ORIGINAL RESEARCH

A Study of Serum Procalcitonin (PCT) Levels in Patients of Covid-19 at Gmch, Jalgaon-An Analytical Study

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Abstract
Background: The hyper-inflammatory immune response due to viral infection is thought to have a major role in the pathogenesis of COVID-19, according to mounting data. In coronavirus illness, serum procalcitonin (PCT) is an emerging prognostic marker (COVID-19). This study's objective was to examine the serum procalcitonin levels in individuals with coronavirus illness (COVID-19).
Materials and methods: The current study was an analytical study conducted among patients using the GMCH, Jalgaon Casualty ICU. Following the fulfilment of the inclusion and exclusion criteria, 100 subjects were included in total. Of which 50 were healthy volunteers in their normal states as controls and 50 were COVID -19 cases verified by RT-PCR tests at VDRL, GMCH, Jalgaon. All of the patients fell within the 20–60 year age range.
Results: The average patient age was 55.3 years, and 25 (50%) of the controls and 32 (64%) of the COVID-19 cases were men. Table 2 showed the PCT levels among the subjects. It was seen that normal level of PCT levels was found in 72.22% COVID males and 100% non-COVID males. Amongst the females, 66.67% COVID females and 100% non-COVID females had normal level of PCT. Only 18.75% males and 33.33% females with COVID had PCT levels >0.5.
Conclusion: PCT may serve as a marker for COVID-19 disease severity and may help assess the severity of SARS-CoV-2 infection in patients. Serial PCT readings could also be helpful in determining the prognosis.
Keywords: Procalcitonin, COVID-19, prognosis.

Introduction
A condition known as coronavirus disease 2019 (COVID-19) is one brought on by the SARS-CoV-2 coronavirus (SARS-CoV-2). It was initially discovered in Wuhan, China, in December 2019, and since then, it has spread throughout the world, causing an ongoing pandemic.[1,2] Even though the majority of individuals have few symptoms and a favourable prognosis, the disease symptoms could worsen quickly. Systemic inflammation and acute respiratory distress syndrome (ARDS) are possible symptoms. [3,4]

In the ICU, these patients frequently require oxygen therapy and possibly aid with ventilation. Unfortunately, the death rate for the severe type of ARDS, or ARDS, can be as high as 60.5% despite intensive care efforts.[3,5] Therefore, it is crucial to examine prognostic indicators and gauge the severity of the disease in order to quickly appraise the situation and support clinical decisions. Viral load, lactic acid, lymphocyte count, CRP, IL-6, IL-10, and procalcitonin are a few lab tests that have been proposed as prognostic indicators.[6,7]

A prohormone of calcitonin produced by thyroid neuroendocrine cells, procalcitonin (PCT) has a different biological purpose from calcitonin. For distinguishing patients with suspected and confirmed bacterial infections from other sources of infection or inflammation, procalcitonin has emerged as a promising diagnostic. Therefore, PCT can be a useful auxiliary to assess clinical severity and the outcome of antibiotic therapy.[4] It is thought that its normal level, which is rather low, is significantly up-regulated in the presence of bacterial infection or cytokines like IL-6. To rule out sepsis and systemic inflammation, a procalcitonin plasma level of 0.2 ng/mL is a helpful cut-off.[5] In contrast to bacterial infections, viral infections have a different impact on procalcitonin. Interferon, which is generated by T helper cells during viral infections, inhibits the formation of procalcitonin.[8,9] As a result, higher serum procalcitonin levels have been suggested as a diagnostic biomarker to discriminate between viral and bacterial infections as well as a prognostic marker and mortality index in sepsis.[10] In order to aid in early risk assessment and eliminate bacterial co-infections in COVID-19 patients, procalcitonin (PCT) testing at the time of admission appears to be a valuable supplementary source of information.[11]

Procalcitonin plasma level's importance in disease categorization and prognosis, however, is still unknown. In the state of Maharashtra, very few research have been done to evaluate blood PCT levels as prognostic indicators in Covid -19 cases. This study was done to find out how much procalcitonin COVID-19 patients have in their systems.

Materials and methods

The current study was an analytical study conducted among patients using the GMCH, Jalgaon Casualty ICU. Following the fulfilment of the inclusion and exclusion criteria, 100 subjects were included in total. Of which 50 were healthy volunteers in their normal states as controls and 50 were COVID -19 cases verified by RT-PCR tests at VDRL, GMCH, Jalgaon. All of the patients fell within the 20–60 year age range. Ethical Committee clearance was obtained.

