

## ORIGINAL RESEARCH

# The magnitude and predictors of self-medication amongst street dwellers in Ethiopia: a multicentre study

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## Abstract

**Background:** Low levels of living standards amongst street dwellers worldwide limit their access to conventional healthcare services, resulting in self-medication use for the treatment of an illness. Nevertheless, self-medication use has risks, including adverse drug reactions, increased polypharmacy, drug resistance, drug dependence, drug interactions and incorrect diagnosis. Ethiopia has a large street-dwelling community; however, there are no studies conducted in Ethiopia assessing self-medication use amongst street dwellers. This study provides insight into self-medication use and predictors amongst street dwellers in Ethiopia.

**Methods:** A community-based, multicentre cross-sectional study was conducted amongst street dwellers from 1 September 2022 to 1 February 2023 at community drug-retail outlets in the three major cities in the Amhara region of Ethiopia. The data were obtained using an interviewer-administered questionnaire. Frequencies and percentages of descriptive statistics were calculated. Bivariable and multivariable logistic regression analyses were employed to indicate predictors of self-medication use. To determine statistical significance, a 95% confidence interval with a *p* value below 0.05 was utilized.

**Results:** The prevalence of self-medication use was 67.4%. Time and financial savings were reported as

the reasons for most self-medication use. The most commonly reported illnesses for which people sought self-medication were gastrointestinal diseases. Low monthly income (adjusted OR 3.72, 95% CI 2.34–5.91) and residing near sewage areas (adjusted OR 3.37, 95% CI 2.03–5.58) were significantly associated with self-medication use.

**Conclusion:** Street dwellers had a high rate of self-medication use. Residing near sewage areas and having a low level of income were factors in self-medication use. Gastrointestinal diseases, respiratory ailments and dermatological conditions were the most frequently reported complaints, whereas antimicrobials and anthelmintics were the most commonly used medications. We recommend that healthcare services enhance outreach programmes to the most vulnerable people, such as street dwellers, especially those with lower monthly incomes and who live near sewage areas, to reduce self-medication rates.

**Keywords:** Ethiopia, self-medication, street dwellers.

## Citation

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## Introduction

People who reside in public areas, such as gardens, open areas, train and bus terminals, funeral homes, building sites, and roads, are referred to as street dwell-

ers.<sup>1</sup> The prevalence of street dwellers has increased as a result of political and financial policies in several countries.<sup>2</sup> Worldwide, more than 500 million homeless people are living on the streets, making this an issue of growing global concern.<sup>3,4</sup> Numerous countries in Africa, including Ethiopia, commonly struggle with housing

issues, leading to overcrowding, homelessness and street dwelling.<sup>5,6</sup> Most of Ethiopia's street dwellers live in metropolitan cities.<sup>7</sup> A case study conducted in the Amhara Region reported that the Amhara ethnic group had the highest percentage of street dwellers within Ethiopia.<sup>8</sup> As street dwellers are highly affected by low socioeconomic conditions and poor personal and environmental hygiene, they are the most disadvantaged and marginalized communities in urban areas.<sup>9</sup> Furthermore, given their overall low levels of living standards and the financial and time constraints linked to their livelihoods, street dwellers have limited access to conventional healthcare services or formal clinics for family planning and reproductive health services,<sup>10</sup> and are therefore extremely likely to self-medicate. Self-medication is the use of medication for self-treatment without visiting a healthcare provider for a prescription or diagnosis or to monitor the course of therapy.<sup>11,12</sup> Self-medication has long been a part of healthcare worldwide, with individuals taking responsibility for their health.<sup>13</sup> Although self-medication can potentially do no harm when practiced correctly, it can have a negative impact on individuals and the healthcare system, especially in countries where prescription drugs are available over-the-counter due to a lack of enforcement of regulations.<sup>14,15</sup> Moreover, self-medication may result in risks such as adverse drug reactions, increased polypharmacy, drug resistance, drug dependence, drug interactions and incorrect diagnosis.<sup>16,17</sup> Despite this, street dwellers commonly attempt to treat an illness through self-medication, visiting a health professional only upon worsening symptoms or lack of disease control, inability to move or work, or when illnesses persists for several days.<sup>18</sup>

