Managing Neurosurgery in the Covid-19 Pandemic

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Abstract

Background

Covid-19 quickly spread around the world as an epidemic with potentially unknown hazards. Like its impacts on various occupations, neurosurgery has undergone changes due to the virus, including changes in surgical planning, inpatient and outpatient clinics, emergency management, and even academic activities. The present study was performed to determine neurosurgery challenges during the Covid-19 pandemic in Iran.

Methods

The present study was conducted as a mixed qualitative and quantitative study in 2021. In the qualitative section using the targeted sampling method, 11 members of the target community were selected using the available sampling method and completed a questionnaire. The qualitative part was conducted in two stages of reviewing texts and interviewing experts and in the quantitative part we evaluated the validity of the structure and the reliability of the questionnaire.

Results

This study examined in detail all aspects of the effects of Covid-19 on neurosurgery. 9 dimensions and 61 items were identified as the challenges of neurosurgery during the Covid-19 pandemic. In order of importance, the aspects were: treatment outcome, manpower, management psychological and physical diseases, education and research, tools and physical space, ethics, financial implications and information technology.

Conclusion

The outbreak of epidemics has different risks for specialties, among them neurosurgery. Accordingly, to observe patients' right to treatment, all necessary measures were first taken to provide instructions, regulations, policies and ethical guidelines.

Background

The outbreak of SARS-CoV-2 challenged neurosurgeons and forced them to change work patterns, patients' triage, staff shifts (1), care patterns and training to respond to patients' demands, and re-design the health care staff in the wards (2). Safety of patients, staff, and surgeons topped the list of priorities, but lack of adequate information about the Covid-19 disease and personal protection facilities, lack of standard protocols, acute and chronic psychological problems, and issues regarding ethics in this pandemic posed greater challenges (3).

As semi-emergency operation, neurosurgery encountered new restrictions or cancellations based on the developed protocols, as the delays and long durations are critical factors (4). In this regard, face-to-face

visits and the number of neurosurgery operations experienced remarkable reduction (5, 6).

For example, in a study conducted in New York (2021), reports showed that the number of neurosurgery operations during the pandemic reached 408 cases, which was equal to 1185 cases in the same period before it showing a decrease of 65.6% (6).

A study in the United States found that the percentage of hospitalization for neurosurgery and spinal cord surgery dropped by 50% and 60.4%, respectively, resulting in a monthly financial loss of nearly \$60 billion in hospitals nationwide. Apart from that, the reduction in the number of surgeries left neurosurgery assistants and other medical interns with dire consequences (7).

In the United Kingdom (2021), the results of a study showed that emergency neurosurgery operations were associated with a 33.6% reduction during the Covid-19 pandemic. Mortality rate was 30% thirty days after the surgery where most patients were infected with the Covid-19 and had underlying diseases or postoperative complications (8).

In a study in India (2020), it was reported that cranial surgery operations increased from 71.2% in the period before the Covid-19 to 88.7% during the pandemic, and the ratio of spinal cases decreased from 27.9% to 11.3%, which is statistically significant ($p=0.043$) (9).

In Isfahan (Iran), the number of neurosurgery operations showed a decrease of 50%. The proposed guideline from the University of California states that neurosurgery planning should be conducted based on patients' triage. Patients requiring a surgery are divided into four categories based on the level of virus infection: green, yellow, red and black, denoting the lowest, medium, high and highest levels, respectively. At the green level are the patients with the Covid-19 positive report who have been hospitalized for 6 days for whom all the planned operations are performed. Patients at the yellow level are those with Covid-19 positive report who have been hospitalized for 7 to 16 days. For them, there is a 25% reduction in surgeries. At the red level, there is a 50% reduction in surgeries for the Covid-19 positive patients who have been hospitalized for more than 17 days. On the black level, only the emergency surgeries are performed. In the proposed model of this university, there is a three-day rotation for the neurologists to reduce the level of exposure (3 days of morning shift and 3 days of rest) (10).

Cerebral hemorrhage, acute hydrocephalus, intracranial pressure tumors, and cranial and spinal cord traumas have been defined as neurosurgical emergencies (11).

A neurosurgeon may be confronted with a variety of conditions. Aneurysmal subarachnoid hemorrhage requires immediate surgery and a non-fatal tumor needs to wait until the pandemic is over (12).

