

Research Article

Correlation of Radiological Findings (High Resolution Computed Tomography Chest) with Anti-SARS-COV-2 Antibodies in Patients Visiting Tertiary Care Hospitals

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Abstract

Background: Coronavirus (COVID 19) pandemic has taken so many lives and has contributed to an increase in morbidity due to its complications. The research is still in infancy and much has yet to be investigated.

Objective: To correlate the HRCT findings on chest with antibody testing in patients visiting tertiary care hospitals in Lahore.

Methodology: Three hundred and thirty-two patients with mild, moderate and severe symptoms of COVID 19 were recruited. Those with raised CRP levels were sent for HRCT chest and PCR testing as protocol of the hospitals. All patients were tested with Rapid antibody kits for reactivity.

Results: Showed that males were affected more than females. Similarly, non-health care workers were more affected. All patients with bilateral involvement of lungs on HRCT chest and positive PCR findings also tested reactive on antibody testing. However, a few people with bilateral lung involvement and negative on PCR testing got reactive results on Rapid antibody testing. Linear regression model shows significant correlation of HRCT chest findings with Anti-SARS-COV 2 antibodies.

Conclusion: HRCT findings (Unilateral and bilateral lung infiltrates) correlated significantly with Anti SARS-COV 2 Antibodies.

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Key Words: Anti _SARS-COV2 antibodies, HRCT, PCR, COVID 19

Introduction:

The second wave of COVID 19 has surfaced worldwide in developed as well as developing countries. The data shows that in Pakistan the severity has increased, 2665 new cases and 59 deaths have been reported in Pakistan as of November 22, 2020¹. Positive infectivity rate in Pakistan is 7.46% (Official website, Government of Pakistan, 2020). The confirmed diagnoses of COVID 19 depend on molecular testing i.e. polymerase chain reaction (PCR of RNA virus). The limited infrastructure created a backlog of testing in developing countries. Peeling et al, 2020 suggested that the Rapid antibody testing of good performing characteristics

may supplement in screening COVID 19 patients and prevent unnecessary isolation of false positive individuals due to cross reactivity with seasonal flu^{2,4}.

Seroconversion period time after the infection of SARS-CoV-2 and formation of IgM and IgG are varied in studies. Studies have stated that the formation of antibodies IgG and IgM after infection with virus were noticed at an early stage after the onset of symptom in some patients, and at intermediate stage or lately in others. The time period of formation of IgM was shorter than IgG^{5,6}. Some studies found that the median seroconversion period was between 10 to 12 days for IgM and 12 to 14 days for IgG^{7,8}. However, another study

reported seroconversion period for IgM was 09 days and 7 – 9 days for IgG after the appearance of symptoms⁹.

The relationship between severity of disease and levels of IgM and IgG were also studied. One study found no relation between the serum values of IgM and IgG and disease severity; however, they found a rapidly increase in antibody response in cases with COVID 19 that concluded in death. Another study observed no significant differences in the values of IgM and IgG antibodies in between patients with different levels of severity of disease. Duration of IgG antibodies in serum of COVID 19 patients is still not established, however it varies from one to three months in some studies^{9,10}.

Although RT-PCR testing is gold standard for detecting COVID 19, some hospitals recommend concomitant HRCT for patients presenting with increased CRP levels. Radiological findings based on HRCT were found to be more specific and sensitive compared to RT-PCR in several studies due to false negative/positive results of PCR testing¹¹⁻¹³.

As the weather turned cold and cases of seasonal flu were on the rise in November in Pakistan, it was not feasible for PCR testing to be done on all patients presenting flu like symptoms due to limited resources in Pakistan. However, to prevent the spread of infection Rapid antibody testing may supplement to identify the true cases of COVID 19. Therefore, the study was designed to determine the Rapid antibody testing in patients presenting symptoms resembling COVID 19. HRCT and PCR testing were done on all patients with similar symptoms but with increased CRP levels.

