Study on health-related quality of life and influencing factors of pediatric medical staff during the COVID-19 outbreak

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Abstract

Aims To evaluate the health-related quality of life (HRQoL) status and explore its associated factors in pediatric medical staff during the COVID-19 epidemic so as to guide hospitals and administrators to formulate suitable interventions.

Methods A cross-sectional study was conducted to investigate the HRQoL of pediatric medical staff. Univariable and multivariable logistic regression were used to analyze the associated factors.

Results A total of 2,997 participants were recruited. Females scored worse than males in terms of emotional functioning (*OR* = 1.6, 95%*CI*: 1.2–2.1) and cognitive functioning (*OR* = 1.4, 95%*CI*: 1.1–1.8). The respondents aged 30–39 years and 40–49 years scored worse in nearly all domains of HRQoL compared health care professionals under 30 years old. Respondents with high education had lower scores in physical functioning (*OR* = 1.3, 95%*CI*: 1.0-1.7) and emotional functioning (*OR* = 1.5, 95%*CI*: 1.2–1.9).Compared with doctors, nurses had higher scores in all domains except for summary score and worry. The respondents whose working places had not set up pediatric fever clinics and isolated observation areas independently had better scores in all domains except for worry. The respondents who had ever treated patients with COVID-19 had lower scores in all domains.

Conclusions During the COVID-19 outbreak, the HRQoL of pediatric medical staff decreased. The factors associated with HRQoL can be used to develop intervention to improve HRQoL in pediatric medical staff.

Background

A Public Health Emergency concerning the novel Coronavirus (COVID-19) was issued [1] in Wuhan, China on 31 December 2019. The virus has been spread to 94 countries outside of China and has infected more than 100,000 people globally (80,859 in China) by 7 March 2020[2][3] Since the outbreak of the pandemic, significant numbers of medical staff have been regularly required to work long shifts. These medical staff not only undertakes high-intensity work, but also faces the risk of infection. According to published literature, the outbreak of COVID-19 in China has caused mental health problems among medical staff and the general public worldwide[4][5][6][7]. To improve the mental health of residents in China during this crisis, the Chinese National Health Commission has released guidelines for local authorities to promote psychological crisis intervention for patients, medical personnel and the public during the COVID-19 outbreak[8][9].

COVID-19 is primarily transmitted *via* respiratory droplets and contact. Fever and respiratory symptoms are two of the most significant clinical manifestations[9]. According to published studies, pediatric outpatients (73.11%) and hospitalized patients (33.09%) are most likely to suffer from respiratory disease as compared with other types of illnesses[10]. During the COVID-19 pandemic,the pediatric medical staff were at high risk of infection. Additionally, since most children come from only-one child family homes, pediatric medical staff often face higher professional pressure on a daily basis as a result of close parental oversight. These considerations together may have an impact on health-related quality of life (HRQoL) of pediatric medical staff[11].

Therefore, in this publication we aim to evaluate the HRQoL and the factors associated with HRQoL of pediatric medical staff during the COVID-19 pandemic. With this study, we aim to provide fundamental evidence for clinicians and administrators to formulate targeted intervention measures to improve the HRQoL in pediatric medical staff during this, and future, pandemics.

Material And Methods

Design and Participants

This study featured a cross-sectional design based on an online survey between 13–17 February 2020. The respondents filled out the questionnaire anonymously, voluntarily and independently. A total of 2,997 pediatric medical staff from 29 provinces in China participated in the survey.

Instrument

Data was collected via a self-administered questionnaire. The first Section was related to the participants' socio-demographic characteristics, including age, gender, occupation, education, major, professional titles, hospital grade, hospital type, province and place of residence. The second Section was related to COVID-19 protection, including whether the pediatric fever clinic and isolation observation area are set up independently, whether they have ever treated COVID-19 or suspected COVID-19 patients, whether their family or colleagues have COVID-19 or suspected COVID-19, whether their family or colleagues have come into contact with COVID-19 patients or suspected patients, and whether they have worked in the clinical field of infectious diseases. The third Section was related to HRQoL. Since the purpose of this study is to analyze the individual HRQoL, after discussion with 5 experts, four sub-scales, including physical functioning(6 items), emotional functioning(5 items), social functioning (4 items), and cognitive functioning(5 items) were selected from the PedsQLTM Family Impact Module scale[12] and considered in the questionnaire. In addition, considering the worry and panic that may be caused by the pandemic, we have included 4 items to evaluate worry status through expert discussion, resulting in a HRQoL scale featuring 5 sub-scales.