There are currently no studies assessing self-medication use amongst street dwellers in Ethiopia. The lack of data on this matter poses a threat to Ethiopian public health as street dwellers without access to proper healthcare can transmit disease.<sup>19</sup> Hence, this study was conducted to provide insight into the self-medication practices and its predictors amongst street dwellers in Ethiopia without access to basic healthcare and other social services. This study aims to assess the prevalence of self-medication use and associated factors, and the findings will assist policymakers and other regulatory bodies, both in Ethiopia and in the wider region, in developing rational drug use policies to prevent public health risks.

## Methods

### Study setting and design

A community-based, multicentre cross-sectional study was conducted at community drug-retail outlets in

three metropolitan cities in Amhara Regional State from 1 September 2022 to 1 February 2023. The Amhara region is found in northwest Ethiopia, which is composed of 3 major cities, 15 zones and 180 districts. The region's major cities are Bahir Dar, Dessie and Gondar, which are situated approximately 552, 727 and 400 km from Addis Ababa (Ethiopia's capital), respectively.<sup>20</sup> In Dessie, there are reportedly 3000 street dwellers.<sup>4</sup> A total of 60 licensed community drug-retail outlets were actively involved in providing services in Gondar at the time of the study,<sup>21</sup> whereas 63 and 11 drug-retail outlets were found in Bahir Dar and Dessie, respectively.<sup>22,23</sup>

### Study participants and inclusion criteria

The source population for this study was composed of adults (18 years and above) who had lived in the streets of major cities of the Amhara region for a minimum of 6 months before the time of data collection. The study population included all adult street dwellers who visited community drug-retail outlets at the selected cities for self-medication during the data collection period. Individuals who came to get medication for someone else were not included in the study.

### Ethics approval and consent to participate

The Declaration of Helsinki was followed in the course of this study. Written informed consent was obtained from all the study participants after fully explaining the nature of the study. For the approximately 21.1% of study participants who were illiterate or unable to read and write, two options were provided: the first was for a member of the research team to read the information on the written consent form clearly to them, and the second was for them to give the written consent form to a person of their choice to read it for them. Finally, those who consented signed the form with their fingerprints to indicate their willingness to participate. Ethical clearance was granted from the Research and Ethics Committees of the University of Gondar, School of Pharmacy (SN: SOP/194/04/22) on 16 April 2022. Additionally, permission from the owners of the drug-retail outlets was obtained to carry out the study at their premises. Furthermore, to maintain the confidentiality of the responses, no personal identifiers were included in the questionnaire.

### Sample size determination

The sample size was determined using a single population proportion formula, considering the following assumptions: 5% margin of error, 50% frequency and 95% confidence level.

$$n = \frac{(za/2)^2 p(1-p)}{d^2},$$

$$n = \frac{(1.96)^2 \times 0.5 \times 0.5}{0.05^2} = 384$$

Finally, we adjusted the non-response rate by adding 10%, resulting in a total sample size of 422.

## Sampling technique

A total of 134 drug-retail outlets were functioning at the time of the study in the selected cities. A simple random sampling technique was applied to select the drug-retail outlets in each city. A proportional allocation method was then used to classify the drug-retail outlets in stratum from different cities. A convenient sampling technique was applied to distinguish street dwellers who came to buy drugs for self-medication. Finally, study participants who met the inclusion criteria were included in the survey.

## Study variables

Self-medication use was a dependent variable. Whilst sociodemographic parameters, including sex, age, religion, residence, housing situation, marital status, educational level, type of work and income level, and variables linked to medication, including reasons for self-medication, type of complaint for self-medication use, client approach whilst requesting to purchase the medication, and source of information about the medications, were included as independent variables.

