ORIGINAL RESEARCH PAPER

Biochemistry

QUANTITATIVE ASSESSMENT OF PROCALCITONIN LEVELS AND ITS CLINICAL CORRELATION AMONG COVID-19 PATIENTS.

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ABSTRACT

Introduction: Whole world is facing a challenge of coronavirus disease 2019 (COVID-19) pandemic, the first case of which found in in the city Wuhan of China in December 2019,caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) .[1] WHO (World health organisation) declared covid 19 as a global pandemic on 11th march 2020. [2] This is an acute respiratory tract infectious disease which may presents as asymptomatic infection to clinically mild to severe type of disease. COVID-19 pandemic has emerged as a global challenge threatening human life worldwide. Early recognition of severe forms of COVID-19 infection is critically essential for timely triaging of COVID-19 patients. Biochemical Parameters correlating clinically with the severity of COVID-19 infection helps in timely management of severe COVID-19 infections. The ever-growing number of COVID-19 patients stresses upon the need to identify effective yet readily available predictors of disease severity to ensure better clinical outcomes. Procalcitonin (PCT) , is a glycoprotein and is produced from C cells of thyroid gland. Among the lung infections such as bacterial pneumonia or other types of viral pneumonia, PCT helps to discriminate between milder cases and more severe cases. PCT also helps to discriminate between severe bacterial pneumonia and mild viral pneumonia. There are earlier evidence which suggests that the use of PCT can help physicians better manage patients with COVID-19.

Aim: In this study, we analysed the role of Procalcitonin levels in assessing the clinical severity of the COVID-19 patients.

Materials and Methods: The present study conducted in a Tertiary care Hospital and Research Center .176 COVID-19 positive patients confirmed by Real Time-Polymerase Chain Reaction (RT-PCR) were included, and classified them into asymptomatic, mild, moderate and severe according to "Clinical Management Protocol: COVID 19", by the Ministry of Health and Family Welfare and Director General of Health Services. Procalcitonin was estimated in the separated serum, using fluroimmuno assay using I-Chroma II immunofluorescence analyser by Weldon Biotech India Pvt.Ltd. Data were presented as percentages for categorical variables.

Results: Among the 176 cases, Procalcitonin levels found to be raised in 23 out of 176 (13.06 %) cases. The proportion of patients with PCT value <1 ng/ ml is 86.93% and these patients were clinically asymptomatic or having mild type of illness. The patients with PCT levels 1 to 10 ng/ml is 10.23% of total cases. 5 cases (2.84%) have severly raised PCT > 10 ng/ ml and all these were in severe form of clinical illness requiring intensive care managment.

Conclusion: Elevation of Procalcitonin levels associated with the severity of clinical course of patients infected with SARS CoV-2 when compared to patients with mild or asymptomatic cases.

INTRODUCTION

COVID-19 is a respiratory and systemic disease that has infected millions of people worldwide. Whole world is facing a challenge of coronavirus disease 2019 (COVID-19) pandemic, the first case of which found in in the city Wuhan of China in December 2019,caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) .[1] WHO (World health organisation) declared covid 19 as a global pandemic on 11th march 2020. [2] This is an acute respiratory tract infectious disease which may presents as asymptomatic infection to clinically mild to severe type of disease. Most covid patients have mild form of the disease but there is a certain percentage of patients who progress to a very severe disease state that requires intensive care and invasive ventilation. In order to ensure better patient management and improved outcomes, early identification of patients who may be at a higher risk of severe infection can play an important role. COVID-19 is a relatively new disease, and there is lot of work to be done for its better management. Among the lung infections such as bacterial pneumonia or other types of viral pneumonia, Procalcitonin (PCT) helps to discriminate between milder cases and more severe cases.[3] PCT also helps to discriminate between severe bacterial pneumonia and mild viral pneumonia. The normal physiological level of PCT in serum is less than 0.1 ng/mL which can increase several folds in systemic bacterial infections.[4]

Procalcitonin (PCT) , is a glycoprotein and is produced from C cells of thyroid gland. PCT is a 116 amino acid long peptide having a molecular weight of 13 KDa.[5] Procalcitonin, it is a precursor of calcitonin, produced by the C-cells of thyroid under the control of the calcitonin gene related peptide 1 (CALC-1) gene.[6] Normally, the expression of the gene is found in the neuroendocrine cells of the thyroid and the lung. However, during microbial infections there is increased CALC-1 gene expression in various extra-thyroid tissues and cells including kidneys, liver, pancreas, leucocytes, and adipose tissue with concomitant release of PCT throughout the body.[7] The pathophysiological role of PCT in sepsis is imperfectly understood.[9] The release of PCT in inflammation is said to be due to either directly toxins and lipopolysaccharides released by microbes ; or alternately indirectly by release of the inflammatory cytokines like interleukin (IL) 1b, IL-6, tumor necrosis factor- (TNF-)[8, 10,11], Although the biological action is largely unknown, the sequence homology between PCT and other human cytokines such as TNF- family, IL6 etc supports that PCT is a mediator of inflammation. [14]

The inflammatory response plays a critical role in COVID 19 and inflammatory cytokine storm increases the severity of COVID 19. [12] There are earlier evidence which suggests that the use of PCT can help physicians better manage patients with COVID-19.Therefore the present study was planned to evaluate the changes in Procalcitonin levels in covid 19 patients to predict mild, moderate and severe form of disease.

