Challenge of Politico-Economic Sanctions on Pharmaceutical Procurement in Iran: A Qualitative Study

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Abstract

Background: Politico-economic sanctions over the recent years have led to significant challenges in the pharmaceutical supply chain (PSC) in Iran. Given the importance of the chain’s resilience for the health system and its impact on accessibility, equity, and public health, this study was conducted to determine the major challenges facing pharmaceutical procurement in Iran after the imposition of these sanctions.

Methods: This study was a qualitative research with a content analysis approach conducted in 2019. Eighteen policymakers and administrative managers in food and drug administration of two Iranian Medical Universities and Iran’s Ministry of Health were included in the present study via snowball sampling and semi-structured interview. The data were analyzed using the framework analysis of MAX QDA10.

Results: Five main themes and 15 sub-themes were identified, which addressed pharmaceutical supply chain challenges under politico-economic sanctions. These included the challenges in financing, purchasing, importing, and manufacturing domestic products in addition to storing and distributing medicines, along with challenges facing the general public, particularly patients.

Conclusion: The results revealed that pharmaceuticals are not immune to politico-economic sanctions, although they are not directly subjected to them. Sanctions, similar to any economic crisis, can affect public health and limit their access to healthcare. Identifying supply chain challenges and planning to address them could help policymakers find solutions to enhance PSC resilience in the future.

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What’s Known

- Politico-economic sanctions have had direct and indirect adverse effects on health systems.
- Pharmaceutical supply chain may lose its resilience against these sanctions.
- The quantity and quality of pharmaceutical access could be restricted as a result of these sanctions.

What’s New

- Sanctions impose several challenges to financing, purchasing, and importing new pharmaceuticals in Iran.
- Sanctions vastly restrict the access to international collaboration in terms of technology transfer and joint research and development.
- Producing domestic products, storing, and distributing them are among other challenges affected by sanctions in Iran.
components of a healthcare system and consists of all the processes, information, resources, financing, technologies, and pharmaceutical industry stakeholders, such as manufacturers, suppliers, brokers, service providers, buyers, and sellers. Therefore, any unexpected shocks on PCS may lead to vast consumption of the resources, which threatens public health. Various interdependencies within national and international domains have accordingly led to complexity, opacity, and uncertainty in the PSC, aggravating its vulnerability and consequently exposing it to greater risks. These risks could also jeopardize the supply chains that have been carefully developed according to scientific principles. Therefore, there is a dire need to manage such risks in the PSC to prepare for and respond appropriately to a wide range of threats. Building resilience in a given chain, especially in critical and abnormal situations, can act as a bulwark against risks in the PSC. Thus, resilience provides the ability for the supply chain to return to its original state or even to a more desirable state than the past and the ability to detect threats. Accordingly, the PSC could predict, regulate, or even prevent potential failures and vulnerabilities. A major threat to the PSC in Iran over recent years has been the imposition of unilateral and multilateral politico-economic sanctions against the country. This situation was exacerbated, when the United States (US) withdrew from the Joint Comprehensive Plan of Action (JCPOA), the agreement aimed at halting Iran's uranium enrichment beyond a certain level, in exchange for the lifting of some sanctions (on May 8, 2018), prompting the other parties to the agreement, such as the European Union (EU), to reinstate all the previous sanctions. This should be seen in the light of the fact that the EU was the primary source of Iranian supplies of medicines. Under this condition, although medicines have not been the direct subject of sanctions against Iran, the PSC has encountered numerous problems, including payment for imported medicines, the supply of raw materials, and the sale of pharmaceutical products.

In this paper, it was highlighted that the US sanctions have caused numerous difficulties in the supply of medical equipment and medicines and widespread problems in Iran’s PSC. Another study also showed that the price of new chemotherapy drugs and new biologic cancer drugs increased significantly after the US sanctions, which restricted patients' access. Setayesh and Mackey also claimed that 73 types of medicines, closely related to the burden of disease in Iran, became scarce following the US sanctions, 44% of which were also classified as essential medicines by the World Health Organization. Sanctions could affect health systems by increasing transportation complications, currency transfer, and lack of money. These, along with limited access to chemotherapeutic agents and severe drug shortages, are cited as the main effects of sanctions on cancer treatment. Barriers to accessing new radiotherapy equipment and limitations in obtaining spare parts for accelerators due to sanctions were other effects of sanctions on public health, particularly on severely ill patients.

