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Original Article

Radiology Section

Can Perinephric Fat Stranding be used as a Predictor of Renal Dysfunction in COVID-19 Patients? A Retrospective Study

NSL SUSMITHA[1], ANU KAPOOR[2], RAMAKRISHNA NARAYANAN[3]

ABSTRACT

Introduction: High Resolution Computed Tomography (HRCT) of the chest is often performed in patients with Coronavirus Disease-2019 (COVID-19) to assess the severity of lung involvement. Multiorgan dysfunction is a well-known complication of COVID-19 infection. Bilateral Perinephric Fat Stranding (PFS) is often observed in cases of COVID-19 infection while reporting the chest Computed Tomography (CT) scans, which might represent associated acute kidney injury. It is still not known whether a correlation exists between the severity of COVID-19 infection and presence of PFS or renal dysfunction.

Aim: To determine the association between PFS, Computed Tomography Severity Index (CTSI) and serum creatinine levels in patients with COVID-19 infection.

Materials and Methods: This retrospective cohort study was conducted in Department of Radiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India, from April 2021 to June 2021. A total of 90 COVID-19 positive patients of age group 21-80 years of either gender, who underwent HRCT of chest were included in the study. The chest scans were retrospectively reviewed for severity of lung involvement using a CTSI. The data collected was analysed from July 2021 to September 2021. The cases were divided equally into two groups A (n=45) and B (n=45). Group A included cases showing PFS on CT and group B included cases with no evidence of PFS. Serum creatinine levels (obtained within 24 hours of the scan) of all patients were noted and analysed to determine any possible association between the PFS, CTSI and serum creatinine levels. Analysis was done using Mann-Whitney U test, for continuous variables and Chi-square test was used for categorical data.

Results: Mean age of cases in group A was 56.16±12.31 years and in group B was 49.91±16.67 years. The mean age of patients (p-value=0.047) and the male to female ratio (p-value <0.001) was significantly higher in group A than in group B. Statistically significant association was found between PFS and serum creatinine (W=1375.500, p-value=0.003). PFS as an indicator of renal dysfunction had a sensitivity of 73.3%, specificity of 54.7%, Positive Predictive Value (PPV) of 24.4%, Negative Predictive Value (NPV) of 91.1% and a diagnostic accuracy of 57.8% with an odds ratio of 3.32.

Conclusion: Presence of PFS at imaging can serve as a useful screening tool for detecting underlying renal dysfunction in patients with COVID-19 infection.

Keywords: Acute kidney injury, Coronavirus disease-2019, Computed tomography severity index, Perirenal

INTRODUCTION

Coronavirus Disease-2019 (COVID-19) pandemic has affected lives across the globe. Since its emergence in December 2019, it has spread expeditiously [1]. The novel coronavirus primarily affects lungs with clinical presentation, ranging from mild symptoms of cough and fever to respiratory failure [2]. It is now well-known that the dysregulated immune and cytokine response in COVID-19 infection leads to systemic inflammatory response syndrome and multiorgan dysfunction syndrome. Cytokine storm and organ cross talk have been described as possible mechanisms in development of Acute Kidney Injury (AKI) in COVID-19 [3]. Prevalence of acute kidney injury in COVID-19 infection results in significant morbidity and mortality [4].

High Resolution Computed Tomography (HRCT) chest is routinely done to assess severity of lung involvement in COVID-19 infection. The upper abdomen included in the chest scans often includes complete or part of both kidneys [5]. The radiologists report includes comments regarding presence of any abnormal findings in the upper abdomen [5]. Perinephric fat stranding is one such finding that is often noted by radiologists while reading the chest scans. As it is a common observation made during pandemic with no existing literature to support.

Bilateral Perinephric Fat Stranding (PFS) is nothing but oedema in normal perinephric fat that surrounds each kidney [6]. It is considered as a non specific sign and is seen in several conditions including trauma, infection, inflammation and obstructive uropathy [7]. When noted in COVID-19 positive patients the presence of PFS might represent underlying acute renal insult and may serve as a clue for multiorgan dysfunction [8].