## Operational definition

**Street dwellers:** people who reside in public areas such as gardens, open areas, train and bus terminals, funeral homes, building sites and roads.<sup>1</sup>

**Self-medication:** the use of medication without consulting a medical professional for a prescription, diagnosis or to monitor the course of treatment.<sup>11,12</sup>

## Data collection tools and procedures

Data were collected using a pretested data-abstracting checklist designed by the authors after reviewing different literature and modified to correspond to local circumstances.<sup>24–28</sup> The data-abstracting checklist was divided into five sections, which included the respondents' sociodemographic details, the illnesses or symptoms that they sought self-medication for, the way in which they made these requests, the sources of information they used, and the kinds of medications they requested for self-medication. The research was conducted in drug-retail outlets found in the selected metropolitan cities, and the data were collected by six trained pharmacists. Study participants were interviewed after they made their requests but before they were provided with information on the drugs they requested.

## Data quality assurance

The research team prepared the questionnaire in English and, to guarantee uniformity, Amharic-speaking

and English-speaking people translated it into the local tongue. The instrument underwent the appropriate modifications based on the translation. The readiness and completeness of the questionnaire were pretested before the start of the real data collection on 5% of study participants at Debre Markos. The findings from the pretest were not incorporated into the end results of the study. The completeness and uniformity of the questionnaire were verified throughout the data entry and at each stage of the data collection process.

## Data processing and analysis

The collected data were verified for accuracy, completeness and clarity prior to analysis. After being entered into Epi-data 4.6, the data were sent to SPSS version 26 for analysis. For categorical variables, including sociodemographic variables and medication-related characteristics, frequency and percentage were calculated; for continuous variables, such as age and duration of life on the street, mean and standard deviation were calculated. Model fitness was checked with the Hosmer and Lemeshow goodness of fit test. Bivariable binary logistic regression analysis was employed to identify factors that were candidates for multivariable analysis at a  $p$  value of less than 0.2. A multivariable binary logistic regression analysis then was fitted to identify factors significantly associated with self-medication use. Furthermore, multicollinearity between the independent variables was assessed with the variance inflation factor to identify and avoid redundant variables that may affect our estimate. The variance inflation factor was in the acceptable range (1–5). An adjusted odds ratio (AOR) at a 95% confidence interval with a  $p$  value of  $<0.05$  was considered statistically significant. The study's findings were then presented utilizing texts, tables and figures depending on the findings.

# Results

## Sociodemographic characteristics of the study participants

A total of 417 street dwellers, yielding a 98.8% response rate, took part in the study. The participants' mean age was 28.9 years, with a standard deviation of  $\pm 9.46$  years. Over 50% of the respondents (63.3%) were men, and 61.6% of the participants' residency was urban. Most participants (35.5%) were street dwellers due to poverty, followed by job insecurity and family problems in 34.3% and 25.2% of respondents, respectively. The mean duration of street living was 4.69 years, with a standard deviation of  $\pm 1.81$  (0.8 years at a minimum and 11 years at the highest). The most common (36.2%) income-generating work mentioned by the participants was street trade, followed by carrying goods and begging by 28.1% and 27.1%

of the respondents, respectively. Regarding their living conditions, more than half of participants (59.7%) lived far from sewage areas, whilst 39.8% of the participants lived with co-inhabitants (Table 1).

**Table 1. Sociodemographic characteristics of street dwellers in Amhara region, Ethiopia, 2023.**

Variable	Frequency (n)	Rate (%)
<b>Age, years</b>		
18–25	198	47.5
26–33	115	27.6
≥34	104	24.9
<b>Sex</b>		
Male	264	63.3
Female	153	36.7
<b>Origin of residence</b>		
Rural	160	38.4
Urban	257	61.6
<b>Religion</b>		
Orthodox	277	66.4
Muslim	112	26.9
Protestant	28	6.7
<b>Marital status</b>		
Single	340	81.5
Married	37	8.9
Divorced	33	7.9
Widowed	7	1.7
<b>Live with co-inhabitant</b>		
Yes	166	39.8
No	251	60.2
<b>Living condition</b>		
Near to sewage	168	40.3
Far from sewage	249	59.7
<b>Duration of street living</b>		
≤4.69 years	184	44.1
>4.69 years	233	55.9
<b>Education level</b>		
Unable to write and read	88	21.1
Able to write and read	121	29.0
Primary education level	110	26.4
Secondary education level	71	17.0