In the United Kingdom, all selective neurosurgery operations were restricted and a large number of road accidents and violence were reduced with the cooperation of the government and the public (13).

Jean et.al (2020) conducted a study entitled "The Impact of Covid-19 on Neurosurgery and Strategy for Conducting Actions" where 646 respondents from 60 countries were surveyed. Two hundred and fifty-

eight patients (52.5%) reported that all selective surgeries were closed by the hospital and 226 respondents (46.1%) reported that the volume of their surgery was reduced by more than 50%. For countries most affected by the Covid-19, this ratio was 54.7%. Respondents also believed that cases involving the arteries needed more immediate treatment (14).

According to the results of various studies, neurosurgery services (both selective and emergency operations) are severely affected by the Covid-19 and the mortality rate in infected patients has increased between 23.8% and 30% (15). Whether or not to perform or delay neurosurgery is currently a dilemma facing the neurosurgeons, so this study was aimed to determine the challenges of neurosurgery during the Covid-19 pandemic in Iran.

Methods

The present study is an analytical-applied and cross-sectional study conducted as a mixed qualitative and quantitative study in Iran in 2021. The target population in the qualitative section included university professors and physicians specializing in neurosurgery area who had at least 5 years of experience and were satisfied to participate in the study.

In the qualitative and quantitative part, using purposive sampling method and snowball until saturation of opinions.

Method of Implementation (Qualitative Part)

The qualitative part of the present study was conducted in two stages. In the first stage, the method of library study and systematic review was used. Persian and English articles and books from domestic and foreign databases such as Elsevier, Scopus, PubMed, Medline, IranMedex, IranDoc with the help of Google Scholar search engines was thoroughly evaluated.

After ensuring the complete search and saturation of the collected information, the content analysis method was used to encode, classify, and conclude the obtained information.

Finally, the variables affecting the management of medical equipment in critical situations were identified as a conceptual model in the form of nine dimensions of manpower, equipment and physical space, therapeutic outcome, management, ethical challenge, financial implications, psychological and physical diseases, information technology, and Training & Research.

In the second stage, to determine the status of each dimensions in the Covid-19 pandemic, the Delphi technique and interviews with experts were used. In this way, a conceptual model was provided to the experts for evaluation. Experts' opinions on adding, modifying, and reviewing various dimensions and sections and determining the variables affecting them in the context of the Covid-19 pandemic were collected in three round-trip stages.

A questionnaire was provided to the experts to evaluate the content validity using content validity ratio (CVR) and content validity index (CVI) indicators. The CVR index in all items was higher than 0.78 and the CVI index in all dimensions, as well as the whole questionnaire, was higher than 0.84. Finally, the content validity of the researcher-made questionnaire for the Neurosurgery in the Covid-19 pandemic was confirmed.

Method of Implementation (Quantitative Part)

Due to the fact that the researcher-made questionnaire was approved by experts in terms of content validity, it is necessary to evaluate the construct validity and reliability. To this end, 11 members of the target community were selected using the available sampling method and completed a questionnaire. Cronbach's alpha index was used to determine the reliability and an exploratory factor analysis technique was employed to determine the construct validity.

Data Collection Tools

The researcher-made questionnaire in this study includes 61 items in 9 dimensions in which the measurement scale of each item was determined by five-choice Likert scale (very low=1,..., very high=5). The dimensions of the questionnaire also included Manpower, Equipment and physical space, Therapeutic outcome, Management, Ethical challenge, Financial implications, Psychological and physical diseases, Information technology, and Training & Research.

After collecting the questionnaires, exploratory factor analysis was used to evaluate the construct validity and Cronbach's alpha index was used to determine the reliability of the dimensions and that of the whole questionnaire. All statistical analyses were performed by SPSS software version 21. The significance level of statistical tests was considered to be 0.05%.

Results

In this study, 11 neurosurgeons in Isfahan that all of them were men in the age group of 40 to 70 years, were studied. In performing exploratory factor analysis, first, the KMO index or the adequacy index of sampling and Bartlett's test was evaluated. The KMO index is used to check small partial correlations between variables. In this study, the KMO index of 0.951 was obtained, which indicates the appropriateness of the information as well as the number of variables of each structure for exploratory factor analysis. Bartlett's test was also obtained in this study ($P < 0.05$) showing that heuristic factor analysis is suitable for identifying the structure (factor model) (KMO:0.951, X^2 :56.307, df:36, P-Value:0.017).

