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Procalcitonin (PCT) as an indicator of Covid-19 infection and disease progression and its correlation with several pro-inflammatory biomarkers

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Abstract *Background:* Procalcitonin (PCT) is protein molecule, present in body as precursor of Calcitonin, initially described in 1984 and noted to possess high levels association in patients with bacterial infection and subsequent sepsis. Due to covid-19 pandemic, screening and diagnostic importance of PCT has increased, due to its ability to differentiate between bacterial and viral infections. *Aim:* Present study described assessment of PCT as a inflammatory biomarker in association with other biomarkers such as D-Dimer, Ferritin, Interleukin-6 (IL-6), C-reactive protein (CRP), and enzymes alanine aminotransfrase (ALT) and creatinine kinase (CPK) currently used in diagnosis and prognosis of Covid-19 infections. *Materials and Methods*: Twenty (Males = 14, females = 6) confirmed admitted cases of SARS-Covid 19 virus, either in Intensive Care Units and High Dependency Units were part of this study carried out during January 2021 till June 2021 . Data were gathered by assessing and evaluating Lab information system (LRS) and after ensuring that all twenty patients had all six inflammatory biomarkers analyzed. Data presented as Regression correlation linear curve with Y intercept and R^2. *Results:* Data showed considerable linearity between PCT and other inflammatory biomarkers and enzymes from 91.17% (PCT vs ALT) to 99.81% (PCT vs D-dimer) suggesting marked precision, correlation and reproducibility amongst variable entities. *Conclusion*: PCT showed marked tendency as an indicative biomarker in early phases of systemic inflammatory flare-up, in addition to its efficacy in further stages of disease progression, in direct correlation with other inflammatory markers.

Keywords Procalcitonin, biomarkers, pro-inflammatory

Introduction

Procalcitonin (PCT) is protein molecule, with 116 amino acid sequence and present in body as precursor of Calcitonin [1-5]. It was initially described in 1984 by a group of scientists lead by Prof Dr Le Moullec. After nearly a decade, in 1993, another group of clinical scientists detailed a significant association between high levels of PCT and patients with bacterial infection and subsequent sepsis [3]. Due to covid-19 pandemic, screening and diagnostic importance of PCT has increased, due to its ability to differentiate between bacterial and viral infections [1-5]. Furthermore, due to non specificity of other markers such as C-reactive protein, which is a commonly used pro-inflammatory marker, to differentiate or diagnose whether patients is suffering from bacterial or viral infections [1-6], importance of PCT has been heightened per se. PCT efficacy, thus, been augmented therefore its been used

routinely for infections such as Covid-19, not only to diagnose correctly but also for the purpose of prognosis as well [1,6]. Recently completed studies also advocated strong biomarker status of PCT in early phases of systemic inflammatory instigation, emitting after any pro-inflammatory stimuli [7-9]. Moreover, it was reported in cohort studies concluded in 2020 and 2021 that PCT showed efficacy as an independent risk factor with 95 percentile for septic patients, in-hospital deaths, in addition to detecting severity of Covid 19 infection progress and depicting association confounded with several confounding factors of Covid-19 gravity [10-13]. In this regard, present study described assessment of PCT as a inflammatory biomarker in association with other biomarkers such as D-Dimer, Ferritin, Interleukin-6 (IL-6), C-reactive protein (CRP), enzymes like alanine aminotransfrase (ALT) and creatinine kinase currently used in diagnosis and prognosis of Covid-19 infections.

