Burnout Among Physicians and Medical Interns: Comparing Time-periods of Coronavirus Disease Outbreak in Shiraz

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Abstract

Background: Physician burnout is a serious issue associated with physician attrition, mental and physical problems, and medical errors. This study aimed to investigate prevalence of overall burnout among Interns-Residents and general physician (GPs)-Specialist during the COVID-19 pandemic in Iran.

Methods: This cross-sectional study was conducted among 220 Interns-Residents and 212 GPs-Specialists in university affiliated hospitals and clinics in Shiraz, Iran. A random sampling method used to recruit the samples and the data gathered using a valid questionnaire. We used covariance analysis and multiple logistic regression to analyze the data.

Results: Multiple logistic regression for GPs-Specialists showed that working in COVID-19 wards during June-July (OR = 13.93) was associated with increasing odds of overall burnout. However, older age was associated with decrease odds overall burnout (OR = 0.94). Multiple logistic regression for Interns-Residents revealed that age (OR = 1.24) and being single (OR = 1.66) were positively associated with overall burnout.

Conclusions: The present finding could remind policy makers the importance of burnout issue among physicians during the pandemics and could persuade them for taking appropriate action in order to prevent this phenomenon. It is suggested that focusing on strategies such as improving organizational resilience, improvement of healthcare working environment, and development of coping skills among physicians could be helpful in this regard.

Introduction

Physician burnout is an important issue, shown its associations with physician attrition, mental and physical health, and self-reported medical errors. The "burnout" phenomenon which is caused by work related stress, is a challenge for academic psychiatry both conceptually and professionally. Until now, more than 140 definitions have been suggested from the first description of burnout in 1974. Therefore, a consensual definition of occupational burnout is currently lacking. However, according to a recent systematic review several studies focusing on burnout issue have used Maslach Burnout Inventory (MBI) to assess burnout. Considering MBI, burnout results from chronic exposure to stress: comprising emotional exhaustion (EE), depersonalization (DP) and a reduced sense of personal achievement (PA). Burnout has been gaining much attention particularly due to its negative impacts such as poor physician health and functional outcomes, lower quality of care, shrinking physician workforce, and compromised patient safety. Burnout for each individual is a result of interplay between his/her personal characteristics and environmental factors. However, Stigma and fear of professional consequences appears to be an important barrier for physicians to express their burnout and access services. Furthermore, this phenomenon has high costs for healthcare systems. Thus, any additional evidence on this subject from all over the world is of great importance.

The coronavirus disease 2019 (COVID-19) pandemic has brought several challenges to an underprepared healthcare system. Health care providers are facing unpredicted acute workplace stress as well as higher rate of physician burnout. The rates of physician burnout, depression, and suicide have been increasing over the past 50 years. However, during the SARS-Cov-2 and COVID-19 pandemics these numbers are predicted to show a steep increase due to the increased work demands, social isolation, decreased self-care, and increased
exposure to emotionally traumatic events at work and home. Although the issue of burnout among physicians is not new, the COVID-19 pandemic is expanding the negative consequences of inadequate support by the authorities for solving this problem. The pandemic has already posed strain on the entire healthcare system, consequently it is vital to provide precise data on the prevalence of burnout during different periods of time since the beginning of pandemic.

Physician burnout during COVID-19 pandemic in Iran has not been determined in previous studies and researches has tended to focus on nursing burnout. The present study aims to estimate the prevalence of overall burnout and its related sub-dimensions (using MBI) among Interns-Residents and general physician (GPs)-Specialists in 3 different periods of time since the beginning of the Pandemic. In addition, our study take a new look at the association between different variables including working in COVID-19 wards with the overall burnout of both mentioned groups.

Materials And Methods

This cross-sectional study was conducted among 220 Interns-Residents and 212 (GPs)-Specialists working at hospitals affiliated with Shiraz University of Medical Sciences, southern Iran. The study was performed in three periods of time, including March-April 2020, June-July 2020, and December 2020-January 2021. These physicians had regular working schedule during the COVID-19 outbreak.

We used a simple random sampling method to recruit participants. To collect data, a trained questioner referred to university affiliated teaching hospitals and their related outpatient clinics in Shiraz. Questionnaires were completed by participants who met inclusion criteria. Experience of at least 6 month presence at clinical wards was considered as inclusion criteria for interns. Willingness to participate in the study was considered as an inclusion criterion for all participants.