Objective:

The objective of the study was to determine the correlation of radiological findings in lungs on HRCT with anti-SARS COV-2 antibodies in symptomatic patients visiting tertiary care hospitals of Pakistan during second wave of COVID 19.

Methodology:

A prospective cross-sectional study conducted from October to December 2020 at Shalamar Medical and Dental College (SMDC), Lahore, and CMH Kohat, Pakistan after approval from Institutional review Boards. The study included 332 adults of both gender

with age range of 18 to 65 years visiting the OPD of the hospitals. Informed consent was taken and methodology explained to them. Those who consented for participation were included in the study.

Those having current symptoms of flu, headache, loss of sense of taste and smell, persistent cough, shortness of breath, diarrhea, redness of eye were included. The ones who were healthy and asymptomatic were excluded. The patients were assessed clinically by the pulmonologist and suspected COVID 19 patients with high CRP levels were asked to get HRCT –chest done and samples were sent for RT-PCR. Mild, moderate and severe cases were characterized on basis NIH COVID treatment guidelines 2020¹⁴.

They were also analyzed for antibodies to SARS-COV 2 virus by rapid antibody test (point of care testing) done in 15 minutes. It was accomplished through using strips (Genrui- Novel Coronavirus (2019n-COV) IgG/IgM test kit) provided by Getz Pharma. The technique is based on lateral flow immunoassay (LFIA) that detects the antibodies within 15 minutes. The score on radiological findings was determined to assess the severity of the disease¹⁵.

Results:

SPSS 23 was utilized for data analysis. Mean \pm Standard deviation were used to present quantitative data and frequency (percentage) was used for qualitative data. Linear regression model was used to determine association of demographic characteristics and clinical markers with antibody status (reactive versus non-reactive). p value was obtained using Chi square test.

p value \leq 0.05 was considered significant.

Table 1 displays age of the patients which is 42.03 years \pm 15.51. There were more male patients compared to

Table 1: Descriptive Characteristics of Symptomatic Suspected COVID 19 patients (n=332)

Characteristics		Statistic (%)
Age		42.03 \pm 15.51
Gender	Male	183 (55.1)
	Female	149 (44.9)
Profession	Medical Students	44 (13.3)
	Doctors	75 (22.6)
	Hospital staff	55 (16.6)
	OPD Patients	158 (47.6)

Symptoms	Mild	176 (53.0)
	Moderate	144 (43.4)
	Severe	12 (3.6)
HRCT results	Normal	185 (55.7)
	Unilateral	38 (11.4)
	Bilateral	109 (32.8)
Rapid antibody Tests	Non-reactive	74 (22.3)
	Reactive	258 (77.7)

Mild Illness: Individuals who have any of the various signs and symptoms of COVID-19 (e.g, fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.

Moderate Illness: Individuals who show evidence of lower respiratory disease during clinical assessment or imaging and who have an oxygen saturation (SpO₂) \geq 94% on room air at sea level.

Severe Illness: Individuals who have SpO₂ <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO₂/FiO₂) <300 mm Hg, respiratory frequency >30 breaths/min, or lung infiltrates >50%.

(NIH COVID treatment guidelines February 2021)

female (55.1% versus 44.9%). Patients visiting hospital OPD (47.6%) were more compared with medical doc-