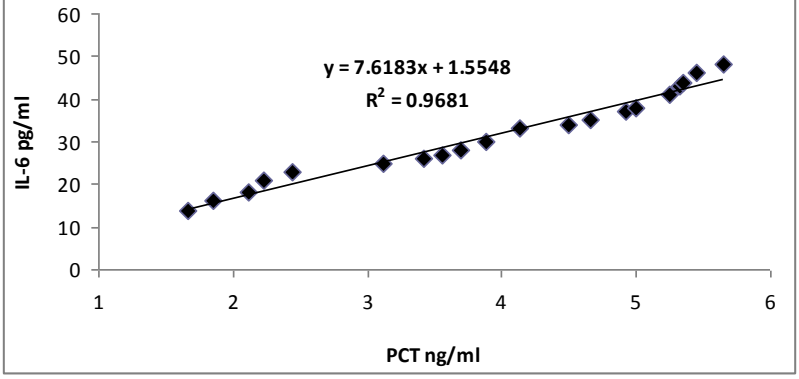
Materials and Methods

Twenty confirmed admitted cases of SARS-Covid 19 virus, either in Intensive Care Units and High Dependency Units were part of this study. Study period was January 2021 till June 2021 and total cases included were n= 20, in which 14 were males and 6 were females. Data gathered by assessing and evaluating Lab information system (LRS) and files (where applicable). It was made sure that all twenty patients had all six inflammatory biomarkers analyzed viz D-Dimer, Pro-calcitonin (PCT), Ferritin, Interleukin-6 (IL-6), C-reactive protein (CRP), Creatine phosphokinase (CPK) and Alanine Aminotransfrase (LDH). Samples were processed and analyzed by protocols described earlier and recently [14-16]. Data presented as Regression correlation linear curve with Y intercept and R^2. Normal reference ranges are D-Dimer < 0.5 µg/ml, Pro-calcitonin (PCT) < 0.5 ng/ml, Ferritin Males 30-400 ng/ml, Females 15-150 ng/ml, Interleukin-6 (IL-6) < 7.0 pg/ml, C-reactive protein (CRP) < 0.5 mg/ml, Creatine kinase (CPK) Males < 174 IU/L (for hospitalized) females < 140 IU/L (hospitalized) and alanine aminotransfrase (ALT) Males < 40 IU/L, Females < 35 IU/L. Regression correlation analysis was performed using SPSS ver 20.0 (USA) and graphs presented by Y intercept and R^2, as PCT vs IL-6, Ferritin, D-Dimer, LDH, CRP and CPK.

Results

Results are summarized in Fig 1 to Fig 5. Data showed considerable linearity between PCT and other inflammatory biomarkers and enzymes from 91.17% (PCT vs ALT, Fig 5) to 99.81% (PCT vs D-dimer, Fig 2) suggesting marked precision, correlation and reproducibility amongst variable entities. Regression correlation date with Y intercept for PCT vs IL-6 was Y = 7.6183x1.5548, R^2 = 0.9681 (Fig 1), PCT vs D-dimer Y = x -0.0475, R^2 = 0.9981 (Fig 2); PCT vs CRP Y = 0.9917 x 0.0105, R^2 = 0.9954 (Fig 3); PCT vs CPK Y = 70.512 x + 203.18, R^2 = 0.9713 (Fig 4) and PCT vs ALT Y = 58.625 x -68.73, R^2 = 0.9117 (Fig 5). Resultant outcome of regression analyses of PCT vs several inflammatory biomarkers used for either diagnosis, screening or prognosis of Covid 19 infections, depicted that all biomarkers elevates when there disease progression and will certainly helping physicians to taking best practice clinical decisions and selecting appropriate medications.

Fig 1: Comparative regression analysis of PCT vs IL-6 in patients with SARS-Covid 19 infection



