

# A Consecutive Series Study of the Frequencies, Intensities, and Natural History of Symptoms Following COVID-19 Infection in Nepali Men

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## ABSTRACT

**Background:** In Nepal, approximately one million individuals, two-thirds men, have tested positive for COVID-19. The recovery picture from this infection is undescribed.

**Methods:** At one major testing institution in Kathmandu, we attempted to contact men three-four months following documentation of a positive PCR Covid test. If the men contacted consented and reported that they had not completely recovered from their Covid infection, we then sought their answers about the presence and intensities of 23 symptoms.

**Results:** Of 2043 consecutive test-positive men, we successfully contacted 1254 men/or family members. 14 men had died before our calls, and two reported having cancer or tuberculosis, providing 1238 individuals. 318 (25.7%) reported that they were unrecovered and 311 of these men were successfully interviewed. At a median of 3.5 months from diagnosis, 216 (17.4%) men reported fatigue, 153 (12.4%) pain, 134 (10.8%) difficulty remembering, 133 (10.7%) reduced physical activity, 114 (9.2%) shortness of breath, and 114 (9.2%) poor sleep. By 6 and 9 months, 108 (8.7%) and 55 (4.4%) of men respectively were still unrecovered.

**Conclusions:** In this PCR Covid test-positive series of symptomatic men, recovery was significantly prolonged compared with other viral illnesses.

**Keywords:** COVID-19; long-COVID; men; recovery; symptoms

## INTRODUCTION

Globally, data in patients beyond 3 months from diagnosis of Covid-19 about symptoms, are limited. High-income country data suggest that 10 to 30% of Covid-infected individuals have persistent functional capacity-limiting symptoms, 6 months later.<sup>1-4</sup> Some persistent symptoms are similar to chronic fatigue syndrome (CFS)- Myalgic Encephalomyelitis (ME).<sup>5</sup> CFS/ME is characterized by six months of muscle weakness exacerbated by physical and social/mental exertion, malaise, non-restorative sleep, and cognitive impairment. The occurrence of persistent symptoms following Covid infection, appears to mimic post-infectious disease syndromes reported for multiple viral illnesses.<sup>6-13</sup>

We designed a study to describe the frequencies, intensities, and natural history of the commonest

reported symptoms in a convenience sample of men testing positive for this infection during the first wave of this pandemic in Kathmandu, when 64% of typed cases were of alpha strain. Testing data in Nepal have suggested that two thirds of Covid cases have occurred in men.

## METHODS

Between March 5 and April 2, 2021, we recruited a consecutive series of men approximately 3 months after they had PCR positive tests for Covid-19 done at a single infectious disease referral institution in Kathmandu during the first wave of the pandemic, which in Nepal occurred from June 2020 through January 2021. Tested individuals were symptomatic with fever, shortness of breath, cough, or anosmia, and had provided cell-phone contact information at the time their blood samples

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for Covid PCR testing were taken, which information was used to send SMS messages reporting test results. Following approval by the Ethics Committee of the Nepal Health Research Council (I.D. #26/2021; date of approval 27th January 2021), and subsequently the Institutional Review Board at Marquette University in the United States, trained Nepali interviewers attempted to call test-positive case men 3 months following their diagnosis. If a family member answered the call and reported that the individual had died, this information was recorded. Three attempts were made to contact test-registration series-identified individuals. When identified cases were successfully contacted, informed consent was sought, and those providing witnessed verbal consent were screened for histories of cancer, tuberculosis, and HIV. If these illnesses were not present, a question about recovery followed. Individuals indicating that they had not recovered were then asked 23 questions about symptoms and their intensities. These individuals were then re-contacted and asked the same questions monthly for months 4-9 from the time of PCR test positivity.