In short, it appears that the politico-economic sanctions have had direct and indirect effects on the drug procurement capabilities of the Iranian PSC. According to Yazdi-Feyzabadi and others, weak health services, high health technology costs, increased prices of drugs and medical supplies, and decreased affordability and accessibility are among the most critical direct effects of sanctions on the health system. The socioeconomic, structural, and intermediate determinants of health also play an essential role, as indirect adverse effects of sanctions, on the health system. According to what was mentioned above, this study investigates and determines the challenges of Iran's PSC in different areas after the imposition of politico-economic sanctions, which may affect the resilience of the supply chain. Identifying the challenges could help policymakers find solutions to increase the resilience of the PSC in the future.

**Methods**

The current work is a qualitative content analysis conducted in 2019. The Ethics Committee of Shiraz University of Medical Sciences approved the proposal of this article under the following ID: IR.SUMS.REC.1397.18779. Herein, semi-structured interviews were conducted with Presidents, Vice-presidents, and Heads of the Food and Drug Administration of Iran’s Ministry of Health, Shiraz University of Medical Sciences and Tehran University of Medical Sciences, to explore the challenges facing the PSC in the wake of politico-economic sanctions. The interviewees were selected using the snowball sampling method. Initially, the Vice-president and executives of the Vice-Chancellor’s Office of Food and Drug were interviewed at Shiraz University of Medical Sciences. Subsequently, they were asked to introduce the individuals interested in the field. The study participants were selected from well-informed individuals, who had sufficient information on drug storage, distribution, and delivery, as well as...
the challenges of the PSC. They were also willing to share their own opinions. One-on-one interviews were conducted with the participants between October and December 2019, mostly at their workplaces by one of the researchers (ZD). At the beginning of the interviews, general explanations about the study objectives and the need for confidentiality of information were given verbally. Written informed consent was also obtained from all the interviewees, and they were ensured that they could withdraw from the study at any time, if they were not satisfied. The average duration of the interview sessions was approximately 50±10 min, and all the interviews were conducted by one of the researchers. The interviews were recorded with the consent of the participants and transcribed within a very short time after completion. The interviews continued until saturation was reached, which was after 18 interviews. To prepare the semi-structured interview guide, which consists of five main items and 18 sub-items, a review of relevant literature and an open-ended pilot interview were conducted. It was then validated by two experts from the Food and Drug Administration associated with Shiraz University of Medical Sciences. In addition, the validity of the interview guide was confirmed after conducting two pilot interviews with the participants. The main questions were as follows: In your opinion, what are the main negative impacts of sanctions on drug procurement in Iran? What are the main barriers in importing, producing, and distributing medicines during the sanctions? How can the politico-economic sanctions impact the PSC? In what areas can the resilience of the supply chain be damaged by the sanctions?

To increase the accuracy and precision of the study, four criteria developed by Guba and Lincoln were considered, namely credibility, confirmability, transferability, and dependability. To increase the credibility of the study, long-term participation and continuous observations were used. As a result, the researchers were fully involved in the study, adequate communication was established with the participants, and general concepts that emerged during the study were accepted. To this end, the interviews and a review of related literature were incorporated. To increase the confirmability of the findings, the participants were presented with the coded data to verify their accuracy. The transferability of the study findings was also promoted by explaining the conditions of the informed study participants and the interview method in a comprehensible manner. An attempt was also made to select the samples entirely in line with the objectives of the study and without any bias. The data were analyzed in parallel with their collection to help the researchers be fully acquainted with the principles of theoretical research. To increase the dependability of the study findings, the process of coding the concepts, themes, audio, and textual information was provided. To ensure this, two research teams analyzed the content individually and discussed the themes to reach a consensus in case of disagreement.

In addition, data analysis was conducted using a five-step framework. The researcher primarily listened to the audio files of the interviews several times, and the transcribed texts were read several times to identify the data. Secondly, to identify a thematic framework, repeated ideas in the identification process were transformed into groups of similar ideas or codes. Thirdly, indexing units or parts of the data that were associated with a particular code were characterized. Subsequently, after indexing, the data were summarized in a code table based on the thematic framework. The data were ultimately combined. Subsequently, graphs and interpretations were employed to define the concepts, show the relationships between the concepts, specify the nature of the phenomenon, and offer explanations to determine the challenges. The coding and classification of the data were performed by two of the researchers (PB and GM), who had enough familiarity and reflexivity with qualitative analysis using the software MAX QDA10 (VERBI GmbH, Germany).

