B and 33%GROUP C were females, which shows that

independent to age group predominantly males are more likely to COVID-19 infection than females. (Table. 1)

Table 1: Demographic features of the study group.			
Parameters	GROUP A (n= 52)	GROUP B (n= 94)	GROUP C (n= 49)
Mean age (MEAN ± SD)	33.9 ± 3.22	50.21 ± 5.36	66.22 ± 5.36
Male %	69%	61%	67%
Female%	31 %	39%	33%

The values are expressed in %.

A significant increase in the biochemical values of renal function test such as urea and creatinine with an increase in the age group was observed, with no difference in uric acid levels under liver function test total protein is found to significantly increase with age, but serum albumin was found to be significantly decrease with increase in age. There is no significant difference in electrolytes levels in various age groups. A statistical significance was observed in inflammatory markers such as ferritin and CRP which increase with age. It is found that diabetic patients with high HbA1C levels with increase age groups are more prone to COVID-19 infection. (Table. 2)

Table 2: Comparison of Mean ± SD of the Measured Biochemical Parameters between GROUP A, B and C.					
PARAMETERS	NORMAL RANGE	GROUP A (n= 52)	GROUP B (n= 94)	GROUP C (n= 48)	p VALUE
LIVER FUNCTION TEST					
Total bilirubin	0.5-1.0 mg/dl	0.68 ± 0.22	0.7 ± 0.21	0.70 ± 0.26	.92
Direct bilirubin	0.2-0.6 mg/dl	0.26 ± 0.1	0.28 ± 0.13	0.27 ± 0.12	.72
Indirect bilirubin	0.7-0.9 mg/dl	0.42 ± 0.14	0.41 ± 0.15	0.43 ± 0.16	.77
AST	8-40 U/L	38.5 ± 10.67	41.24 ± 21.73	40.6 ± 16.26	.82
ALT	5-35 U/L	43.41 ± 21.09	39.10 ± 20.41	35.5 ± 17.89	.19
ALP	40 – 125 U/L	62.64 ± 23.07	70.95 ± 35.97	76.47 ± 27.46	.14
GGT	10-50 U/L	40.96 ± 17.7	48.57 ± 25	48.35 ± 18.32	.27
Total protein	6-8 g/dl	6.72 ± 0.96	6.79 ± 1.11	7.1 ±0.85	.009**
Albumin	3.5-5.0 g/dl	4 ± 0.68	3.95 ± 0.94	3.59 ± 0.44	.02*
Globulin	2.5 3.0 g/dl	2.72 ± 0.43	2.84 ± 0.57	2.61 ± 0.67	.16
A/G Ratio	1.1-2.5	1.48 ± 0.28	1.46 ± 0.53	1.50 ± 0.62	.94
RENAL FUNCTION TEST					
Urea	15-40 mg/dl	33.5 ± 12.1	34.87 ± 18.25	43.68 ± 21.50	.004**
Creatinine	0.5-1.2 mg/dl	0.76 ± 0.24	0.79 ± 0.25	1.33 ± 0.92	<.0001***
Uric acid	3.0-7.2 mg/dl	4.17 ± 1.57	3.25 ± 1.32	5.14 ± 7.54	.05
ELECTROLYTES					
Sodium	135-150 mmol/L	136.6 ± 4.2	133.6 ± 15.22	134.33 ± 5.07	.39
Potassium	3.5-5.0 mmol/L	4.19 ± 0.43	4.16 ± 0.46	4.25 ± 0.67	.66
Chloride	95-105 mmol/L	104.5 ± 3.85	103.9 ± 6.46	103.11 ± 5.04	.48
INFLAMMATORY MARKERS					
LDH	250-480 U/L	349.51 ± 156.04	390.33 ±171.48	354 ± 141.61	.37
Ferritin	20-250 ng/ml	512.21 ± 426.45	564.9 ± 346.54	661.7 ± 336.3	<.0001***
CRP	< 10 mg/L	2.53 ± 3.46	2.56 ± 1.21	3.78 ± 2.09	.004
BLOOD GLUCOSE LEVELS					
RBS	70-140 mg/dl	150.67 ± 76.51	230.10 ± 109.4	238.1 ± 107.2	.0001***
HbA1C	4.5-6.0 %	6.26 ± 1.04	7.19 ± 1.57	7.23 ± 1.23	.004**