There are not established reliable and validated data-collection instruments for investigation of post-Covid populations, much less instruments usable in different cultural settings and in translations. In this context, using reported Covid-case data, and data about symptoms in patients with CFS/ME, the investigators created an instrument with questions about 23 symptoms and their intensities.<sup>1,3,4</sup> Because of the continuous symptom states investigated, patients were asked for their symptom presence and intensity ratings over the last 3 days. The symptoms assessed were worst pain/ache, pain/ache according to location (muscle, back/whole body, head, joints, chest), mental and physical fatigue/tiredness, poor unrefreshing sleep, fever and/or chills, shortness of breath, cough, feeling sad/depressed, anxious/worried, rapid or irregular heartbeat, change in sense of smell, change in sense of taste, mental confusion or disorientation, difficulty thinking and concentrating, difficulty remembering, difficulty in word-finding, lack of motivation, numbness in fingers or toes, light-headedness or dizziness on standing, heat or cold intolerance, reduced physical activity, increased sensitivity to sound or light, and increased/delayed fatigue the day after more-than-usual physical or social activity. For several symptoms, combined word language was presented. These choices were made based on lengthy investigator experience with common understandings of symptom descriptions in thousands of patients, particularly where translations of the English language terms are made.<sup>14,15</sup> For some items, the

consequence of the symptom was asked about, because of the vagueness of the symptom itself; for example, we have asked about loss of motivation, which is the major consequence of malaise, a poorly definable English word. Several symptom questions follow from available reports, and also agreed-upon key/cardinal symptoms which characterize CFS/ME.<sup>4,5</sup> Instead of an often-used 11-point (0-10) Likert scale for severity ratings, we chose a 6-point Likert scale (0-5) because in our multi-country experiences with 11-point scales, patients have repeatedly expressed annoyance with attempting to elicit such fine-tuned differences in their ratings.<sup>14</sup> Using a translation, cultural and limited cognitive validation process for this English questionnaire, the investigators prepared a translation of this instrument for use and evaluation in Nepal as follows: 1. The questionnaire was translated from English into Nepali independently by two bilingual medical experts, who then compared and resolved their Nepali language differences. 2. A third independent bilingual individual then back-translated into English the agreed-upon Nepali questionnaire version. 3. The Nepali version was then reconciled by the three translators together. 4. Preliminary reliability of this Nepali version of the questionnaire was determined by instrument use twice on the same day by 7 Covid-affected Nepali patients, with whom there was also linguistic validation and discussion about understanding and clarity of the questions, and initial evaluation of the validity of each of the items by a “think out loud” activity with these patient users.

## RESULTS

Using the Covid test registry at the Sukraraj Tropical and Infectious Disease Hospital, interviewers attempted to contact by telephone 2043 men who at the time of the calls were 3-4 months from Covid-19 PCR test positive status. In 1254 cases, contact was made with the case or an appropriate family member who consented to provide health information. 14 calls determined that the test man had died (1.1%) In these cases no causal attribution information was sought. In two cases the individual reported having cancer or tuberculosis. 1238 men were thus determined to be study eligible.

Interviewers' inability to contact 789 (38.6%) men or family members after 3 phone calls, was attributed to: no answer, wrong number, left the country, number change and new number unknown, and refusal to be interviewed.

Among the 1238 study eligible men (age 18-92 years, median 36.5 years; timepoint from diagnosis 2.6-4.6 months, median 3.5 months), 318 (25.7%) (18-92 years;

median 38 years) (timepoint from diagnosis 2.6-4.5 months, median 3.5 months) self-assessed that they had not completely recovered from their Covid infection at this first interview timepoint (Figure 1). These median age and median time points from diagnosis in the total population of 1238 men and in the 318 men reported to be unrecovered, are not statistically different. Among the study eligible men, 18.4% were over age 50, while among those 318 that had not completely recovered at the first interview timepoint, 17.3% were over this age (N.S.). Out of 318 men, 311 were successfully interviewed within the timepoint parameters recorded above.

Figure 1 and Tables 1, 2, and 3 present the key symptom-descriptive findings for these 311 men self-assessed as unrecovered at 3.5 median months from diagnosis. As can be seen in Table 2, at three months, on a Likert scale of 0-5, 184 (15%) of 1238 men reported scores of two or more (and thus of significant intensity and likely functionally important) for fatigue, for pain 126 (10%), reduced physical activity 116 (9.4%), difficulty remembering 110 (9.0%), shortness of breath 98 (7.9%), and 95 (7.7%) poor sleep. Table 3 shows that by 6 months, the frequencies for each of these symptoms were reduced by two thirds or more. By six and nine months of the 108 (8.7%) and 55 (4.4%) men respectively still reported incomplete recovery; significant levels of pain, difficulty remembering, and fatigue were their commonest symptomatic problems.