**Results**

All the 18 respondents were male (100%) and had a mean age of 55.25±8.3 years. The results of the analysis of the interviews contributed to the identification of five main themes and 15 sub-themes related to the challenges facing the PSC during the politico-economic sanctions. As represented in table 1, the main themes included the following challenges: financing medicines, purchasing and importing medicines, domestic production of medicines, storage and distribution of medicines, and community and patient-associated challenges.

**Financing Challenges**

Challenges related to drug financing were composed of four sub-themes, namely international transaction banks, lack of financial resources, interactions with international organizations, and reverse trafficking. All the respondents believed that sanctions have caused numerous challenges in the PSC through disruptions in electronic transaction
### Table 1: Challenges facing the pharmaceutical supply chain under politico-economic sanctions

| Main Themes                  | Sub-themes                        | Final Codes                                                                 |
|------------------------------|-----------------------------------|-----------------------------------------------------------------------------|
| Financing challenges         | International transaction banking | Disruption of electronic and banking transactions and social networks       |
|                              |                                   | Challenges in the procurement of pharmaceutical and medical equipment       |
|                              |                                   | Inability in cash exchange                                                 |
|                              |                                   | Lack of political communication and systems for transporting foreign currency|
|                              |                                   | Lack of cooperation from multinational companies                           |
|                              | Lack of financial resources        | Lack of negotiation and contracting skills with international companies     |
|                              |                                   | Lack of political power of compliant with lack of commitment from vendors   |
|                              |                                   | Lack of medicines in government centers due to lack of resources             |
|                              |                                   | Blockage of financial resources in bankrupt insurance organizations        |
|                              |                                   | A sudden increase in drug prices due to currency fluctuations               |
|                              |                                   | Lack of allocating the other goods’ impost for compensating pharmaceutical funds |
| Interactions with international organizations |                                   | Restriction of operations of international companies                      |
|                              |                                   | Challenges in transporting money to international companies                 |
|                              |                                    | The low proportion of bids from international companies                    |
| Reverse trafficking          |                                   | Destruction of market tranquility due to exchange rate fluctuations         |
|                              |                                   | Reverse trafficking due to an imbalance between the exchange rate inside and outside the country |
|                              |                                   | Smuggling medicines through the country’s borders to neighboring countries   |
| Purchasing and importing challenges | Inadequate attention to pharmaceutical needs | Lack of access to disease characteristics locally as a prerequisite for drug procurement |
|                              |                                   | Lack of estimation of annual order requirements by importers                |
|                              |                                   | A mismatch between demand and imports                                       |
|                              |                                   | Forfeiture of drugs due to incorrect estimation                            |
|                              |                                   | Issues related to Iran’s Customs Administration and clearance procedures    |
|                              |                                   | Delay in the timely clearance of pharmaceuticals from the customs department|
|                              |                                   | Challenges in customs-related software                                       |
|                              |                                   | Instability of customs tariffs                                              |
|                              |                                   | Varying customs tariffs and legislation                                      |
|                              |                                   | Time-consuming processes for clearance of vital goods                       |
|                              |                                   | Many decision points for the clearance of medicines                         |
|                              |                                   | The complexity of the control process and separation of original and contraband medicines |
|                              |                                   | Little cooperation between Iran’s Customs Administration and the Ministry of Health |
| Medication import processes  |                                   | Lack of assessment of importers’ capabilities                               |
|                              |                                   | Lack of planning for the importation of medicines                           |
|                              |                                   | Instability and delay in the importation of drugs and medical devices       |
|                              |                                   | Decreasing competition due to restriction of importers and OTCs             |
|                              |                                   | Challenges in importing drugs from monopolists                              |
|                              |                                   | High activity-based costing of importing initial materials and products     |
| Challenges facing domestic production | Hoarding by manufacturing companies | Lack of control and hoarding of medicines in warehouses                     |
|                              |                                   | Hoarding of drugs by manufacturers                                          |
|                              |                                   | Lack of economic justification for pharmaceutical producers                 |
|                              |                                   | Lack of raw materials for production                                         |
|                              |                                   | Dependence on non-pharmaceutical products in the production process         |
|                              |                                   | High dependence on imported raw materials and technologies                  |
|                              |                                   | Lack of infrastructure to support pharmaceutical production                 |
|                              | Inability to update scientific knowledge | Lack of access to new knowledge                                              |
|                              |                                    | Influence on scientific relations with other countries                       |
|                              |                                   | Lack of success with new packaging, new formulations, and technologies      |
| Storage and distribution challenges | Exploitation by stakeholders and brokers | Storage of medicines in pharmacies                                          |
|                              |                                   | The emergence of a pharmaceutical black market                              |
|                              |                                   | Easy and cheap smuggling of medicines from the country by brokers            |
|                              | No control over medical products   | Inadequate control of import channels and distribution centers              |
|                              |                                    | Unclear structures and process of distribution of pharmaceutical and medical devices |
|                              | Problems with prescribing and supply| Vulnerability of medical devices and pharmaceuticals                        |
|                              |                                   | Brand prescribing due to prescribers’ loyalty, inclination, or conflict of interest |
|                              |                                   | Lack of substitution of pharmaceutical therapies with other interventions    |
banking and money transfer. In this regard, one of the respondents said:

“Everything relies on electronic banking transactions. All electronic transaction banking services have been disrupted, and there is even limited access to social networks in our country. Therefore, we are indirectly affected by the sanctions on medicines.” [P1]

Several interviewees also acknowledged that the unavailability of foreign currency and Iranian Rial meant that medicines could not be delivered. In this regard, one of the participants said:

“Unfortunately, the funds for the supply of medicines are currently in the hands of the health insurance companies, which are unable to pay due to insolvency.” [P6]

In addition, some of the interviewees assumed that interactions with international organizations were very limited under the sanctions. Despite this, these organizations also provided some support to Iran in this area; for example, one of the participants said:

“Before the sanctions, international organizations did not help our country much in terms of financial problems. Their support was also not strong enough in the field of health. During the sanctions, remittance procedures overshadowed such contributions.” [P4]

Most interviewees mentioned reverse trafficking triggered by Iran’s exchange rate fluctuations as one of the challenges facing the PSC. In this regard, one of the participants said:

“Prices in our country are not set at a real rate, and exchange rate fluctuations can create a two-price market and lead to reverse trafficking.” [P15]

Challenges in Purchasing and Importing medicines included the three sub-themes of inadequate attention to medicine requirements, problems associated with Iran’s Customs Administration and clearance procedures, and the processes involved in importing medicines. Certain respondents cited the lack of attention to medical needs in Iran and the lack of estimation of annual needs in ordering medicines from importers as challenges in purchasing and importing medicines; for instance, one of the participants stated:

“Information on diseases, such as information on the prevalence and incidence of certain diseases in different regions of Iran, is of the utmost importance to make an initial estimate of the needs, which should be based on accurate information about actual needs.” [P3]

Most of the respondents also included Iran’s Customs Administration and clearance procedures among the challenges of the PSC. They believed that the clearance of medicines was delayed by Iran’s Customs Administration and especially the procedures for the clearance of essential items were time-consuming. In this regard, one of the participants opined that:

“Currently, there are few interactions between the Ministry of Health and Medical Education and Customs Administration. I think the authorities in Iran’s Customs Administration must know that the timely release of items is of great importance to avert harm to the pharmaceutical market.” [P7]

Almost all the respondents said that importation of medicines faced many challenges, such as lack of assessment of importers’ capabilities, instability and delays in importing medicines and medical devices, and reducing competition due to the limited number of companies importing one-item products. In this regard, one of the participants said:

“Unfortunately, currently, government
corruption and rent-seeking related to imported items are rife, and the government has created a kind of self-imposed sanction against medicine imports.” [P5]

Challenges Facing Domestic Production

The challenges facing the domestic production of drugs included three sub-themes: hoarding by manufacturing companies, lack of raw materials for production, and inability to update scientific knowledge. Some interviewees pointed to hoarding by manufacturing companies as one of the challenges facing the PSC during the sanctions; for example, one of the participants stated:

“In case of the current sanctions, some manufacturing companies are hoarding a large amount of the most expensive prescription drugs, which may lead to increased prices and unavailability of certain items in short intervals.” [P11]

From the perspective of the majority of the interviewees, the lack of raw materials for production was seen as a challenge facing the PSC. In this regard, one of the participants noted:

“Although we can produce drugs, we are highly dependent on imported raw materials, especially those for packaging.” [P9]

The inability to update scientific knowledge was also mentioned by three interviewees as a challenge for the PSC. In this regard, one of the participants added:

“Sanctions have stopped us from updating our knowledge, which is their least important effect; for example, there is no possibility of progress in terms of new packaging, new formulations, and scientific techniques without any contact with the outside world.” [P7].