Values are expressed in mean ± standard deviation. The values are statistically significant based on the p value. p value <0.05, p value <0.01**, p value <.001***, NS-Not Significant.*

A significant decrease in the eosinophil count and increase in basophil count was observed with an increase in age group and hemoglobin, PCV, MCH decreases significantly with increase in age group, but insignificantly MCV and MCHC also decrease with increasing age. ESR an inflammatory marker significantly increases with age group. (Table. 3)

Table 3: Comparison of Mean ± SD of the Measured Hematological Parameters between GROUP A, B and C.

PARAMETERS	NORMAL RANGE	GROUP A (n= 52)	GROUP B (n= 94)	GROUP C (n= 48)	p VALUE
Total cell count	4500-11000/ microliter	8166.7 ± 4757.8	8671.6 ± 4364.4	8152.6± 4068.5	.82
Neutrophils	40-80 %	74.19 ± 18.58	78.87 ± 16.37	81.65 ± 11.14	.08
Lymphocytes	20-40%	18.6 ± 15.06	21.23 ± 9.5	24.51 ± 14.14	.09
Eosinophil	1-3%	1.67 ± 1.52	1.1 ± 1.03	1.28 ± 0.98	.04*
Basophils	0-1%	0.76 ± 0.7	1.24 ± 1.04	2.37 ± 2.27	<.0001***
Monocytes	4-8%	2.19 ±2.03	2.74 ± 2.26	2.74 ± 2.53	.42
Hemoglobin	12-15.5 g/dl	14.1 ± 1.56	13.08 ± 1.66	12.36 ± 2.27	<.0001***
RBC	4.5-6.0 million	4.4 ± 0.5	4.36 ±0.49	4.26 ± 0.49	.39
PCV	35.5-44.9 %	39.95 ± 4.6	36.95 ± 4.88	36.56 ± 6.63	.007**
MCV	80-100 fl	85.7 ± 15.03	84.82 ± 9.9	83.66 ± 9.67	.69
MCH	27-31 pg/cell	30.93 ± 4.19	30.86 ± 7.4	29.84 ± 3.81	<.0001***
MCHC	32-36 g/dl	34.88 ± 0.98	34.82 ± 1.39	34.78 ± 1.49	.58
ESR	0-29 mm/hr	39.12 ± 17.3	47.5 ± 18.3	64.58 ± 21.02	<.0001***

Values are expressed in mean ± standard deviation. The values are statistically significant based on the p value. p value <0.05, p value <0.01**, p value <.001***, NS-Not Significant.*

