Original Article

Comparison of Features of Corona Virus in Confirmed and Unconfirmed Patients In Lahore

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Abstract

Introduction: Coronavirus has spread rapidly in Pakistan. These patients were kept at quarantine facilities on suspicion, even before RT-PCR was done. We were able to collect clinical, laboratory, and management features from them.

Objective: To assess the features of Corona confirmed and unconfirmed patients, and compare them. It could help in deciding if confirmed and unconfirmed patients were correctly identified and managed appropriately.

Material and Methods: Retrospective, Descriptive, Crossectional study between 8th April to 30th April 2020. Patient data was collected from different sites retrospectively, on a Performa. Clinical, Laboratory, and Management data as collected. It was analyzed on SPSS 23. All patients in quarantines and ICU were included, irrespective of their corona PCR status, if the treating physicians had a strong suspicion. Home quarantine and less than 15-year old patients were excluded.

Results: Clinical features showed more preponderance for males and smokers. Chronic disease patients were also significantly involved. Fatigue, nasal congestion, runny nose, sickness, and vomiting were more common in confirmed patients. CURB 65 scores 3 and 4 were more in unconfirmed patients. CT involvement was more common in unconfirmed patients as was high white cells and neutrophils. More patients had mechanical ventilation in the unconfirmed group, and they also had more secondary infections and shock. Antibiotic use was more common in the confirmed group.

Conclusion: Corona was more common in males and smokers. Though fever and cough were common, the presence of fatigue, runny nose, nasal congestion sickness, and vomiting discriminated confirmed patients. Antibiotics should be used irrespective of RT-PCR results, especially if CT showed an abnormality.

Keywords: Coronavirus, Confirmed, Features, Fatigue, Antibiotic.

Introduction

Since the reporting of the first case in Pakistan of coronavirus in February 2020, it was evident that the disease will spread here.[1] Steps were taken to decrease the impact, but it was inevitable. With current positive cases exceeding 54000, the burden of disease was anticipated more here as compared to developed countries, due to lack of resources. Even developed nations were finding it difficult to address problems related to it.[2]

Different features were already reported in studies, with evidence suggesting the presence of them in both confirmed and unconfirmed patients. Quarantine was a very important part of management to tackle spread.[3] We also faced an additional problem because of the scarcity of testing kits for coronavirus, initially. Because there was a deficiency in information about the novel coronavirus, healthcare professionals were also not sure about many things, including which type of mask was needed for them, let alone deficiency of Personal protective equipment.[4] There were a lot of patients with symptoms, who came in contact with health professionals and were either not tested, or their results came back negative. Even ARDS patients were reported in an emergency without test report availability. It emphasized the need to compare confirmed and unconfirmed patients. Coronavirus had affected global economies, and China was the only country, documenting positives out of it.[5] Pakistan being a developing country, it became more important to identify cases clinically and decrease the burden of disease.

Liu et al[6] compared the clinical features of the elderly with middle age and young patients of Covid-19. They found that elderly patients had higher mortality with this disease. This study was on a very small number, and just targeted confirmed pneumonia patients. Our study identified the difference in features of all unconfirmed and confirmed patients in different age groups. We had different patterns of co-morbidities, exposure to infections, and vaccination patterns. It was worth including all such cases and observing in our setup. Cao et al[7] studied case series of only 102 adult patients of Covid-19. They compared treatments, features, and laboratory results, with outcomes retrospectively. Our study was different from them. The policy adopted by relevant authorities was to quarantine all suspected and probable patients, before testing in a supervised facility, until tested negative or developed features warranting further observation despite being negative. Therefore, we had higher admissions of those who were later discharged as Corona PCR was negative. It was therefore possible for us to include these patients and observe their features in comparison with those who were tested positive.

The study aimed to assess the features of Corona confirmed and unconfirmed patients, and compare them. These features included clinical, laboratory, and treatment features. It can help us in deciding if confirmed and unconfirmed patients were correctly identified and managed appropriately, and decrease mortality and burden on the resources.

Material & Methods

According to the policy of the government, all patients were kept in quarantine, having strong suspicion, at different designated areas in the city. After testing, PCR negative patients were allowed to go home. We collected this data in quarantine areas only, which were multiple. Retrospectively, the collection was done after Ethical Committee approval. Also, data was collected from patients who were admitted in different intensive care facilities in serious condition. They were confirmed as well as unconfirmed, as admission was in serious condition with insufficient time for testing. Some patients were serious but reported negative, but still, their clinicians were suspecting Covid-19 strongly, and re-sampling was sent.