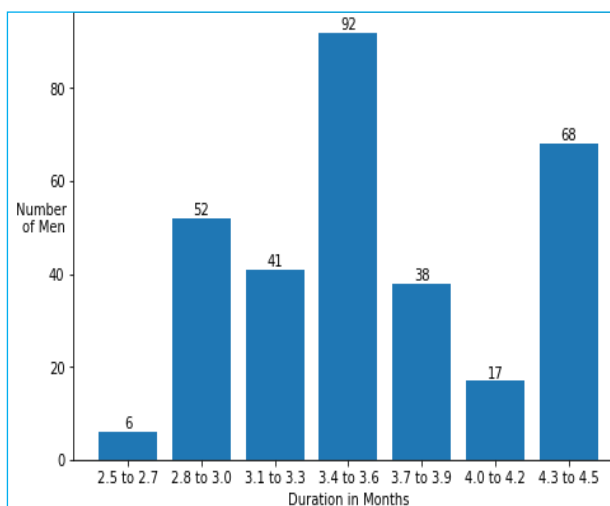


Figure 1. Distribution of time from positive PCR Covid test to first successful interview in 314 men self-assessed as unrecovered at this timepoint. Three of these men have been excluded in the detailed symptom reports because of unclear data.

Table 1. Frequencies of the six most commonly-reported symptoms in 311 men successfully interviewed, who reported being incompletely recovered at 3-4 months from diagnosis of Covid 19, and among 1238 PCR positive eligible men.

Symptom	Number of men reporting symptom	% of 1238 eligible
Fatigue	216	17.4%
Pain	153	12.4%
Difficulty remembering	134	10.8%
Reduced physical activity	133	10.7%
Shortness of breath	114	9.2%
Poor, unrefreshing sleep	114	9.2%

Table 2. Presence and intensity of 23 symptoms at 3-4 months from diagnosis in 311 men self-assessed to be incompletely recovered from Covid-19 infection who were successfully interviewed.

	Not present			Very severe		
	0	1	2	3	4	5
Worst pain or ache	157	28	55	51	8	12
Pain/ache locations:						
Muscles	26					
Back/whole body	62					
Head	41					
Joints	14					
Chest	41					
Mental and physical fatigue or tiredness	93	34	65	80	27	12
Poor, unrefreshing sleep	197	19	32	29	26	8
Fever and/or chills	280	4	14	9	4	0
Shortness of breath	196	17	44	31	17	6
Cough	255	12	19	14	8	3
Feeling sad or depressed	244	9	19	27	5	7
Anxious or worried	242	10	24	18	10	7
Rapid or irregular heart beat	228	11	31	26	8	7
Change in sense of smell	275	5	12	6	7	6
Change in sense of taste	280	6	12	7	5	1
Mental confusion or disorientation	247	12	28	15	6	3
Difficulty thinking and concentrating	218	22	34	19	13	5
Difficulty remembering	176	25	36	46	17	11

Difficulty in word-finding	251	11	19	17	8	5
Lack of motivation	226	11	34	24	12	4
Numbness in fingers or toes	254	0	17	16	10	14
Light-headedness/dizziness on standing	233	12	39	15	8	4
Heat or cold intolerance	243	5	25	17	16	5
Reduced physical activity	177	18	48	46	14	8
Increased sensitivity to sound or light	230	12	29	21	12	7
Increased/delayed fatigue the day after more-than-usual physical or social activity	204	14	37	33	21	2

Table 3. Percentage frequencies of 6 commonest symptoms with intensity scores of 2 or more in 311 men reporting being unrecovered at 3-4 months who were successfully interviewed, at 3, 6, and 9 months from Covid diagnosis. The frequencies of these symptoms of significant intensity in the entire eligible PCR test-positive cohort of 1238, can be calculated by dividing the percentage figures shown in the table by 4.

