



Long-Term Physical Manifestations among Patients Recovered From COVID-19 Infection

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Abstract

Background/ Purpose of the Research: The post COVID-19 syndrome is defined as unexplained development of signs and symptoms during and after recovery from COVID-19 infection. This research was conducted to identify the relative risk of developing physical manifestations (loss of smell and taste, irregular heartbeats, headache, dizziness dyspnea and fatigue) among individuals who have recovered from Covid 19 infection.

Materials and Methods: A comparative cross-sectional study was conducted on two matched groups: one group included recovered individuals from Covid 19 infection and the other group included individuals without past history of infection. They were matched as regard sociodemographic criteria and history of smoking and chronic diseases.

Results: It was found that individuals exposed to Covid 19 infection were at significant risk of developing the following symptoms: fatigue, loss of smell, loss of taste, irregular heartbeat and dyspnea (the relative risk was 1.1, 7.3, 13.5, 1.2 and 1.1, respectively, $P < 0.05$). The highest mean score of the physical manifestations was for loss of smell and the least score was for dyspnea. There was a significant negative correlation between time that passed since recovery and the intensity of fatigue, irregular heartbeats and dyspnea ($p < 0.05$).

Conclusions: Individuals who were exposed to Covid 19 infection were at risk of developing some physical symptoms after recovery. The longer the time passed since recovery from Covid-19, the less the intensity of these manifestations: fatigue, irregular heartbeat and dyspnea.

Keywords: Post COVID-19 Syndrome; Fatigue; Dyspnea

Introduction

In December 2019, the outbreak of the novel coronavirus SARS-Cov-2 (COVID-19) occurred in Wuhan, China. The virus was

identified as a member of the genus betacoronavirus, grouping it with severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) by Zhu N., et al. [1]. According to Peeri NC., et al. its global spread was rapid within one month

via droplet infection, after which the World Health Organization declared a health emergency, and all countries became concerned with the first of February 2020 [2,3]. The total confirmed cases with COVID-19 were 44,884,868 cases in the United State (USA). Also, India, Brazil, United Kingdom (UK) and Russia had high number of confirmed cases according to Alyami MH., *et al.* [2,3].

Based on the ministry of health in Saudi Arabia (MOH), one of the earliest countries that commence measures and precautions was the kingdom of Saudi Arabia (KSA), they also forebode the severity of the disease. The Kingdom has a major role in politics, strategies and the economy. Therefore, its efforts to limit the spread of Corona were not only locally, but also at the international level [4].

On 27th of February 2020, there was a restriction on the holy sites for the first time in KSA, and citizens from countries affected with COVID-19 were banned to enter KSA according to Al-Rabiaah A., *et al.* [5]. After the first reported case, the rate of confirmed cases was continuing to rise. From the first report until 23 October 2021, the total of confirmed cases in KSA were 547,931 [3].

According to the ministry of health (MOH) of Saudi Arabia, the total number of recovered patients from COVID-19 in September 25th, 2021 was 208,557,433 internationally and in Saudi Arabia 2021, it was 536,900 [6].

According to Greg Vanichkachorn., *et al.* the post COVID-19 syndrome (PCS) was defined as unexplained development of signs and symptoms during and after COVID-19, continue for more than 4 weeks [7]. There were a high prevalence of post covid conditions presented in physical symptoms such as fatigue, dyspnea or exercise intolerance [8]. Few studies were conducted to investigate post Covid syndrome in Saudi Arabia. This study was conducted to identify the relative risk of developing physical manifestations (loss of smell and taste, irregular heartbeats, headache, dizziness dyspnea and fatigue) among individuals recovered from Covid 19 infection compared to individuals without past history of infection.

Materials and Methods

Study design

A comparative cross-sectional study was conducted on two matching groups of adults: one group included those who have recovered from COVID-19 infection for more than 4 weeks and the other group included those without past history of infection.

Both groups were matched as regard sociodemographic criteria (age, gender, marital status, educational level, working status and income level) as well as history of smoking and chronic diseases.

Study setting and study population

Different sectors of Riyadh city, Kingdom of Saudi Arabia. Study population were all adults living in Riyadh city of both genders and aged 18 years or more.

Inclusion criteria

All individuals who are 18 years and older of both gender with or without past history of infection with COVID-19 have been included in the study.

Exclusion criteria

Out of those with history of COVID-19 infection, we excluded all non-recovered patients or recovered since less than 4 weeks [7].