tors, medical students and hospital staff (22.6%, 13.3% and 16.6% respectively. 53% were mild cases, 43.4% moderate and 3.6% were patients with severe symptoms according to NIH COVID treatment guidelines February 2021. HRCT results shows bilateral infiltrates in 32.8% cases while were unilateral in 11.4% cases. The rest were normal with no infiltrates (55.7%). Rapid antibody test was positive in 258 (77.7%) cases. Association of demographic characteristics and clinical markers with antibody status (reactive versus non-reactive) was determined by Linear regression model Table 2). Odds Ratio was determined and significance correlated. The odds of the individual having moderate symptoms were 22 times higher with respect to non-reactive antibody results. The odds of unilateral and bilateral HRCT results with reactive antibody results increased many folds, adjusting the model for age gender, profession and symptoms. The HRCT results with infiltrates were significant when adjusted with antibody reactivity. PCR test was done in 147 patients in whom infiltrates were detected on HRCT (Table 3). Out of 147 patients, 109 had bilateral infiltrates of which 33.3% were PCR positive and 40.8% PCR negative. However, 51.02% were reactive on antibody test. Unilateral infiltrates were found in 38 cases amongst which, 1.36% were PCR positive and 2.04% were reactive on antibody test. Out of 185 symptomatic patients who were taken as normal and were not recommended PCR, 180 were found to be

Table 2: Association of Demographic Characteristics and Clinical Markers with Antibody Status

Characteristic		Crude OR	95% CI	Adjusted OR	95% CI
Age		1.03	1.01-1.05	1.02	0.99-1.04
Gender	Male	1.00		1.00	
	Female	0.95	0.56-1.59	1.03	0.58-1.83
Profession	Student	1.00		1.00	
	Hospital faculty	0.89	0.40-2.00	0.60	0.23-1.53
	Hospital staff	1.23	0.51-2.98	0.77	0.28-2.13
	Patient	2.46	1.12-5.39	0.86	0.32-2.34
Symptoms	Mild	1.00		1.00	
	Moderate	2.46	1.40-4.32	0.22	0.07-0.67*
	Severe	4.61	0.58-36.65	0.36	0.03-4.46
HRCT results	Normal	1.00		1.00	
	Unilateral	9.07	2.12-38.92	28.90	4.84-172.81*
	Bilateral	4.99	2.43-10.24	15.40	4.19-56.63*

Association was determined by applying Linear Regression Model

Table 3: RT-PCR and Rapid antibody Tests in Patients with Unilateral and Bilateral Infiltrates

HRCT N=147 (%)	PCR positive	PCR Negative	Rapid Antibody Reactive	Rapid Antibody Non- Reactive	P value
Bilateral infiltrates (n=109)	49(33.3%)	60(40.8%)	75 (51.02%)	34 (23.1%)	<0.0001
Unilateral Infiltrates (n=38)	2(1.36%)	36(24.48%)	3(2.04%)	35(23.80%)	

P value was obtained by applying Chi square test. P value <0.05 was considered significant

