



Development and Validation of a Tool for Measuring Knowledge, Attitude, and Behavior Regarding Unused Household Medicine Management

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ABSTRACT

Background: Today, one of the environmental problems in the world is pharmaceutical waste, which has the potential to be hazardous, toxic, and pathogenic with a long half-life and cumulative properties. This study aimed to develop and validate a tool to measure knowledge, attitude, and behavior of household pharmaceutical waste disposal in urban households.

Methods: The initial items of the questionnaire were developed based on existing guidelines, standards, literature, and experts' opinions. Content validity ratio (CVR) and content validity index (CVI) were used to confirm the content validity of the tool. Item impact score was used to determine face validity. The internal consistency of the instrument was evaluated using Cronbach's alpha. Test-retest analysis was used for examining over time consistency. All the data were analyzed using SPSS version 21.

Results: Based on the results of CVI, CVR, and impact scores, 36 items remained. The tool's internal consistency and over time consistency were confirmed with Cronbach's alpha coefficient of 0.82 and correlation coefficient of 0.9, respectively.

Conclusion: The results indicated proper psychometric properties of the questionnaire and confirmed that it is valid for measuring urban households' knowledge, attitude, and behavior about the disposal of pharmaceutical waste.

1. Introduction

Today, one of the world's environmental problems is the entry of substances that can be dangerous, toxic, and pathogenic such as household pharmaceutical waste. Increasing the amount and diversity of these wastes has raised environmental pollution and essential health hazards. Therefore, proper management in the disposal of this waste

can prevent pollution in the environmental resources such as water, soil, air, etc. Today, environmental pollution caused by pharmaceutical waste is reaching alarming levels in low-income countries [1].

Moreover, the burden of diseases related to the effects of waste is increasing and is not sufficiently known [2]. The most important reason for investigating and controlling drug contaminants in the environment is the possibility of these



contaminants entering the food cycle and drug resistance resulting from them, which leads to many environmental and medical hazards. Due to the existence of more than 4000 active substances in drug production (only in Europe), the combination of these substances with different chemical structure and various physical and chemical properties, and production of thousands of drugs (12000 drugs for humans and 2500 drugs for animals), this issue has faced many aspects and challenges [3, 4].

According to the studies, more than 16 million tons of waste is produced annually in Iran. Consequently, an average of 45,000 tons of household waste, 400 tons of hospital waste, and 500 tons of infectious waste are produced daily. The leachate of this waste, containing various hazardous chemical and biological substances, can cause irreparable damage to environmental resources such as soil, water, and humans [5]. Today, a wide range of destructive effects of medicinal wastes including physiological effects, growth inhibition or stimulation in aquatic plants and algal species, effects on the fertility and fish growth, reptiles, and aquatic invertebrates have been identified [6, 7]. In 2006, the effects of drug residues were observed in the environment, which included identifying 12 different drug compounds in the Rudbolder Basin in Colorado by scientists from the U.S. Geological Survey [8].

Assessing the environmental impact of pharmaceutical waste is very difficult and complex. Since 1980, the U.S. Food and Drug Administration (FDA) has been assessing the environmental risks of human and veterinary drugs and their effects on aquatic and terrestrial organisms before they enter the market. However, the destructive effects of most drugs remain unknown and require evidence-based studies [9].

Although the concentration of drugs in the environment may be low or less effective in direct and short-term experiments (does not show the biological effect of these drugs), the target organs are exposed to these drugs and accumulate in them over time, causing risks [10].

Part of the waste management problems in Iran is caused by the executive agents of waste management, namely municipalities. As the main custodians of municipal waste management, municipalities should be evaluated from citizens' perspective; since there is a direct relationship between public oversight of municipal performance and the quality of services provided by them [11].

Regarding municipal waste management, evaluating two components of awareness and attitude among municipal waste producers can help the waste management system continuously improve its programs [12].

Considering the importance of pharmaceutical waste and its effects on the environment and humans, as well as creating various disease cycles, researching in this area is important. So, an accurate tool should be provided to measure pharmaceutical waste management at the level of urban households and collect appropriate data. Therefore,

this study aimed to provide an effective tool to understand the status of pharmaceutical waste management better and assess behavior, knowledge, and attitude of waste disposal at the level of urban households.