5. DISCUSSION

SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), is the virus that causes COVID-19 (coronavirus disease 2019), has spread quickly and became pandemic.[11] Although the disease affects all the age groups of the population, it is seen that older ones are more vulnerable to the COVID-19 infection compare to other age groups.[12,13] A study by Mélodie Monod et al, showed that adult and older age groups disproportionate to the size of the population are susceptible to COVID-19 disease.[14] In this study, the mean ages of Group A, Group B, and Group C were 33.9 ± 3.22 years, 50.21 ± 5.36 years and 66.22 ± 5.36 years respectively. Among 195 subjects about 69% Group A, 61% Group B, and 67% Group C were male and 31 % Group A, 39% Group B, and 33% Group C were female, which shows that independent to age group predominantly males are more susceptible to COVID-19 diseases than female.[15] It is seen that COVID-19 severity is associated with alteration of several biochemical and hematological laboratory parameters.[3,16,17,18] In this study, a significant increase in the biochemical values of renal function tests such as urea and creatinine with an increase in the age group was observed, so that the patient may develop kidney damage due to COVID -19. It is found that serum albumin is found to decrease with an increase in the age group with significance which states that there is an increase in proteinuria with loss of albumin. A study by Xiucui Han et al, showed that COVID-19 affect kidney may develop kidney damage and also complicate the condition of the patient with kidney disease, with the most commonly patient present with proteinuria.[19] A study by QingxianCai et al, showed that above 24% of COVID-19 patients have elevated ALT and GGT levels and COVID-19 positive individuals with abnormal liver function test may progress to more severe COVID-19 condition,[20] but this study did not support the above study where there is no significant rise was observed with age group. There is no significant difference in electrolytes levels in various age groups, but a statistical significance was observed with inflammatory markers such as ferritin, ESR and CRP that increase with increasing age group age. A study by Muammer Yucelet al, showed that the severity of COVID-19 is associated with an increase in the rate of inflammatory markers such as ferritin, ESR, CRP, procalcitonin, D-dimer, and fibrinogen.[21] Other studies also support that assessment of the inflammatory marks can be used to observe the condition of COVID-19.[22,23] In this study, it is found that diabetic patients with high HbA1C levels with an increasing age group are more prone to COVID-19 infection, similar to the study of Zhenzhou Wang et al.[25] A study by Michal Shauly-Aharonov et al, showed that pre and post blood glucose raise in COVID-19 positive individuals result in severe complications of disease.[26] This study shows significant decreases in the eosinophil count and increased basophil count with an increase in age group and hemoglobin, PCV, MCH decreases significantly with increase in age group, but insignificantly MCV and MCHC decrease with increasing age. Which is similar to the study by Guoguang Lu et al, showed that there is a decrease in eosinophil and lymphocyte count and also supports that there will be an increase in hemoglobin and RBC levels in COVID-19 positive individuals.[27] But a study by Qin C, Ziwei MP et al, showed that there will be a decrease in basophil count in COVID-19 patients which is in contrast to this study where the basophil levels are raised.[28] As several studies suggest that the severity of the COVID-19 condition can be analyzed by the clinical parameters,[4] this study shows that assessment of biochemical and hematological parameters are association with different age groups.

6. CONCLUSION

Compared to younger age groups, older ones with COVID-19 are associated with an increase in the markers of immune and inflammatory response such as ferritin, CRP,ESR and increase in markers of tissue and major organ failure including urea and creatinine, with a decrease in serum albumin levels. Markers of the adaptive immune response have changed, with eosinophils decreasing and basophils increasing significantly with age. The clinical utility of these markers should be investigated in order to assess the risk of age criteria and track the clinical progress of COVID-19. As a result, continuous monitoring and additional care must be

provided to the elderly in order to reduce the severity of COVID-19 among the South Indian population.

7. AUTHORS CONTRIBUTION STATEMENT

analysis was done by Dr.Jainulavudeen Mohamed Rabeek and Dr. Mary Chandrika Anton.

8. ACKNOWLEDGEMENT

We acknowledge the Department of Biochemistry, Departments of General Medicine of Sree Balaji Medical College and Hospital for giving us support to complete this project.

9. ETHICAL STANDARDS

The study involved human participants following the ethical standards of the tertiary health care institution where the study was conducted.

10. LIMITATIONS OF THE STUDY

The study population shall be enlarged as it was relatively less.

11. CONFLICT OF INTEREST

Conflict of interest declared none.

12. REFERENCES

1. Sarkar Arnab, Chakrabarti Alok Kumar, Dutta Shanta. Covid-19 infection in India: A comparative analysis of the second wave with the first wave. Pathogens. 2021 Sep 21;10(9):1222. doi: 10.3390/pathogens10091222, PMID 34578254.
2. Kumar Saurabh. Second wave of COVID-19: emergency situation in India. J Travel Med. 2021;28(7):1-2. doi: 10.1093/jtm/taab082, PMID 34037783.
3. RamananLaxminarayan Brian Wahl, Shankar Reddy Dudala, K. Gopal , Chandra Mohan B , S. Neelima, K. S. Jawahar Reddy, J. Radhakrishnan, Joseph A. Lewnard. Epidemiology and transmission dynamics of COVID-19 in two Indian states. Science 06 Nov 2020:Vol. 370, Issue 6517, pp. 691-697. DOI: 10.1126/science.abd7672.
4. Letelier Pablo, Encina Nicole, Morales Pablo, Riffo Alejandra, Silva Halett, Riquelme Ismael, Guzmán Neftalí. Role of biochemical markers in the monitoring of COVID-19 patients. J Med Biochem. 2021 Mar 12;40(2):115-28. doi: 10.5937/jomb0-29341, PMID 33776561.
5. Moutchia Jude, Pokharel Pratik, Kerri Aldiona, McGaw Kaodi, Uchai Shreeshti, Nji Miriam, Goodman Michael. Clinical laboratory parameters associated with severe or critical novel coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. PLOS ONE. 2020;15(10):e0239802. doi: 10.1371/journal.pone.0239802, PMID 33002041.
6. Mardani Rajab, Ahmadi Vasmehjani Abbas, Zali Fatemeh, Gholami Alireza, Mousavi Nasab Seyed Dawood Mousavi, Kaghazian Hooman, Kaviani Mehdi, Ahmadi Nayebali. Laboratory parameters in detection of COVID-19 patients with positive RT-PCR; a