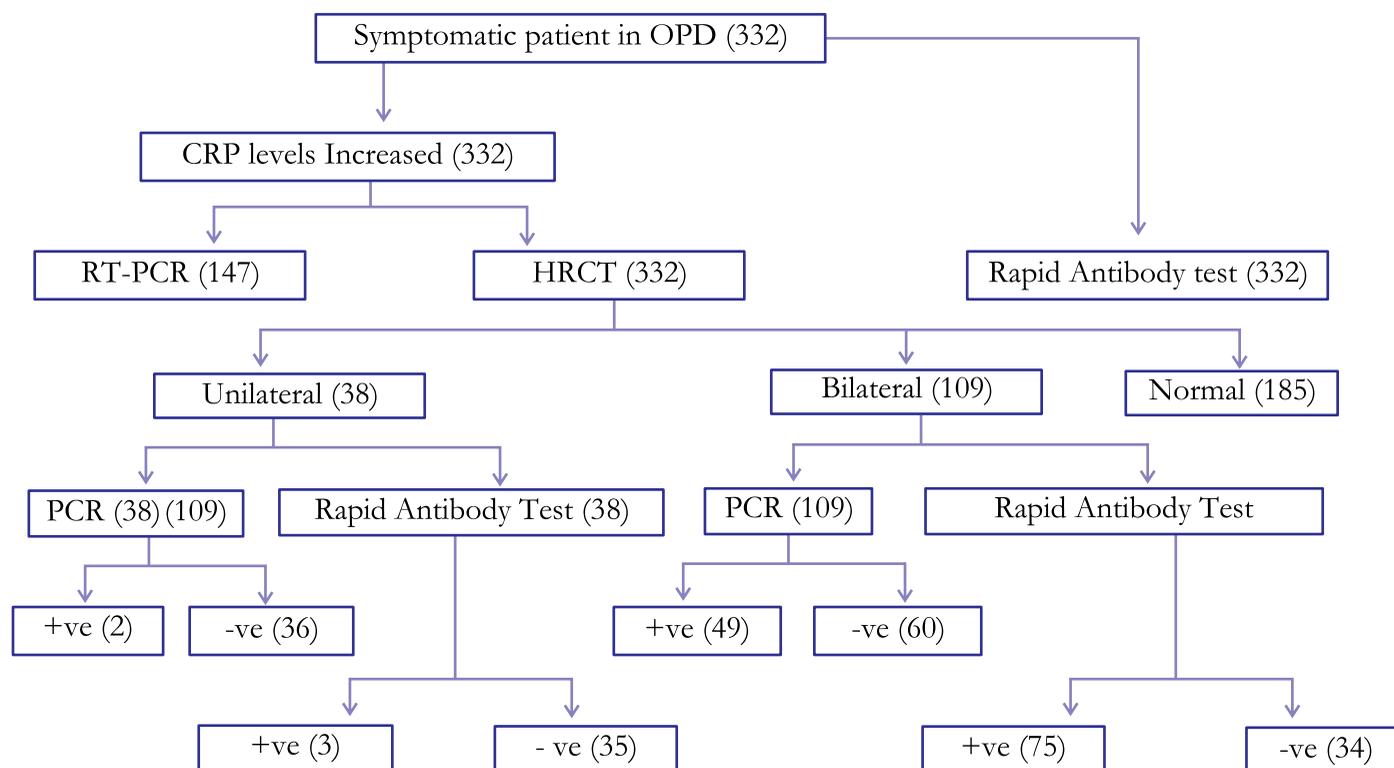
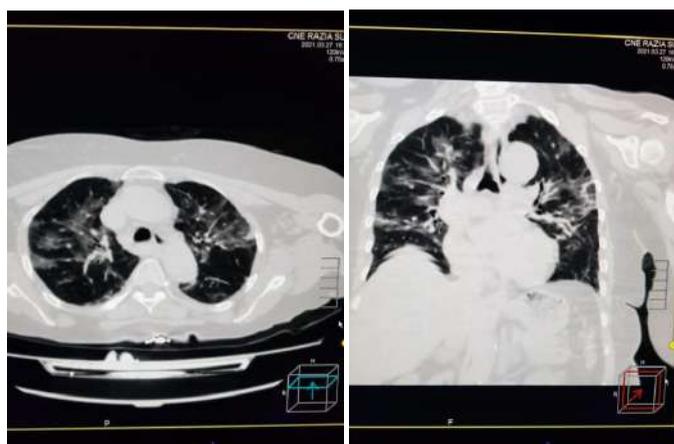
**Figure 1:** Flow chart showing Number of Patients with Investigations done on Visit to Tertiary Care Hospital

Figure: 2A

Figure 2B

Bilateral patchy random ground glass opacities and septal thickening in upper lobes, representing pneumonia, COVID-19 pattern.

Figure 2: HRCT Chest Axial and Coronal Images

reactive on antibody test. This shows that these cases were missed and were considered as normal flu but detected on antibody testing.

Figure 1 shows the details of the investigations done on number of patients presenting in hospitals. Figure 2 shows HRCT findings showing infiltrates in lungs.

Discussion:

The second wave of COVID 19 was seen in November-December 2020 in Pakistan, but the dilemma was that most of the people normally experience flu like symptoms every year with changing weather situations. This year it was difficult to differentiate between flu and COVID 19 as false negative reports by PCR testing was also on rise. The study included symptomatic patients visiting tertiary care hospital pulmonology department

with symptoms of flu, loss of taste and smell, sore throat, persistent cough, redness of eye or diarrhea. Suspected COVID 19 patients were referred for HRCT and PCR after CRP was found to be raised. Rapid antibody testing was also done in all patients with mild, moderate or severe symptoms.