In this study we gathered data using a researcher-made checklist and a valid questionnaire. The checklist comprises demographic features and job characteristics, including working experience and taking care of COVID-19 patients. We also applied a valid Persian version of the Maslach Burnout inventory (MBI), which included 9 items on emotional exhaustion, 8 items on depersonalization, and 5 items on personal accomplishment. The MBI has frequency and intensity ratings. To avoid redundancy, the intensity rating was used in this study.

In this study, a physician with a high score for either the depersonalization and/or emotional exhaustion dimensions was considered as having at least one manifestation of job burnout. The level of emotional exhaustion was classified high if the score was greater than 26, intermediate if it was from 17 to 26, and low if the score was less than 17. In the depersonalization dimension, the overall score of more than 12 was considered high depersonalization, and the scores from 7 to 12 and less than seven were deemed to be intermediate and low levels, respectively. Personal achievement dimension score include higher than 39 (top level), from 32 to 38 (moderate level), and those below 32 (low level).

According to the Li et al. an exhausting score equal to or more than 27 or a depersonalization score equal to or more than 13 was considered as overall burnout.
Statistical methods

We analyzed data using IBM SPSS 18. Quantitative and qualitative variables were described by mean ± standard deviation (SD) and frequency (percent). The Chi-square test were used to compare qualitative variables between the groups. Total score of burnout and related sub-dimensions were compared between the periods of time using analysis of covariance adjusted for age and sex. To determine factors related to the overall burnout, we employed a multiple logistic regression. A P-value less than 0.05 was considered statistically significant.

Results

The participants’ characteristics are shown in Table 1. The Mean age of participants was 25.33 ± 1.89 (ranged 21 to 31) years for Interns-Residents and 37.55 ± 9.01 (ranged 26–62) years for GPs-Specialists. Most of GPs-Specialists were married and female. Working experience in COVID-19 centers was significantly lower in December-January than March-April.
Table 1
Participants’ Characteristics measured in different periods of time

| Characteristics | Interns-Residents | GPs- Specialists |
|-----------------|-------------------|------------------|
|                 | Mar-Apr (n = 158) | Dec-Jan (n = 62) | P | Mar-Apr (n = 76) | Jun-Jul (n = 43) | Dec-Jan (n = 93) | P |
| Age (years)     | 25.11 ± 1.83      | 25.88 ± 1.95     | 0.01 | 30.90 ± 4.43 | 41.62 ± 9.99 | 41.09 ± 8.24 | 0.01 |
| Work experience (years) | 2.62 ± 1.01 | 2.25 ± 1.36 | 0.03 | 5.27 ± 2.62 | 11.51 ± 8.58 | 10.81 ± 8.35 | 0.01 |
| Gender          | Male 86 (54.43)   | 25 (40.32)       | 0.06 | 35(46.05)    | 20(46.51)     | 44(47.31)     | 0.98 |
|                 | Female 72 (45.56) | 37 (59.67)       |     | 41(53.94)    | 23(53.48)     | 49(52.68)     |     |
| Marital Status  | Single 140(88.60) | 51(82.25)        | 0.21 | 45(59.21)    | 18(41.86)     | 16(17.20)     | 0.01 |
|                 | Married 18(11.39) | 11(17.74)        |     | 31(40.78)    | 25(58.13)     | 77(82.79)     |     |
| Working in COVID-19 ward | No 14(8.86) | 40(64.51) | 0.01 | 12(15.78) | 0(0.00) | 40(43.01) | 0.01 |
|                 | Yes 144(91.13)    | 22(35.48)        |     | 64(84.21)    | 43(100)       | 53(56.98)     |     |
| Experience of resuscitation maneuver for COVID-19 patients | 0 30(18.98) | 39(62.90) | 0.01 | 13(17.10) | 27(62.79) | 42(45.16) | 0.01 |
|                 | 1–4 101(63.92)    | 11(17.74)        |     | 43(56.57)    | 12(27.90)     | 30(32.25)     |     |
|                 | >=5 27(17.08)     | 12(19.35)        |     | 20(26.31)    | 4(9.30)       | 21(22.58)     |     |
| Experience of dealing with patients died from COVID-19 | 0 19(12.02) | 18(29.03) | 0.01 | 11(14.47) | 23(53.48) | 25(26.88) | 0.01 |
|                 | 1–4 81(51.26)     | 22(35.48)        |     | 23(30.26)    | 15(34.88)     | 26(27.95)     |     |
|                 | 5–9 38(24.05)     | 9(14.51)         |     | 21(27.63)    | 2(4.65)       | 12(12.90)     |     |
|                 | >=10 20(12.65)    | 13(20.96)        |     | 21(27.63)    | 3(6.97)       | 30(32.25)     |     |