   diagnostic accuracy study. Arch Acad Emerg Med. 2020;8(1):e43. PMID 32259132.
7. Mahat Roshan Kumar, Panda Suchismita, Rathore Vedika, Swain Sharmistha, Yadav Lalendra, Sah Sumesh Prasad. The dynamics of inflammatory markers in coronavirus disease-2019 (COVID-19) patients: A systematic review and meta-analysis. Clin Epidemiol Glob Health. 2021 Jul–Sep;11:100727. doi: 10.1016/j.cegh.2021.100727.
8. Moutchia J, Pokharel P, Kerri A, Mc Gaw. K, Uchai S, Nji MAM, et al. Clinical laboratory parameters associated with severe or critical novel coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis of observational studies. PROSPERO; 2020.
9. Szklanna Paulina B, Altaie Haidar, Comer Shane P, Cullivan Sarah, Kelliher Sarah, Weiss Luisa, Curran John, Dowling Emmet, O'Reilly Katherine MA, Cotter Aoife G, Marsh Brian, Gaine Sean, Power Nick, Lennon Áine, McCullagh Brian, Ní Áinle Fionnuala, Kevane Barry, Maguire Patricia B. Routine hematological parameters may be predictors of COVID-19 severity. Front Med (Lausanne). Jul 16 2021;8:682843. doi: 10.3389/fmed.2021.682843, PMID 34336889.
10. Samprathi Madhusudan, Jayashree Muralidharan. Biomarkers in COVID-19: an up-to-date review. Front Pediatr. 2020;8:607647. doi: 10.3389/fped.2020.607647, PMID 33859967.
11. Paramanantham P. Management of neonates born to coronavirus(covid-19) infected pregnant mother. Int J Pharm Biol Sci. 2020;11(4):154-61.
12. Han Yujuan, Luo Zujin, Zhai Wenliang, Zheng Yue, Liu Huan, Wang Yanran, Wu Endong, Xiong Fang, Ma Yingmin. Comparison of the clinical manifestations between different age groups of patients with overseas imported COVID-19. PLOS ONE. 2020;15(12):e0243347. doi: 10.1371/journal.pone.0243347, PMID 33275609.
13. Ningthoujam Ramananda, Khomdram Deepa. WHO statement – "Older people are at highest risk from COVID-19": should the hypothesis be corroborated or rejected? Med Hypotheses. 2020 Nov;144:109896. doi: 10.1016/j.mehy.2020.109896.
14. Monod Mélodie, Blenkinsop Alexandra, Xi Xiaoyue, Hebert Daniel, Bershan Sivan, Tietze Simon, Baguelin Marc. Age groups that sustain resurging COVID-19 epidemics in the United States. Science. 2021;371(6536):1336. doi: 10.1126/science.abe8372, PMID 33531384.
15. Pradhan Ajay, Olsson Per-Erik. Sex differences in severity and mortality from COVID-19: are males more vulnerable? Biol Sex Differ. 2020;11(1):Article number: 53. doi: 10.1186/s13293-020-00330-7.
16. Sarhan Adil R, Hussein Thaer A, Flaih Mohammed H, Hussein Khwam R. A biochemical analysis of patients with COVID-19 infection. Biochem Res Int. 2021;2021:Article ID 1383830. doi: 10.1155/2021/1383830, PMID 34703628.
17. Gemcioglu Emin, Davutoglu Mehmet, Catalbas Ramis, Karabuga B, Kaptan E, Aypak A, Kalem AK, Özdemir

M, Yeşilova NY, Kalkan EA, Civak M, Kücüksahin O, Erden A, Ates I. Predictive values of biochemical markers as early indicators for severe COVID-19 cases in admission. Future Virol. 2021;16(5):353-67. doi: 10.2217/fvl-2020-0319.