Sample size

The sample size was calculated using N4Studies software to be 381 [9]. It was calculated based on the Saudi Arabia dashboard COVID-19 recovery data of Riyadh and Riyadh total population and 80% power of the study [6,10]. After data collection, we analyzed 550 participants who met the inclusion criteria. 148 adults who have recovered from Covid 19 infection for more than 4 weeks and 402 matching adults without past history of infection. That increase in the sample size led to increase in the power of the study to be more than 90%.

Sampling technique

A convenient sampling technique was used. A self-administered questionnaire was designed as an online survey questionnaire, specifically by google form and distributed through social media applications (e.g., WhatsApp, Twitter and Telegram).

Data collection tools

A self-administered questionnaire was used. It consists of 3 sections: The first section included socio-demographic criteria with 11 questions, for example: age, income, educational level and marital status. It also included data about past history of smoking and chronic diseases. The second section included the COVID-19 information, e.g.: "Have you been admitted to a hospital due to COVID-19?" and duration of the disease.

The third section was about physical symptoms. It included questions about loss of smell or taste, headache, dizziness irregular heartbeats and dyspnea. These symptoms were assessed using a self-reported intensity of the symptoms from 0 to 100, where 0 indicates not present at all and 100 indicates suffering from it all the time. A score more than 33.3% for any of these symptoms was considered “present” and if less than that was considered “absent”. According to Chalder T, *et al.* fatigue have been assessed with 7 questions with 5 points Likert scale, for example” I suffer from fatigue”, “I need to relax” and “I feel sleepy most of the time” [11]. With the following responses: strongly agree, agree, neutral, disagree and strongly disagree. 5 points Likert scale is used to score these questions. Strongly agree scored 5 points and strongly disagree scored 1 point [11]. The total possible score for this data was 35; total score was converted to a percentage by the equation: (score obtained\35) *100. In that way 0 indicates not having fatigue at all and 100 indicates having it all the time. A score of 50 or less was considered absent and more than 50 was considered present.

Validity of the questionnaire of fatigue

Reliability test was done using Cronbach’s α which resulted in α = 0.82. Validity was tested for all questions and they were significantly correlated with the overall score with r > 0.5.

Statistical analysis

Statistical analysis was performed with the JMP software version 14.2 [12]. Continuous variables were presented as mean and ± standard deviation (SD), and categorical variables were presented as numbers and percentage (%). Categorical variables were compared to ensure matching of both groups using the

Likelihood Ratio and Fisher’s exact test. The relative risks of developing physical manifestations after infection with COVID-19 with 95% confidence intervals were calculated. Attributable risk percent was calculated for each of these manifestations, to get the percentage of that manifestation among exposed persons to COVID-19 infection that is attributed to this exposure. Spearman correlation test was done to test the correlation between intensity of physical symptoms and time that passed since recovery (time was collected as a categorical ordinal variable). MANOVA was conducted to illustrate which of these manifestations was most affected by COVID-19 infection. 0.05 was the cutoff point of significance.

Ethical consideration

Informed consent has been taken from all participate before filling in the questionnaire. Also, there is a completely privacy and confidentiality of the participant’s information. IRB approval have been taken before starting this study (IRB Log Number: 21-0486).

Results

Table 1 demonstrates matching of both groups (exposed and non-exposed to Covid 19 infection) as regard sociodemographic criteria as well as history of smoking and chronic diseases. It was found that there was no significant difference between both groups as regard any of the sociodemographic criteria. P value > 0.05 for age, gender, marital status, working status, income level, educational level and family members. As regard the smoking status X² = 5.1, P > 0.05, which indicates that there was no significant difference in both groups. The same was observed regarding chronic diseases as there was no significant difference in both groups (P > 0.05).

Variable	Have been infected with COVID-19				Test of significance
	No		Yes		
	N	%	N	%	
Age category					
18-21 years	209	52.25%	71	48.30%	LR = 0.9148
22-35	110	27.50%	48	32.65%	
36-50	64	16.00%	21	14.29%	
more than 50 years	17	4.25%	7	4.76%	
Gender					