The comparison of total score of burnout and related sub-dimensions is presented in Table 2. For Interns and Residents, the mean score of burnout, depersonalization, and reduced achievement were significantly higher in December-January than March-April. In the June-July, GPs and Specialist reported highest level of burnout, emotional exhaustion, and depersonalization. Emotional exhaustion for interns and Residents, and reduced achievement for GPs and Specialists were not significantly different between the periods of time.
Table 2
Comparison of total score of burnout and related sub-dimensions

| Burnout Dimensions | Interns-Residents | GPs-Specialists | p* | Interns-Residents | GPs-Specialists | p* |
|--------------------|------------------|----------------|-----|------------------|----------------|-----|
|                    | Mar-Apr           | Dec-Jan         |     | Mar-Apr           | Jun-Jul         | Dec-Jan |     |
| Burnout            | 55.24 ± 9.97      | 60.66 ± 12.24   | 0.01| 53.65 ± 13.28a   | 55.83 ± 9.27b   | 47.02 ± 20.04ab | 0.01|
| Emotional exhaustion| 27.99 ± 7.32      | 28.40 ± 7.19    | 0.94| 29.31 ± 7.64a    | 32.83 ± 6.93a   | 23.45 ± 12.09a  | 0.01|
| Depersonalization  | 8.86 ± 4.60       | 10.98 ± 4.86    | 0.01| 7.40 ± 4.66      | 8.65 ± 4.38a    | 6.12 ± 5.49a    | 0.02|
| Reduced Achievement| 18.38 ± 6.00      | 21.27 ± 5.22    | 0.01| 16.93 ± 6.45     | 14.34 ± 4.35    | 17.44 ± 7.77    | 0.05|

* Comparisons between the periods of time are adjusted for age and sex; In the rows, same lower letters indicate significant differences between the periods of time.

One-hundred and fifty-seven (71.4%) Interns-Residents and 141 (66.5%) GPs-Specialists had overall burnout. The prevalence of overall burnout was not statistically different between the two groups (P = 0.27).

In the univariate analysis, for interns-residents, all determining factors except age (OR = 1.18, P = 0.04, 95% C.I.: 1.01–1.38) were not significantly associated with overall burnout (P > 0.05). Working in COVID-19 wards during the studied periods of time was not significantly related to overall burnout (OR = 1.04, P = 0.94, 95% C.I.: 0.33–3.24). Multiple logistic regression revealed that age (OR = 1.24, P = 0.01, 95% C.I.: 1.04–1.47) and being single (OR = 1.66, P = 0.02, 95% C.I.: 1.09–2.51) were positively associated with overall burnout. Detailed results are shown in Table 3.
### Table 3
Determinant factors of overall burnout among Interns and Residents.