The results showed that the constructs designed in the researcher-made questionnaire from library studies and systematic review, as well as the opinion of experts based on the mathematical model, justify more than 92.82% of the variance related to the purpose of the study, i.e. Neurosurgery in the Covid-19 pandemic. In other words, the questionnaire has the necessary capability to evaluate the management of

Neurosurgery in the event of a Covid-19 pandemic and can be cited. Therefore, this result confirms the validity of the structure. According to the obtained results, Therapeutic outcome and financial implications showed the most and the least amount of variance in the structure of management of Neurosurgery in Covid-19 pandemic conditions, respectively.

Reliability evaluation showed that all constructs and the whole questionnaire had a Cronbach's alpha greater than 0.7. In other words, reliability in the target population shows that the researcher-made questionnaire has good reliability, stability, accuracy, and reliability.

Finally, in the target population, the study prioritized each of the factors affecting the management of Neurosurgery in Covid-19 pandemic. According to the answers to the questions, the instruction dimensions and then the management dimensions had higher priority and the physical space dimensions had the lowest priority in the management of Neurosurgery in Covid-19 pandemic (Table 1).

Table 1. Researcher-Made Questionnaire after Confirming the Content Validity

dimensions	Number of Questions	Cronbach's Alpha Index	Cumulative Variance Percent	Average Rating	Priority	P-value
Therapeutic outcome	12	0.701	14.157	9	1	0.0001
Manpower	6	0.799	27.077	5.45	5	
Management	8	0.716	37.774	6.32	4	
psychological and physical diseases	5	0.735	49.663	3.59	6	
Training & Research	9	0.862	59.115	7	3	
equipment and physical space	11	0.710	68.155	7.23	2	
Ethical challenge	4	0.796	76.744	2.73	7	
financial implications	3	0.744	84.801	1.68	9	
Information Technology	3	0.764	92.821	2	8	
Questionnaire	61	0.778	100.000	-		

Table (2) shows the prioritization of 61 items available in each dimensions by priority in dimension and overall priority (X^2 :138.140, df:59, P-Value:0.001).

Table 2. 61 items available in 9 dimensions

Dimension	Items (Reference)	Mean±SD	General Prioritization
Therapeutic outcome	Elimination of elective surgeries (10, 16-20)	4.18±0.75	1
	Identify high-risk groups (10, 16, 18-20)	4.09±1.04	2
	Type of surgery (13, 20-23)	4.08±0.70	3
	hospitalized for a period (23-25)	4.00±1.00	4
	Necessary screening tests (22)	3.90±1.22	5
	Group decision-making (11, 16, 17, 23, 26)	3.88±0.83	6
	Chronic disease in the staff (8, 19, 23)	3.81±0.98	7
	Laboratory requests (20, 23)	3.80±1.07	8
	Imaging requests (20)	3.72±1.19	9
	False negative results of screening test (20, 23, 27)	3.63±1.28	10
	Alternative treatment methods (11, 17, 21, 23)	3.54±1.03	12
	Provide daily reports (20, 23)	3.36±1.20	14
Manpower	Employing minimum staff (11, 16)	3.81±0.67	7
	Presence of assistants in the ward (20, 23)	3.81±1.07	7
	Transfer personnel to Covid-19 wards (8, 10, 17)	3.56±1.21	11
	Lack of nurses (17, 18, 28)	3.36±1.36	14
	Identifying on-call physician (20)	3.27±1.27	15
	Unconventional work schedule (11, 23)	3.00±1.18	19
Management	Guideline Development Process (17, 18, 22, 28)	3.45±1.36	13
	Operation in hospitals with special ward of corona (10, 19)	3.36±1.02	14
	Contradictory rules (10, 27, 29)	3.18±1.47	16
	Prohibition of visits and companion (13, 29)	2.90±1.57	20
	Risk assessment of virus transmission (13, 20, 23)	2.89±1.22	21
	Inter-departmental coordination (20, 23)	2.87±1.30	22
	Holding a case review committee (13, 20)	2.80±1.44	25
	Pharmaceutical supply chain (13, 30)	2.72±1.10	29