Peeling et al., in the study emphasized the need for rapid antibody testing in countries where molecular testing capacity by PCR is limited. Developing countries do have challenges with molecular tests due to limited facilities and financial resources, therefore rapid serology tests are cost effective alternative. It helps to identify the true cases and avoid unnecessary quarantine to subjects with seasonal flu².

Our study showed that males were more affected than females. Patients presenting in OPD were more as compared to healthcare workers and medical students. This may be due to the fact that males in our society have to go out for work and other shores as compared with females who prefer to remain indoor. Majority patients presents with mild symptoms followed by moderate and severe cases. Similarly HRCT results were normal in most cases followed by bilateral and then unilateral involvement of the lungs. Several studies also demonstrates the highly specific role of HRCT chest in confirming the diagnosis of COVID 19 compared with RT-PCR and Chest radiography¹⁶⁻¹⁸. Rapid antibody tests were reactive in most cases. 33% with bilateral infiltrates were positive on PCR testing but 51.0 % were reactive on antibody testing. However only 2 cases with unilateral infiltrates who had atelectasis, tuberculosis or emphysema on HRCT had PCR positive results and 3 showed reactive antibody tests. A study conducted in Radiology department Lahore General Hospital done on 94 patients revealed that 83% patients had positive HRCT chest findings of COVID-19, 17% had negative HRCT chest findings; while 40.4% had positive and 59.6% had negative first PCR. The sensitivity, specificity, NPV, PPV and accuracy of HRCT chest was 92%, 23%, 81%, 45%, and 51%; while of first RT-PCR was 45%, 81%, 23%, 92% and 51%, respectively¹⁷. The cause may be due to inadequate sampling for PCR or may be the time of presentation of patients is more than ten days after which PCR gets negative. Most of the patients do not want to visit hospital until it is absolutely necessary due to social stigma of COVID 19 and

limited resources of the patients in Pakistan. It is also evident from the results of our study that antibody tests of these patients were reactive which occurs after 7 to 10 days of illness. Linear regression model was applied to determine the correlation of demographic characteristics and clinical markers with antibody status. The study showed that the odds of the individual having moderate symptoms were 22 times higher with respect to non-reactive antibody results. It may be the result of time duration of onset of symptoms and the antibody testing done or false negative results of antibody testing. The odds of HRCT results with reactive antibody results increased many folds, adjusting the model for age gender, profession and symptoms. This showed the significance of Rapid antibody testing in patients in addition to PCR testing. The missed cases may be detected through this method which is cheap and less time consuming especially in developing countries where resources are limited and patients are reluctant to spend more on their health than to provide themselves with basic needs².

A study conducted in Peru where 42534 cases out of 355, 604 tested positive and 26 362 were positive by rapid test. This leads to identification of group of symptomatic subjects in the society. This results in relief in the backlog, waiting time reduction and prevents burden on health-care system. A study in China shows that rapid antibody testing may result in more detection of COVID-19 symptomatic patients. Further long-term prospective studies are needed to get an insight into the performance and efficacy of rapid antigen-antibody tests and the timing of testing. Large number of individuals with mild or no symptoms, have been shown in studies to transmit infection¹⁵.

Conclusion:

HRCT chest findings correlate significantly with Anti-SARC-COV2 antibodies. The patients with bilateral infiltrates but PCR negative were observed to be reactive on Rapid antibody testing. Moreover most of the mild cases were also reactive to Rapid antibody testing.

Recommendations:

Rapid antibody test may be able to pick up the cases which are not recommended for PCR testing either due to limited resources or considered as seasonal flu.

Ethical Approval: Given

Conflict of Interest: The authors declare no conflict of interest.

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