| Determinant Factors | Overall Burnout | Univariate logistic Regression | Multiple logistic Regression |
|---------------------|-----------------|-------------------------------|-----------------------------|
|                     | No | Yes | OR | 95% CI | P | OR | 95% CI | P |
| **Periods of time * Working in COVID-19 ward** | | | | | | | | |
| Dec-Jan * work (Yes) | 5(22.7) | 17(77.3) | 1.40 | 0.49–3.99 | 0.52 | 1.04 | 0.33–3.24 | 0.94 |
| Dec-Jan * work (No) | 10(25) | 30(75) | | | | | | |
| Mar-Apr * work (Yes) | 43(29.9) | 101(70.1) | - | - | - | - | - | - |
| Mar-Apr * work (No) | 5(35.7) | 9(64.3) | - | - | - | - | - | - |
| **Periods of time** | | | | | | | | |
| Dec-Jan | 15(24.2) | 47(75.8) | 1.36 | 0.69–2.68 | 0.36 | - | - | - |
| Mar-Apr | 48(30.4) | 110(69.6) | - | - | - | - | - | - |
| **Working in COVID-19 ward** | | | | | | | | |
| No | 15(27.8) | 39(72.2) | - | - | - | - | - | - |
| Yes | 48(28.9) | 118(69.6) | 0.94 | 0.47–1.87 | 0.87 | - | - | - |
| **Age (years)** | 24.92 ± 1.97 | 25.50 ± 1.84 | 1.18 | 1.01–1.38 | 0.04 | 1.24 | 1.04–1.47 | 0.01 |
| **Gender** | | | | | | | | |
| Male | 33(29.7) | 78(70.3) | - | - | - | - | - | - |
| Female | 30(27.5) | 79(72.5) | 1.11 | 0.62–2.00 | 0.71 | 1.19 | 0.64–2.32 | 0.56 |
| **Marital status** | | | | | | | | |
| Single | 52(27.2) | 139(72.8) | - | - | - | - | - | - |
| Married | 11(37.9) | 18(62.1) | 0.61 | 0.27–1.38 | 0.23 | 0.31 | 0.12–0.81 | 0.02 |
| **Experience of resuscitation maneuver for COVID-19 patients** | No | 22(31.9) | 47(68.1) | - | - | - | - | - |
| 1–4 | 34(30.4) | 78(69.6) | 1.07 | 0.56–2.05 | 0.82 | 0.83 | 0.37–1.83 | 0.64 |
| >=5 | 7(17.9) | 32(82.1) | 2.14 | 0.81–5.59 | 0.12 | 2.21 | 0.67–7.22 | 0.18 |
| **Experience of dealing with patients died from COVID-19** | No | 15(40.5) | 22(59.5) | - | - | - | - | - |
| 1–4 | 30(29.1) | 73(70.9) | 1.65 | 0.75–3.62 | 0.20 | 1.67 | 0.66–4.23 | 0.27 |


| Determinant Factors | Overall Burnout | Univariate logistic Regression | Multiple logistic Regression |
|---------------------|-----------------|-------------------------------|-----------------------------|
|                     | No | Yes | OR | 95% CI | P | OR | 95% CI | P |
| 5–9                 | 11(23.4) | 36(76.6) | 2.23 | 0.87–5.72 | 0.09 | 2.03 | 0.66–6.24 | 0.21 |
| >=10                | 7(21.2) | 26(78.8) | 2.53 | 0.88–7.32 | 0.08 | 1.99 | 0.57–6.94 | 0.27 |

a: To prevent redundancy, main effects of periods of time and Working in COVID-19 ward were not included in the multiple logistic model.

According to the univariate analysis, higher level of burnout among the GPs-Specialists was reported in the June-July (OR = 4.44, P = 0.02, 95% C.I.: 1.23–16.03) and males (OR = 2.03, P = 0.01, 95% C.I.: 1.12–3.66). Also, higher level of overall burnout is reported in December-January (OR = 0.29, P = 0.01, 95% C.I.: 0.15–0.57) and older age GPs-Specialists (OR = 0.95, P = 0.01, 95% C.I.: 0.93–0.99). Multiple logistic regression depicted that working in COVID-19 wards during June-July (OR = 13.93, P = 0.01, 95% C.I.: 3.62–53.51) was associated with increasing odds of overall burnout. However, older age was associated with decrease odds overall burnout (OR = 0.94, P = 0.01, 95% C.I.: 0.90–0.98). Detailed results of overall burnout and its determinant factors are presented in Table 4.
Table 4
Determinant factors of overall burnout among general physician and specialist

