

Covid-19 effects on the workload and mental health of Iranian healthcare workers

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Abstract

Background

Workload and mental health problems of health care workers (HCW_s) in the COVID-19 pandemic is a concern. These problems increase medical error and mortality of patient and can reduce performance HCW_s.

Methods

We studied 495 HCW_s in Iran between March and April 2020. Three online questionnaires (NASA-TLX, GHQ-12, and demographic) were distributed to them via social networks. Data were entered into software SPSS v.25 and T-test, ANOVA, Regression methods were used for data analysis.

Results

Task load and mental disorder were significantly higher in HCW_s who encountered COVID-19 patients ($p < 0.001$). Among HCWs, nurses had the highest workload (71 ± 16.13 , $p < 0.001$). Females had significantly higher GHQ scores compared to males (6.54 ± 1.84 vs. 5.90 ± 2.21 , $p = 0.003$). Regarding the ward of work, health workers in the Corona part had more total task load scores compared to workers in health centers (71.56 ± 17.40 vs. 63.94 ± 17.36 , $p = 0.003$). Total GHQ score had significant positive correlation with age ($r = 0.12$, $p = 0.008$), education level ($r = 0.09$, $p = 0.03$), and experience level ($r = 0.15$, $p = 0.001$). A positive significant correlation was observed between mental demand and age ($r = 0.12$, $p = 0.007$) and experience level ($r = 0.10$, $p = 0.024$). Task Load score, mental demand, temporal demand, and performance demand had a negative correlation with education level ($p < 0.05$).

Conclusions

This study suggests the following recommendations for reducing workload and mental disorders: Psychological intervention to mental support of medical staff, especially nurses and health experts, Attention to macro ergonomics factors and work shift planning according to psychophysiological characteristics workers can improve mental health.

Background

In December 2019, the 2019 novel coronavirus (COVID-19) pneumonia widespread prevalence was appeared in Wuhan, China. On 30th January 2020, due to spreading to other countries following a logarithmic growth, WHO stated the outbreak of COVID-19 as a Public Health Emergency of International Concern (PHEIC)[1]. COVID-19 is occurred by SARS-CoV-2 that is a positive-sense single-stranded RNA virus belonging to the subgenus Sarbecovirus (beta-CoV lineage B)[2]. COVID-19 epidemic is more widespread than prevalence previous coronaviruses, indicating the extremely high transmission potential of the virus. However, the

mortality rate from the SARS-CoV-2 is lower than other coronaviruses such as SARS, MERS and other viral infections such as AIDS and Ebola[3]. Currently, due to the lack of effective treatment and vaccines, the best way to deal with this condition is prevention of virus spread through protective measures and personal hygiene[2].

In any emerging infection, health workers are unfortunately at risk due to involvement in examination and treatment patients. In COVID-19 pandemic, factors such as increasing the number of patients, increasing working hours, fatigue, the sense of danger and uncertainty, as well as lack of knowledge about the process of COVID-19 increase workload among health worker[4, 5]. Mental demand, physical demand, temporary demand, effort, performance and frustration level are important dimensions on workload[6]. Increasing the mental workload among health workers in this condition is very important; some studies have shown that the increased mental workload of these employees can lead to medical errors and put co-workers, patients, and his or her family at risk[7, 8]. The increased mental workload can also cause burnout, dissatisfaction, stress, and reducing the patient's safety and health[9, 10]. According to the Institute of Medicine (IOM) report, as many as 44,000 to 98,000 people die in the United States hospitals every year because of medical errors[5]. Since the mental health problems of health workers in the COVID 19 pandemic is a concern, we aimed to evaluate the impact of the COVID-19 epidemic on the workload of medical service staff in Iran in 2020.

Methods

Participants and data collection

The present cross-sectional study was carried out between March 5th to April 5th, 2020. We targeted all of health care worker that works in Iran ministry of health and medical education such as nurses, doctors, emergency medical service staffs, clinical, and public health technicians. Informed written consent was obtained from each participant. Then, the anonymous online questionnaires were distributed to them via social networks. Every health worker could fill the questionnaire only one time.