Dimension	Items (Reference)	Mean±SD	General Prioritization
psychological and physical diseases	Job stress (20, 31)	3.81±1.05	7
	Anxiety (11, 31)	3.72±0.78	9
	Incidence of skin problems, headache, nausea (20)	3.36±1.12	14
	Fear of infecting the family (19, 20)	3.09±1.30	17
	Fear of developing Covid-19 disease (17, 19)	2.81±1.53	24
Training & Research	Conduct clinical research and new research opportunities related to the disease (13, 17, 23)	4.09±0.94	2
	More emphasis on writing systematic review articles and meta-analyzes (23)	3.27±1.42	15
	The effect of e-learning for assistants and staff (8, 32, 33)	3.18±1.16	16
	Training and application of personal protective equipment instructions (11, 16, 34, 35)	3.00±1.41	19
	Proper skills training (17, 33)	2.72±1.27	29
	Ethical guide training (22, 23)	2.70±1.10	30
	Holding online meetings of case report (13, 23)	2.54±1.36	33
	Holding virtual conferences (10, 13, 17, 23, 32)	2.45±1.21	36
Equipment and physical space	Disease Education and Awareness (symptoms and modes of transmission) (13, 20, 23, 33-35)	2.00±0.77	40
	Observe the physical distance (10, 20, 36)	2.90±1.13	20
	Continuous ventilation and replacement of filters (21, 37)	2.83±1.32	23
	Infection control (20, 27, 38)	2.80±1.53	25
	General disinfection (20, 36)	2.79±1.55	26
	Corona waste (17, 20, 36)	2.75±1.48	28
	Reuse personal protective equipment (16, 20, 36)	2.72±1.27	29
	Long-term use of personal protective equipment (16)	2.57±1.36	31
	Type of disinfectant (20)	2.54±1.21	33
	Type of mask used (20, 36, 39)	2.45±0.82	36

Dimension	Items (Reference)	Mean±SD	General Prioritization
	The degree of transmission of infection in different objects with different materials (20)	2.27±1.00	37
	Restrictions on beds (8, 16)	2.18±0.98	39
Ethical challenge	Develop an ethical guide (13, 23)	3.09±1.30	17
	Age of patients (8, 23)	2.77±1.25	27
	Injustice in the selection of patients (13, 17, 23)	2.56±1.03	32
	Unfair access to care (13, 17)	2.54±1.01	33
Financial implications	The treatment cost of patients (39)	2.50±1.36	34
	Consume more electricity and water energy (39, 40)	2.48±1.27	35
	Decrease in medical center revenue (39, 40)	2.20±1.10	38
Information Technology	E-learning (electronic educational technology) (8, 10, 12)	3.08±1.32	18
	Telemedicine (13, 20, 25, 41-44)	2.90±1.44	20
	Online Neurosurgeon Consultation via Video Call (12, 20, 23, 27, 45)	2.72±1.34	29

As can be observed, this study examined in detail all aspects of the effects of Covid-19 on neurosurgery. All studies performed in this dimension have examined only some aspects of the effects of Covid-19 on neurosurgery. In this study, 9 dimensions and 61 items were identified as the challenges of neurosurgery during the Covid-19 pandemic.

In order of importance, the aspects were: treatment outcome, manpower, management, psychological and physical diseases, education and research, Equipment and physical space, Ethics challenge, financial implications and information technology.

The three most important items in each aspect are:

Therapeutic outcome: Elimination of elective surgeries, Identification of high-risk groups and Type of surgery.

Manpower: Employing minimum staff, Presence of assistants in the ward, Transfer personnel to Covid-19 wards.

Management: Guideline Development Process, Operation in hospitals with special ward of corona, Contradictory rules.

Psychological and physical diseases: Job stress, Anxiety and Incidence of skin problems, headache, nausea.

Education and research: Conduct clinical research and new research opportunities related to the disease, more emphasis on writing systematic review articles and meta-analyses, The effect of e-learning for assistants and staff.

Equipment and physical space: Observe the physical distance, Continuous ventilation and replacement of filters, Infection control.

Ethics challenge: Develop an ethical guide, Age of patients, Injustice in the selection of patients.

Financial implications: cost of treating patients, consuming more electricity and water, reducing the income of the medical center.