| Determinant factors                                      | Overall burnout | Univariate logistic Regression | Multiple logistic Regression |
|----------------------------------------------------------|-----------------|--------------------------------|----------------------------|
|                                                          | No              | Yes                            | OR                           |
| Periods of time * Working in COVID-19 ward               | Dec-Jan * Work (Yes) | 27(50.9) | 26(49.1) | 0.52 | 0.27–1.02 | 0.06 | 0.73 | 0.33–1.57 | 0.42 |
|                                                          | Dec-Jan * Work (No) | 22(55) | 18(45) | - | - | - | - | - | - |
|                                                          | Jun-Jul * Work (Yes) | 3(7) | 40(93) | 7.28 | 2.12–25.02 | 0.01 | 13.93 | 3.62–53.51 | 0.01 |
|                                                          | Jun-Jul * Work (No) | 0(0) | 0(0) | - | - | - | - | - | - |
|                                                          | Mar-Apr * Work (Yes) | 18(28.1) | 46(71.9) | - | - | - | - | - | - |
|                                                          | Mar-Apr * Work (No) | 1(8.3) | 11(91.7) | - | - | - | - | - | - |
| Periods of time                                          | Dec-Jan | 49(52.7) | 44(47.3) | 0.29 | 0.15–0.57 | 0.01 | .a | .a | .a |
|                                                          | Jun-Jul | 3(7) | 40(93) | 4.44 | 1.23–16.03 | 0.02 | .a | .a | .a |
|                                                          | Mar-Apr | 19(25) | 57(75) | - | - | - | - | .a | .a | .a |
| Working in COVID-19 ward                                 | No | 23(44.2) | 29(55.8) | - | - | - | - | .a | .a | .a |
|                                                          | Yes | 48(30) | 112(70) | 1.85 | 0.97–3.52 | 0.06 | .a | .a | .a |
| Age (years)                                              | 39.83 ± 8.77 | 36.40 ± 8.95 | 0.95 | 0.93–0.99 | 0.01 | 0.94 | 0.90–0.98 | 0.01 |
| Gender                                                   | Male | 25(25.3) | 74(74.7) | 2.03 | 1.12–3.66 | 0.01 | 1.89 | 0.98–3.64 | 0.06 |
|                                                          | Female | 46(40.7) | 67(59.3) | - | - | - | - | - | - |
| Marital status                                           | Single | 20(25.3) | 59(74.7) | - | - | - | - | - | - |
|                                                          | Married | 51(38.3) | 82(61.7) | 0.54 | 0.29–1.01 | 0.05 | 0.99 | 0.45–2.15 | 0.97 |
| Experience of                                            | No | 29(35.4) | 53(64.6) | - | - | - | - | - | - |
### Determinant factors

| Determinant factors                                           | Overall burnout | Univariate logistic Regression | Multiple logistic Regression |
|---------------------------------------------------------------|-----------------|--------------------------------|-----------------------------|
|                                                               | No              | Yes                            | OR  | 95% CI  | P   | OR  | 95% CI  | P   |
| resuscitation maneuver for COVID-19 patients                  |                 |                                |     |         |     |     |         |     |
| 1–4                                                           | 29(34.1)        | 56(65.9)                       | 1.05| 0.55–1.99| 0.86| 0.90| 0.39–2.05| 0.80|
| >=5                                                           | 13(28.9)        | 32(71.1)                       | 1.34| 0.61–2.96| 0.45| 1.87| 0.65–5.35| 0.23|
| Experience of dealing with patients died from COVID-19        |                 |                                |     |         |     |     |         |     |
| 0                                                             | 20(33.9)        | 39(66.1)                       | -   | -       | -   | -   | -       | -   |
| 1–4                                                           | 19(29.7)        | 45(70.3)                       | 1.21| 0.56–2.59| 0.61| 1.35| 0.52–3.50| 0.53|
| 5–9                                                           | 9(25.7)         | 26(74.3)                       | 1.48| 0.58–3.75| 0.40| 1.63| 0.51–5.20| 0.40|
| >=10                                                          | 23(42.6)        | 31(57.4)                       | 0.69| 0.32–1.48| 0.34| 0.83| 0.28–2.41| 0.73|

a: To prevent redundancy, main effects of periods of time and Working in COVID-19 ward were not included in the multiple logistic model.

### Discussion

In this study we have provided further information on overall job burnout and its related sub-dimensions among interns-residents and GPs-Specialists during three separated periods of time in the era of the COVID-19 pandemic. In addition, we have searched for significant association between sex, age and working in covid-19 wards with the overall burnout in both groups.