Literature regarding associated renal dysfunction and PFS in patients with COVID-19 infection is sparse [9]. Hence, the present study was conducted with an aim to evaluate any association between PFS, severity of lung involvement as mentioned by Computed Tomography Severity Index (CTSI) and serum creatinine as a predictor of renal dysfunction in patients with COVID-19 infection.

MATERIALS AND METHODS

This retrospective cohort study was conducted in Department of Radiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India, from April 2021 to June 2021. A total of 90 COVID-19 positive patients were included in the study and the data collected was analysed from July 2021 to September 2021.

Inclusion and Exclusion criteria: A total of 90 nasopharyngeal swab, Reverse Transcription-Polymerase Chain Reaction (RT-PCR) test positive COVID-19 patients of age range (21-80 years) and irrespective of gender, who underwent HRCT of chest were included in the study. All mild, moderate, severe cases were also included in present study. Patients with pre-existing renal pathology such as obstructive calculi, acute pyelonephritis, chronic kidney disease were excluded from the study. Pre-existing diabetic and hypertensive patients were also excluded.

The cases were divided equally into two groups

- **Group A** (n=45): This group included cases showing Perinephric Fat Stranding (PFS) on CT
- **Group B** (n=45): This group included cases with no evidence of PFS.

Study Procedure

HRCT Chest of all patients were performed on 16-slice Multidetector Computed Tomography (MDCT) (Brilliance 16TM, Philips, Netherlands). Patients were placed in a supine position with single breath hold. Scanning parameters were as follows: scan direction (craniocaudally), tube voltage (120 kV), tube current (100-600 mA)-smart mA dose modulation, slice collimation (16×0.75 mm), width (0.625×0.625 mm), pitch (0.938), rotation time (0.5 sec). All axial images were reconstructed at 1 mm slice thickness and 1 mm interval.

HRCT images were evaluated using lung window settings with window width of 1200 HU and window level of -600 HU. Severity of lung involvement was assessed following a semi-quantitative scoring system proposed by Pan F et al., which depends on the visual assessment of area of each lobe involved. The sum total of the individual lobar scores indicates the overall severity as follows [10] [Table/Fig-1]:

Severity (category):

- Mild: 1-7
- Moderate: 8-17
- Severe: 18-25

Percentage of lobar parenchymal involvement	Score
<5%	1
5%-25%	2
26%-49%	3
50%-75%	4
>75%	5

[Table/Fig-1]: Semi-quantitative lobar scoring system based on percentage of involvement.

Presence or absence of perinephric fat stranding was assessed by a single radiologist with 20 years of experience in thoracic imaging who was blinded to clinical data and serum creatinine values. All images were reviewed and evaluated using soft tissue setting with window width of +400 HU and window level of +60 HU with a slice thickness of 1 mm.

PFS was defined as thin or thick soft tissue attenuation strands extending radially or parallel to the renal capsule and/or any coalescent perirenal fluid [11].

Serum creatinine: Quantitative estimation of creatinine in serum samples were evaluated using Roche COBAS C501 clinical chemistry analyser. The normal biological reference values for serum creatinine as per our institute laboratory were as follows:

Male: 0.7-1.2 mg/dL

Female: 0.6-1.0 mg/dL

Serum creatinine values were obtained for all patients within 24 hours of the CT scan. The results were evaluated to determine any possible correlation between the PFS, CTSI and serum creatinine levels.

STATISTICAL ANALYSIS

Statistical analysis was performed by using Statistical Package for Social Sciences (SPSS) version 24.0 (SPSS, IBM, New York, NY). The continuous data were expressed as mean±standard deviation. Normality of data was checked using Shapiro-Wilk test. Spearman's correlation coefficient was used to analyse correlation between different parameters. Analysis was done using Mann-Whitney U test, for continuous variables and Chi-square test was used for categorical data. Specificity and sensitivity of PFS as a predictor of abnormal serum creatinine was calculated. A p-value of <0.05 was considered as statistically significant.

