

Original Article

Travel History Based Symptom Analysis of COVID-19 Patients

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^{1,2,3,4} Conception of study

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Abstract

Background: A meager amount of literature is present on the relationship of different COVID-19 symptoms in various regions of the world. Individuals who have been infected with strains from abroad and are traveling to Pakistan inadvertently create a distinction in terms of the strain causing the illness among patients. The local elements, such as climate, remain consistent for all cases.

Objectives: To test if there lies any varying symptomatology among foreign travelers and non-travelers.

Materials & Methods: This comparative retrospective study was carried out among patients visiting the Infectious Diseases Department at Holy Family Hospital, Rawalpindi, using simple random sampling. A Self-structured questionnaire was used comprising of socio-demographic details, presenting Complaints and details of comorbidities. Only confirmed COVID-19 patients, through laboratory testing (PCR) and Chest X-ray findings, were included in this study. The patients were divided into two groups: without traveling history (local cases) and with foreign traveling history. The Cronbach's alpha was 0.73, indicating reliable internal consistency. Continuous variables were compared using Mann-Whitney *U* test, and enumeration variables were compared by Pearson χ^2 or Fisher exact test, where appropriate.

Results: Out of 81 patients, 62(76.5%) were non-travelers, and 19 (23.5%) were travelers. Among travelers, 15 (78.9%) were vitally stable, while 4 (21.1%) were unstable at the time of presentation. Out of the 32 (39.6%) with multiple symptoms, 6 (31.6%) were travelers, while 26 (41.9%) were non-travelers. However, there was neither statistically significant difference between presenting complaints nor number of symptoms among the study groups ($p > .05$).

Conclusion: There was a difference in frequency of presenting symptoms among COVID-19 patients including both travelers and non-travelers, but this difference was not statistically significant.

Keywords: COVID-19, travelers, Pakistan, non-travelers.

Introduction

At the end of 2019, Wuhan, an emerging business hub of China, experienced an outbreak of the coronavirus, which killed more than 1,800 people and infected more than 70,000 people during the first five days of the epidemic.¹ On January 30, 2020, the World Health Organization announced the COVID-19 outbreak as the sixth Public Health Emergency of International Concern (PHEIC), and, when international travelers from China spread it to a considerable number of countries, a pandemic on March 11, 2020.² In Pakistan, the first case of COVID-19 was confirmed by the Ministry of Health, the government of Pakistan, on February 26, 2020, in Karachi, Sindh province. The first 20 cases had all recently arrived from Iran, Syria, and London.³ This suggests that it is not a local disease and was brought into Pakistan by immigrants.

Coronavirus Disease 2019 (COVID-19) behaves like a typical respiratory coronavirus in its mechanism, infection, and replication. But some mutations allow it to bind tighter to host receptors and increase its transmissibility, which is thought to make it more infective.⁴ Thus, many different strains of the virus are now affecting various parts of the world.⁵ According to the report published by the WHO in 2021 five COVID variants of concerns (VOC) have been named since the commencement of the COVID-pandemic: Alpha (B.1.1.7): first VOC identified in the United Kingdom (UK) in late December 2020, Beta (B.1.351): first reported in South Africa in December 2020, Gamma(P.1): first reported in Brazil in early January 2021, Delta (B.1.617.2): first

reported in India in December 2020 and Omicron (B.1.1.529): first reported in South Africa in November 2021.⁶

A study done by Shakeel M et al. assessed the viral strains during different waves of COVID. B.1.36, B.1.160, and B.1.255 were common strains in the first wave, B.1.36 and B.1.247 strains in the second wave, B.1.1.7 (Alpha variant) and B.1.36 strains in the third wave, and B.1.617.2 (Delta) in the fourth wave. Surprisingly, the B.1.36 variants was present throughout all the waves signifying their rigid fitness to survive.⁷

