Impact of Medical Professionals on Carbapenem-Resistant Pseudomonas Aeruginosa: Moderation Effect of Workload Based on the Panel Data in China

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Research article

Keywords: carbapenem-resistant Pseudomonas aeruginosa; medical professionals; workload; moderation effect; fixed-effect model

DOI: https://doi.org/10.21203/rs.2.15355/v3

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Abstract

**Background:** Antimicrobial resistance (AMR) causes serious increase in morbidity, mortality and costs, especially carbapenem-resistant Pseudomonas aeruginosa (CRPA). Medical professionals play an important role in tackling AMR. Available studies overlooked the impact of workload on medical professionals in the relationship between medical professionals and AMR. This study explored the relationship between medical professionals and CRPA rate and the moderation effect of medical professionals’ workload in this relationship.

**Methods:** Based on provincial-level panel data in China, hierarchical regression analysis was used to explore moderation effect of workload on medical professionals and CRPA rate. Fixed-effect model was applied to estimate the moderation effect models. Medical professionals were measured by the numbers of physicians, registered nurses, pharmacists, clinical microbiologists per 1000 populations. Workload was measured by the number of daily visits of physicians.

**Results:** The numbers of physicians, registered nurses, pharmacists and clinical technicians were significant negative with CRPA rate (Coef. = -0.889, -0.775,-1.176, -0.822; P= 0.003, 0.003, 0.011, 0.007, respectively). Workload had significant positive moderation effect between physicians, registered nurses, pharmacists, clinical technicians and CRPA rate (Coef.= 1.270, 1.400, 2.210, 1.634; P=0.004, 0.001, 0.035, 0.003, respectively).

**Conclusions:** Increasing medical professionals may help curb CRPA. Measures to reduce medical professionals' workload should be implemented to improve CRPA performance further.

**Background**

Many countries are facing the challenge of antimicrobial resistance (AMR). About 25,000 people die from AMR a year in European countries [1], and data from India, Nigeria, Pakistan and the democratic republic of Congo indicate that a large number of newborn deaths are caused by drug-resistant sepsis [2]. AMR in particular carbapenem-resistant Pseudomonas aeruginosa (CRPA) threatens global public health security [3]. Since Pseudomonas aeruginosa is the main pathogens of healthcare-associated infection (HAI) [4], and Pseudomonas aeruginosa infections are often challenging to treat because of its intrinsic nonsusceptibility to many antimicrobials. Pseudomonas aeruginosa causes an estimated 51,000 HAI in the United States annually and was the third most common gram-negative cause of selected HAI [5]. The increasing rate of carbapenem-resistant Pseudomonas aeruginosa worldwide limiting its therapeutic options as well as increasing costs and risk of mortality [6, 7]. Carbapenems are considered by WHO as critically important antimicrobials[CIs and have become important antimicrobials for serious Pseudomonas aeruginosa infections [5, 7].

In 2011, WHO marked “antimicrobial resistance: no action today, no cure tomorrow”. A consensus in the antimicrobial stewardship is to establish the multidisciplinary team of medical professionals, and include an infectious disease physician, a clinical pharmacist and a clinical microbiologist, with expertise and
professional involvement in the diagnosis, prescriptions, prudent use and evaluation of antimicrobials [8]. Registered nurses are often included in the team since they always serve as the most consistent providers of care at the bedside and one of the integral executors of AMR stewardship such as preventative and proactive infection prevention programmes [9].

The relationship between medical professionals and AMR is a significant concern of health service research and health economics [10]. Prior studies mainly focus on the direct relationship between medical professionals and AMR. For instance, Liu et al. [10] found that increasing the number of clinical microbiologists could significantly reduce Staphylococcus aureus and coagulase-negative staphylococci rate, by using the provincial panel data in China. Another typical study found that pharmacist-led antimicrobial stewardship program had a lower mortality rate (19.3% vs 29.0%) and a lower multidrug-resistance (23.8% vs 31.7%) compared to the control group in a multicenter prospective cohort study on 577 patients [11].