Parameters	Perinephric fat stranding	
	Group A (n, %)	Group B (n, %)
Age (year)		
21-30	1 (2.2%)	6 (13.3%)
31-40	4 (8.9%)	8 (17.8%)
41-50	5 (11.1%)	10 (22.2%)
51-60	22 (48.9%)	10 (22.2%)
61-70	7 (15.6%)	5 (11.1%)
71-80	6 (13.3%)	6 (13.3%)
Gender		
Male	44 (97.8%)	30 (66.7%)
Female	1 (2.2%)	15 (33.3%)

[Table/Fig-2]: Demographic characteristics of patient with COVID-19.

RESULTS

Mean age of cases in group A was 56.16±12.31 years and in group B was 49.91±16.67 years [Table/Fig-2]. The mean age of patients and the male to female ratio was significantly higher in group A than in group B, (p-value=0.047) and (p-value <0.001) respectively. Mean CTSI for cases in group A was 11.38±5.63 and for group B was 10.18±6.09. The mean serum creatinine value for cases in group A was 1.17±0.79 and for group B was 0.90±0.26. Statistically significant association was found between PFS and serum creatinine (W=1375.500, p-value=0.003) [Table/Fig-3].

Parameters	Perinephric fat stranding		p-value
	Group A (n, %)	Group B (n, %)	
Computed tomography severity index (Mean±SD)	11.38±5.63	10.18±6.09	0.384[2]
Severity (category)			0.313[1]
Mild	14 (31.1%)	20 (44.4%)	
Moderate	24 (53.3%)	17 (37.8%)	
Severe	7 (15.6%)	8 (17.8%)	
Serum creatinine (mg/dL) (Mean±SD)	1.17±0.79	0.90±0.26	0.003[2]

[Table/Fig-3]: Radiological and Laboratory parameters of patient with COVID-19.
*p-value <0.05 was considered as statistically significant
1. Chi-Square test,
2: Wilcoxon-Mann-Whitney U Test

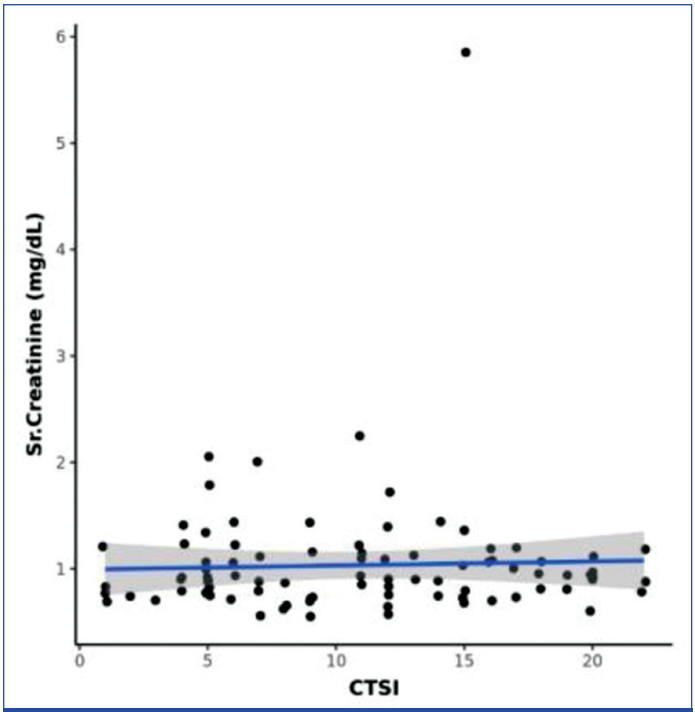
No significant association was found between presence of perinephric fat stranding and severity of disease (p-value=0.313) [Table/Fig-3].

Non parametric tests (Spearman correlation) were used to explore the correlation between the two variables, as atleast one of the variables was not normally distributed. There was a weak positive correlation between CTSI and serum creatinine (mg/dL) values, and this correlation was not statistically significant (rho=0.04, p-value=0.715) [Table/Fig-4].