2. Materials and Methods

The tool was developed and adopted based on existing guidelines, standards, literature, and 'experts' opinions about household pharmaceutical waste disposal. The designed tool included closed-ended questions about demographic characteristics (age, level of education, marital status), physical and mental health status, various forms of existing unused medicine at home such as tablets, syrups, ampules, vials, ointments, sprays. 50 initial items were about knowledge, attitudes, and behavior regarding the management of unused medicine at home. The knowledge domain included 7 multiple-choice questions.

The attitude domain was developed using 16 statements. Responses to these statements were measured on a five-point Likert scale, ranging from very agree to very disagree. The behavior section consists of 27 statements including always, often, sometimes, rarely, and never. For assessing the content validity of items, we used content validity ratio (CVR) and content validity index (CVI). CVR and CVI were calculated based on the feedback from a panel of 10 experts in related fields. For calculating CVR, the experts' panel was asked to assess each item based on a three-part spectrum (necessary, useful but unnecessary, unnecessary). Based on the answers, the CVR was calculated using Equation 1. According to 'Lawshe's table, the items with CVR equal to or more than 0.62 (based on the evaluation of 10-panel experts) were preserved in the questionnaire.

Equation (1):

$$\text{CVR} = \frac{ne - n/2}{n/2}$$

Where ne is the number of experts who have selected the necessary option and n is the total number of specialists.

For assessing the CVI, the experts' panel was asked to assess the items in terms of three characteristics including simplicity, specificity, and clarity ranging from lowest (score 1) to highest (score 4). Then, according to Equation 2, the CVI of each question was calculated.

Equation (2):

$$\text{CVI} = \frac{\text{number of specialists who gave the item a score of 3 and 4}}{n}$$

For evaluating the qualitative face validity, difficulty level, appropriateness, and ambiguity of each item were examined. A 5-point Likert scale questionnaire was considered in quantitative face validity: 1 (not important at all) to 5 (absolutely important). Based on the answers of twenty

individuals in the target group, the impact score of each item was calculated using Equation 3. Equation (3):

$$\text{Impact Score} = \text{Frequency (\%)} \times \text{Importance}$$

Frequency refers to the percentage of people who have given a score of 4 or 5 to the item. Importance is the average of importance scores based on the above Likert scale for each item. After performing these calculations, if the calculated impact score was more than 1.5, the item was preserved in the tool.

To assess the developed tool's reliability, Cronbach's alpha coefficient was used to evaluate internal consistency and the test-retest method was used to measure the over-time consistency. For assessing over-time consistency, the developed tool was completed in two-week intervals by 30 urban households and the correlation coefficient was calculated.

3. Results and Discussion

Different sections of the researcher-made questionnaire are as follows:

- Demographic information
- Little information about keeping medicines at home
- Examining responsive behavior with the response scope of the items including always - often - sometimes - rarely - never
- Examining the responsive attitude with the response scope of the items including strongly agree-agree- have no opinion- disagree and strongly disagree
- Examining responsive knowledge using multiple-choice questions with one correct option.

The result of this study is the production of tools to measure the knowledge, attitude, and behavior of pharmaceutical waste management in urban households. The content of this tool is summarized in Tables 1 to 3.

The results of calculating the CVR showed that for the attitude component 6 questions (out of 16), for the behavior component 7 questions (out of 27), and the knowledge component 1 question (out of 7) were deleted due to the score less than 0.62.

The results of calculating the CVI showed that 3 questions (out of 16) were deleted for the attitude component and for the behavior component, no question was deleted. For the knowledge component, 1 question (out of 7) was deleted from the questionnaire due to the score of less than 0.79. At the end of this stage, the mean CVR index was 0.96, the CVI index was 0.93, and the tool's validity was confirmed.

The face validity of the instrument was determined by 20 people and the impact score of each question was counted and compared with the relevant standard. The impact score in all the questions was higher than 1.5.