Symptoms experienced by the patients include fever, nonproductive cough, dyspnea, myalgia, and fatigue.⁸ Different studies suggest that the COVID-19 infection targets groups of humans in close contact; it is more likely to affect older men with comorbidities and result in ARDS. There are multiple reports that confirmed cases of human to human transmission.^{9,10} Symptoms of COVID-19 have been different for different regions of the world, mainly fever, nonproductive cough, and dyspnea were observed in China⁹ and Italy.¹¹ At the same time, a European study added loss of, or change in, the normal sense of taste (ageusia) or smell (anosmia) along with fever and cough.¹² Furthermore, microvascular injury and thrombosis have been associated with COVID-19 in China and the USA, further emphasizing the disease's different symptomatology in different geographical settings.^{13,14,15} A study conducted in USA by Stokes et al. reported that among 373,883 diagnosed COVID-19 cases, 70% of them experienced fever, cough, shortness of breath, 36% had myalgia, and 34% suffered from

headache.¹⁶ A study conducted in England among 1,542,510 adults studying variant specific symptoms of COVID-19 concluded that among the VOCs, Alpha, and Delta, were associated with loss or change of sense of smell or taste, while Omicron BA.1 and BA.2 reported influenza-like and cold-like symptoms.¹⁷

Given the spread of the new coronavirus and its impacts on human health, the research community has responded rapidly to the novel virus. Many preliminary research articles have already been published about this epidemic. However, a meager amount of literature was found regarding the relation of different symptoms with varying regions of the world. We presume that the virus's ability to replicate and get mutated is responsible for this difference. On the other hand, different local factors, such as the climate, may also play a modifying role in the disease's symptomatology. The people infected with foreign strains and traveling from other countries to Pakistan create a natural division based upon the strain infecting patients presenting with the disease. The local factors (e.g., climate) are the same for each. Thus, using these natural groups, this study was aimed to test whether the various strains of the virus cause the varying symptomatology in different geographical areas or whether there are other local factors, such as the climate, diet, etc., involved. If there is a difference in the symptomatology between our two groups (i.e., travelers and non-travelers), this would highlight the various attributing strains. On the other hand, no significant difference in the symptoms will indicate that local factors might play a much more significant role than previously established.

Materials and Methods

Approval to carry out the study was given by the ethical and research committee of Rawalpindi Medical University. The confidentiality of all the participants was taken into consideration. The participants' personal information (names, identity numbers, and addresses) was not collected.

It is a retrospective comparative cross-sectional study done from March 2020 to May 2020. The study was carried out at the Department of Infectious Diseases, Holy Family Hospital, Rawalpindi. Simple random sampling technique using computer-generated random numbers was performed. A self-made questionnaire was used. The questionnaire consisted of 1) Sociodemographic details, 2) Presenting Complaints, and 3) Comorbidities details. The outcome was defined as either dead or discharged. Only confirmed COVID-19 patients, through laboratory testing (PCR) and chest X-ray findings, were added in this study. The patients were divided into two groups: without traveling history and with foreign traveling history, over the last two weeks; as COVID symptoms usually appear 2 to 14 days post-exposure.¹⁸ The Cronbach's alpha was 0.732, indicating reliable internal consistency.

Data were collected from the doctors' and nurses' notes of patients admitted to the Infectious Diseases Department, Holy Family Hospital, Rawalpindi, Pakistan.

Continuous variables were described as Mean (Standard Deviation) or Median (Interquartile Range) accordingly, while categorical variables were presented as counts (frequencies and percentages). Sociodemographic characteristics were described in terms of frequencies and percentages. Continuous variables were compared using the Mann-Whitney *U* test, and enumeration variables were compared by Pearson χ^2 or Fisher exact test, where

appropriate. A two-tailed $p < 0.05$ was considered statistically significant. Analysis was carried out using the Statistical Package for Social Sciences (SPSS) v.23.0.

The median age was 44 (28-56) years, with the majority 31 (38.27%) lying in the 41 to 60 years old age group. Out of 81 patients, 62 (76.5%) were non-travelers, and 19 (23.5%) were travelers. Eleven patients (13.6%) were referred from other hospitals of Rawalpindi and Islamabad. There was significant difference in COVID contact history between the travelers and non-travelers ($P=0.008$). Table No. 1 shows sociodemographic details among travelers and non-travelers.

Results

Table-I: Sociodemographic details among travelers and non-travelers (n=81).