Information technology: E-learning (electronic educational technology), Telemedicine, Online Neurosurgeon Consultation via Video Call

The general priorities of the items, disregarding the scope, are as follows:

The highest mean was related to the items of elimination of selected surgeries, identification of high-risk groups and type of surgery, respectively, and the lowest mean was related to the decreased income of the medical center, bed shortage and patient education (symptoms and means of transmission), respectively.

The Covid-19 pandemic highlighted the need to set up and improve management infrastructures in the country such as information technology, medical planning, Pharmaceutical supply chain, etc. It is hoped that by implementing various schemes such as telemedicine and Online Neurosurgeon Consultation via Video Call, many of the risks facing patients, such as disease transmission, can be avoided. Also, using the results of this study, the necessary measures can be taken to reduce mortality from neurosurgery.

Discussion

Out of the 9 dimensions identified for neurosurgery, Therapeutic outcome is the most important and financial implications is the least. Regarding the Therapeutic outcome, the central items were the removal of selected surgeries, identification of high-risk groups, and the type of surgery. Attempts have been made to address all the challenges in treating patients in this dimensions.

Since many surgeries were canceled during the Covid-19 pandemic, including selective neurosurgery operations, patient dissatisfaction rose remarkably due to pains and sufferings, which necessitated alternative surgical methods. After the elimination of elective surgeries (10,16-20), identification of high-risk groups came as a high priority (10, 16, 18-20).

Also, as specified in instructions, after performing the necessary screening tests (22), the patients underwent surgeries by observing health standards.

After surgery, patients needed to be hospitalized for a period (23-25). Patients hospitalized after a surgery had both a risk of infection and transmission. Preoperative screening tests, sometimes with false negative results (20, 23, 27), led to further surgeries which eventually caused contamination of staff and associated problems. The implementation of the Group decision-making of neurosurgery operation was a great help in order to observe justice and select patients for performing surgery (11, 16, 17, 23, 26). Also, an ethical guide for hospitalization of patients in neurosurgery wards was developed where patients' age, type of surgery, condition and deterioration were considered (22, 23).

Presence in Corona wards increased the risk of contamination with the Covid-19 in the personnel with underlying diseases, so there were transferred to other wards and the problem of staff shortage became more apparent than before (8,10,11, 16, 17, 18, 28).

On the other hand, diagnostic procedures such as imaging and laboratory, in addition to the long queues, made patients act as disease carriers for surgeons and staff (20, 23).

In the meantime, false negative results of screening tests also led to surgery, which greatly increased the risk of infection (20, 23, 27).

In this regard, it is necessary to prepare daily and weekly reports about the condition of the Covid-19 in the neurosurgery wards (20, 23), identify risk factors in a meeting with professors and assistants of this field, and take the necessary measures to reduce mistakes.

Identifying an on-call physician (20) who is aware of all the group's guidelines and regulations and can act according to the group's policies was another issue at the onset of the Covid-19 pandemic. The unconventional work schedule (11, 23) of physicians and staff caused confusion in the training of medical assistants and other students, and exposed training to a serious risk. In addition, the staff faced the challenge of job insecurity and instability in the workplace, multiple deaths, even among the medical staff, each of which caused some psychological problems such as anxiety, job stress and fear (11, 19, 20, 31).

In addition, the personnel were afraid of infection and traumatized at the probability of having infected family members (19, 20). On the other hand, long-term use of personal protective tools and observing some protocols has caused skin reactions, respiratory problems, headache, nausea and other physical problems for the personnel, so the psychological and physical diseases dimension were also formed.

In the field of management, instructions were developed at the outset of the pandemic, but due to the variability of the virus behavior in infecting patients, some rules contradicted others. For example, at the beginning of the virus outbreak, hand washing was emphasized, but after the disease continued and the virus behavior was identified, masking received more attention than hand washing. Therefore, rules should be updated regularly with regards to the behavior of the virus. Based on the problems created

following the occurrence of Covid-19, hospital committees examined patients' files with more accurately and were held more regularly. On the other hand, inter-departmental coordination (20, 23). was performed in diagnostic and Covid-19 wards in order to reduce patients' waiting time for diagnostic procedures.

Family visit and having a companion were prohibited in the Covid-19 wards, but by the persistence of the disease and staff shortage, companions were allowed into the wards. Neurosurgery operations in hospitals with Corona wards caused some risks and concerns for staff, surgeons and patients, so that emergency operations were selected more strictly.