Medical professionals’ workload is closely related to health care related outcomes. Some previous studies have focused on the impact of workload on medical professionals. For instance, a systematic review pointed out that high workload harms medical professionals’ well-being, such as being prone to job burnout and staffing turnover in ICU [12]. Other studies have explored the relationship between medical professionals’ workload and AMR. A 3 year cohort study in Portugal showed physicians’ workload (OR = 0.97, 95% CI: 0.94-1.00; p < 0.05) was related to poor quality of antimicrobials prescribing [13], which could cause AMR. Similar result has been found in an observational study in Norway that odds of prescribing antimicrobials for acute respiratory infections were 1.64 (95% CI: 1.33-2.03) times higher among general practitioners with higher workload [14].

The available studies examined medical professionals and workload as independent predictors of AMR and overlooked the potential interaction effects among medical professionals and their workload. So the interesting questions is whether workload could moderate the relationship between medical professionals and AMR. And what is the action path of workload on this relationship from a macro perspective. Since CRPA caused great concern, this study explored the relationship between medical professionals and CRPA rate and moderation effect of workload in the relationship with the 2014-2017 provincial balanced panel data in China.

**Hypothesis**

Hypothesis 1: The increase number of medical professionals is negatively associated with CRPA rate in China at this stage. Since many kinds of medical professionals play different critical roles in monitoring, guiding and rational use of antimicrobials and preventing from CRPA. Physicians prescribe the necessary antimicrobial agents according to the patient’s disease symptoms and guidelines related. Nurses are directly involved in the administration, management and monitoring of antimicrobials, assessing patient suitability for outpatient antimicrobial management, identifying errors in a timely manner, and providing appropriate education for patients [15]. Pharmacists play an integral role in educating physicians and patients on appropriate use of antimicrobials, monitoring and auditing outcomes of antimicrobial usage,
and reviewing individual patient regimens to optimize therapy [16]. Clinical microbiologists report on isolation and drug susceptibility tests which can provide evidence for the selection of antimicrobials with their professional knowledge [17]. As China has not established effective practitioner-based referral system, it is common for a medical professional to see around 100 patients daily in the outpatient department in large hospitals. The time spent with each patient is usually less than 3 minutes [18]. For these reasons the time they spent on antimicrobial stewardship and infection prevention and control is very limited. Increasing medical professionals may help them better undertake these tasks.

Hypothesis 2: Workload moderate the association between medical professionals and CRPA rate. Increasing the number of medical professionals helps to improve the hospitals’ service capacity with monitoring, guiding, and providing education for antimicrobials and enhance the rational use of antimicrobials. However, medical professionals’ excessive workload may decrease the quality of medical care and nursing [19]. A retrospective study conducted in Turkey showed a significant correlation between increased nurse workload and multidrug-resistant organism colonization or infection [20].

Methods

Variable Measurement and Data Sources

This study created 30 provincial balanced panel data of China from 2014 to 2017. The main variables and data sources were as follows.

The numbers of physicians, registered nurses, pharmacists, clinical microbiologists per 1000 populations were selected as independent variables. The number of clinical microbiologists was estimated by technicians. Since physicians, pharmacists, clinical microbiologists are involved in the diagnosis, prescription, and prudent use of antimicrobials, and registered nurses are consistent executors, they are core members of AMR stewardship [8,9,21]. Divide the number of physicians, registered nurses, pharmacists, clinical microbiologists by 1000 populations, to adjust the deviation caused by population differences.

The number of daily visits of physicians in hospitals was used as moderation variable since the increase of daily visits of physicians indicates that the medical professionals need to work longer hours or take fewer breaks to meet medical demand. It has become one of the factors to be considered in measuring medical professionals’ workload [18]. Rodrigues et al. [13] used the number of daily visits of physicians as workload, and found that workload influenced physicians’ antimicrobials prescriptions. Gjelstad et al. [14] used the number of consultations to explore general practitioners’ workload and antimicrobials prescriptions.

The number of tertiary hospitals was used as the control variable. Due to the incomplete establishment of hierarchical diagnosis and treatment system in China, patients tend to choose large general hospitals which with high quality medical resources. Large hospitals are usually overcrowded and concentrate most cases of pseudomonas aeruginosa infections. CRPA rates, diagnostic proficiency, diagnostic
availability and competence with infection control practices in every province are also hospital-specific and are influenced by the number of large hospitals.

The rates of CRPA were obtained from the China Antimicrobial Resistance Surveillance System (CARSS) 2014-2017. The independent variables, moderation variable and control variable were obtained from China Health and Family Planning Statistical Yearbooks 2015-2018[22,23,24,25,2021,22, 23].