While there was not any significant difference between the prevalence of overall burnout among interns-residents and GPs-Specialists, the highest mean score of burnout and its sub-dimensions including depersonalization, and reduced achievement for interns-residents was attributed to December-January. This score for GPs-Specialists was at highest level during June-July with the exception in the sub-dimension of reduced achievements. The higher values of overall burnout score in December and January correlates fairly well with the study written by Amanullah et al.(17) and further support the concept of increasing burnout resulting from the increasing workload due to COVID-19. This substantiates previous findings in the literature which has shown statistically significant decrease in EP wellness during the pandemic of COVID-19 as a result of the followings: 1-feeling less happy while being at work, 2-having more stress on days not being at work, 3-having more trouble falling asleep, 4- having a sense of dread when thinking of work needing to be done and 5-being more concern about ones’ health and the health of the beloved ones.(18) A recent study (19) has shown that burnout levels among emergency physician remained stable during the initial weeks of the pandemic. However, the impact of COVID-19 on the work environment and personal perceptions as well as fears about its impacts on lifestyle have affected physicians’ well-being. On the other hand, Sophie et al. proposed that the development of peer support networks during the pandemic may lead to reduced physician burnout in a paper of 2020.(20) Therefore, exposure to COVID-19 does not necessarily correlate with increased burnout and there
is an area for more research. Moreover, given that our findings are based on a limited number of participants, the result from such analysis should be considered with the utmost caution.

Moving through the rest of our results, the most striking point was the correlation between working in COVID-19 wards and burnout in June-July for GPs-Specialists versus lack of any similar correlation for Interns-Residents, according to both univariate and multivariate analysis. On the other side, age was correlated with burnout for both groups of GPs-Specialists and Interns-residents. Further tests carried out by Sunjaya et al. points to the higher risk of experiencing depressive symptoms and burnout for the health care personnel which are responsible for treating COVID-19 patients and have direct contact to them(21) As reviewed by Rikinkumar et al. (22), contributors to physician burnout could be categorized to 1-work factors such as excessive workloads, long working hours and specialty choice, 2-Personal characteristics including age and sex and 3-organizational factors. Furthermore, physicians with more experience demonstrated lower rates of burnout, while early-career physicians demonstrated higher rates of burnout.(23) More recent evidence suggests that among trainee physicians, workplace-related factors, including concerns about patient care, poor work-life balance, excessive work demands, a dysfunctional work environment, and poor career development, demonstrated stronger association with burnout whereas the feeling of stress compared with non-work-related factors, such as sex and financial worries.(24, 25) Therefore it could be hypothesized that in the case of Interns-Residents as trainee physicians, although there wasn’t any specific correlation between burnout and working in COVID-19 wards, there are many workplace-related factors leading to burnout which could be exist in all wards of the hospital including COVID-19 wards as well.

Study Limitations

The most important limitation of this study was the reluctance of participants to complete the questionnaires due to the high volume of activities. In this regard, we tried to address this problem by describing the importance of research to participants.

Conclusion

Taken together, evaluating the prevalence of overall burnout during the Covid-19 pandemic in addition to finding its correlative factors could be usefully employed in providing information for the policymakers. The present finding has the potential to remind policy makers the importance of burnout issue among physicians during the era of pandemic and to persuade them for taking appropriate action in order to prevent this phenomenon. Focusing on the organizational resilience and the connecting dimensions between organizations and their physicians could be a helpful framework in addressing physician mental health.(26) Also, fostering a healthcare working environment that supports intrinsic motivation and improves work hours as well as rewarding physicians fairly and equitably may prevent them from burnout and job dissatisfaction.(27) Doolittle et al. (28) suggests that amelioration of burnout requires both intrinsic strategies such as creative writing (29) or longitudinal mindfulness trainings (30) that emphasize physician coping skills as well as extrinsic strategies that address institutional support.

Abbreviations

GP: General physician
OR: Odds ratio

MBI: Maslach Burnout Inventory

EE: Emotional exhaustion

DP: Depersonalization

PA: Personal achievement

C.I.: Confidence interval

Declarations

Ethics approval and consent to participate

Research protocol of this study was evaluated and approved by the Ethics Committee of Shiraz University of Medical Sciences (code: IR.SUMS.REC.1398.877). All the participants were asked to fulfil their written consent form before completing the questionnaires. All the participants completed the questionnaires willingly and were ensured of the confidentiality of the collected data.

Consent to publish

Not applicable

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests

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Authors’ contributions

**YS and ST** contributed in designed the study, analyzed the data, and interpreted the results, wrote the manuscript drafting. **MSM, AE, and LZ** contributed in analysis of data and interpretation the results. **SSh, KKh, GhRS, and PK** contributed in interpretation the results wrote the manuscript drafting. **KBL** contributed in interpretation the results and designed the study. The final version was confirmed by all authors for submission.
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