**Table 1. (Continued)**

Variable	Frequency (n)	Rate (%)
Higher education level	27	6.5
<b>Reasons for being a street dweller</b>		
Poverty	148	35.5
Search for job	143	34.3
Family problem	105	25.2
Other <sup>a</sup>	21	5.0
<b>Income-generating work</b>		
Street trade	151	36.2
Carrying goods	117	28.1
Begging	113	27.1
Car washing and protection	23	5.5
Other <sup>b</sup>	13	3.1
<b>Monthly income</b>		
≤475.6 ETB	231	55.4
>475.6 ETB	186	44.6

<sup>a</sup>Illness, being an orphan.

<sup>b</sup>Shoe-shine boy, street sweeper.

## Prevalence of self-medication amongst study participants

The study revealed that 67.4% of street dwellers self-medicate. The primary reasons mentioned for self-medication amongst most participants (74.3%) were savings in time and money, followed by prior experience of the disease or medication and the belief that the disease is not serious (66.5% and 53.0% of participants, respectively). Regarding complaints, gastrointestinal diseases, such as abdominal cramps, diarrhoea and vomiting, were the most frequently reported (52.3%), followed by skin-related diseases and respiratory diseases (43.0% and 37.5%, respectively). Most participants (75.8%) requested medications by describing the symptoms (Table 2).

Regarding medications used, antimicrobials and anthelmintics were the most commonly used medications, followed by analgesics; amoxicillin was the most utilized medication amongst participants (Table 3).

## Predictors of self-medication amongst study participants

Results from the multiple logistic regression analysis indicated level of income, type of income-generating work, living conditions and living with co-inhabitants

**Table 2. Self-medication-related characteristics amongst street dwellers in Amhara, Ethiopia, 2023.**

Variable	Frequency (n)	Rate (%)
<b>Reasons for self-medication</b>		
For saving time and money	209	74.3
Prior experience	187	66.5
Disease is not serious/ minor problem	149	53.0
Less waiting time in community pharmacy	87	30.9
Other <sup>a</sup>	13	4.6
<b>Type of ailment complaint for self-medication use</b>		
Gastrointestinal diseases	147	52.3
Skin-related diseases	121	43.0
Respiratory diseases	106	37.7
Fever	72	25.6
Headache	56	19.9
Urogenital disease	39	13.8
Eye diseases	34	12.0
Other <sup>b</sup>	9	3.2
<b>Clients approach whilst requesting to purchase the medication</b>		
Describing symptoms	213	75.8
Describe physical characteristics of the medication	47	16.7
Showing old sample	19	6.7
Presenting piece of paper	13	4.2
Mention name of the drug	8	2.8
<b>Information source regarding medications</b>		
Have no information	206	73.3
Advised by friends/family	98	34.8
Recommendation from healthcare professional	11	3.9
Others <sup>c</sup>	6	2.1

<sup>a</sup>Emergency use, distance to health facility.

<sup>b</sup>Dysmenorrhea, joint pain, mechanical injury, insomnia.

<sup>c</sup>Advertisement/promotion, own initiative.

who lived near sewage areas was 3.37 times higher than that those who lived far from sewage areas (AOR 3.37, 95% CI 2.03–5.58) (Table 4).