Symptom	3 months	6 months	9 months
Fatigue	59%	18%	7%
Pain	40%	12%	6%
Reduced physical activity	37%	6%	1%
Shortness of breath	31%	8%	4%
Poor, unrefreshing sleep	30%	7%	1%
Difficulty remembering	35%	11%	8%

## DISCUSSION

This report suggests that in comparison with recovery following seasonal influenza, recovery following Covid infection is slow among Nepali men, and characterized by significant intensities of symptoms. This conclusion should be interpreted in the following contexts. First, the men studied were a convenience sample of individuals living in the Kathmandu valley, who self-referred themselves to an infectious disease specialty hospital because of symptoms of Covid infection. Notably, this is not a cohort of men who were hospitalized with Covid. Thus, these studied men were mostly urban area residents, and were likely better educated, generally younger, and healthier at the time of diagnosis than their fellow men countrymen. The circumstances suggest that

the levels of symptoms among these men are of lower levels than are likely among all Nepali men. Second, we did not investigate similar men who tested negative and never developed clinical or test evidence of Covid infection, to determine usual levels of these symptoms in non-affected individuals, and thus we cannot rigorously attribute the symptom experiences reported to Covid infection. However, the symptom picture that we report here is consistent with reported data from several populations and is internally consistent over time (with specific decreases in symptoms), suggesting that these data reports are giving a reliable and valid qualitative portrait of the post Covid situation in Nepali men. Further in a much larger study of Nepali women from the same testing institution, using the same symptom instrument, and obtaining data in a consecutive series of all women six months after Covid PCR testing, the 15% of women who reported being unrecovered had the same symptoms as those of the men in the current study, and critically, those who reported recovery and those who had tested negative and had never had Covid infection symptoms, had negligible levels of these symptoms (Shrestha et al; data submitted for publication). These observations strongly suggest that the symptoms reported in the demographically similar men in the current series are indeed consequent to their earlier Covid infections and are not likely to be from other causes. Third, we sought no detailed health status or health history data from studied subjects and acquired no data about their treatment experiences or functional status. These circumstances limit any assessment of confounding factors contributing to these symptoms and their functional impact. Four, we were able to contact only 1254 (61%) of the estimated and study possible 2043 test-positive men. The non-interviewed men were demographically similar to those interviewed. The interviewers' explanations for this shortfall are logical and credible in the social circumstances of Kathmandu during the Covid pandemic. It is however well possible that our data reflect better outcomes than might have been found with significantly higher response rates. Five, this study is of men likely infected with the initial Covid virus alpha variant, based on limited variant type testing being done in Kathmandu at the time.

The strengths of this study lie in: the large studied men numbers, and in the facts and circumstances that: 1. symptom data were obtained directly from the patients themselves; 2 the follow-up symptom data were obtained by the same interviewers; 3. the case status was defined by a laboratory PCR test; 4. the symptoms' descriptions were for periods of 3 days; 5. the case recovery determinations were made both by patients

themselves and by descriptions of their symptoms; and 6. the symptom questionnaire had reliability and validity information suggesting reasonable credibility for the study population investigated.<sup>16</sup> These strengths all support an argument that these observational data are of high quality.

## CONCLUSIONS

The principal findings from this study are that: In a self-referred population of 1238 Nepali men PCR test-positive for Covid, after 2.6-4.6 months, 25.7% self-assessed themselves as incompletely recovered. Their most common symptoms were fatigue, pain, reduced physical activity, difficulty remembering, shortness of breath and poor sleep. The patient-reported intensities of these symptoms were of magnitudes likely to impair function and interfere with many activities of daily living.

By 6 months 108 (8.7%) men were still unrecovered, and the frequencies for each of these symptoms were reduced by about half from the initially assessed levels. By 9 months, 55 (4.4%) men reported incomplete recovery with fatigue, difficulty remembering, and pain.

The constellation of the most common symptoms, while suggestive of CFS/ME like syndromes because of their prolonged durations (>6 months), were infrequent—occurring in less than a low percentage—under 4%—of all symptomatic men in the studied cohort, after several months.

These detailed persistent symptom data should be useful to clinicians assessing patients in the several months following Covid-19 infection.

## CONFLICT OF INTEREST

The authors declare no conflict of interest

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