Female	292	72.64%	112	75.68%	P = 0.9148 ^a
Male	110	27.36%	36	24.32%	
Marital Status					
Single	290	72.14%	102	68.92%	LR = 0.544
Married	107	26.62%	44	29.73%	
Divorced or Widower	5	1.24%	2	1.35%	
Occupational status					
Working	99	24.63%	37	25.00%	LR = 0.190
Student	238	59.20%	85	57.43%	
Not working	65	16.17%	26	17.57%	
Income					
Not enough	118	29.35%	44	29.73%	LR = 1.167
Enough	180	44.78%	72	48.65%	
Enough and saving	104	25.87%	32	21.62%	
Education level					
Less than High school	8	1.99%	4	2.70%	LR = 3.121
High school	207	51.49%	81	54.73%	
Higher education	32	7.96%	6	4.05%	
Bachelors	155	38.56%	57	38.51%	
Smoking					
Quit smoking	10	2.49%	5	3.38%	LR = 5.156
No	335	83.33%	132	89.19%	
Yes	57	14.18%	11	7.43%	
Family members					
1-5 members	119	29.75%	43	29.25%	LR = 1.425
6-8 members	182	45.50%	74	50.34%	
9 or more	99	24.75%	30	20.41%	
Chronic diseases					
No	349	86.82%	129	87.16%	P = 0.9148 ^a
Yes	53	13.18%	19	12.84%	

Table 1: Matching of both groups (exposed and non-exposed to Covid 19 infection) as regard sociodemographic criteria as well as history of smoking and chronic diseases.

LR = Likelihood Ratio, a = Fisher’s Exact Test.

Table 2 demonstrated data about the history of infection with Covid 19 among recovered patients in the studied sample (n = 148). As regard time passed since recovery from the infection, most of them have recovered since more than 6 months (74.32%), and only 10% since 1 or 2 months. It was found that 53.3% of the recovered patients had been suffering from Covid 19 for less than 10 days and one third of them for 11 to 14 days. It was also found that the majority of recovered patients (97.97%) did not require hospital admission during the infection.

Variable	N	%
Time passed since recovery		
More than 6 months	110	74.32%
2 months to 6 months	23	15.54%
From one month to less than 2 months	15	10.14%
Duration of the infection with Covid 19		
Less than 10 days	79	53.38%
11 to 14 days	50	33.78%
15 to 30 days	9	6.08%
More than a month	10	6.76%
Hospital admission due to infection of COVID-19		
No	145	97.97%
Yes	3	2.03%

Table 2: Data about history of infection with Covid 19 among recovered patients (n = 148).

Table 3 demonstrated the relative risk of developing physical manifestations after infection with COVID-19. It was found that individuals exposed to Covid 19 infection were at significant risk of developing all of the following symptoms compared to others who were not exposed: fatigue, loss of smell, loss of taste, irregular heartbeat and dyspnea (the relative risk was 1.1, 7.3, 13.5, 1.2 and 1.1, respectively, P < 0.05 for each of them). Also, it was also found that relative risks for developing both headache and dizziness were not statistically different between both groups (exposed and non-exposed to COVID-19 infection) with P > 0.05 for both of them. Attributable risk percent was calculated for each of these manifestations, it was highest among loss of taste, where 92.60% of this manifestation among exposed persons to COVID-19 infection was attributed to this exposure. The attributable risk percent for loss of smell was 86.40%. And the least attributable risk percentage was for headache and dizziness (5.2% and 10.5%, respectively).

Multivariate Analysis of Variance was conducted to illustrate the most prominent physical manifestations after recovery from Covid 19 infection as shown in table 4. The variables entered the model as dependent variables were: the score of loss of taste, score of loss of smell, score of irregular heartbeat, score of dyspnea and fatigue

Variable	Past history of Covid 19 infection				Relative Risk (CI)	Attributable risk
	Yes		No			
	N	%	N	%		
Fatigue						
Yes	122	82.43%	291	72.39%	1.1 (1.1-1.3)*	12.2%
No	26	17.57%	111	27.61%		
Loss of smell						
Yes	92	62.16%	34	8.46%	7.3 (5.2-10.3)**	86.4%
No	56	37.84%	368	91.54%		
Loss of taste						
Yes	80	54.05%	16	3.98%	13.5 (8.2-22.4)**	92.6%
No	68	45.95%	386	96.02%		
Headache						

Yes	127	85.81%	327	81.34%	1.1 (0.9-1.1)	5.2%
No	21	14.19%	75	18.66%		
Dizziness						
Yes	107	72.30%	260	64.68%	1.1 (0.9-1.2)	10.5%
No	41	27.70%	142	35.32%		
Irregular heartbeat						
Yes	78	52.70%	175	43.53%	1.2 (1.1-1.5)*	17.4%
No	70	47.30%	227	56.47%		
Dyspnea						
Yes	93	62.84%	211	52.49%	1.2 (1.1-1.4)*	16.4%
No	55	37.16%	191	47.51%		

Table 3: Relative risk of developing physical manifestations after infection with Covid 19.