Each item of the HRQoL scale has 5-Likert response options: 0 (never a problem), 1 (almost never a problem), 2 (sometimes a problem), 3 (often a problem) and 4 (almost always a problem). The item is then linearly converted to a score of 100 (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0),and the score of each subscale is the sum score of its items divided by the number of items. Therefore, the higher the score, the better the HRQoL (i.e., less negative impact)[13].

The Cronbach's α coefficient and Split-Half Coefficient were used to assess the reliability of the third Section of the questionnaire. The Cronbach's α coefficient and Split-Half Coefficient of the HRQoL scale and all its subscales were all above 0.70.

Statistical analysis

Continuous variables were presented as Mean ± standard deviation$(\mathrm{mean} \pm sd)$.Categorical variables were presented as frequencies and percentages [n(%)]. One-way analysis of variance (ANOVA) or t-test was used to compare scores among groups defined by each characteristic. Multiple forward stepwise logistic regression analyses (Entry=0.05, Removal=0.1) were used to explore the factors associated with HRQoL. The dependent variables were the summary of HRQoL values and all their domains which were converted into a dichotomous variable(≤ P25=1,>P25=0) according to its 25th percentile of the score. The independent variables were the demographic characteristics and COVID-19 protection-related characteristics. Statistical significance was set at p-value < 0.05. SPSS 23.0 software package for Windows was used to carry out all analyses.

Results

Demographic characteristics and HRQOL

A total of 2,970 respondents correctly filled and submitted the questionnaires out of a total of 2,997 respondents, and the effective rate of questionnaire collection was 99.1%. The respondents represented 29 provinces, among which Shaanxi province accounted for 43.3% of the responses. The vast majority of the respondents (88.8%) were women and most (47.9%) were aged 30–39 years. 52.4% of subjects were doctors. The mean score of the Summary HRQoL was 69.7 (SD

= 15.9), and the mean scores of its five subscales were worry(58.9 ± 19.0), physical functioning (70.5 ± 19.1), emotional functioning (71.1 ± 20.2), cognitive functioning (71.5 ± 19.5) and social functioning (75.5 ± 19.5).Further details of the participants' characteristics can be found in Table 1.

Table 1 presents the univariate analyses results. Male respondents have higher scores than female respondents in emotional functioning but lower score than female respondents in social functioning (72.5 vs 75.9).The respondents under 30 years old had the highest scores in all HRQoL domains, while respondentsaged40-49 years old had the lowest scores. Respondents with higher education (Masters and above) had lower scores than those with lower education (Bachelors and below) in all domains. Doctors had lower scores in all domains except for worry when compared to nurses. Respondents working in the tertiary class-A hospital had higher scores in social functioning and had lower scores in worry compared to respondents working in second-class hospitals.

Table 1

HRQoL based on socio-demographic characteristics(mean$\pm sd$)