Table 1: Evaluation of the validity of the questions related to the components of attitude, behavior, and knowledge

| Attitude | | | |
|-----------------|--|-----|------|
| Row | Question | CVR | CVI |
| 1 | The drug should be taken only with a doctor's prescription | 0.8 | 0.9 |
| 2 | When preparing the drug, its expiration date should be considered | 1 | 0.93 |
| 3 | The rest of the used drugs should be given to acquaintances | 0.4 | 0.93 |
| 4 | The rest of the used drugs should be given to government centers / Red Crescent | 0.6 | 0.9 |
| 5 | The rest of the used medicine should be thrown in the trash | 1 | 1 |
| 6 | The rest of the used drugs must have a collector | 1 | 0.93 |
| 7 | Having some medications at home is essential for emergencies | 1 | 0.87 |
| 8 | The drug should be discontinued if it has side effects on the body | 0.2 | 0.73 |
| 9 | Self-medication should be avoided when you have headaches, fever, earache, sore throat, etc. | 0.8 | 0.87 |
| 10 | You can prepare the medicine you need according to the guidance of those around you | 1 | 0.87 |
| 11 | The drug should be stopped if it does not have a therapeutic effect | 0 | 0.73 |
| 12 | The remaining drugs should be disposed of according to the disposal method of the drug recorded on the brochure | 1 | 0.8 |
| 13 | The use of medications prescribed for other family members is sometimes not a problem | 0 | 0.77 |
| 14 | Improper disposal of the remaining drugs causes damage to the environment | 1 | 0.83 |
| 15 | Improper disposal of the remaining drugs causes them to be transferred to the food chain of humans and animals | 1 | 0.83 |
| 16 | Public awareness of how to dispose of medicines left in their homes is low | 0.6 | 0.87 |
| Behavior | | | |
| Row | Question | CVR | CVI |
| 17 | I prepare and take medicine with a doctor's prescription | 0.4 | 0.9 |
| 18 | With the guidance of friends and acquaintances, I prepare and take the medicines I need | 0.2 | 0.83 |
| 19 | When I feel headaches, heartburn, earache, eye pain, back pain, knee pain, etc., I prepare and take medicine without a doctor's prescription. | 1 | 0.83 |
| 20 | When I have fever, nausea, lethargy, runny nose, itching, muscle cramps, cough, sneeze, and shortness of breath I prepare and take medicine without a doctor's prescription. | 1 | 0.83 |
| 21 | When necessary, I use medications that have been prescribed for other family members and are already at home. | 0.6 | 0.87 |
| 22 | When preparing the medicine, I pay attention to its expiration date | 1 | 0.97 |
| 23 | I read the brochure and guide inside the medicine package | 1 | 1 |
| 24 | I pay attention to the label of the Ministry of Health on the package or bottle of medicine | 0.8 | 0.9 |

Table 1: Evaluation of the validity of the questions related to the components of attitude, behavior, and knowledge (Continue)

| | | | |
|------------------|---|------------|------------|
| 25 | I read the label or the instructions for how to dispose of the medicine, which is in the medicine package or bottle | 1 | 1 |
| 26 | I read the label or the guide for the storage conditions of the medicine, which is in the medicine package or bottle | 1 | 1 |
| 27 | I keep the rest of the unused medicines at home for later treatment | 1 | 1 |
| 28 | I donate the rest of the unused medicines to charities | 1 | 1 |
| 29 | I sell the rest of the unused drugs | 1 | 1 |
| 30 | I give the rest of the unused medicines to my friends and acquaintances | 1 | 1 |
| 31 | I give the rest of the unused medicines to health centers or the Red Crescent | 1 | 1 |
| 32 | I give the rest of the unused medicine to the pharmacy | 1 | 1 |
| 33 | I throw the rest of the unused and expired drugs in the toilet | 1 | 1 |
| 34 | I dump the remaining unused and outdated medicines in the bathroom or toilet | 0.6 | 1 |
| 35 | I put the rest of the unused and expired medicines in the sink | 1 | 1 |
| 36 | I burn the remnants of unused and outdated drugs | 0.8 | 0.97 |
| 37 | I throw the leftovers of unused and outdated medicines in the trash along with other household waste. | 1 | 1 |
| 38 | I throw the rest of the unused and outdated drugs in the separate trash | 1 | 1 |
| 39 | I leave the rest of the unused and outdated drugs in the mountains, forests, sea, and river | 0.8 | 1 |
| 40 | I bury the rest of the unused and outdated medicines in the garden soil | 0.8 | 1 |
| 41 | If the medicine used does not have a therapeutic effect, I will stop taking it without the doctor's permission | 0 | 0.87 |
| 42 | If the medicine I use has side effects (shows side effects in my body), I will stop taking it | 0.4 | 0.8 |
| 43 | If the medicine I use is bad-tasting or smelly, should I stop taking it despite my doctor's prescription? | 0.2 | 0.8 |
| Knowledge | | | |
| Row | Question | CVR | CVI |
| 44 | What is the best place to store medicines at home? | 1 | 1 |
| 45 | What is the best way if the prescribed medicine shows side effects in the body? | 1 | 1 |
| 46 | What is the best way to get rid of leftover medicine at home? | 1 | 1 |
| 47 | What is the best source of information on how to dispose of leftover drugs? | 1 | 1 |
| 48 | Which environment is the most harmful to disposing of medicine in household waste? | 1 | 1 |
| 49 | If the prescribed drug has a bad taste, color, and smell for the consumer, what is the best decision about that drug? | 0.6 | 0.78 |
| 50 | Which environment does the medicine in the sink/toilet do the most damage? | 1 | 1 |