* P < 0.05, **P < 0.001.

score. The independent variable was the exposure to COVID-19 infection. The whole model was statically significant with F = 0.2, P < 0.0001. The highest mean score of the physical manifestations was for loss of smell (67.8 ± 29.7) followed by fatigue (63.6 ± 15.5) and then loss of taste (63.5 ± 30.2). The least score was for dyspnea

(48.8 ± 22.7). This difference of the mean scores of the physical manifestations was statistically significant within subjects exposed to Covid 19 infection (F = 0.5, P < 0.0001) and between both groups with and without past history of COVID-19 (F = 0.3, P < 0.0001).

Variable	Past history of Covid 19 infection				MANOVA within subjects (physical manifestations)	MANOVA between subjects (past history of COVID-19)
	No		Yes			
	Mean	SD	Mean	SD		
Score of loss of taste	35.2	9.9	63.5	30.2	F = 0.5**	F = 0.3**
Score of loss of smell	37.0	12.8	67.8	29.7		
Score of irregular heartbeat	52.2	23.7	59.5	27.6		
Score of dyspnea	42.0	18.6	48.8	22.7		
Score of fatigue	59.3	15.7	63.6	15.5		

Table 4: Multivariate Analysis of Variance to illustrate the most prominent physical manifestations after recovery from Covid 19 infection.

**p < 0.0001.

Table 5 demonstrated spearman correlation between the time that passed since recovery from Covid 19 and intensity of physical manifestations. There was significant negative correlation between

the time that passed since recovery from the infection and the intensity of all of the following symptoms: fatigue, irregular heartbeats and dyspnea (p < 0.05).

Variable	By variable	Sperman p	P-value
Time passed since recovery from the infection	Fatigue	-0.1637	0.0468*
	Irregular heartbeats	-0.2110	0.0101*
	Dyspnea	-0.2590	0.0015**
	Headache	-0.0485	0.5585
	Loss of smell	0.0081	0.9226
	Loss of taste	-0.0187	0.8214
	Dizziness	-0.1025	0.2149

Table 5: Correlation between time passed since recovery from Covid 19 and intensity of physical manifestations.

*P < 0.05; **P < 0.01.

Discussion

The objectives of the present research were to identify the relative risk of developing physical manifestations (loss of smell and taste, irregular heartbeats, headache, dizziness dyspnea and fatigue) among individuals recovered from Covid 19 infection compared to individuals without past history of infection. The results have revealed that the relative risk showed significant difference of having physical symptoms (loss of smell and taste, irregular heartbeats, dyspnea and fatigue) between participants who have history of COVID-19 infection and participants without past history. Based on Mayo clinic, this virus can damage several organs which increases the possibility of having persistent symptoms after recovery, even in mild cases [13]. Besides that, COVID-19 was associated with dysfunction in many organs after hospital discharge [14]. According to Selina Kikkenborg Berg, *et al.* physical manifestations including headache, dizziness and fatigue were significantly higher in recovered COVID-19 participants than control who have not experienced COVID-19 infection [15].

Based on this study, the mean score of the physical manifestations was statistically significantly higher among those who recovered from of COVID-19 for more than one month compared to others with no history of infection. Similarly, another cross sectional study reported that 13% of those with anosmia and 11% with ageusia continued with these symptoms even after relapse of the acute manifestation of the disease by 3 months [16].

This study findings showed that there was significant negative correlation between time passed since recovery from the infection and the intensity of the physical manifestations. Similarly, another

study [17] was conducted in which patients after recovery from covid 19 were followed up in 6-weeks, 6 months, and 12-month visits. That study showed that the loss of smell, loss of taste, headache and dyspnea symptoms were decreased over time by 50% for each symptom between the period from more than one month to more than 12 months. But that study found that the highest frequency of symptoms occurrence was after more than month of recovery. In a cohort study [18] patients who recovered after 5 months from COVID-19 infection have been followed for 5 months then 9 months until 12 months. It showed that in the period from 5 months to 12 months, fatigue and dyspnea symptoms have increased (from 41.7% to 53.1%, and from 27.1% to 37.5% respectively). And the highest frequency of symptoms occurrence was in the period while they were infected with COVID-19 in fatigue and dyspnea symptoms. The is probably due to the difference in the study population as regard age and gender as in this study most of participants were aged from 18 to 21 years and most of them were females. While in the other two studies, one had most of the participants aged 42 years and most of them were males, and the other study participants were all males and aged mostly 57 years. Also, the two studies considered the same sample for different periods of follow up. This study did not require follow up.