Variables		Total		Traveling Status				P-values
				Non-travelers		Travelers		
		N	%	N	%	N	%	
Gender								.238
Males		55	67.9	40	64.5	15	78.9	
Females		26	32.1	22	35.5	4	21.1	
Age Group(years)								.134
1 – 20		8	9.9	7	11.3	1	5.26	
21-40		27	33.3	20	32.3	7	36.8	
41-60		31	38.3	25	40.3	6	31.6	
61-80		14	17.3	10	16.1	4	21	
>80		1	1.23	-	-	1	5.26	
COVID History	Contact							.008*
Yes		57	70.4	49	79	8	42	
No		8	9.88	4	6.45	4	21	
Unknown		16	19.8	9	14.5	7	36.8	
Hospital visits within last 14 days								.107
Yes		12	14.8	7	11.3	5	26.3	
No		69	85.2	55	88.7	14	73.7	
*P<0.05								

* $P < 0.05$

Presenting symptoms:

Out of 19 travelers, 15(78.9%) were stable, while 4 (21.1%) were unstable at the time of presentation. On the other hand, fifty-six (90.3%) non-travelers were stable. Out of 5 patients shifted to ICU, four (80%) were non-travelers, and one (20%) was a traveler. The median duration of fever recorded in patients with no traveling history was 4 (4-6) days, while for those with traveling history, it was 3 (2-6.5) days. On the other hand, the median

duration of shortness of breath in non-travelers was 2 (2-3.5) days, while in travelers was 3 (3-3) days. However, there was no significant difference in the medians of the duration of fever ($P=0.260$) and shortness of breath ($P=0.714$) between travelers and non-travelers. Only one patient (1.23%), non-traveler, reported the loss of taste at the time of presentation. Table no. 2 shows the presenting symptoms of patients.

Table-II: Presenting symptoms of COVID-19 patients(n=81).

Presenting symptoms	Traveling status						<i>P</i> -value
	Total (n=81)		Non-Travelers (n=62)		Travelers (n=19)		
	N	%	N	%	N	%	
No. of symptoms							.406
No symptoms	39	48.1	28	45.2	11	57.9	
Single	10	12.3	8	12.9	2	10.5	
Multiple	32	39.6	26	41.9	6	31.6	
General symptoms							.317
Generalized Weakness							
Yes	15	18.5	10	16.1	5	26.3	
No	66	81.5	52	83.9	14	73.7	
History of fever							.125
Yes	29	35.8	25	40.3	4	21	
No	52	64.2	37	59.7	15	79	
Headache							.926
Yes	9	11.1	7	11.3	2	10.5	
No	72	88.9	55	88.7	17	89.5	
Runny nose							.370
Yes	2	2.5	1	1.6	1	5.3	
No	79	97.5	61	98.4	18	94.7	
Respiratory symptoms							
History of persistent cough							.238
Yes	26	32.1	19	30.6	7	36.8	
No	55	67.9	43	69.4	12	63.2	
Type							.196
Dry	23	88.5	18	94.7	5	71.4	

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	Total (n=81)		Non-Travelers (n=62)		Travelers (n=19)		
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No. of symptoms							.406
No symptoms	39	48.1	28	45.2	11	57.9	
Single	10	12.3	8	12.9	2	10.5	
Multiple	32	39.6	26	41.9	6	31.6	
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History of fever							.125
Yes	29	35.8	25	40.3	4	21	
No	52	64.2	37	59.7	15	79	
Headache							.926
Yes	9	11.1	7	11.3	2	10.5	
No	72	88.9	55	88.7	17	89.5	
Runny nose							.370
Yes	2	2.5	1	1.6	1	5.3	
Productive	3	11.5	1	1.6	2	10.5	
Sore throat							.737
Yes	19	23.5	14	22.6	5	26.3	
No	62	76.5	48	77.4	14	73.7	
Gastrointestinal symptoms							
Diarrhea							.370
Yes	2	2.5	1	1.6	1	5.3	
No	79	97.5	61	98.4	18	94.7	
Nausea/Vomiting							.683
Yes	6	7.4	5	8.06	1	5.3	
No	75	92.6	57	91.14	18	94.7	
* p<0.05							

* p<0.05

Patients with multiple symptoms:

At the time of presentation, 42(51.9%) were symptomatic, which led them to get themselves tested. Out of these 42, 32(39.6%) had multiple

symptoms. Table no 3 shows the frequencies and percentages of multiple symptoms among travelers and non-travelers.