	N(%)	Physical Functioning	Emotional Functioning	Social Functioning	Cognitive Functioning	Worry	Summary Score
Gender							
Male	334(11.2)	69.2 ± 19.2	73.2 ± 20.3	72.5 ± 18.9	70.5 ± 19.8	59.9 ± 19.8	69.3 ± 16.7
Female	2636(88.8)	70.6 ± 19.1	70.9 ± 20.2	75.9 ± 17.8	71.6 ± 19.5	58.7 ± 18.9	69.8 ± 15.8
P value		0.193	0.046	0.001	0.324	0.269	0.601
Age (years)							
< 30	805(27.1)	74.9 ± 18.2	75.4 ± 19.9	79.5 ± 17.3	77.1 [a]±19.1	59.9 ± 20.1[ab]	73.7 ± 15.6
30–39	1277(4.0)	69.3 ± 19.1	70.4 ± 20.5	75.2 [b]±17.9	71.1 [b]±19.6	57.8 ± 18.9 [b]	69.0 ± 16.0
40–49	541(18.2)	66.8 ± 18.8	68.2 ± 19.0	71.7 [c]±18.2	65.4 [c]±18.0	58.3 ± 18.2 [b]	66.2 ± 15.0
≥ 50	347(11.7)	69.9 ± 19.7	68.5 ± 19.8	73.6 [bc]±17.7	69.5 [b]±19.0	61.3 ± 17.5[a]	68.7 ± 15.7
P value		< 0.001	< 0.001	< 0.001	< 0.001	0.006	< 0.001
Education							
Bachelor and below	2540(85.5)	71.2 ± 18.9	72.3 ± 20.1	76.4 ± 17.7	72.4 ± 19.4	59.5 ± 19.0	70.6 ± 15.7
Masterandabove	430(14.5)	66.1 ± 19.3	64.5 ± 19.6	70.4 ± 18.7	66.5 ± 19.4	54.9 ± 18.3	64.7 ± 15.9
P value		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Occupation							
Doctors	1557(52.4)	67.7 ± 18.9	68.4 ± 19.8	72.1 ± 18.1	68.0 ± 19.1	58.6 ± 17.7	67.1 ± 15.4
nurses	1413(47.6)	73.5 ± 18.9	74.2 ± 20.2	79.3 ± 17.1	75.4 ± 19.2	59.2 ± 20.3	72.6 ± 15.9
P value		< 0.001	< 0.001	< 0.001	< 0.001	0.390	< 0.001
Professional titles							
Senior	747(25.2)	67.5 ± 19.3	68.3 ± 19.8	71.8 ± 17.9	67.1 ± 18.2	59.4 ± 17.6	67.0 ± 15.4

	N(%)	Physical Functioning	Emotional Functioning	Social Functioning	Cognitive Functioning	Worry	Summary Score
intermediate	883(29.7)	69.0 ± 19.3	69.3 ± 19.9	74.5 ± 18.1	69.4 ± 19.8	57.8 ± 19.2	68.2 ± 15.9
junior	1340(45.1)	73.1 ± 18.5	73.9 ± 20.2	78.3 ± 17.5	75.3 ± 19.3	59.2 ± 19.5	72.3 ± 15.8
P value		< 0.001	< 0.001	< 0.001	< 0.001	0.122	< 0.001
Hospital grade							
Tertiary class-A hospital	2172(73.1)	70.6 ± 19.3	71.0 ± 20.5	75.9 ± 18.0	72.2 ± 19.5	58.2 ± 19.3	69.8 ± 16.1
Secondclass hospital	798(26.9)	69.9 ± 18.6	71.4 ± 19.3	74.5 ± 18.0	69.8 ± 19.4	60.7 ± 18.1	69.4 ± 15.4
P value		0.372	0.655	0.065	0.003	0.001	0.540
Hospital type							
Comprehensive hospital	2224(74.9)	70.6 ± 19.4	71.6 ± 20.1	75.7 ± 18.0	71.5 ± 19.6	59.4 ± 19.1	70.0 ± 16
Specialized hospital	746(25.1)	70.0 ± 18.3	69.8 ± 20.4	75.0 ± 18.1	71.5 ± 19.3	57.1 ± 18.4	69 ± 15.7
P value		0.475	0.033	0.354	0.956	0.004	0.124
Pediatrics major							
Internal medicine	1836(61.8)	70.4 ± 19.1	70.9 ± 19.9	74.9 ± 17.9	71.2 ± 19.4	59.2 ± 19.1	69.6 ± 15.8
Respiratory	193(6.5)	71.0 ± 19.4	72.6 ± 22.5	76.1 ± 18.4	72.0 ± 18.6	58.1 ± 20.7	70.2 ± 16.8
Infection	79(2.7)	71.6 ± 19.0	74.8 ± 20.8	77.0 ± 17.6	74.2 ± 21.4	60.4 ± 17.4	71.8 ± 15.7
Critical medicine	274(9.2)	69.5 ± 20.0	71.6 ± 19.9	76.8 ± 17.7	73.6 ± 20.3	58.6 ± 18.8	70.2 ± 16.2
Others	588(19.8)	70.6 ± 18.7	70.7 ± 20.2	76.5 ± 18.2	70.9 ± 19.5	58.0 ± 18.3	69.6 ± 15.6
P value		0.879	0.375	0.196	0.214	0.615	0.726
Place of residence							
City	2730(91.9)	70.5 ± 19.2	71.1 ± 20.2	75.5 ± 18.0	71.6 ± 19.4	58.9 ± 18.9	69.8 ± 15.9
Rural	240(8.1)	70.1 ± 18.2	71.3 ± 19.7	75.6 ± 17.6	70.8 ± 20.2	58.5 ± 19.6	69.5 ± 15.7
P value		0.788	0.932	0.955	0.561	0.739	0.793
Province							
Hubei	83(2.8)	63.6 ± 15.9	56.8 ± 18.3	67 ± 16.9	63.8 ± 16.6	41.0 ± 15.0	59.0 ± 12.2