Limitations and strengths

Recall bias may be found as the information was gathered from participants regarding previous events. The strengths of this study include the power of the study as the sample size was adequately calculated based on 80% power and even more participants than the calculated figure were included which increased the power over 90%.

Conclusions

It was found that individuals who were exposed to Covid 19 infection were at risk of developing all of the following symptoms compared to others who were not exposed: fatigue, loss of smell, loss of taste, irregular heartbeat and dyspnea. The highest mean score of the physical manifestations was for loss of smell followed by fatigue and then loss of taste. The least score was for dyspnea. Finally, the longer the time passed since recovery, the less the intensity of these manifestations: fatigue, irregular heartbeat and dyspnea.

Recommendations

Post COVID-19 syndrome awareness campaigns are necessary to educate the patients about the possible symptoms and their duration. Also, to encourage them to commit with the post COVID-19 syndrome clinics. Further studies are needed to investigate other possible physical as well as any mental manifestations after recovery from COVID-19.

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Bibliography

- Zhu N., *et al.* "A Novel Coronavirus from Patients with Pneumonia in China, 2019". *New England Journal of Medicine* 382.8 (2020): 727-733.
- Peeri NC., *et al.* "The SARS, MERS and novel coronavirus (COVID-19) epidemics, the newest and biggest global health threats: what lessons have we learned?" *International Journal of Epidemiology* 49.3 (2020): 717-726.
- Alyami MH., *et al.* "Epidemiology of COVID-19 in the Kingdom of Saudi Arabia: An Ecological Study". *Frontiers in Public Health* 8 (2017): 506.
- MOH Publications - Saudi Arabia's Experience in Health Preparedness and Response to COVID-19 Pandemic (2022).
- Al-Rabiaah A., *et al.* "Middle East Respiratory Syndrome-Corona Virus (MERS-CoV) associated stress among medical students at a university teaching hospital in Saudi Arabia". *Journal of Infection and Public Health* 13.5 (2022): 687-691.
- COVID 19 Dashboard: Saudi Arabia (2022).
- Vanichkachorn G., *et al.* "Post-COVID-19 Syndrome (Long Haul Syndrome): Description of a Multidisciplinary Clinic at Mayo Clinic and Characteristics of the Initial Patient Cohort". *Mayo Clinic Proceedings* 96.7 (2022): 1782-1791.
- Donnelly JP., *et al.* "Readmission and Death After Initial Hospital Discharge Among Patients With COVID-19 in a Large Multihospital System". *JAMA* 325.3 (2021): 304-306.
- n4Studies 1.4.0 Free Download (2021).
- Riyadh, Saudi Arabia Metro Area Population 1950-2022 | MacroTrends (2022).
- Chalder T., *et al.* "Development of a fatigue scale". *Journal of Psychosomatic Research* 37.2 (1993): 147-153.
- SAS Downloads: JMP 14.2 Annual License Updaters (2022).
- COVID-19 (coronavirus): Long-term effects - Mayo Clinic (2022).
- Ayoubkhani D., *et al.* "Post-covid syndrome in individuals admitted to hospital with COVID-19: retrospective cohort study". *BMJ* (2021): 372.
- Kikkenborg Berg S., *et al.* "Long COVID symptoms in SARS-CoV-2-positive adolescents and matched controls (LongCOVIDKidsDK): a national, cross-sectional study". *The Lancet Child and Adolescent Health* 6.4 (2022): 240-248.
- Sampaio Rocha-Filho PA., *et al.* "Headache, anosmia, ageusia and other neurological symptoms in COVID-19: a cross-sectional study". *Journal of Headache and Pain* 23.1 (2022): 1-11.
- Rank A., *et al.* "One Year after Mild COVID-19: The Majority of Patients Maintain Specific Immunity, But One in Four Still Suffer from Long-Term Symptoms". *Journal of Clinical Medicine* 10.15 (2021).
- Seeßle J., *et al.* "Persistent symptoms in adult patients one year after COVID-19: a prospective cohort study". *Clinical Infectious Disease* (2021).