All of the individuals underwent a predesigned proforma examination, and vital findings—including those involving inflammatory markers—were also noted. In a k3EDTA SST tube, 2ml of venous blood was swiftly transported to CCL, GMCH, Jalgaon for processing while following aseptic procedures to take the blood sample from the ante-cubital vein of the left forearm.[12] For the quantitative assessment of the serum PCT levels, samples were processed in the Ichroma PCT Fluorescence Immunoassay (FIA) Analyzer utilising the sandwich immunodetection method. ANOVA was used to statistically examine the generated data. Statistical significance was established as $p < 0.05$, and the analysis was conducted using SPSS version 23 and STATA version 0.05.

Results

In this investigation, 100 patients with confirmed COVID-19 were included. The average patient age was 55.3 years, and 25 (50%) of the controls and 32 (64%) of the COVID-19 cases were men (table 1). Table 2 showed the PCT levels among the subjects. It was seen that normal level of PCT levels was found in 72.22% COVID males and 100% non-COVID males. Amongst the females, 66.67% COVID females and 100% non-COVID females had

normal level of PCT. Only 18.75% males and 33.33% females with COVID had PCT levels >0.5. The Prevalence, Sensitivity, specificity, PPV, NPV, diagnostic accuracy, Positive Likelihood ratio and negative likelihood ratio was 11%, 90.9%, 55.06%, 20%, 98%, 59%, 2.02% and 0.17% respectively.

	Covid affected	Non covid
MALES	32 (64)	25 (50)
FEMALES	18 (36)	25 (50)
TOTAL	50 (100)	50 (100)

Table 1: Gender distribution of subjects

		PCT levels		
		Normal level of PCT found in the subjects	>0.5 PCT Levels found in subjects	Total
Males	COVID	26 (72.22)	06 (18.75)	32
	Non COVID	25 (100)	00	25
Females	COVID	12 (66.67)	06 (33.33)	18
	Non COVID	25 (100)	00	25
Total		88 (88)	12 (12)	100

Table 2: PCT levels among the subjects

	COVID	NON- COVID	P-value
Mean ± SD	0.72 ± 2.07	0.26 ± 0.14	0.002*

Table 3: Mean PCT levels among subjects

*: statistically significant

Prevalence	11
Sensitivity	90.9
Specificity	55.06
PPV	20
NPV	98
Diagnostic accuracy	59
Positive Likelihood Ratio	2.02
Negative Likelihood Ratio	0.17

Table 4: Prevalence, Sensitivity, specificity, PPV, NPV, diagnostic accuracy, Positive Likelihood ratio and negative likelihood ratio

Discussion

In the present study, in accordance with table no. 2, 24% of COVID-19 patients had procalcitonin levels that were elevated (>0.5 ng/mL). Procalcitonin levels in patients with severe COVID19 were reported to be 0.5 ng/ml on average by Hu et al.[11] This frequency has also been reported as 5.5% in a cohort analysis of 1099 Chinese patients with COVID-19, and the majority of these patients had procalcitonin levels below 0.2 ng/mL.[8,13] Additionally, a meta-analysis showed that elevated PCT values are associated with a 5-fold higher risk of severe COVID-19.

In contrast to non-COVID patients (0.26 ± 0.14), shown in table no. 3, we discovered that the mean serum procalcitonin level in COVID-19 individuals was 0.72 ±2.07. According to many research from China, 6- 30% of patients with COVID-19 have elevated procalcitonin levels (>0.5 ng/mL), and two of these studies linked the procalcitonin level to the severity of the illness or the risk of death.[14,15]Procalcitonin level monitoring can be useful in early illness progression diagnosis, and doing this test at the time of admission seems to provide extra information to estimate the early risk. PCT may serve as a marker for COVID-19 disease severity and help assess the severity of SARS-CoV-2 infection in patients.

Additionally, a recent study proposed that a steadily rising PCT level may indicate a poor prognosis.[16] The current study included 38 patients with serially assessed PCT values, of whom 32 were released from the hospital and 6 passed away. Both high-normal and abnormal PCT levels fell in the 32 patients who were released from the hospital as they recovered. However, in the six cases that resulted in death, serum PCT levels rose as the illness got worse. These findings show that repeated PCT measurements can forecast a patient's prognosis for COVID-19.