The summary statistics of the above variables were shown in Table 1. The number of registered nurses per 1000 people was the highest, followed by physicians, clinical microbiologists and pharmacists.

Table 1. Variable definitions and summary statistics
| Variable | Definition | N  | Mean  | SD    | Min  | Max  |
|----------|------------|----|-------|-------|------|------|
| CRPA     | Rate of carabapenem-resistant *Pseudomonas aeruginosa* | 120 | 21.445 | 6.514 | 8.7  | 36.4 |
| PHY      | The number of physicians per 1000 population | 120 | 1.959  | 0.476 | 1.3  | 4.1  |
| NUR      | The number of registered nurses per 1000 population | 120 | 2.524  | 0.525 | 1.65 | 4.8  |
| PHA      | The number of pharmacists per 1000 population | 120 | 0.325  | 0.083 | 0.186| 0.648|
| MCB      | The number of clinical microbiologists | 120 | 0.335  | 0.065 | 0.236| 0.587|
gists per 1000 population

| WORKL | The number of daily visits of physicians in hospitals
|-------|--------------------------------|
|       | 120 | 7.170 | 2.520 | 3.7 | 15.20 |

| HOS   | The number of tertiary hospitals
|-------|--------------------------------|
|       | 120 | 71.825 | 40.757 | 7 | 170 |

SD: standard deviation.

**Statistical Analysis**

Hierarchical regression analysis was used to test the moderation effect. The following equation was constructed to test the relationship between the number of medical professionals and CRPA rate firstly: (see Equation 1 in the Supplementary Files)

Secondly, in order to test the effect of the number of medical professionals on CRPA rate under the moderation of workload, it was gradually incorporated into the workload (equation (2)) and the interaction term between workload and the number of medical professionals (equation (3)). To avoid multi-collinearity effects, variables in the interaction terms were mean-centered in equation (3). If the regression coefficients of interaction term were statistically significant, the moderation effect of workload was significant [26]: (see Equations 2 and 3 in the Supplemental Files)

Where \( i = 1, 2, 3, \ldots, 29, 30 \) indicated province, and \( t = 1, 2, 3, 4 \) indicated year, \( \mu_i \) was an unobservable regional effect, \( \epsilon_{it} \) was a random error term. STAFF indicated one type of medical professionals as physicians, registered nurses, pharmacists, clinical technicians. Each variable was taken in logarithmic form to eliminate the influence of heteroscedasticity.

Panel data model is a quantitative method for longitudinal data, which could increases the estimator precision by increasing observations and obtain more dynamic information than a single cross-sectional
data [27]. The pooled ordinary least squares (OLS) model, fixed-effect (FE) model and random-effect (RE) model are often used to estimate panel data. Because OLS does not control for the fixed effect of provinces, the estimation caused by endogenous problems may be biased. FE model or RE model is further applied for estimation. RE model is relatively more effective, but exogenous variables and individual effects are not required to be correlated, while FE model, although there is no requirement between the exogenous variables and individual effects, consumes more degrees of freedom [28]. Hausman test can determine which model was more appropriate for result estimation. As shown in Table 2, every test rejected the null hypothesis, indicating that FE model was more reasonable (Table2).

Table 2. Panel data model estimation

| Variable | FE  | RE  | FE  | RE  | FE  | RE  | FE  | RE  |
|----------|-----|-----|-----|-----|-----|-----|-----|-----|
| ln PHY   | -0.888*** | -0.706*** |     |     |     |     |     |     |
| ln NUR   |      |      | -0.757*** | -0.833*** |     |     |     |     |
| ln PHA   |      |      |      |      | -1.126*** | -0.731*** |     |     |
| ln MCB   |      |      |      |      |      |      | -0.785*** | -0.728*** |
| ln WORK  | 0.001 | 0.524*** | 0.181 | 0.537*** | 0.398 | 0.678*** | 0.296 | 0.486*** |
| L        |      |      |      |      |      |      |      |      |
| ln HOS   | -0.418*** | 0.046 | -0.316** | 0.094 | -0.443*** | 0.021 | 0.433*** | 0.039 |
| Constant | 5.289*** | 2.285*** | 4.646*** | 2.359*** | 2.764** | 0.790 | 3.345*** | 1.119** |
| Hausman  | 33.30*** | 24.72*** | 33.45*** |     |     |     |     |     |
| test value | 0.000 | 0.0001 | 0.000 | 0.000 |     |     |     |     |

FE: Fixed-effect (FE) model; RE: random-effect (RE) model;

*** p<0.01, ** p<0.05, * p<0.1

STATA\textregistered version 13.0, Stata Corp., College Station, Texas, USA\textregistered was used for the statistical analysis.