Cronbach's alpha test and test-retest were used to evaluate the reliability and stability of the tool. Due to the nature of attitude and behavior components items as a Likert scale, attitude and behavior components items entered the reliability analysis of Cronbach's alpha calculation. The results of Cronbach's alpha analysis were calculated separately for each component (attitude and behavior) and for all the attitude and behavior items. According to the results obtained from the reliability test, by deleting the component's of second question, the tool's internal correlation behavior increased from 0.78 to 0.82. Reliability of knowledge section using Kuder-Richardson coefficient was confirmed with a correlation coefficient of 0.76. Then, to determine the time reliability (tool stability), the test-retest was used and the stability of the prepared tool was confirmed with a correlation coefficient of 0.9.

In the present study, the initially designed questionnaire had 50 items. Based on the 'experts' opinions, 14 items with CVR less than 0.62 were deleted, and 36 items remained. The highest CVR was assigned to the knowledge component among the questionnaire questions. This study was based on the method used to determine the reliability of the questionnaire in previous studies, like the study by Poletti *et al.* (1994) [13] and Ebadi *et al.* (2002) [14]; since tool design is increasing in various fields. The process of designing a tool is long, complicated, and it has its own rules and principles. Neglecting of each rule can lead to a poor quality tool, resulting in invalid results of the data collected by that tool. Therefore, before designing tools, the tool designer must ask himself/herself what he/she needs to measure and why. The other question is whether or not the required information can be obtained from the available sources [15]. It is very important to pay attention to the psychometric quality of the tool to design or use a tool. Two main features of psychometrics are the validity and reliability of tools. Calton and Covert stated that there is no set rule for determining the number of primary items, but it depends on whether one or more components are to be measured. The number of items increases with the increase of the measured components. They believe that a pool of items should be formed, and then the items should be selected from this pool. Forming this tool can also help to design parallel forms. These authors believe that one-fourth of the primary items usually remain in the previous edition of the tool [16].

In this study, the research team designed a pool of 100 items at the beginning, which was decreased to 35 items in the final stage. The remaining items were more than a quarter of the primary items. In terms of the questionnaire's content, common words and phrases among the people were used and specialized phrases and words that may affect a person's perception of the questions were refrained. Although there is no specific rule for the number of items to be extracted, it should be remembered that tools with small number of items have a lower response error (due to less fatigue of respondents). Items should also represent the intended content. At least three items are required for each component to achieve proper internal correlation [17].