## Discussion

According to the findings of our study, the rate of self-medication use was 67.4%, which was much higher than that reported in previous studies,<sup>27–31</sup> likely due to the low levels of living standards in the study population consisting of street dwellers. In contrast to other communities, street dwellers cannot access conventional healthcare services, with a subsequently greater tendency to self-medicate. Indeed, previous studies have indicated that, for disadvantaged people such as street dwellers, the first point of access to healthcare services is commonly at drug-retail outlets rather than at healthcare facilities.<sup>32–34</sup> Additionally, as previous observations indicated, in Ethiopia, most community drug-retail outlets do not follow regulations for dispensing medications, which allows and supports people in accessing drugs easily without a prescription, thus increasing the rate of self-medication use.<sup>28,35</sup> The prevalence of self-medication use in our study was comparable to that in a study conducted amongst college students in

**Table 3. Frequency of commonly used medications amongst street dwellers in Amhara, Ethiopia, 2023.**

Medication	Frequency (n)	Rate (%)
Amoxicillin	275	65.9
Ciprofloxacin	196	47.0
Albendazole	153	36.6
Metronidazole	173	41.4
Mebendazole	47	11.2
Permethrin	24	5.7
Benzyl benzoate	9	2.1
Tetracycline	13	3.1
Paracetamol	117	28.0
Ibuprofen	16	3.8
Diclofenac	31	7.4
Tramadol	14	3.3
Artemether/lumefantrine (coartem)	17	4.0
Metoclopramide	56	13.4
Other <sup>a</sup>	19	4.5

<sup>a</sup>Diphenhydramine, norethindrone, dextromethorphan syrup, omeprazole, bisacodyl, oral rehydration salt.

were associated with self-medication, whilst low monthly income and residing near sewage were predictors of self-medication. Accordingly, patients who had low income were about 3.72 times as likely to practice self-medication (AOR 3.72, 95% CI 2.34–5.91), whereas the likelihood of self-medication use amongst participants

**Table 4. Predictors of self-medication use amongst street dwellers in Amhara, Ethiopia, 2023.**

Variable	Self-medication use		Bivariable analysis			Multivariable analysis		
	Yes	No	p value	COR	CI	p value	AOR	CI
<b>Age, years</b>								
18–25	133	65	0.59	0.86	0.52–1.45			
26–33	75	40	0.43	0.79	0.45–1.40			
≥34	73	31		1				
<b>Sex</b>								
Male	178	86	0.98	1.00	0.65–1.53			
Female	103	50		1				
<b>Religion</b>								
Orthodox	193	84	0.84	1.08	0.47–2.50			
Muslim	69	43	0.54	0.76	0.31–1.83			
Protestant	19	9		1				
<b>Educational level</b>								
Unable to read and write	39	24	0.75	1.18	0.41–3.35			
Able to read and write	77	32	0.27	1.75	0.64–4.75			
Primary education	129	59	0.34	1.59	0.60–4.15			
Secondary education	25	13	0.56	1.39	0.45–4.33			
Higher education	11	8		1				
<b>Marital status</b>								
Single	224	116	0.76	0.77	0.14–4.04			
Married	31	6	0.44	2.06	0.32–13.25			
Divorced	21	12	0.69	0.70	0.11–4.17			
Widowed	5	2		1				
<b>Origin of residence</b>								
Rural	106	54	0.69	0.92	0.60–1.40			
Urban	175	82		1				
<b>Coinhabitant</b>								
Present	162	89	0.12	0.71	0.47–1.10	0.29	0.77	0.48–1.25
Absent	119	47		1			1	
<b>Living condition</b>								
Near to sewage	140	28	0.00	3.83	2.37–6.17	<b>0.00*</b>	3.37	2.03–5.58
Far from sewage	141	108		1			1	
<b>Reason for living on the streets</b>								
Poverty	115	33	0.27	1.74	0.65–4.67			
Search for job	79	64	0.32	0.61	0.23–1.62			
Family problem	73	32	0.79	1.14	0.42–3.09			
Others	14	7		1				
<b>Duration of living on the streets</b>								
<5 years	121	63		1				
≥5 years	160	73	0.52	1.14	0.75–1.72			

(Continued)

Table 4. (Continued)