Study Design:

It was a Descriptive, Crossectional Study, with data collection retrospectively from 8th April to 30th April 2020, after ERC approval.

Included were all patients admitted in quarantine with suspicion, probable or confirmed, and were above the age of 15. Excluded were all non-admitted patients who were having suspicion but not meeting criteria for admission. We also excluded those who were in self-isolation at homes.

Statistical Analysis:

Data was divided into Continuous and Categorical variables. Continuous variables as mean and ranges and Categorical variables as numbers (percentages). A correlation was calculated in categorical data and P values in Continuous variables were determined through ANOVA Test.

The statistical software package of social sciences (SPSS 23.0) was used for analysis and P values <0.05 were considered significant.

Results

Features were compared in three different tables, described as under:

Basic Clinical Features (Table 1)

A total of 488 patients were included. The majority were confirmed patients. The elderly and young and middle-age patients in both confirmed and unconfirmed groups were almost equal and statistically not significant. Male patients were predominant in the confirmed group as was smoking history, and females more frequent in the unconfirmed group. The P-value was also significant for Gender and smoking. There was a more frequent history of chronic liver disease, chronic kidney disease, ischemic heart disease, and cerebrovascular accidents in unconfirmed patients, whereas diabetes, hypertension, and persistent atrial fibrillation were more prevalent in confirmed patients. These findings were all statistically insignificant.

The cough was more common in unconfirmed patients. Fever was equally present in both groups. Both these values were statistically insignificant. Fatigue, nasal congestion, running nose, and sickness and vomiting were more frequent in confirmed patients and these were also statistically significant. When CURB 65 score was applied, scores 0, 1, and 2 were almost comparable in both groups. However, score 3 and 4 were more frequent in the unconfirmed group, but statistically insignificant.

Table 1: Basic Clinical Features

	Confirmed Cases(%)	*Unconfirmed Cases %*	*P-Value*
Total	**321 (65.8%)**	**167 (34.2%)**	
Age			
Elderly	31 (9.7%)	21 (12.6%)	0.323
Young & Middle Aged	290 (90.3%)	146 (87.4%)	
Gender			
Male	270 (84.1%)	119 (71.3%)	0.001
Female	51 (15.9%)	48 (28.7%)	
Smoking History	126 (39.3%)	29 (17.4%)	0.000
Past Medical History			
Chronic Liver Disease	4 (1.3%)	3 (1.8%)	0.631
Chronic Kidney Disease	9 (2.8%)	9 (5.4%)	0.151
Diabetes	40 (12.5%)	18 (10.8%)	0.579
Hypertension	98 (30.5%)	43 (25.7%)	0.270
Ischemic Heart Disease	5 (1.6%)	7 (4.2%)	0.075
Persistent Atrial Fibrillation	3 (0.9%)	0 (0%)	0.211
Cerebro-vascular Accident	2 (0.6%)	5 (3.%)	0.037
Clinical Symptoms			
Cough & Sputum	79 (24.6%)	64 (38.3%)	0.054
Fever	269 (83.8%)	139 (83.8%)	0.873
Fatigue	251 (78.7%)	107 (64.1%)	0.000
Nasal Congestion	153 (47.8%)	35 (21%)	0.000
Runny Nose	162 (50.8%)	33 (19.8%)	0.000
Sick & Vomit	86 (27%)	25 (15%)	0.003
Curb 65 Score			0.332
0	269 (86.5%)	143 (86.56%)	
1	29 (9.3%)	14 (8.4%)	
2	10 (3.2%)	5 (3.0%)	
3	1 (0.3%)	2 (1.2%)	
4	2 (0.6%)	3 (1.8%)	

Laboratory Features (Table 2)

During hospitalization, unconfirmed patients had more involvement of CT scan for multiple lobe lesions, single lobe lesions or no involvement at all. Single lobe was more involved than multiple lobes and Pleural Effusion was more common in the confirmed group. The P-value was not significant. There was a significant number in the confirmed group where CT was not performed.

In the routine blood examination, high white cell count, high neutrophil count, lower lymphocyte count and, low C-reactive protein were documented in unconfirmed patients. P-value was also significant in all, except white cell count. Hemoglobin, Platelet, and serum creatinine were similar in both groups.