As mentioned, the creation of alternative medicine methods by improving the country's pharmaceutical infrastructure and launching the Pharmaceutical supply chain could be a great help in drug management during the Covid-19 epidemic. The use of information technology was the basis for improving the pharmaceutical infrastructure and creating the Pharmaceutical supply chain (13, 30).

Information technology is an important dimension that can be of great help in controlling the disease and treatment in pandemic and non-pandemic conditions. Telemedicine (13, 20, 25, 41-44) is an effective measure to treat patients remotely, as well as Online Neurosurgeon Consultation via Video Call (12, 20, 23, 27, 45) for patients who have previously undergone surgery and are unable to have in-person visits during the pandemic. In the meantime, using the right tools to train assistants is of prime importance. In the last two years, due to the prevalence of epidemiology, training of assistants has faced many challenges (13, 20, 23, 33-35).

The number of surgeries has decreased and the number of cases that assistants face has risen. Therefore, it is necessary to adopt appropriate training methods for assistants, hold case report sessions (13, 23), and present online some rare cases of brain diseases during the Covid-19 pandemic. Also, surgical skills should be taught to assistants using simulated software (17, 33).

In this period, the personnel also need special training and skills which bring them experiences beneficial to other staff members. It should be borne in mind that the development of ethical guidelines (13, 23) and instructions cannot be effective alone, but should be taught to staff online and put on the agenda of neurosurgery wards.

Additionally, research continued with vigor during the Covid-19 pandemic. During this period, more emphasis was placed on conducting systematic review studies and meta-analyzes (23), so that the behavior of the Coronavirus family of MERS and SARS was examined.

The Covid-19 pandemic had a devastating effect on the economy of countries and consequently, on the revenues of the health care sector, so that the share of health care in GDP was decreased. The routine activity of the neurosurgery ward faced major alteration. Hospitalization of patients with the Covid-19 in the intensive care unit also led to higher cost of treatment and a shortage of beds for the non- Covid-19 patients with brain and spinal cord problems (39, 40).

The need for medical equipment was no exception. Disinfection of equipment and environment related to neurosurgery procedures, use of disinfectants and infection control were prioritized by neurologists as well as patients who had to perform necessary surgeries (20, 36).

Observing physical distance and using personal protective equipment also had their own challenges. In addition, hospitals have increasingly been obliged to create appropriate ventilation systems to prevent infection of patients, staff, and surgeons. It was also seen in some cases that some personal protective equipment was used twice or for a long time, which had its own risks and complications (11, 16, 34, 35).

The disposal of the Covid-19-related waste had its own hardships, which, by the lack of timely and unprincipled disposal, exacerbated the situation. To address this problem, planners, especially environmental health professionals, need to play more active roles. It is noteworthy that any non-compliance with health norms and regulations leads to pose a risk not only to the individual, but also to those who are in contact with him. Attention to risk management and implementation of crisis management systems is also essential for neurosurgery (13, 20, 23).

Finally, surgical instrument contains the virus longer than other devices, an issue which requires attention (20).

Conclusion

As can be observed, the neurosurgery wards faced several problems during the pandemic and several articles were written around the world, but in Iran, there is no comprehensive study to address existing challenges with regard to local conditions, type of the pandemic and effects on neurosurgery. In summary, the outbreak of epidemics has different risks for specialties, among them neurosurgery. Accordingly, to observe patients' right to treatment, all necessary measures were first taken to provide instructions, regulations, policies and ethical guidelines. After training and informing staff, assistants and neurosurgeons, attempts were made to reduce the risks to a minimum. Finally, it is hoped that using the results of this study, the necessary measures and strategies can be taken to improve the situation in the 9 dimensions under study.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethics Committee of Esfahan University of Medical Science (IR.MUI.MED.REC.1399.785).

Consent for publication

Not applicable

Availability of data and materials

The datasets involved during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Nil.

Authors' contributions

BA contributed to study design, the literature review, article preparation, MM contributed to the quality assessment and scientific correspondence. MSH & MS completed the draft of the article, MH conceived of the study, quality assessment, data extraction, DST contributed to study design, article review and correspondence. All authors read and approved the final manuscript.

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