Table 2: Impact Score of the final questionnaire

| Row | Question | Impact score |
|-----|--|--------------|
| 1 | When I feel light and intermittent pain such as headache, heartburn, earache, eye pain, back pain, etc., I prepare and take medicine without a doctor's prescription. | 2.1 |
| 2 | When I have fever, nausea, lethargy, runny nose, itching, muscle cramps, cough, sneeze, and shortness of breath I prepare and take medicine without a doctor's prescription. | 2.4 |
| 3 | When preparing the medicine, I pay attention to its expiration date | 3.8 |
| 4 | I read the brochure and guide inside the medicine package | 3.1 |
| 5 | I pay attention to the approval label of the Ministry of Health (health I.D.) on the package or bottle of medicine when preparing the medicine | 3.1 |
| 6 | I read the label or the instructions for how to dispose of the medicine, which is in the medicine package or bottle | 2 |
| 7 | I read the label or the guide for the storage conditions of the medicine, which is in the medicine package or bottle | 2.8 |
| 8 | I keep the rest of the unused medicines at home for later treatment | 2.1 |
| 9 | I donate the rest of the unused medicines to charities | 2.1 |
| 10 | I sell the rest of the unused drugs | 1.7 |
| 11 | I give the rest of the unused medicines to my friends and acquaintances | 2 |
| 12 | I give the rest of the unused medicines to health centers or the Red Crescent | 1.7 |
| 13 | I give the rest of the unused medicine to the pharmacy | 2.7 |
| 14 | I throw the rest of the unused and expired drugs in the toilet | 1.9 |
| 15 | I put the rest of the unused and expired medicines in the sink | 3.2 |
| 16 | I burn the remnants of unused and outdated drugs | 2.3 |
| 17 | I throw the leftovers of unused and outdated medicines in the trash along with other household waste. | 2.2 |
| 18 | I throw the rest of the unused and outdated drugs in the separate trash | 1.7 |
| 19 | I leave the remnants of unused and outdated drugs in the mountains, forests, sea, and river | 2.7 |
| 20 | I bury the rest of the unused and outdated medicines in the garden soil | 3.2 |
| 21 | The drug should be taken only with a doctor's prescription | 3.4 |
| 22 | When preparing the drug, its expiration date should be considered | 4.2 |
| 23 | The rest of the used medicine should be thrown in the trash | 2.8 |
| 24 | The rest of the used drugs must have a collector | 3.6 |
| 25 | Having some medications at home is essential for emergencies | 2.4 |
| 26 | Self-medication should be avoided when you have headaches, fever, earache, sore throat, etc. | 1.8 |
| 27 | You can prepare the medicine you need according to the guidance of those around you | 1.7 |

| | | |
|----|--|-----|
| 28 | Drugs left at home If you have a drug disposal brochure, the disposal should be done according to the method recorded on the brochure. | 2.7 |
| 29 | Does improper disposal of excess home remedies in the environment cause environmental damage? | 4.3 |
| 30 | Improper disposal of leftover drugs at home causes them to enter the food chain of humans and animals | 4.3 |
| 31 | What is the best place to store medicines at home? | 1.5 |
| 32 | What is the best way if the prescribed medicine shows side effects in the body? | 2.7 |
| 33 | What is the best way to get rid of leftover medicine at home? | 2.2 |
| 34 | What is the best source of information on how to dispose of leftover drugs? | 2.4 |
| 35 | Which environment is the most harmful to disposing of medicine in household waste? | 3.4 |
| 36 | Which environment does the medicine in the sink/toilet do the most damage? | 4 |

According to Waltz *et al.* (2014) experts should consider the four criteria of necessity, simplicity, clarity, and relevance of the item when assessing the items of a tool in terms of content [18]. In the present study, the experts based on the opinion of Waltz *et al.* (2014) considered all four criteria for the items [18]. In addition to qualitative methods, quantitative methods that provide more objective results were used to ensure face and content validity. Tool designers also involve the target group for whom the tool was made in the tool designing process. Accurate and step-by-step implementation of the face and content validity both qualitatively and quantitatively improves the level of instrument and makes the analysis easier [19]. It seems that the present study is one of the first studies related to the design and instrumentation of measuring knowledge, attitude, and disposal of household pharmaceutical waste and its evaluation at the level of urban households. The questionnaire provided an opportunity to measure knowledge, attitude, and behavior items on all three scales. In Iran, no review study has been conducted to examine the quality of appropriate tools. The study of tools designed for health and tools for measuring psychological constructs, have shown that tool designers have not considered all aspects of psychometrics. Knowledge of the tool's psychometric properties can guide researchers to choose the appropriate tool for research in the field of health. It can also help tool designers to design and provide a tool with the desired psychometric quality [20].

In the reliability stage, the behavior and attitude questions consisted of 5 options including always (5 points), often (4 points), sometimes (3 points), rarely (2 points), and never (1 point). The questions of the knowledge section were multiple-choice. In the case of selecting the correct answer, the score was 1, and in the case of an incorrect answer, the score was zero.