Table-III : Patients with multiple symptoms at the time of presentation(n=32)

Symptoms				Traveling Status						
				Total (n=32)		Non-Travelers (n=26)		Travelers (n=6)		P-value
								N	%	
Fever and Headache	6	7.4	5	8.1	1	5.26	.404			
Runny nose and Headache	1	1.2	1	1.6	0	0	.661			
Generalized weakness and Fever	10	12.3	7	11.3	3	15.8	.316			
Generalized weakness and Headache	4	4.9	2	3.2	2	10.5	.412			
Cough and Sore throat	10	12.3	7	11.3	3	15.8	.265			
Diarrhea and Tastelessness	1	1.2	1	1.6	0	0	.166			
GIT and Respiratory Complaints	8	9.9	6	9.7	2	10.5	.422			

Notes: GIT=Gastrointestinal

Comorbidities:

Out of 81 patients suffering from COVID-19, 57 (70.4%) didn't have any comorbidities. Among those having comorbidities 24 (29.6%), there were 6 (7.4%) patients with diabetes and hypertension. Five (6.2%) patients were suffering from

pulmonary disease. On chi square test, there was a significant difference in comorbidities between travelers and non-travelers ($p < 0.05$). Figure no.1 shows the distribution of comorbidities among COVID-19 patients.

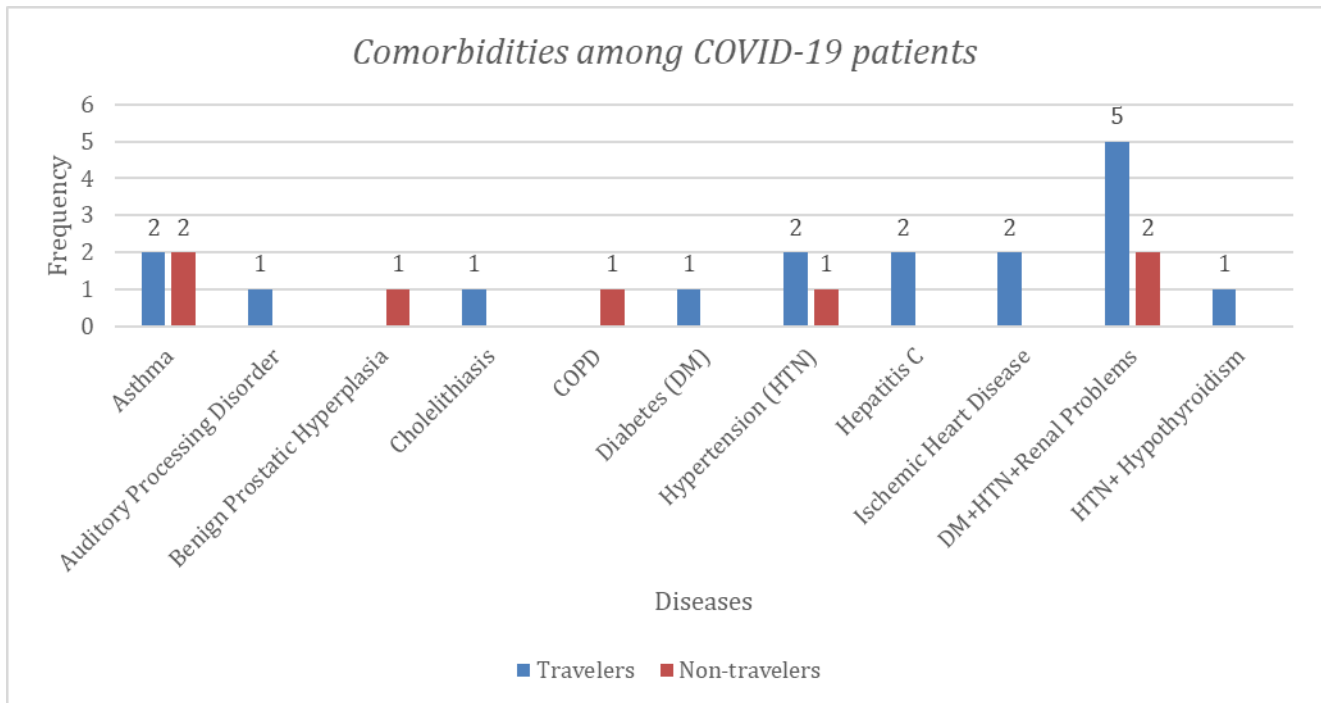


Figure 1: Distribution of comorbidities among COVID 19 patients. Comparison of the frequencies of comorbidities/diseases among travelers(blue) and non-travelers(red) being recorded as a part of history on presentation. *Note:* DM: Diabetes; HTN: Hypertension; COPD: Chronic Pulmonary Obstructive Disorder.

Out of 62 patients with no travel history, 60 were discharged while all the 19 with travel history were also discharged. Two patients out of 10 unstable patients died, giving an overall case

fatality rate of 2.47%. No significant difference was found between the mortality rates of both groups ($p=0.428$).