Questionnaires

Demographic Questionnaire

This questionnaire included Sociodemographic information such as age, marital status, sex, job title, shift working (fixed morning, fixed evening, fixed night or rotational), type of employment (contractual or permanent), number of over times per month, duration of employment (in years), educational level (diploma, bachelor's, master's, doctoral and higher), Governmental workplace (yes or no), facing with COVID- 19 patients at workplace (yes or no), interest in job (yes or no), Increased working hours due to COVID-19 prevalence (yes or no), ward of work (ICU, operating room, laboratory, emergency, radiology, nursing station, COVID-19 service center or other).

NASA-TLX Questionnaire

To assess workload, we applied the NASA-TLX (NASA -Task Load Index) technique. This technique was developed by the Human Performance Group at NASA Ames Research Center and involved 6 subscales, including mental demands, physical demands, temporal demands, performance, effort, and frustration. Twenty step bipolar scales are used to obtain ratings for these subscales. The score of each scale is from 0 to 100. NASA-TLX score is calculated by multiplying each subscale rate to its weight. The overall workload is obtained by summing across scales and dividing by 15[11, 12]. Acceptable reliability of the NASA-TLX among health workers was indicated by Mohammedi et al. with Cronbach's alpha = 0.897[13].

General health Questionnaire (GHQ-12)

To evaluate the mental health (the psychosocial well-being), the General Health Questionnaire-12 (GHQ-12) was applied. GHQ developed by Goldberg & Williams in 1972. This instrument had originally 60-item, but now there is a range of brief versions of the questionnaire, including the GHQ-30, the GHQ-28, the GHQ-20, and the GHQ-12. The GHQ-12 is short and easy to complete, and its application in research settings appropriate. The GHQ-12 comprises 12 items (six of which are positively phrased and six negatively phrased). Each item is responded to on a 4-point scale (less than usual, no more than usual, rather more than usual, or much more than usual). We used Goldberg's original scoring method (0, 0, 1, and 1). This method supplies scores ranging from 0 to 12[14]. Good reliability of Persian translation of the GHQ-12 was shown by Montazeri et al. study, with Cronbach's alpha = 0.87[15].

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics software (Version 23) (IBM SPSS Statistics, Armonk, USA). The normality of variables was confirmed using the Kolmogorov- Smirnov test. A chi-square test was used to compare the categorical data between groups. and was applied to compare parametric data between the groups. The comparisons of the variables difference between the groups were performed with the independent Student's t-test and ANOVA. Linear regression analysis in 3 models (Model 0, linear regression analysis without adjustment; Model I, linear regression analysis with adjustment for encounter to corona virus; Model II, linear regression analysis with correction for encounter to the corona virus, age, sex, marital, job, experience, type of employment, shift, education, governmental, interested, and ward of work) was used for determination of the association between overtime with total Task Load score and GHQ score. Moreover, Spearman- test was used for correlation between total Task Load score, NASA-TLX questionnaire components an GHQ score with age, education, and experience. A p-value of less than 0.05 was regarded to be statistically significant.

Results

We analyzed 495 of the 1,000 health workers who filled out the questionnaire, 505 questionnaires with incomplete data were excluded from the study. In terms of gender, 71.3% of the subjects were women. The

majority of subjects were nurses (65.9%). Regarding facing COVID- 19 patients at the workplace, 83.8 percent of subjects reported that they encountered to COVID- 19 patients. The participants' Characteristics across the type of gender are shown in Table 1. The differences in the job, ward of work, and encounter with COVID-19 patients were significant between females and males ($p < 0.05$). Moreover, males had significantly higher over time due to the prevalence of COVID-19 compared females (76.57 ± 75.87 vs. 58.49 ± 61.95 , $p = 0.01$). (Table 1)

Table 1
The characteristics of the subjects in the male and female groups

Variable	Female (n = 353)	Male (n = 142)	<i>P-value*</i>
Education (N) (%)			
Doctoral degree and higher	9 (2.5)	9 (6.3)	0.058
Master	44 (12.5)	23 (16.2)	
Basic Sciences	259 (73.4)	89 (62.7)	
Diploma	41 (11.6)	21 (14.8)	
Age category (year), (N) (%)			
20-30	141(39.9)	60(42.3)	0.117
31-40	143(40.5)	35(36.6)	
41-50	64(18.1)	23(16.2)	
> 50	5(1.4)	7(4.9)	
Marital (N) (%)			
Single	133(37.7)	43(30.3)	0.073
Married	220(62.9)	99(69.7)	
Job (N) (%)			
Nurse	256(72.5)	70(49.3)	<0.001
Doctor	32(9.1)	11(7.7)	
Health expert	6(1.7)	9(6.3)	
Health assistant	15(4.2)	22(15.5)	
Lab/radiology	6(1.7)	8(5.6)	
Other	38(10.8)	22(15.5)	
Experience (year), (N) (%)			
1-5	145(41.1)	62(43.7)	0.554
6-10	60(17)	24(16.9)	
11-15	77(21.8)	22(15.5)	
16-20	34(9.6)	15(10.6)	
>20	37(10.5)	19(13.4)	
Type of employment (N) (%)			