Results

This 4-year balanced panel data included 120 records. The equations (1), (2) and (3) were tested in turn to explore the moderation effect of workload on the relationship between medical professionals and CRPA rate.

**Correlation analyses between the variables**
As shown in Table 3, workload was significantly and positively correlated with CRPA rate (r=0.363; p=0.000). However, the association between numbers of physicians, registered nurses, pharmacists, clinical technicians and CRPA rate were not statistically significant, respectively (r=0.120, r=0.109, r=0.095, r=0.136; p=0.194, p=0.236, p=0.301, p=0.140).

| Variable | 1  | 2  | 3  | 4  | 5  | 6  | 7  |
|----------|----|----|----|----|----|----|----|
| 1. ln PHY | 1.000 |    |    |    |    |    |    |
| 2. ln NUR | 0.788*** | 1.000 |    |    |    |    |    |
| 3. ln PHA | 0.788*** | 0.794*** | 1.000 |    |    |    |    |
| 4. ln MCB | 0.731*** | 0.849*** | 0.766*** | 1.000 |    |    |    |
| 5. ln WOR | 0.302*** | 0.388*** | 0.486*** | 0.225** | 1.000 |    |    |
| KL       | 0.109 | 0.128 | 0.086 | -0.037 | 0.158* | 1.000 |    |
| 7. ln CRPA | 0.120 | 0.109 | 0.095 | 0.136 | 0.363*** | 0.461*** | 1.000 |

*** p<0.01, ** p<0.05, * p<0.1

**Relationship between Medical Professionals and CRPA**

As shown in Table 4, there were significant negative correlations between physicians, registered nurses, pharmacists, clinical technicians and CRPA rate, respectively (Coef. = -0.889, -0.775, -0.1.176, -0.822; P=0.003, 0.003, 0.011, 0.007). That meant the increase in medical professionals was associated with lower CRPA rate. Hypothesis 1 was supported.

| Variable | 1  | 2  | 3  | 4  | 5  | 6  | 7  |
|----------|----|----|----|----|----|----|----|
| 1. ln PHY | 1.000 |    |    |    |    |    |    |
| 2. ln NUR | 0.788*** | 1.000 |    |    |    |    |    |
| 3. ln PHA | 0.788*** | 0.794*** | 1.000 |    |    |    |    |
| 4. ln MCB | 0.731*** | 0.849*** | 0.766*** | 1.000 |    |    |    |
| 5. ln WOR | 0.302*** | 0.388*** | 0.486*** | 0.225** | 1.000 |    |    |
| 6. ln HOS | 0.109 | 0.128 | 0.086 | -0.037 | 0.158* | 1.000 |    |
| 7. ln CRPA | 0.120 | 0.109 | 0.095 | 0.136 | 0.363*** | 0.461*** | 1.000 |

*** p<0.01, ** p<0.05, * p<0.1

**Table 4. Relationship between medical professionals and CRPA rate**
| Variable | Model (1)       | Model (2)       | Model (3)       | Model (4)       |
|----------|----------------|----------------|----------------|----------------|
| ln PHY   | -0.889***      |                |                |                |
|          | (0.276)        |                |                |                |
| ln NUR   |                | -0.775***      |                |                |
|          |                | (0.240)        |                |                |
| ln PHA   |                |                | -1.176**       |                |
|          |                |                | (0.434)        |                |
| ln MCB   |                |                |                | -0.822***      |
|          |                |                |                | (0.283)        |
| ln HOS   | -0.418***      | -0.322**       | -0.465***      | -0.445***      |
|          | (0.120)        | (0.143)        | (0.125)        | (0.126)        |
| Constant | 5.302***       | 5.034***       | 3.560***       | 3.922***       |
|          | (0.354)        | (0.403)        | (0.959)        | (0.791)        |
| R-squared| 0.431          | 0.457          | 0.404          | 0.412          |
| F        | 66.77***       | 64.89***       | 50.88***       | 55.55***       |