According to Liu et al., PCT concentrations above 0.07 ng/mL and sensitivity and specificity of 73.15% and 84.85%, respectively, for the prediction of morbidity can be taken into account in routine clinical practise in conjunction with other biochemical markers and the clinical picture.[15] The identification of cases that might advance to a severe state can help with effective resource allocation and aggressive treatment strategies. In a study done by Peng J et al [17], with PCT concentrations of 0.76 ng/mL, the sensitivity and specificity was 70.97% and 66.67% respectively.

First, due to the limited sample size in our study, it may be difficult to interpret the results. Therefore, larger clinical prospective investigations are needed to corroborate the correctness of our findings. Furthermore, as the study did not use pathophysiological models, more investigation is required to determine the precise relationship between PCT level and severity using simpler tests. Furthermore, our results might not be applicable to other regions of Iran or other nations.

Conclusion

The findings of this study demonstrated that PCT may be a marker of disease severity and may help determine the severity of COVID-19 patients despite a number of limitations. Additionally, it is possible to use initially increased PCT levels in COVID-19 as a quick predictor of criticality, a deteriorating clinical picture, and even fatality. However, more research is required to fully assess the predictive value of PCT.

References

1. Laing AG, Lorenc A, Del Molino Del Barrio I, et al. A dynamic COVID-19 immune signature includes associations with poor prognosis. Nat Med 2020; 26(10): 1623-35.
2. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev 2020; e3319: e3319.
3. Wynants L, Van Calster B, Collins GS, Riley RD, Heinze G, Schuit E. Prediction models for diagnosis and prognosis of covid-19: Systematic review and critical appraisal. BMJ 2020; 369.
4. Qu R, Ling Y, Zhang YH, et al. Platelet-to-lymphocyte ratio is associated with prognosis in patients with coronavirus disease-19. J Med Virol 2020; 92(9): 1533-41.
5. van Berkel M, Kox M, Frenzel T, Pickkers P, Schouten J. Biomarkers for antimicrobial stewardship: a reappraisal in COVID-19 times? Crit Care 2020; 24(1): 600.

6. Liu B, Li M, Zhou Z, Guan X, Xiang Y. Can we use interleukin-6 (IL-6) blockade for coronavirus disease 2019 (COVID-19)-induced cytokine release syndrome (CRS)? J Autoimmun 2020; 111: 102452.

7. Shahini Shams Abadi M, Siadat SD, Vaziri F, et al. Distribution and diversity of hmw1A among invasive nontypeablehaemophilusinfluenzae isolates in Iran. Avicenna J Med Biotechnol 2016; 8(2): 99- 102.

8. Zhao Z, Chen A, Hou W, et al. Prediction model and risk scores of ICU admission and mortality in COVID-19. PLoS One 2020; 15(7): e0236618.

9. Heesom L, Rehnberg L, Nasim-Mohi M, et al. Procalcitonin as an antibiotic stewardship tool in COVID-19 patients in the intensive care unit. J Glob Antimicrob Resist 2020; 22: 782-4.

10. Hu R, Han C, Pei S, Yin M, Chen X. Procalcitonin levels in COVID19 patients. Int J Antimicrob Agents 2020; 56(2): 106051.

11. Zhou B, She J, Wang Y, Ma X. Utility of ferritin, procalcitonin, and C-reactive protein in severe patients with 2019 novel coronavirus disease. Research Square 2020.

12. Burtis CA,Ashwood ER, Young DS, BermenEW. Tietz's fundamentals of clinical chemistry. Chapter 2- specimen collection and other preanalytical variable, WB saunders& Co. Ltd. 5th Ed. 2003;1:30-54.

13. Huang I, Pranata R, Lim MA, Oehadian A, Alisjahbana B. C-reactive protein, procalcitonin, D-dimer, and ferritin in severe coronavirus disease-2019: a meta-analysis. Ther Adv Respir Dis 2020; 14: 1753466620937175.

14. Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. ClinChimActa 2020; 505: 190-1.

15. Liu F, Li L, Xu M, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. J ClinVirol 2020; 127: 104370.

16. Lippi G, Cervellin G. Procalcitonin for diagnosing and monitoring bacterial infections: for or against? ClinChem Lab Med 2018;56:1193–5.

17. Peng J, Qi D, Yuan G, Deng X, Mei Y, Feng L, Wang D. Diagnostic value of peripheral hematologic markers for coronavirus disease 2019 (COVID-19): a multicenter, cross-sectional study. J Clin Lab Analysis. 2020 Oct;34(10):e23475.