Perinephric fat stranding as an indicator of renal dysfunction had a sensitivity of 73.3%, Specificity of 54.7%, PPV of 24.4%, NPV of 91.1%, Diagnostic Accuracy of 57.8% with an odds ratio of 3.32. The likelihood of elevated serum creatinine levels is 3.32 times higher in cases with PFS when compared to those without PFS [Table/Fig-5]. Some of the illustration of cases of this study are shown in [Table/Fig-6-8].

DISCUSSION

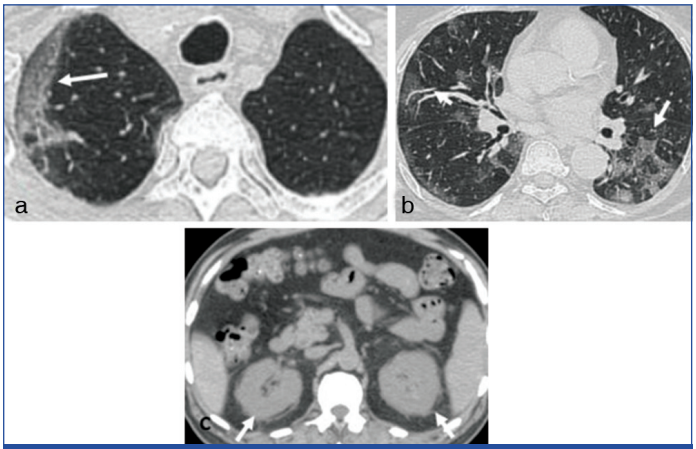
The mean age of patients and the male to female ratio was significantly higher in group A than in group B, (p-value=0.047) and (p-value <0.001) respectively. Thickened soft tissue strands in perirenal space noted in the elderly population have been described as senescent changes and do not always imply an underlying renal pathology [12]. PFS is more commonly observed in males. There



[Table/Fig-4]: Correlation between CTSI and serum creatinine (mg/dL) (n=90). The scatter plot depicts the correlation between CTSI and serum creatinine (mg/dL). Discrete points represent individual cases. The blue trend line represents the general trend of correlation between the two variables. The shaded grey area represents the 95% confidence interval of this trend line.

Variable	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
Perinephric fat stranding	73.3% (45-92)	54.7% (43-66)	24.4% (13-40)	91.1% (79-98)	57.8% (47-68)

[Table/Fig-5]: Study parameters for predicting serum creatinine.

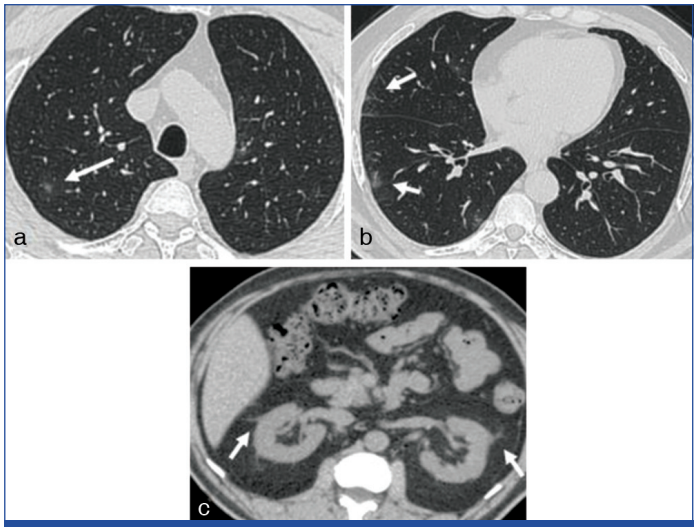


[Table/Fig-6]: A 63-year-old male patient with COVID-19 infection of moderate severity (CTSI=15), serum creatinine 0.95mg/dL. Axial non enhanced HRCT scan sections of chest in lung window, showing; a) patchy ground glass opacities in right upper lobe; b) bilateral subpleural ground glass opacities in middle lobe and bilateral lower lobes (arrows); c) Axial non enhanced soft tissue window sections showing wisps of perinephric fat stranding around both kidneys (arrows).