AIMS AND OBJECTIVES-
To estimate levels of PCT in COVID 19 positive patients.
TO analyze the role of Procalcitonin levels in assessing the clinical severity of the COVID-19 patients.

MATERIAL & METHODS

The study was done at Tertiary care Hospital and Research Center. A total 176 cases of covid 19 were taken as study samples, admitted in department of medicine. The patients with confirmed covid 19 infection, positive for RTPCR (Real time polymerase chain reaction) assay of 2019-nCoVRNA were included as study group. We enrolled 176 in-patients of Medical College in this single centre observational study and classified them into asymptomatic, mild, moderate and severe according to "Clinical Management Protocol: COVID 19", by the Ministry of Health and Family Welfare and Director General of Health Services. Procalcitonin was estimated in the separated serum, using fluroimmuno assay using I-Chroma II immunofluorescence analyser by Weldon Biotech India Pvt.Ltd. The PCT was done by principle which uses a sandwich immunodetectction method; the detector antibody in buffer binds to antigen in sample, forming antigen antibody complexes and migrates onto nitrocellulose matrix to be captured by the other immobilized antibody on test strip. The more antigen in sample forms the more antigen antibody complex and leads to stronger intensity of fluorescence signal on detector antibody, which is processed by instrument ICHROMA II to show PCT concentration in the sample. Data were presented as percentages for categorical variables.

RESULTS

Table 1 Gender Distribution Among Cases

GENDER	CASES	
	NO	%
MALE	112	63.63
FEMALE	64	36.36
TOTAL	176	100

Table 2 Procalcitonin Levels In Covid 19 Patients

PCT LEVELS	Mean + SD	CASES (n=176)	PERCENTAGE
<1 ng/ml	0.22±0.09	153	86.93%
1 -10 ng/ml	3.096±1.03	18	10.23%
>10 ng/ml	14.114±4.54	5	2.84%

Table 1 shows gender distribution in study groups. It is evident that number of males 63.63% (112/176) were more as compared to females 36.36% (64/176) and female to male ratio 1.57 .

Table 2 shows values of serum PCT in Covid 19. Among the 176 cases, Procalcitonin levels found to be raised in 23 out of 176 (13.06 %) cases. The proportion of patients with PCT value <1 ng/ ml is 86.93% and these patients were clinically asymptomatic or having mild type of illness. The patients with PCT levels 1 to 10 ng/ml is 10.23% of total cases. PCT levels severely raised in 2.83% cases (5 /176) in which values found to be > 10ng/ml. These 5 cases (2.84%) which have PCT > 10 ng/ ml and all these were in severe form of clinical illness requiring intensive care management. In our study the highest level of PCT was found to be 23ng/ml. While most of the asymptomatic and mild form of cases have PCT values less than 0.1ng/ml. Severely raise PCT correlates with increase hospital stay as well requirement of intensive care management.

DISCUSSION

The covid 19 and inflammation has a strong correlation; inflammatory cytokine strome increases the severity of COVID 19 infection.[12] The levels of PCT increases significantly in severe form of covid infection suggesting high inflammation in lung and tissues.

Most COVID-19 patients have very low PCT levels <0.1ng/ml at the time of admission, were in clinically mild and asymptomatic cases while raised pct was found in clinically moderate to severe category only. Raised PCT in Covid suggests concomitant bacterial infections. The role of PCT in sepsis has been proposed that in inflammation, the release of PCT by toxins and lipopolysaccharides released by microbes alternately the inflammatory cytokines like interleukin (IL) 1b, IL-6, tumour necrosis factor- (TNF-) etc may indirectly influence PCT production .[8,11,12]

We found PCT increased in 13.06 % (23/176) of cases. PCT levels severely raised in 2.83% cases (5 /176) in which values found to be > 10ng/ml. While most of the asymptomatic and mild form of cases have PCT values less than 0.1ng/ml. Fang Liu et al et al has found raised PCT in 5.7% of cases on admission.[12] Rui Hu et al also found raised PCT in Moderate to severe covid cases.[13] Some authors mention PCT levels may rise above 100 in severe form of infection and associated systemic manifestation.[14] In our study the highest level of PCT was found to be 23ng/ml. Thus PCT value may be helpful in determination of clinical severity, PCT values may be influence by preexisting comorbid conditions, such as CKD and congestive cardiac failure.[14]

As for covid patients more severe cases shows marked rise in PCT. Our study shows Increase in pct in covid cases and that was predominant in severe clinical illness. While most of the asymptomatic and mild form of cases have PCT values less than 0.1ng/ml. PCT value remains within normal ranges in patients with noncomplicated covid infections and increase in its level is associated with bacterial coinfection and the development of more critical type of illness.

LIMITATION(S) – The current study was conducted at a single centre with limited sample size. Hence, further study may be needed to extrapolate the findings to wider patients populations.

CONCLUSIONS-

The serum PCT levels increased with clinical severity of covid 19. Elevated procalcitonin levels associated with the severity of clinical course of patients infected with covid 19 when compared to patients with mild or asymptomatic clinical presentations. Hence, this reinforces the fact that PCT levels helps to predict the clinical course of the disease and is a definite guide for early management of complications like added bacterial sepsis.

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