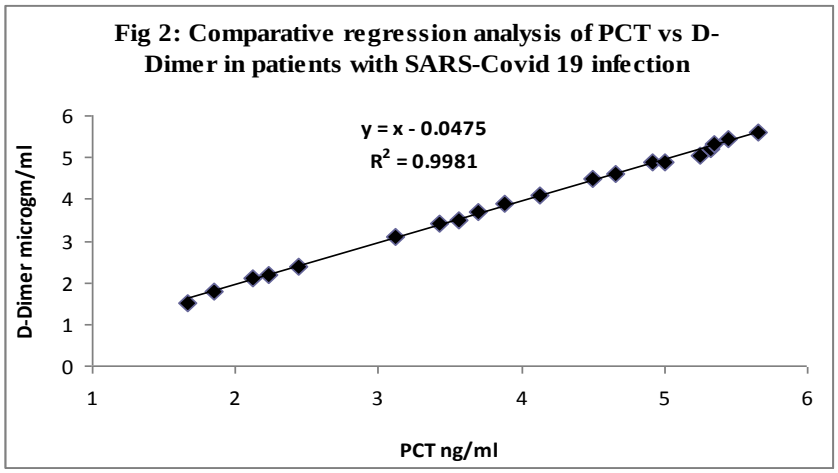


Fig 2: Comparative regression analysis of PCT vs D-Dimer in patients with SARS-Covid 19 infection

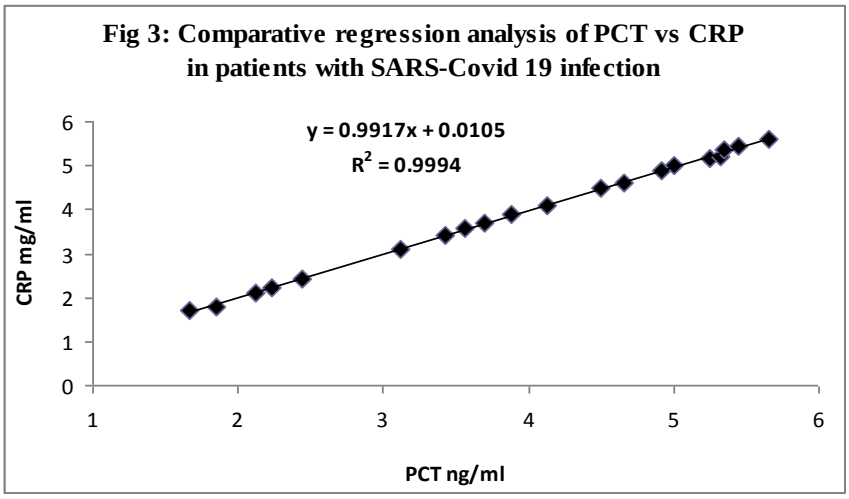


Fig 3: Comparative regression analysis of PCT vs CRP in patients with SARS-Covid 19 infection

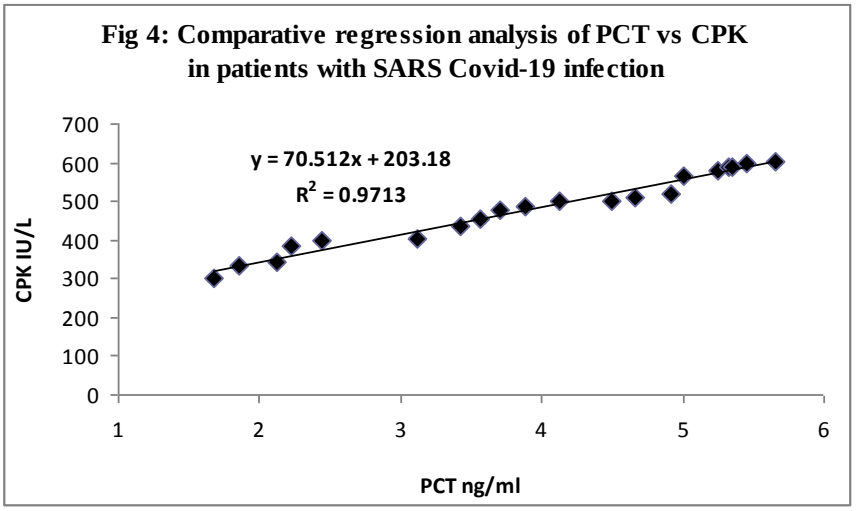
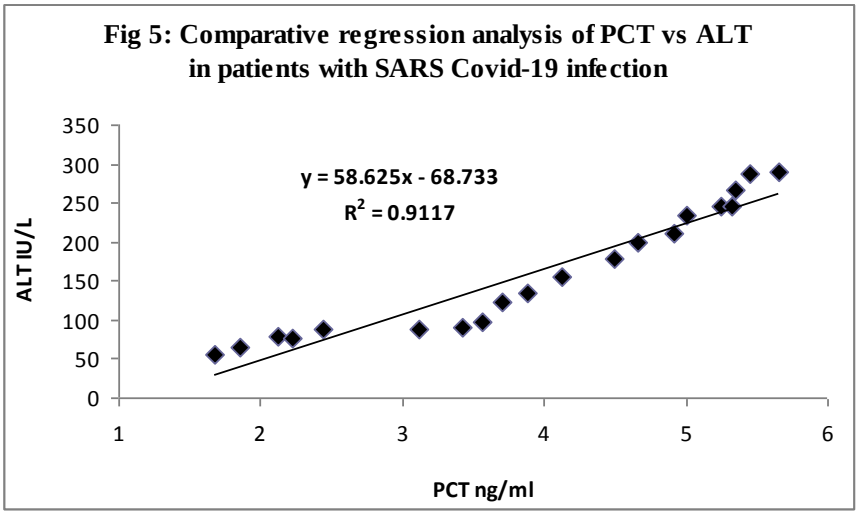