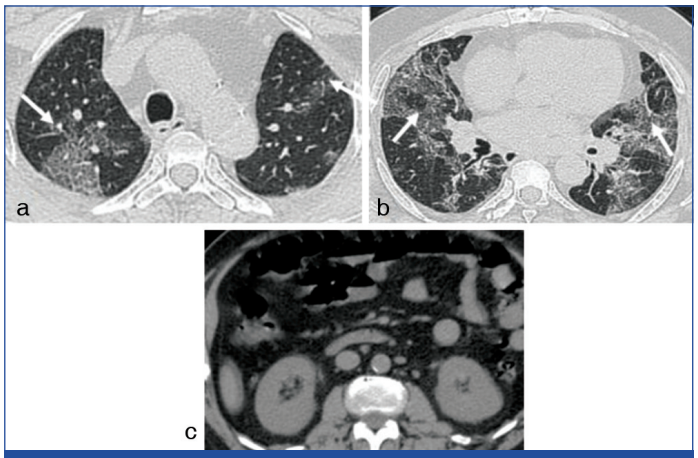
was not much difference between mean CTSI of both the groups. So, the occurrence of PFS is not determined by CT severity score.

There was no significant correlation between CTSI and serum creatinine. Cheng Y et al., found that patients with elevated serum creatinine were more likely to develop AKI in patients with COVID-19 infection [13]. Thus, laboratory monitoring is required in all the patients irrespective of CT severity score.

In the present study, the mean serum creatinine value for cases in group A was higher than group B (p-value=0.003). The current study showed that PFS as an indicator of renal dysfunction had a sensitivity of 73.3%, specificity of 54.7%, PPV of 24.4%, NPV 91.1%. PFS as a sign had moderate sensitivity and specificity, low PPV, high NPV. Odds of having raised serum creatinine in presence of PFS was 3.32 times those when PFS was absent.



[Table/Fig-7]: A 58-year-old male male patient with COVID-19 infection of mild severity (CTSI=6), serum creatinine 1.38 mg/dL; a) Axial non enhanced HRCT scan sections of chest in lung window, showing ground glass opacity in right upper lobe, (arrow); b) subpleural ground glass opacities in middle lobe and right lower lobe (arrows); c) Axial non enhanced soft tissue window sections showing wisps of bilateral perinephric fat stranding (arrows).



[Table/Fig-8]: A 62-year-old male patient with COVID-19 infection of severe category (CTSI=20), serum creatinine 0.9 mg/dL; a); b) Axial non enhanced HRCT scan sections of chest in lung window showing subpleural patchy ground glass opacities in bilateral upper lobes, middle lobe and bilateral lower lobe (arrows); c) Axial non enhanced soft tissue window sections showing absence of perinephric fat stranding.

This study also has sparse literature to support the hypothesis, as COVID-19 is a recent disease. Further evaluation of PFS in a larger cohort of COVID-19 patients with age and sex matched controls is recommended.

Limitation(s)

The limitations include, a small sample size and lack of age and sex matched controls.

CONCLUSION(S)

Presence of PFS at imaging can serve as a useful screening tool for detecting underlying renal dysfunction in patients with COVID-19 infection. However, due to its low sensitivity and specificity, it cannot be used as diagnostic test. Presence of this sign should be interpreted with caution in elderly, needs to be mentioned in report, so that it can alert clinicians for possibility of underlying renal dysfunction.

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PARTICULARS OF CONTRIBUTORS:

1. Postgraduate Student, Department of Radiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.
2. Professor, Department of Radiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.
3. Associate Professor, Department of Radiology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. NSL Susmitha,
Postgraduate Student, Department of Radiology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad-500082, Telangana, India.
E-mail: susmithanarakuchi@gmail.com

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