Table 2: Laboratory Features

	Confirmed Cases %	*Not Confirmed Cases %*	*P-Value*
Total	**321 (65.8%)**	**167 (34.2%)**	**0.475**
CT Results			
Multiple Lobe Lesion	19 (5.9%)	11 (6.6%)	
Single Lobe Lesion	25 (7.8%)	48 (28.7%)	

Pleural Effusion	8 (2.5%)	2 (1.2%)	
Not Done	184 (57.3%)	4 (2.4%)	
None	75 (23.4%)	98 (58.7%)	
Lab Indicators at Admission			
White Blood Cell Count	7.44 (3.50-12.90)	7.79 (4 - 33)	0.083
Total White Blood Cell Increased	59 (18.4%)	26 (15.6%)	0.438
Total White Blood Cell Increased	262 (81.6%)	141 (84.4%)	0.438
Neutrophil proportion	71.6 (3.20 - 92)	71.46 (50 - 96)	0.846
Increased Neutrophil Proportion	53 (16.5%)	90 (53.9%)	<0.001
Lymphocyte Ratio	26.92 (8 - 35)	21.68 (7 - 76)	<0.001
Decreased Lymphocyte Ratio	296 (92.2%)	157 (94.0%)	0.466
C-Reactive protein	7.39 (2 - 35)	3.93 (0.8 -35)	<0.001
Hemoglobin	12.35 (8 - 16)	12.55 (4.1 - 16)	0.221
Platelet	*260.62 (105 - 554)*	*244.14 (50 - 432)*	*0.005*
Serum Creatinine	28.72 (12 - 85)	30.53 (13 - 87)	0.025

Management Features (Table 3)

It was observed that there were more patients with Invasive ventilation in the unconfirmed group. The confirmed group had more non-invasive ventilation. P-value was not significant here. There were less Discharged and Healed patients in the unconfirmed group, as was more frequent death in this group. The P-value was not significant. Acute Kidney Injury, Secondary Infection, and Shock were more frequent in the unconfirmed group, whereas ARDS, Acute Heart Injury was more frequent in the confirmed group. The P-value of only Secondary Infection was significant in favour of unconfirmed patients. Patients in both groups were treated symptomatically equally, but the antibiotic use was more frequent in the confirmed patient. Chloroquine or Hydroxychloroquine use was more frequent in the unconfirmed group. The P-value was again not significant.

Table 3: Management Features

	Confirmed Cases %	*Unconfirmed Cases %*	*P-Value*
Total	**321 (65.8%)**	**167 (34.2%)**	
Comorbidities			
Acute Respiratory Distress Syndrome (ARDS)	24 (7.5%)	5 (3.0%)	0.115
Acute Heart Injury	1 (0.3%)	0 (0%)	**0.470**
Acute Liver Injury	**0 (0%)**	**0 (0%)**	**-**
Acute Kidney Injury	5 (1.6%)	8 (4.8%)	0.036
Secondary Infection	4 (1.3%)	9 (5.4%)	0.007
Shock	3 (0.9%)	3 (1.8%)	0.413
Treatment Given			
Symptomatic	285 (88.8%)	149 (89.2%)	0.12
Antibiotic	35 (10.9%)	11 (6.6%)	
Chloroquine or Hydroxychloroquine	1 (0.3%)	3 (1.8%)	
Mechanical Ventilation			
Invasive	1 (0.4%)	3 (1.9%)	0.113
Non-Invasive	276 (99.6%)	159 (98.1%)	
Prognosis			
Healed & Discharged	318 (99.1%)	161 (96.4%)	0.038
Death	3 (0.9%)	6 (3.6%)	

Discussion

Comparing clinical, laboratory, and management feature was important in understanding this disease. Evidence was scarce on this virus locally, especially when it was already here and spreading rapidly. Guo et al[8] had documented that adults with co-morbidities were more likely to be victims of this virus with an average age of around 58 years. An important observation in our study was that the young and middle-aged population was almost equally affected in both groups. Qin et al[9] documented that more males had severe disease. Vardavas and Nikitara et al[10] had published more severity of Covid-19 in smokers. Our

study also suggested similarly. The reason for male predominance in the confirmed group was not known in our population but could be postulated to our social circumstances, where males go out for work and were more exposed. The same reason could also be postul ated for smoking, as smokers had badly affected the lungs. More studies were needed to confirm these findings.

Wickmann et al[11] performed autopsies in patients to document the cause of death. They confirmed the role of chronic diseases, especially of the lung in their studies. Also, viral levels were found high in other organs in their study. We could not justify why few chronic diseases were more frequently involving unconfirmed group, and others like diabetes and hypertension more in the confirmed group. One possibility was that the presence of chronic disease affects the immune status, making them more likely to be involved. But why the unconfirmed group had more organ involvement, was not explainable. A possibility could be that they were affected due to already existent disease, or involvement due to some other secondary cause. Further clinical evidence is needed in support. Lie et al[12] documented false-negative results in their study and emphasized the importance of correct technique for the collection of the RT-PCR test. In our study, we raised a question on the methodology used for doing PCR for Covid-19, the area from where a sample was taken, competency of the person taking the sample, and reliability of laboratory. These questions could also be further analyzed in future studies.