Table 3: Correlation coefficient of the questionnaire questions in the components of behavior and attitude

| Row | Questions | Cronbach's alpha |
|-----|---|------------------|
| 1 | When I feel light and intermittent pain such as headache, heartburn, earache, eye pain, back pain, etc., I prepare and take medicine without a doctor's prescription. | 0.839 |
| 2 | When preparing the medicine, I pay attention to its expiration date | 0.797 |
| 3 | I read the brochure and guide inside the medicine package | 0.79 |
| 4 | I pay attention to the approval label of the Ministry of Health (health I.D.) on the package or bottle of medicine when preparing the medicine | 0.793 |
| 5 | I read the label or the instructions for how to dispose of the medicine, which is in the medicine package or bottle | 0.805 |
| 6 | I read the label or the guide for the storage conditions of the medicine, which is in the medicine package or bottle | 0.806 |
| 7 | I keep the rest of the unused medicines at home for later treatment | 0.831 |
| 8 | I donate the rest of the unused medicines to charities | 0.812 |
| 9 | I sell the rest of the unused drugs | 0.828 |
| 10 | I give the rest of the unused medicines to my friends and acquaintances | 0.818 |
| 11 | I give the rest of the unused medicines to health centers or the Red Crescent | 0.81 |
| 12 | I give the rest of the unused medicine to the pharmacy | 0.837 |
| 13 | I throw the rest of the unused and expired drugs in the toilet | 0.826 |
| 14 | I put the rest of the unused and expired medicines in the sink | 0.833 |
| 15 | I burn the remnants of unused and outdated drugs | 0.826 |
| 16 | I throw the leftovers of unused and outdated medicines in the trash along with other household waste. | 0.832 |
| 17 | I throw the rest of the unused and outdated drugs in the separate trash | 0.827 |
| 18 | I leave the remnants of unused and outdated drugs in the mountains, forests, sea, and river | 0.829 |
| 19 | I bury the rest of the unused and outdated medicines in the garden soil | 0.825 |
| 20 | The drug should be taken only with a doctor's prescription | 0.813 |
| 21 | When preparing the drug, its expiration date should be considered | 0.812 |
| 22 | The rest of the used medicine should be thrown in the trash | 0.834 |
| 23 | The rest of the used drugs must have a collector | 0.812 |
| 24 | Having some medications at home is essential for emergencies | 0.814 |
| 25 | Self-medication should be avoided when you have headaches, fever, earache, sore throat, etc. | 0.82 |
| 26 | You can prepare the medicine you need according to the guidance of those around you | 0.821 |
| 27 | Drugs left at home If you have a drug disposal brochure, the disposal should be done according to the method recorded on the brochure. | 0.82 |

| | | |
|----|---|-------|
| 28 | Improper disposal of excess home remedies in the environment causes environmental damage | 0.815 |
| 29 | Improper disposal of leftover drugs at home causes them to enter the food chain of humans and animals | 0.82 |

After designing the final questionnaire by confirming its validity, reliability, and reproducibility, it can be said to what extent this tool, if applied at the community level, can indicate individuals' knowledge, attitude, and behavior regarding the disposal of pharmaceuticals waste. In this study, the pre-introduction steps were performed accurately and step by step, and the desired results were counted. The questionnaire for measuring the knowledge, attitude, and disposal of household pharmaceutical waste and its evaluation at the urban households level with 19 questions in the behavior section, 10 questions in the attitude section, and 6 questions in the knowledge section, as well as the internal consistency assessment (Cronbach's alpha) of all the items of the questionnaire, indicated a good correlation between different items, in similar conditions, by the target group. In other words, people had almost the same perception of this tool. The results of Cronbach's alpha 0.82 and correlation coefficient 0.9 indicated the internal stability and high internal consistency of the designed items which confirmed that the tool was valid.

4. Conclusion

According to the results of this study, examining the validity and reliability indicators related to the researcher-made questionnaire indicated proper psychometric properties of the questionnaire and confirmed its validity for measuring knowledge, attitude, and behavior in household pharmaceutical waste disposal. Moreover, it can be used in future studies in related fields at the urban households level.

Authors' Contributions

Samira Abbasi: Data Curation; Investigation; Resources; Visualization; Writing-original draft. **Gholamreza Sadeghi:** Conceptualization; Formal analysis; Funding acquisition; Supervision; Methodology; Project administration; Validation; Writing-original draft; Writing-review and editing. **Fatemeh Jafari:** Formal analysis; Methodology; Validation; Writing-review and editing.

Conflicts of Interest

The Authors declare that there is no conflict of interest.

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