Contractual	44(12.5)	13(9.2)	0.321
Permanent	137(38.8)	47(33.1)	
Employment contracts	86(24.4)	40(28.2)	
Temporary contracts	86(24.4)	42(29.6)	
Shift working (N) (%)			
Rotational	238(67.4)	95(66.9)	0.613
Night	10(2.8)	2(1.4)	
Morning	105(29.7)	45(31.7)	
Ward of work (N) (%)			
ICU	42(11.9)	8(5.6)	0.002
Operating room	18(5.1)	8(5.6)	
Laboratory	14(4)	6(4.2)	
Emergency	44(12.5)	41(28.9)	
Corona	45(12.7)	13(9.2)	
Radiology	13(3.7)	5(3.50)	
Health center	140(39.7)	47(33.1)	
other	37(10.5)	14(9.9)	
Governmental workplace (N) (%)			
Yes	299(84.7)	114(80.3)	0.231
No	54(15.3)	28(19.7)	
Facing with COVID- 19 patients at workplace (N) (%)			
Yes	311(88.1)	104(73.2)	<0.001
No	42(11.9)	38(26.8)	
Interest in job (N) (%)			
Yes	280(79.3)	111(78.2)	0.776
No	73(20.7)	31(21.8)	
Overtime (hour)	58.49 ± 61.95	76.57 ± 75.87	0.01

The results are described as mean ± SD for quantitative data and number (%) for qualitative data.

* P <0.05 was considered as significant using Independent t-test for comparison between the two groups and Chi-square test for parametric and categorial data, respectively.

As shown in Table 2, females had significantly higher GHQ scores compared to males (6.54 ± 1.84 vs. 5.90 ± 2.21 , $p = 0.003$).

Table 2

Total Task Load score, NASA-TLX questionnaire components and GHQ score between the male and female groups

Variable	Female (n = 353)	Male (n = 142)	<i>P-value*</i>
Mental pressure	15.42±4.25	14.7±4.28	0.101
Physical pressure	13.79±5.49	13.06±5.55	0.218
Temporal	14.75±4.48	13.69±4.55	0.018
Performance	10.77±7.01	12.66±6.3	0.006
Effort	12.35±6.17	13.8±5	0.005
Frustration (failure)	14.2±6.05	13.23±6.01	0.110
NASA-TLX overall score	67.79±17.85	68.95±17.96	0.514
GHQ score	6.54±1.84	5.90±2.21	0.003
The results are described as mean ± SD. <i>*P < 0.05</i> was considered as significant using Independent t-test for comparison between the two groups.			
Abbreviation: NASA-TLX: NASA Task Load Index, GHQ: General health Questionnaire.			

Total Task Load score and GHQ score according to different qualitative variables are presented in Table 3. Health workers who encountered COVID- 19 patients, subjected to more task load and weak mental health compared to who didn't face COVID- 19 patients at the workplace ($p = 0.001$). Total Task Load score was significantly higher in nurses compared to doctors and health assistances (71 ± 16.13 vs. 56.35 ± 20.45 , $p < 0.001$; 71 ± 16.13 vs. 58.96 ± 15.28 , $p < 0.001$). Moreover, health experts had a higher task load compared to doctors (69.40 ± 8.85 vs. 56.35 ± 20.45 , $p = 0.012$). The difference of Total Task Load score was not significant between nurses and health experts ($p = 0.999$) and radiology and laboratory experts ($p = 0.868$) and other jobs ($p = 0.517$). Regarding the ward of work, health workers in the Corona part had more total task load scores compared to workers in health centers (71.56 ± 17.40 vs. 63.94 ± 17.36 , $p = 0.003$). (Table 3)

Table 3

Total Task Load score and GHQ score according to different qualitative variables Values are expressed as means \pm SD.