Jin et al[13] documented a whole series of gastrointestinal and other features in patients with Covid-19. They concluded that some symptoms could also appear, other than classical symptoms outside china. This was also a significant finding in the symptomatology in our study. Although fever was the most common symptom in both groups, Fatigue, nasal congestion, running nose, sickness, and vomiting were more frequent in the unconfirmed group, and more statistically significant in the confirmed group. The cough was more in the unconfirmed group and statistically insignificant. It suggested that the presence of these features were a better indicator of corona infection. Is it a feature that was different in our patients? We don't know yet, but should also be investigated in the future. We know from the literature that cough and fever appear early, whereas fatigue was present later in the disease, as was sickness and vomiting.[6] It appeared that if the Covid-19 test was negative, we should recheck, especially if the patient developed fatigue, runny nose, and sickness and vomiting.

Chen et al[14] documented the features and calculated MuLBSTA score for predicting mortality in severe pneumonia cases due to Covid-19. We used CURB 65 score, as it was convenient for us, but it was unexpected finding to note high scores of 3 and 4 in unconfirmed patients. A possible explanation could be another infection, bacterial or viral, causing this deterioration. This was supported by high white cell count, high neutrophils, and low lymphocytes in this group. But we could not explain then, why C-reactive protein was low in these patients. It was therefore required to do more studies to confirm these findings in this setup. Another possibility was poor testing quality due to multiple reasons.

Rothan and Byrareddy[15] found that CT was more convincing in confirmed patients for diagnosis. We also found that a CT scan was an important tool to confirm lung findings, but we could not do it in many patients in this study. The reason could be the condition of the patient or lack of resources. However, to find that more unconfirmed patients had multiple lobes or single lobe involvement was unexpected, especially with single lobe more in unconfirmed patients. It meant that either there was another pathology which could not be found, or the unconfirmed group had a false negative result, which should have been rechecked. It was also a different finding and suggested that further studies should be carried out in our setup.

Misra et al[16] published in Rheumatological patients that cytokine storm in Covid-19 patients can cause susceptibility to infections. They however emphasized that immune-suppressive treatment should be continued. In our study, we expected that chronic disease patients would be more, and was documented as well, but why Kidney injury, Secondary infection and shock was more frequent in the unconfirmed group, was unexplained. A possible reason could be missing secondary infection, inappropriate treatment, and hydration status in this group. This was also suggested by documentation of less frequent antibiotic use in the unconfirmed group. We knew that patients were initially kept in quarantine before tests, but discharged with medication once a single Covid-19 test was negative. Did they took that treatment at home, and was that including antibiotics could not be confirmed in this study. We suggest more studies to endorse it. Yazdany and Kim et al[17] documented that use of Chloroquine and Hydroxychloroquine should be restricted until sufficient data is available through

randomized controlled trials. They also recommended against prophylaxis, until the evidence is available. Our study findings were that there was more use of Chloroquine or Hydroxychloroquine in the unconfirmed group. Has it interfered with the Covid-19 PCR? Was it helpful or not? We cannot say through this study and suggest the need to confirm it in future studies. We also found that death was more frequent in unconfirmed patients in this study. A possible explanation could be a secondary infection, decreased use of antibiotics, frequent discharge, and readmission once developed a serious complication.

Conclusion

We concluded that Covid-19 was present in both adults and young and middle ages in our study. Males were predominantly affected, as were smokers. Chronic disease patients were present on both confirmed and unconfirmed patients, but diabetics and hypertensive were more common in the confirmed group. Though cough and fever were most common in both groups, Fatigue, runny nose, nasal congestion, sickness, and vomiting if present, strongly favoured Covid-19 and if RT-PCR was negative, it should be repeated in such patients. All severely sick patients should receive antibiotics aggressively, especially if a CT scan showed pulmonary involvement, irrespective of the RT-PCR result. We could not conclude on the affectivity of Chloroquine or Hydroxychloroquine and suggest randomized controlled studies for both prophylaxis and empirical use.

Limitations

There were several limitations to our study. First, it was a descriptive crossectional study. It would have been better if a randomized control study could be planned in the future. Secondly, non-admitted patients were missed in this study. We could only gather information from admitted patients in quarantine. Another limitation was being unable to carry out all the acute inflammatory parameters due to a lack of resources.

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