*** p<0.01, ** p<0.05, * p<0.1, cluster-robust standard errors in parentheses.

The Moderation Effect Test of Medical Professionals Workload

Model (5), model (7), model (9) and model (11) displayed that there were significant positive correlations between the number of physicians, registered nurses, pharmacists, clinical technicians and CRPA rate after the addition of workload, respectively (Coef. = -0.888, -0.757, -1.125, -0.785; P=0.005, 0.004, 0.017, 0.008). Model (6), model (8), model (10) and model (12) showed that the interaction terms of workload and medical professionals (ln WORKL* ln PHY, ln WORKL* ln NUR ln WORKL* ln PHA, ln WORKL* ln PHY, ln WORKL* ln MCB) were significantly positive with CRPA rate, respectively (Coef. = 1.270, 1.400, 2.210, 1.634; P=0.004, 0.001, 0.035, 0.003). This indicated that workload moderated the impact of the number of medical professionals on CRPA rate, and the increase in workload may lead to CRPA rate increased. Therefore, hypothesis 2 was supported (Table 5).

Table 5. Workload’ moderation effect on the relationship between medical professionals and CRPA rate
### Discussion

The following findings were worth discussing on the relationship between medical professionals and CRPA rate, and the moderation effect of medical professionals’ workload on the relationship.
A 0.899% decrease in CRPA was associated with a 1% increase in the number of physicians. Some studies might explain why it happened. Reducing misuse of antimicrobials by physicians can reduce the proportion of colonized or infected with multidrug-resistant organism[17]. Previous study has shown that increasing the allocation of infectious disease physicians can better optimize antimicrobial therapy (11.4% vs. 18.5%; P = 0.012) and may improve clinical outcomes in bloodstream infections patients [29]. In fact, previous studies have found a significant positive association between physician practice activity and their antimicrobials prescription rates [14,30]. Physicians with high workload may feel it is too time consuming to discuss alternative therapeutic approaches with patients. Antimicrobials prescribing even a broader spectrum agent may thus be a time-saving strategies[14]. Therefore, the increased allocation of physicians allow them more time to reasonably prescribe antimicrobials and educate patients on the rational use of antimicrobials, which are conducive to containing of AMR by cooperation of physicians and patients.

There was a positive association between the increase in the number of registered nurses and the decrease in CRPA rate (Coef. = -0.775; P = 0.003). Similar result has been found in critical care populations that risks of respiratory failure and reintubation increased when the nurse-patient ratio was 1:3, compared with ratios of 1:1 or 1:2[31]. Zhang et al. [32] found that the higher the nursing workload, the lower the adherence to hand hygiene. Sadule-Rios [33] found that 51.0% of nurses reported the main cause of low adherence to hand hygiene was their high workload. A shortage of nurses leads to high workload[34] and, further, high workload and lack of time are the main factors affecting the adherence of hand hygiene which can effective and efficient precaution for reducing the incidence of HAI's [33,35]. Increase the number of registered nurses make them have a relatively sufficient time improving adherence to regulations such as hand hygiene, ward disinfection and isolation systems, which can reduce the incidence of CRPA by responsible work. As the increase of registered nurses also allows them to have more time in monitoring prescription decisions and reducing prescribing errors, following up on missed doses[15].

This study also found that increasing the number of pharmacists may reduce CRPA rate. (Coef. = -1.176; P = 0.011). This is similar to findings from previous studies. A antimicrobial stewardship programs at Mount Sinai Hospital and The University Health Network showed that increasing pharmacists to monitor and intervene in antimicrobial use led to about 15% drop in the consumption of antimicrobials in ICU and 5%–17% increase in the susceptibility of isolates of Pseudomonas spp. to antimicrobials [36]. Zhang et al.[37] found a significant negative correlation between rational carbapenem use and the prevalence of CRPA.

Antimicrobial stewardship has become a platform for pharmacists because of the rising rate of AMR [38]. However, implementation of clinical pharmacy is in its infancy in many developing countries [39]. There is a shortage of pharmacists to meet increasing demand by providing suggestions on prescription and promoting the rational use of antimicrobials in China [40,41]. In particular, more than half of these pharmacists concentrated in the more developed Eastern regions of China [41]. Increased pharmacists can more fully support prescribers to optimize patient antimicrobial regimens, manage entry of new
antimicrobials onto hospital formularies, including critical reviews of new agents and their place in treatment, and thereby improve rational use of antimicrobials to reduce CRPA rate.