Variables	Total Task Load score	GHQ score
Age category (year), (n=495)		
20-30 (n=201)	66.46 \pm 18.16	6.10 \pm 2.01
31-40 (n=195)	68.96 \pm 18.57	6.49 \pm 2.11
41-50 (n=87)	70.26 \pm 15.38	6.49 \pm 1.55
> 50 (n=12)	66.75 \pm 17.71	7.41 \pm 0.51
<i>P- value</i>	0.32*	< 0.001**a
Marital (n=495)		
Single (n=176)	66.79 \pm 17.52	5.98 \pm 1.93
Married (n=319)	68.31 \pm 18.09	6.56 \pm 1.96
<i>P- value</i>	0.744*	0.002**
Job (n=495)		
Nurse (n=326)	71 \pm 16.13	6.43 \pm 1.89
Doctor (n=43)	56.35 \pm 20.45	6.67 \pm 1.98
Health expert (n=15)	69.40 \pm 8.85	6.73 \pm 2.46
Health assistant (n=37)	58.96 \pm 15.28	5.62 \pm 2.21
Lab/radiology (n=14)	65.66 \pm 20.41	6.78 \pm 2.26
Other (n=60)	66.82 \pm 22.11	6 \pm 1.93
<i>P- value</i>	<0.001**a	0.076*
Marital Status		
Single(n=176)	66.79 \pm 17.52	5.98 \pm 1.93
Married(n=319)	68.31 \pm 18.09	6.56 \pm 1.96
<i>P- value</i>	0.744***	0.002***
Experience (year)		
1-5(n=207)	66.97 \pm 18.61	6.04 \pm 2.04
6-10(n=84)	68.97 \pm 17.36	6.63 \pm 1.96
11-15(n=99)	69.54 \pm 14.73	6.31 \pm 2.14

16-20(n=49)	72.18±18.02	6.55±1.55
>20(n=56)	65±20.30	7.05±1.48
<i>P- value</i>	0.240*	0.006 ^{*a}
Type of employment		
Contractual(n=57)	66.83±18.25	6.91±1.70
Permanent(n=184)	69±17.89	6.68±1.84
Employment contracts(n=126)	70.51±18.40	6.15±1.96
Temporary contracts(n=128)	65.07±16.87	5.86±2.15
<i>P- value</i>	0.081*	<0.001 ^{**a}
Shift working		
Rotational(n=333)	70.58±17.13	6.39±1.99
Night(n=12)	75.22±15.88	6.58±1.44
Morning(n=150)	61.50±17.95	6.26±1.96
<i>P- value</i>	<0.001 ^{*a}	0.741*
Education		
Doctoral degree and higher(n=18)	68.15±14.41	6.72±2.27
Master (n=67)	68.93±16.8	5.67±2.36
Basic Sciences (n=348)	70.17±16.23	6.40±1.89
Diploma (n=62)	55.76±23.34	6.77±1.74
<i>P- value</i>	<0.001 ^{**a}	0.008 ^{*a}
Ward of work		
ICU(n=50)	73.68±16.22	6.50±1.48
Operating room(n=26)	82.32±10.31	6.88±1.17
Laboratory(n=20)	69.11±16.38	6.15±1.72
Emergency(n=85)	71.88±16.38	6.83±1.69
Corona(n=58)	71.56±17.40	6.25±1.91
Radiology(n=18)	66.76±16.98	7.33±1.57
Health center(n=187)	63.94±17.36	5.90±2.25
Other(n=51)	60.70±20.82	6.88±2
<i>P- value</i>		

	<0.001 ^{*a}	<0.001 ^{**a}
Governmental workplace		
Yes(n=413)	68.52±17.89	6.47±1.88
No(n=42)	66.11±17.75	5.80±2.30
<i>P- value</i>	0.265 ^{***}	0.015 ^{***}
Facing with COVID- 19 patients at workplace		
Yes(n=415)	69.28±17.50	6.52±1.84
No(n=80)	62.11±18.68	5.53±2.39
<i>P- value</i>	0.001 ^{***}	0.001 ^{***}
Interest in job		
Yes(n=391)	67.11±18.27	6.46±1.99
No(n=104)	61.93±15.83	5.99±1.85
<i>P- value</i>	0.015 ^{***}	0.031 ^{***}
* <i>P</i> <0.05 was considered as significant using One-way ANOVA test (F test). a. Post hoc with LSD test.		
** <i>P</i> <0.05 was considered as significant using One-way ANOVA test (Welch test), a. Post hoc with LSD test.		
*** <i>P</i> <0.05 was considered as significant using Independent t-test for comparison between the two groups.		
Abbreviation: NASA-TLX: NASA Task Load Index, GHQ: General health Questionnaire.		