Storage and Distribution Challenges

Challenges in the storage and distribution of medicines included the three sub-themes of exploitation by stakeholders and brokers, no control over medical products, and problems in prescribing and supplying. Accordingly, certain participants believed that exploitation by some stakeholders and brokers could be a challenge for the PSC under sanctions. In this regard, one of the participants stated:

“Since a big proportion of the profits belong to the manufacturing and distribution companies, pharmacies stockpile drugs to increase prices and disrupt the supply and demand cycle. After the scarcity sets in, they sell them at high prices and gradually enter the black market.” [P13]

Some interviewees identified the lack of control over medical products and devices as one of the challenges facing the PSC. In this regard, one of the participants said:

“There are a few problems in terms of controlling and monitoring medicines, but there is less monitoring in the area of consumables due to the volume of activities and delivery points. Thus, pharmacies are inspected at least twice a month, yet medical products are not inspected.” [P2].

The problem with prescriptions and providers was also mentioned by some interviewees as one of the challenges related to medication sanctions. In this regard, one of the participants stated:

“In the current situation, it is not possible to talk about replacing and changing your medication regime.” [P14]

Community and Patient-Associated Challenges

Challenges related to community and patients also included two sub-themes: social and psychological impact on the community and compromised health and well-being. Almost all the respondents believed that sanctions have caused negative social and psychological impacts, such as feelings of insecurity and high dissatisfaction, among people. One of the participants said:

“I think the most important problem related to sanctions is social dissatisfaction and the reduction of social capital. I think the trust between the people and the government is damaged.” [P12]

In addition, most respondents acknowledged that sanctions would jeopardize the health and well-being of the community and that patients with chronic illnesses, in particular, would suffer. In this case, one of the respondents stated:

“Since medicines and equipment are imported with delay, the cost of treatment delays is one of the problems associated with sanctions. Since drugs are available for a limited duration and difficult to get at other times, the treatment is not completed, and the course of treatment is prolonged.” [P8]

Discussion

The findings of this study revealed that the challenges facing the PSC during the period of politico-economic sanctions included financing, purchasing, importation, production, storage, and distribution of drugs, in addition to community and patient-associated challenges.

As mentioned earlier, the findings of this study indicated that the difficulty of working with international transaction banks, lack of financial resources, limited interaction with international
organizations, and reverse trafficking were among the challenges in financing medicines. It should be noted that Iran has faced various regional and international sanctions in foreign trade and financial and banking services over the recent decade, imposed by the US after May 2018. On the other hand, Iran's pharmaceutical industry usually plays an important role in providing medicines and necessary medical services to patients. Although medicines are exempted from sanctions, pharmaceutical companies have encountered many difficulties importing raw materials and medicines after the sanctions due to foreign exchange restrictions. A study by Cheraghali and others also revealed that one of the weaknesses of the PSC under sanctions, which reduces its resilience, was the mode of payment for imported drugs and raw materials. Similarly, according to Kokabiasgahi, politico-economic sanctions have had severe effects on the macroeconomy in decreasing government revenues, increasing inflation, depreciating national currency, and unemployment, among others. Such macroeconomic criteria could directly lead to a progressive deterioration in the well-being and health of the community and reduce access to healthcare and medicine.

Challenges in procuring and importing drugs also included lack of attention to drug needs, problems with Iran's Customs Administration and clearance process, and the processes involved in importing drugs. It appears that lack of access to prevalence rates of diseases in different regions of Iran has been attributed to an inaccurate assessment of treatment needs. In addition to shortfalls in certain items, some other medicines expire due to excessive imports and orders, resulting in a loss of financial resources. In addition, the abundance and variety of stringent regulations in Iran's Customs Administration have resulted in a time-consuming clearance process that can delay access to essential medicines. As a result of sanctions, medicines are imported exclusively by a limited number of companies, which has led to reduced monitoring and inadequate assessment of importers. Similarly, Moret highlighted the negative impact of sanctions on access to and use of medicines by the citizens of Iran and Syria. This restriction may be partially due to the importation of essential medicines.