	N(%)	Physical Functioning	Emotional Functioning	Social Functioning	Cognitive Functioning	Worry	Summary Score
Others	2887(97.2)	70.7 ± 19.1	71.6 ± 20.1	75.8 ± 18	71.7 ± 19.5	59.4 ± 18.8	70.0 ± 15.9
P value		0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Total	2970(100.0)	70.5 ± 19.1	71.1 ± 20.2	75.5 ± 18	71.5 ± 19.5	58.9 ± 19.0	69.7 ± 15.9

Covid-19 Protection Related Characteristics And HRQOL

As shown in Table 2, the hospitals in which 68.1% of the respondents worked had independent pediatric fever clinics and isolated observation areas. Univariate analyses found that the respondents whose working places had not set up independent pediatric fever clinics and isolated observation areas had lower HRQoL scores, except for worry. The respondents who had treated patients with COVID-19 or suspected COVID-19 had lower scores than those who had not. Respondents whose family members or colleagues had ever suffered from COVID-19 or suspected COVID-19 had lower HRQoL than those who did not.

Table 2

HRQoL based on COVID-19 protection related characteristics($\overline{x} \pm s$)

	N(%)	Physical Functioning	Emotional Functioning	Social Functioning	Cognitive Functioning	Worry	Summary Score
The pediatric fever clinic and the isolated observation set up independently							
No	946(31.9)	68.1 ± 19.7	69.3 ± 20.1	73.0 ± 18.3	67.6 ± 19.5	58.0 ± 18.3	67.4 ± 16.0
Yes	2024(68.1)	71.6 ± 18.7	72.0 ± 20.1	76.7 ± 17.7	73.4 ± 19.2	59.3 ± 19.3	70.8 ± 15.7
P value		< 0.001	0.001	< 0.001	< 0.001	0.077	< 0.001
Whether you have ever treated patients with COVID-19							
No	2484(83.6)	71.5 ± 19.1	72.2 ± 20.0	76.5 ± 17.8	72.4 ± 19.3	60.0 ± 18.9	70.7 ± 15.7
Yes	486(16.4)	65.2 ± 18.4	65.7 ± 20.2	70.7 ± 18.4	67.0 ± 19.7	53.2 ± 18.5	64.6 ± 15.7
P value		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Whether your family or colleagues have ever suffered from COVID-19							
No	118(4.0)	64.5 ± 18.2	64.4 ± 21.8	70.5 ± 18.2	66.7 ± 18.4	51.8 ± 18.8	63.8 ± 15.3
Yes	2852(96.0)	70.7 ± 19.1	71.4 ± 20.1	75.7 ± 17.9	71.7 ± 19.5	59.1 ± 18.9	70.0 ± 15.9
P value		0.001	< 0.001	0.002	0.006	< 0.001	< 0.001
Whether your family or colleagues have ever contact with COVID-19 patients							
Yes	364(12.3)	65.8 ± 17.2	65.3 ± 19.5	70.1 ± 17.8	67.0 ± 17.5	53.1 ± 17.6	64.6 ± 14.4
No	2606(87.7)	71.1 ± 19.2	72.0 ± 20.1	76.3 ± 17.9	72.2 ± 19.7	59.7 ± 19	70.5 ± 16.0
P value		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Whether you have ever worked in the clinical field of infectious diseases							
No	2362(79.5)	71.1 ± 19.0	71.8 ± 20.1	76.2 ± 17.9	72.3 ± 19.5	59.0 ± 19.1	70.3 ± 15.8
Yes	608(20.5)	67.9 ± 19.3	68.7 ± 20.5	72.8 ± 18.2	68.4 ± 19.4	58.3 ± 18.5	67.4 ± 16.0
P value		< 0.001	0.001	< 0.001	< 0.001	0.381	< 0.001
Total	2970	70.5 ± 19.1	71.1 ± 20.2	75.5 ± 18.0	71.5 ± 19.5	58.9 ± 19.0	69.7 ± 15.9