In terms of the subscale score of NASA-TLX, nurses had more mental pressure compared to doctors ($p < 0.001$) and health assistance ($p = 0.002$). The health experts, laboratory, and radiology experts had more mental pressure vs. doctors ($p < 0.05$). Moreover, nurses were exposed to more physical pressure, time pressure(temporal) and, frustration compared to the rest of jobs ($p < 0.05$) except for laboratory and radiology experts. Doctors had higher frustration score vs. health experts ($p = 0.026$). (Table 4).

Table 4
Subscale score of NASA-TLX according to type of job.

Job	Mental pressure	Physical pressure	Temporal	Performance	Effort	Frustration
Nurse (n=326)	15.64±3.94	14.85±4.89	15.26±4.04	11.19±6.76	13.05±5.73	15.15±5.50
Doctor (n=43)	13.13±5.49	11.07±5.16	11.16±4.90	9.76±7.28	11.04±7.03	12.11±5.56
Health expert (n=15)	16.4±4.27	9.26±6.65	13.53±6.28	15.73±4.99	15.66±4.89	8.27±5.22
Health assistant (n=37)	13.40±4.50	9.38±4.79	12.03±4.40	11.29±6.34	11.32±5.55	9.70±6.16
Lab/radiology (n=14)	17.14±2.10	13.64±3.93	16.28±3.15	8.43±7.91	10.71±7.15	13.43±6.68
Other (n=60)	14.78±4.44	11.82±6.59	13.71±4.90	12.65±6.69	13.35±5.64	12.70±6.85
<i>P- value</i> ^{*a}	0.001	<0.001	<0.001	0.01	0.046	<0.001
* $P < 0.05$ was considered as significant using One-way ANOVA test (Welch test). a. Post hoc with LSD test.						
Abbreviation: NASA-TLX: NASA Task Load Index						

As shown in Table 5, total GHQ score had significant positive correlation with age ($r = 0.12, p = 0.008$), education level ($r = 0.09, p = 0.03$), and experience level ($r = 0.15, p = 0.001$). A positive significant correlation was observed between mental pressure and age ($r = 0.12, p = 0.007$) and experience level ($r = 0.10, p = 0.024$). Task Load score, mental pressure, temporal, and performance had negative correlation with education level ($p < 0.05$). (Table 5)

Table 5

The relationship between total Task Load score, NASA-TLX questionnaire components an GHQ score with age, Education, and Experience

Variables	Age category		Education level		Experience level	
	R value*	P-	R value*	P-	R value*	P-
GHQ score	0.12	0.008	0.09	0.03	0.15	0.001
Task Load score	0.07	0.098	-0.12	0.005	0.04	0.387
Mental pressure	0.12	0.007	-0.17	<0.001	0.10	0.024
Physical pressure	-0.06	0.179	0.01	0.777	-0.08	0.049
Temporal	-0.03	0.522	-0.10	0.023	-0.04	0.389
Performance	0.06	0.205	-0.13	0.004	0.05	0.236
Effort	0.05	0.224	-0.05	0.274	0.02	0.585
Frustration (failure)	-0.04	0.346	0.05	0.255	-0.03	0.536

*. $P < 0.05$ was considered as significant using Spearman- test for correlation between variables. R was considered as correlation coefficient.

Abbreviation: NASA-TLX: NASA Task Load Index, GHQ: General health Questionnaire.