The challenges associated with the domestic production of drugs are also related to hoarding by manufacturing companies, lack of raw materials for production, and failure to update scientific knowledge. It seems that manufacturing companies are taking advantage of this chaotic situation in Iran and exacerbating the crisis through storage and hoarding. In addition, there is extreme dependence on pharmaceutical and non-pharmaceutical products and advanced equipment and machinery for domestic production, which is hindered by sanction-related conditions and the inability to access new pharmaceutical production science. The results of the study by Ghiasi and others also showed that access to imported and domestic medicines for the treatment of asthma has reduced by 19% and 42%, respectively, due to sanctions, which has increased patients' suffering. Storage and distribution challenges were also associated with exploitation by stakeholders and brokers, lack of control and monitoring of medical products, and problems in prescribing and supply. Unfortunately, it appears that pharmacies, as the last link in the PSC, are storing away drugs and creating a black market. Moreover, the limited access of manufacturing companies to the best treatments based on scientific and experimental resources causes numerous problems for patients. The results of a study by Kheirandish and others indicated that sanctions have reduced access to medicines for asthma and cancer patients, mainly imported medicines and those whose raw materials depend on imports.

Ultimately, the challenges associated with the community and patients included the social and psychological impact on people and the threat to health and well-being. Sanctions have also created a hostile social and psychological atmosphere, a sense of insecurity, a decline in public trust in the government, reduced social capital, and higher levels of dissatisfaction among people. In this regard, the good performance of pharmaceutical companies and their adherence to ethical obligations and provision of affordable medicines, specifically for the poor, have resulted in an increase in social capital and better social welfare in Bangladesh. Furthermore, the lack of timely provision of medicines endangers patients' lives and increases the severity of their diseases. Examining data on infants and children in 69 countries, Petrescu found that underweight infants and children in countries subject to sanctions are most likely to die before the age of three. The current status of the drug market in Iran suggests that sanctions have affected the general public and community health sectors, leading to limited access to necessary medicines in the domestic market and increased patient suffering. Similarly, Aigbogun and others cited environmental fluctuations, external pressures, high sensitivity of the PSC, and dependencies on and linkages
with external elements' as the main challenges to PSC resilience in Malaysia; this is consistent with the findings of the present study.

To sum up, the present findings implied that politico-economic sanctions can harm the PSC and raise several issues for public health. Evidence from other countries’ experiences also shows that sanctions can limit many diagnostic and treatment services. According to a report on North Korea, the food crisis, the decline in medical research, and the number of therapeutic and diagnostic items available for citizens are among the greatest challenges resulting from the imposition of sanctions on that country.29

Another study from Cuba also reported that despite the negative impact of sanctions on the health system, proper management of the PSC could mitigate their adverse effects.30

Based on the aforementioned discussion, paying attention to the role of suppliers and producers and to the role of the medical community and consumers as a strategy to address the challenges of the PSC under politico-economic sanctions can go a long way in improving the quality of medicines, increasing production and exports, and addressing the challenges posed by sanctions in the pharmaceutical sector. Most importantly, policymakers should consider informing the medical community and using alternative medicines and methods, the role of providers in cases of poor brand loyalty, and consumer-patient collaboration. The present paper has certain limitations, which could be as follows: the national document analysis could be merged with the data achieved from semi-structured interviews for more data robustness and achieving triangulation for qualitative research.

**Conclusion**

The findings of this study implied that pharmaceuticals may be affected by politico-economic sanctions in five main areas, namely financing, purchasing and importing, manufacturing of domestic products, storage and distribution of medicines, and challenges to people and patients. Identifying supply chain challenges and planning to address them can inform policymakers on how to increase PSC resilience in the future.

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**Authors’ Contribution**

P.B: Study concept, Interpretation of data, Critical revision of the manuscript for important intellectual content; Z.D: Study concept, Interpretation of data, Drafting of the manuscript; S.M.K: Study design, Drafting of the manuscript; H.D: Acquisition of data, Drafting of the manuscript; M.M: Study design, Drafting of the manuscript; Gh.M: Analysis of data, Critical revision of the manuscript for important intellectual content; All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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