Factors associated with HRQoL

As shown in Table 3, logistic regression analysis shows that females had lower emotional functioning scores (OR = 1.6, 95%CI: 1.2–2.1) and cognitive functioning scores (OR = 1.4, 95%CI: 1.1–1.8) when compared to males. The respondents aged 30–39 years and 40–49 years had lower scores in all domains, except for worry, compared to those aged less than 30 years. Respondents with higher education level (Masters and above) had lower summary (OR = 1.5, 95%CI: 1.2–1.9), physical functioning (OR = 1.3, 95%CI: 1.0-1.7) and emotional functioning (OR = 1.5, 95%CI: 1.2–1.9) scores than those with lower education level (bachelor and below). Nurses had higher scores in all domains, except for the summary score and worry, compared to doctors.

Table 3
Logistic regression analysis of HRQoL (OR,95%CI)

	Physical Functioning	Emotional Functioning	Social Functioning	Cognitive Functioning	Worry	Summary Score
Gender (ref="Male")						
Female	—	1.6(1.2–2.1)	—	1.4*(1.1–1.8)	—	—
Age (ref="<30")						
30–39	1.6**(1.3-2.0)	1.6**(1.3-2.0)	1.3*(1.1–1.7)	1.6**(1.3–2.1)	1.1(0.9–1.4)	1.8**(1.4–2.2)
40–49	1.6*(1.2–2.1)	1.7**(1.3–2.2)	1.4*(1.1–1.9)	2.0**(1.6–2.8)	0.9(0.8–1.2)	2.0**(1.5–2.6)
≥ 50	1.3(0.9–1.8)	1.3(0.9–1.8)	1.1(0.8–1.5)	1.5*(1.1–2.1)	0.7*(0.5–0.9)	1.3(0.9–1.8)
Education (ref=" Bachelor and below")						
Masterandabove	1.3*(1.0-1.7)	1.5*(1.2–1.9)	—	—	—	1.5**(1.2–1.9)
Occupation (ref=" Doctors")						
Nurses	0.8*(0.6–0.9)	0.8*(0.7–0.99)	0.6**(0.5–0.7)	0.7*(0.6–0.9)	—	—
Province(ref="out of Hubei")						
Hubei	—	2.2*(1.4–3.5)	1.8*(1.1–2.9)	1.6*(1.0-2.6)	6.3**(3.4–11.5)	2.2*(1.4–3.6)
Whether the pediatric fever clinic and the isolated observation area are set up independently (ref="Yes")						
NO	1.3*(1.03–1.5)	1.2*(1.01–1.4)	1.2*(1.03–1.5)	1.6*(1.3–1.9)	—	1.5**(1.3–1.8)
Whether you have ever treated patients with COVID-19 or suspected COVID-19 (ref="No")						
Yes	1.3**(1.1–1.7)	1.6**(1.3–1.9)	1.5*(1.2–1.8)	1.4*(1.2–1.8)	1.6**(1.3-2.0)	1.7**(1.4–2.1)
Whether your family or colleagues have ever suffered from COVID-19 or suspected COVID-19(ref="No")						
Yes	1.8*(1.2–2.6)	—	—	—	—	—
Whether your family or colleagues have ever contact with COVID-19 patients or suspected patients(ref="No")						
Yes	—	—	1.3*(1.0-1.6)	—	—	—

Notes: Statistical significant at ** $p < 0.001$, * $p < 0.05$

The respondents whose working places had no independent pediatric fever clinics and isolated observation areas had lower scores in all HRQoL domains, except for worry, than those who had. The respondents who had treated patients

with COVID-19 or suspected COVID-19 had lower scores in all HRQoL domains than those had not treated patients with COVID-19 or suspected COVID-19. The respondents whose family members or colleagues had ever suffered from COVID-19 or suspected COVID-19 had lower physical functioning scores(OR = 1.8, 95%CI: 1.2–2.6) than those whose family members or colleagues had not suffered from COVID-19 or suspected COVID-19.The respondents whose family members or colleagues had contact with COVID-19 patients or suspected patients had lower social functioning scores (OR = 1.3, 95%CI: 1.0-1.6) than those whose family members or colleagues that had no contact with COVID-19 patients or suspected patients. Respondents living in Hubei Province had lower scores for all domains, except physical functioning, than those living in other Provinces.