Discussion

As definitive information about Covid-19 and its symptomatology is not yet available, any information in this regard is invaluable. Patients may present with a variety of symptoms, including systematic and general complaints. Our study suggests minor differences in the presenting symptoms of Covid-19 patients traveling from foreign countries and those with local transmission.

According to our study, the most common presenting complaints of patients irrespective of traveling history are fever (35.8%), cough (32.1%),

and sore throat (23.5%). Similarly, Guan et al. stated that the most common presenting complaints were fever (43.8%) and cough (67.8%). However, some patients did not have a fever and presented with abnormal radiological findings.¹³ Another study reported pharyngodynia (12.4%), nasal congestion (3.7%).¹⁹ Chen et al. found that patients presented with fever (83%), cough (82%), and shortness of breath (31%) as the most common findings. Most of them (89%) had more than one of these signs and symptoms.²⁰ As the proportion of patients with different symptoms (i.e., fever, cough, sore throat, etc.) varies in various studies, we presume that this difference in the presentation of symptoms may be due to

several factors. These variations may be attributed to regional factors such as climate, diet, ethnicity, or infections with different virus strains. In a European study, the highest number of people presented with headaches (70.3%), loss of smell (70.2%), nasal obstruction (67.8%), and asthenia (63.3%). This contrasts with our study and the studies conducted in China, where a higher proportion of patients presented with fever and cough. At the same time, a headache was only reported by a minority of patients.^{12,15,20} Thus, studies from China and Europe stated the diverse symptomatic characteristics of the patients. Hence, symptomatic presentation of patients traveling from different regions of the world may vary.

Our study's median age was 44 years; the same median age was reported by Wu et al.¹⁸ The majority of non-travelers (40.3%) had ages ranging between 41-60 years old, while 36.8% of travelers were within the 21-40 years age group. As stated in a Chinese study, the patients' median age was 47, and 55.1% were in the age group 15-49 years old. In a European study, the mean age was 37, and 94% of patients reported were under 60 years of age.^{12,15,21} Thus, in different regions of the world, the presentation age fluctuates a bit, explaining that the presentation age of travelers and non-travelers is not following the same trend ($P=0.134$). Most non-travelers had contact history (79%), making the relation statistically significant. In comparison, a Chinese study showed 60.4% of patients had a contact history with confirmed cases, and 10.9% of them had no contact history.²² The reason can be a false sense of insecurity in non-travelers about their virus-free gatherings. In contrast, travelers ought to face unfamiliar crowds during their travel, and so take better precautions.

Presenting symptoms are somewhat varying amid travelers and non-travelers; however, the

results are not statistically significant. Non-travelers showed a slightly changed trend with the highest number of them either having no (45.2%) or multiple complaints (41.9%). These changes may be due to different strains of viruses, creating other symptomatic presentations. Chen et al. stated that 90% of patients were presented with multiple complaints.²⁰ However, the higher detection of asymptomatic cases could also be attributed to the stringent screening procedures being carried out at airports during these times. Thus, cases that may not have been reported unless they became symptomatic are being detected, thus creating the current picture.

Our study suggests a slight disparity between the two groups regarding the percentage of patients with general symptoms. General weakness, fever, and headache were the most common in travelers in this order. In contrast, fever was a more common general symptom among non-travelers, followed by general weakness and headache. Duration of fever was also longer among non-travelers than travelers.

Distribution of comorbidities among different COVID-19 patients depends on the patient's characteristics rather than traveling history. However, specific comorbidities are prevalent in certain areas, which created a significant difference in comorbidities among travelers and non-travelers. The outcome, on the other hand, was also not statistically significant. The overall mortality rate was 2.47 %, which is significantly lower than other studies such as the one by Tian et al. in China.²²

All the inherent drawbacks that apply to comparative retrospective studies are valid in this study as well. Furthermore, the sample size available in this study is small. In addition to this, the analyses have not been adjusted for multiple comparisons. Hence, given the potential for type

1 error, the findings are in no way, shape, or form generalizable and should be interpreted as exploratory and descriptive. However, this study may open gateways for further, more extensive studies that investigate the specific symptomatology in relation to geographical factors affecting COVID-19 occurrence and progression.

Conclusion

There was statistically insignificant difference in frequency of presenting symptoms among COVID-19 patients including both travelers and non-travelers. Future studies with large sample size and more factors should be carried out for more conclusive results.

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