The increase of clinical microbiologists was positively associated with the decrease of CRPA rate (Coef. = -0.822; P=0.007). Liu et al. [10] found a same result that clinical microbiologists was a significant predictor of lower Staphylococcus. aureus and coagulase-negative staphylococci from a macro perspective based on the panel data in China (Coef. = -0.191, -0.351; p = 0.070, 0.004, respectively). Since clinical microbiologists are more familiar with the microbial characteristics of pathogens than other medical professionals, their recommendations for antimicrobial therapy are usually compelling and ensure a high degree of compliance with treatment modifications if necessary. They can also help the clinic identify CRPA as soon as possible and provide appropriate targeted therapy based on microbiology susceptibility test results.

Workload had moderation effect between physicians, registered nurses, pharmacists, clinical microbiologists and CRPA rate, respectively (Coef. = 1.270, 1.400, 2.210, 1.634; P=0.004, 0.001, 0.035, 0.003), which meant that control workload would increase the impact of medical professionals on CRPA. It confirmed that high workload was a main associated factor of poor hand hygiene adherence which could lead to the spread of pathogens and aggravation of AMR [32]. Excessive workload may make medical professionals neglect the implementation of monitoring, guiding, rational use of antimicrobials and infection control measures, meanwhile, it may also make it difficult for pharmaceutical care and microbiological testing to meet the demand, which can greatly increase the spread of drug-resistant organism. As the same time excessive workload may lead to CRPA worse by creating job burnout, a lack of responsibility and sympathy of medical professionals [42].

Implications and Limitations

This study provided evidence of an association between the increased number of medical professionals and reduced CRPA rate by paying attention to the deep correlation and potential value between medical professionals and CRPA. Since provincial-level panel data transcends the details of individual behaviors and help increased understanding of underlying connections [10].

Workload moderated the relationship between medical professionals and CRPA rate. This study also found that increased workload increased CRPA rate. Those results may provide the evidence for more strategic and systematic suggestions in allocation of different kinds of health professional resources in curbing CRPA.

Some suggestions based on our findings were also proposed as follows: to increase the allocation of medical professionals on tackling CRPA; to improve the overwork of medical professionals by guiding patients to visit hospitals rationally, so as to reduce CRPA rate for improvement medical quality and safety.
There were also some limitations. Firstly, the existing provincial balanced panel data contains only 4 years and the data volume was relatively small, which may limit the robustness and statistical significance of the estimation and therefore dynamic panel model was not adopted. Secondly, since the characteristic variables of medical professionals and patients were not available, only the hospital level can be controlled in the model. Thirdly, this study focused on the adequacy of medical professionals, but economic and political characters of the medical professionals were not discussed. Increasing medical professionals may improve CRPA performance but also means more input. If more data are available, the economic and political factors should be considered to provide further evidence on medical professionals allocation and utilization. Fourthly, We used the number of daily visits of physicians instead of more complex definitions as workload due to data unavailable and it may affect the generalization of the results of this study.

**Conclusion**

The study found an association between increased medical professionals and reduced CRPA rate, and workload showed a moderation effect between medical professionals’ numbers and CRPA rate. It was recommended that the measures increasing medical professionals allocation and reducing their excessive workload to curb AMR should be implemented.

**Abbreviations**

AMR, Antimicrobial resistance; CRPA, carbapenem-resistant Pseudomonas aeruginosa; HAI, healthcare-associated infection; CARSS, China Antimicrobial Resistance Surveillance System; OLS, pooled ordinary least squares; FE, fixed-effect; RE, random-effect.

**Declarations**

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

**Availability of data and materials**

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

**Conflicts of Interest**

The authors declare that they have no competing interests.
Funding

No funding was received for this manuscript.

Authors' contributions

MH contributed to the study design, data collection, data analysis and interpretation, manuscript drafting. XPZ provided important assistance in study conceive and design, and revised the study critically. All authors read and approved the final manuscript.

Acknowledgements

We sincerely thank Junjie Liu for his help in improving this manuscript.

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