Discussions

In a pandemic, health care workers face greater risk of infection and undertake higher work intensity as compared with the general population. This can lead to excessive fatigue and tension which led to anxiety, sadness, grievance, helplessness, and depression, among other emotions[14]. As our results showed, 8.2% of the respondents frequently felt anxious, which is similar to the findings from Liu et al[15].

Multivariate analysis showed that the socio-demographic characteristics associated with HRQoL of the respondents were gender, age, occupation and education. Females were associated with worse scoring than males in emotional functioning and cognitive functioning. We hypothesize that the HRQoL of doctors was worse than that of nurses because doctors receive patients first, and they need to conduct physical patient examinations (e.g., pharynx examinations), leading to a relatively higher risk of infection than nurse. The HRQoL of respondents living in Hubei Province was worse, which may be related to the more serious epidemic situation and higher risk of infection.

Multivariate analysis also showed that HRQoL was closely related to COVID-19 protection-related characteristics, especially establishment of independent settings for the fever clinic and isolation area, as well as the treatment of patients with COVID-19 or suspected COVID-19. We hypothesize that these two factors were closely related to the risk of infection. The higher the possibility of infection, the more likely professionals are to suffer from anxiety[16]. According to the joint investigation report from the China-World Health Organization and the relevant data released by the Chinese government, nosocomial infections among medical staff largely occurred in the early stage of COVID-19 infection, primarily in Wuhan when there was a lack of materials and experience in dealing with the disease[17].These findings suggest that it is critical to strengthen the safety of health care workers. Measures should be taken to reduce the risk of nosocomial infection, such as triage outside of hospitals (e.g., in tents or other shelters), establishment of an independent fever clinic and isolation area, and an adequate supply of protective equipment[18].

After the outbreak of the epidemic, the National Health Commission of China issued the guideline for emergency psychological crisis intervention during the outbreak of COVID-19 on January 26, 2020[19]. This guideline has formulated psychological intervention programs and key points for different personnel, such as people infected with COVID-19, personnel under quarantine, front-line staff, and the general public. According to our results, we believe that in addition to adopting the guidelines for daily psychological crisis intervention, we should also consider more targeted interventions according to the characteristics of pediatric medical staff to allay their concerns and improve their HRQoL. If the conditions permit, measures could be taken to meet their personal needs, such as care of an older family member and providing front-line staff with accommodations near the hospital. This would help maintain individual and team performance over the long run and improve the mental and physical health of these health care professionals.

There are some limitations in this study. First, since this study is a cross-sectional survey it is not possible to elucidate causal relationships[20]. Second, the survey was conducted online, which may result in respondent bias. However, face-to-face surveys were not possible during the pandemic.

Conclusion

During the outbreak of COVID-19, the HRQoL of pediatric medical staff was impacted. The respondents with different demographic characteristics and COVID-19 protection-related characteristics were impacted to varying degrees. Therefore, clinicians and administrators should focus on developing interventions according to the characteristics of different groups to improve the HRQoL of pediatric medical staff.

Abbreviations

HRQoL
Health-Related Quality of Life
COVID-19
coronavirus disease 2019

Declarations

Ethics approval and consent to participate

This study was approved by the ethical board of the Fourth Military Medical University and all participants provided written informed consent.

Consent for publication

Not applicable

Availability of data and materials

The data set supporting the conclusion of this article is available on request to the corresponding author.

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

All authors on this manuscript made significant contributions to the study design. Jiang Xun and Shang Lei have made substantial contributions to design of the work; Huang Feng and Yang Zhe were responsible for the data analysis and interpretation of data, as well as drafting the manuscript. Wang Yue, Zhang Wei, Lin Yan, Zeng Ling-chao were involved in the acquisition of data. All authors read and approved the final manuscript.

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