18. Waris Abdul, Din Misbahud, Khalid Atiqa, Abbas Lail Raees Abbas, Shaheen Asmat, Khan Nida, Nawaz Mehboob, Baset Abdul, Ahmad Imtiaz, Ali Muhammad. Evaluation of hematological parameters as an indicator of disease severity in Covid-19 patients: Pakistan's experience. J Clin Lab Anal. 2021 Jun;35(6):e23809. doi: 10.1002/jcla.23809, PMID 34028884.

19. Han Xiucui, Ye Qing. Kidney involvement in COVID-19 and its treatments. J Med Virol. 2021;93(3):1387-95. doi: 10.1002/jmv.26653, PMID 33150973.

20. Cai Qingxian, Huang Deliang, Yu Hong, Zhu Zhibin, Xia Zhang, Su Yinan, Li Zhiwei, Zhou Guangde, Gou Jizhou, Qu Jiuxin, Sun Yan, Liu Yingxia, He Qing, Chen Jun, Liu Lei, Xu Lin. COVID-19: abnormal liver function tests. J Hepatol. 2020 Sep;73(3):566-74. doi: 10.1016/j.jhep.2020.04.006, PMID 32298767.

21. Yucel M, Avsar C. The effect of COVID-19 pandemic on biochemistry laboratory test consumption numbers and variety. Turk J Biochem. 2020;45(3):339-41. doi: 10.1515/tjb-2020-0239.

22. Zeng Furong, Huang Yuzhao, Guo Ying, Yin Mingzhu, Chen Xiang, Xiao Liang, Deng Guangtong. Association of inflammatory markers with the severity of COVID-19: A meta-analysis. Int J Infect Dis. 2020;96:467-74. doi: 10.1016/j.ijid.2020.05.055, PMID 32425643.

23. Panda Suchismita, Nanda Rachita, Tripathy Prasanta Kumar, Mangaraj Manaswini. Immuno-inflammatory predictors of disease severity in COVID-19: A systematic review and meta-analysis. J Family Med Prim Care. 2021 Mar;10(3):1102-16. doi: 10.4103/jfmpc.jfmpc_2196_20, PMID 34041137.

24. Terpos Evangelos, Ntanasis-Stathopoulos Ioannis, Elalamy Ismail, Kastritis Efstathios, Sergentanis Theodoros N, Politou Marianna, Psaltopoulou Theodora, Gerotziafas Grigoris, Dimopoulos Meletios A, Grigoris Gerotziafas, and Meletios A. Dimopoulos. Hematological findings and complications of COVID-19. Am J Hematol. 2020 May 23;95(7):834-47. doi: 10.1002/ajh.25829, PMID 32282949.

25. Wang Zhenzhou, Du Zhe, Zhu Fengxue. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. Diabetes Res Clin Pract. 2020 Jun;164:108214. doi: 10.1016/j.diabres.2020.108214.

26. Shauly-Aharonov Michal, Shafrir Asher, OraPaltiel Ronit, Calderon-Margalit RifaatSafadi, RoeeBicher Orit Barenholz-Goultschin, Stokar Joshua. Both high and low pre-infection glucose levels are associated with increased risk for severe COVID-19: new insights from a population-based study. PLOS ONE. Jul 22, 2021.

27. Lu Guoguang, Wang Jing. Dynamic changes in routine blood parameters of a severe COVID-19 case. Clin Chim Acta. 2020 Sep;508:98-102. doi: 10.1016/j.cca.2020.04.034, PMID 32405079.

28. Qin C, Ziwei MP, Tao SY, Ke PC, Shang MM. Dysregulation of immune response in patients with COVID-19 in Wuhan, China; Clinical Infectious Diseases; Oxford Academic. Clin Infect D.