The relationship between overtime with total Task Load score and GHQ score is illustrated in Supplemental Table. In the unadjusted model, there was a significant association between Total Task load score and overtime ($B = 0.025$, $p = 0.04$), which didn't remain significant after further adjustment for the encounter to COVID-19 patients (Model1) and adjusted for the encounter to the COVID-19 patients, age, sex, marital, job, experience, employment status, shift, education, governmental workplace, interested in the job, and ward of work(Model 2).(Supplemental Table)

Discussion

In the present study, the workload and mental health resulting from the COVID-19 outbreak were assessed among Iranian health care staff. More than 80 percent of the participants encountered COVID-19 patients in the workplace. The variables such as age, marital status, experience, education, type of employment, ward of work interest in the job, and facing COVID_19 patients in the workplace affected on the score of GHQ. Moreover, jobs, the shift of work, education level, and facing COVID-19 affect the score of NASA-TLX. The NASA_TLX and GHQ scores of medical workers were high in the present study. That scores, generally, NASA-TLX and GHQ scores in nursing and health experts were higher than other health staff groups. Several studies have also reported that health care workers have depression and anxiety due to the COVID-19 outbreak[16–18]. The results of this study indicated that the total workload and mental health of staff who contracted COVID-19 patients were significantly higher than those who didn't face COVID-19 patients.

Limited knowledge about COVID-19, the lack of an effective drug, and the importance of prevention of virus spread has increased the workload nurses and health experts in the front line of the fight against COVID-19.

The current study showed that workload and type of work shift had significant association and night shift had higher workload scores compared to rotational and morning shifts. It was consistent with the findings of the Hoonakker et al. study. They showed that night shifts had a higher workload than the morning shift. Also, their study showed that shifts with an 8hr cycle time had lower mental workload in compare with 12-hr shift time[19]. Shortening work shifts and adjusting shifts to psychophysiological characteristics workers can increase mental, physical capacity, and improve worker performance[20]. Based on the results of the current study, mean workload and mental health scores in the nurses of operation ward were highest and intensive care unit (ICU), coronavirus, and emergency wards were in the next ranks. Hoonakker et al. [19]and Nasirizad Moghadam et al. [21] showed that mental workload is the highest in the ICU ward, and Yuan Wu et al. showed burnout of front line of fight COVID-19 was lower[16]. In this study, the front-line ward (emergency, coronavirus, and ICU) had the highest rank after the operation ward.

According to the result, this study workload and mental health scores increased among those who interesting in his or her job. Tajvar et al. reported no significant correlation between mental disorders and job interest[22]. Job satisfaction, commitment, and job enrichment can decrease workload and mental disorders[23–25]. Increasing COVID-19 patient numbers in hospitals, effort to treat them, lack of effective treatment protocol, increased responsibility probably increase workload, and mental disorders those who were interested in their job. Some studies have identified the relationship between workload and mortality and infection in hospitals [10, 26]. Although knowledge of COVID-19 is limited but increasing workload and decreasing mental health in health care staff can increase medical errors [27] and number death of COVID-19 patients.

Conclusions

Given the importance of workload and mental disorders in health care workers, this study suggests the following recommendations for reducing workload and mental disorders:

- Psychological intervention to mental support of medical staff, specially nurses and health experts.
- Attention to macro ergonomics factors to increase motivation, job involvement, job enrichment, and commitment.
- Work shift planning according to psychophysiological characteristics workers with aimed to more resting workers, especially in operation, ICU, corona, and emergency.
- Finance and social support for staff to make them interested in the job.

The limitations of this study were first, the small size of the health worker group, second, bored of the health worker staff in the days of the spread of COVID-19, and lack of response to the questionnaire.

Abbreviations

HCW_s: healthcare workers; PHEIC: Public Health Emergency of International Concern; IOM: Institute of Medicine; WHO: world health organization; AIDS: Acquired immunodeficiency syndrome; NASA-TLX: National Aeronautics and Space Administration-Task Load Index; GHQ-12: General health Questionnaire; ANOVA: Analysis of variance; ICU: intensive care unit; COVID-19: Coronavirus disease 2019.

Declarations

Ethics approval and consent to participate

This research approved by the Medical Ethics Committee of Esfarayen University Medical Science (approval number: IR.ESFARAYENUMS.REC.1398.021). Informed written consent was obtained from each participant.

Consent for publication

No individual or personal data is included in this manuscript.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have no competing interests to declare.

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Authors' contributions

E S.H., V A., and A A. contributed to the conception and design of the study and the study protocol. M G., H B. and M D. managed the running of the study. A C.H., K.H N. and H R.M. conducted data analysis and all authors helped with data interpretation. This manuscript was written by V A. with input from all co-authors. All authors read and approved the final version of the manuscript.

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