Fig 4: Comparative regression analysis of PCT vs CPK in patients with SARS Covid-19 infection



Discussion

It was recently reported that in patients with severe Covid 19 infections and those who needed hospitalization due to deteriorating conditions, PCT seems to be positively correlated with meta-analysis of 1.77, 95% CI: 1.38-2.29 [7]. Data analyzed in 7716 participants provided considerable correlated outcome of PCT with severity of Covid 19, hospital/ICU/HDU stays and fatality [7]. PCT known to instigate and accelerate surface markers on neutrophils and lymphocytes, and then subsequently up regulates cytokine mechanism, production of reactive oxygen species (ROS) [7], which correlates with each to induce clinical severity in Covid 19 patients [7, 17]. Moreover, correlation of PCT with disease severity and other inflammatory cytokines and markers, suggests its strong candidacy as a potential biomarkers to predict disease progression and probable prognosis [1]. Regarding liver function tests (LFTs) and muscle markers, it was reported that liver dysfunction and its markers can be used as agents of detecting disease progression and severity [10, 18]. All parameter of LFTs tends to be elevated, however not markedly, in cases of minor Covid 19 infections [10, 18]. About 24% of patients with Covid 19 infections seem to be trend altered ALT and gama-Glutamyl Transpeptidase (gGT) concentrations. Moreover, it was reported that both ALT and gGT tends to get further elevated as hospitalization prolonged and/or disease progressed [10, 18-20]. It has also been documented that patients with elevated LFTs are classified as Hepatocyte type and most likely progressed to more severe form of Covid 19 infections [10, 18-20]. Furthermore, use of antiviral drugs, which saves lives of more critically ill patients, also has a tendency to induce liver damage and thus altering hepatic enzymes. Arguably, PCT alterations as per disease progression correlated well inflammatory biomarkers (IL-6, D-Dimer, CRP), muscle (CPK) and hepatic (ALT), suggesting strong synergy amongst immunological system. Studies done in recent years also suggested similar findings, as we have seen in our study that PCT manifest strong biomarker tendency not only in early phases of systemic inflammatory instigation, but also at later stages of disease progression, in direct correlation with other inflammatory markers [7-9].

Conclusion

Present study exhibited considerable linearity between PCT and other inflammatory biomarkers (IL-6, D-dimer, CRP) and enzymes (CPK, ALT) from 91.17% to 99.81% confirming marked precision, correlation and reproducibility amongst variable entities. Conclusion drawn that PCT showed marked tendency as a indicator biomarker not only in early phases of systemic inflammatory flare-up, but also at further stages of disease progression, in direct correlation with other inflammatory markers.

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