Variable	Self-medication use		Bivariable analysis			Multivariable analysis		
<b>Income-generating work</b>								
Street trade	87	64	0.65	0.73	1.90–2.82	0.60	0.68	0.15–2.93
Carrying goods	83	34	0.87	1.11	0.28–4.36	0.77	0.80	0.18–3.53
Begging	89	24	0.18	0.40	0.10–1.54	0.17	0.37	0.08–1.56
Car washing and protection	12	11	0.15	0.32	0.07–1.50	0.23	0.36	0.07–1.92
Other	10	3		1			1	
<b>Monthly income level</b>								
<475.6 ETB	186	45	0.00	3.95	2.56–6.11	<b>0.00*</b>	3.72	2.34–5.91
>475.6 ETB	95	91		1			1	

\*Statistically significant. AOR, adjusted odds ratio; COR, crude odds ratio.

urban areas of the Amhara region, which is unsurprising as urban living is associated with self-medication practices.<sup>36</sup>

Regarding complaints reported by participants, gastrointestinal diseases (such as diarrhoea or abdominal cramps), skin-related diseases and respiratory ailments (such as cough) were amongst the most prevalent complaints. A possible reason for the high prevalence of intestinal infections and respiratory ailments in our study might be inadequate sanitation, contaminated drinking water and malnutrition, which are significant amongst street dwellers, making them more vulnerable to such diseases.<sup>37</sup> Scabies was also a common complaint in our study, likely due to a lack of personal hygiene, overcrowding and inadequate treatment; indeed, dermatological infections are the most common health problems in homeless populations.<sup>38,39</sup> Moreover, scabies constitutes one of the typical problems with public health amongst people with low standards of living conditions in Ethiopia.<sup>40,41</sup> In comparison, the most prevalent illnesses mentioned in studies conducted in Mekele and Harer in Ethiopia and another in India were fever and headache.<sup>13,29,42</sup> These differences in the findings of various studies demonstrate that there is widespread use of self-medication across a range of diseases.<sup>43,44</sup>

Regarding medications used by the participants, antimicrobials, including antimicrobials and anthelmintics, were the most commonly used drug class. This finding was similar to those of a study conducted in an Indian community.<sup>45</sup> These findings are not surprising given that gastrointestinal infections, respiratory ailments and dermatological conditions are commonly treated with antimicrobials. According to multiple studies conducted

around the world,<sup>46–48</sup> even if rules forbid such practices, antimicrobials can be easily bought without a valid prescription. Furthermore, self-medication with antimicrobials is common,<sup>13,28,29</sup> leading to the well-known problem of antimicrobial resistance.<sup>49</sup> Generally, the lack of adequate national regulations and precise criteria for antimicrobial sales in community medication retail outlets might be partially responsible for the high prevalence of non-prescription sales and access to antimicrobials in our study.

Concerning reasons for self-medication, participants reported that they preferred to visit drug-retail outlets directly rather than hospitals because it was less expensive – both regarding direct payments and regarding time costs; these findings are similar to those of previous studies.<sup>13,27,30</sup> Furthermore, these factors are exacerbated by street dwellers lives being marked by an ongoing struggle for survival, lack of income, inconsistent work, job insecurity and poor living standards.<sup>50</sup>

The most common method for street dwellers to obtain the required medications was by symptom description; conversely, a study in India reported that presenting a prior prescription or recalling the name of the medication from prior prescriptions was the most common approach to requesting medications.<sup>42</sup> This variation might be attributed to educational level – compared with other studies,<sup>29,42</sup> most participants in our study had low literacy levels. A previous study claimed that those with high educational levels normally utilize a prior prescription for the same complaints, whereas those with low educational levels obtain their medications from pharmacists by simply reporting their symptoms.<sup>51</sup>

The current study also assessed predictors of self-medication use, which included lower monthly income and residing near sewage areas. The low or poor standard of living, low monthly income level, and high charges by hospitals might lead to street dwellers favouring community drug-retail outlets. Self-medication has been shown to increase due to poverty and inaccessibility to healthcare services.<sup>52</sup> Moreover, individuals living near sewage and waste matter areas have a high risk for diseases such as intestinal parasite infections, which increases the use of self-medication.<sup>53</sup> A study conducted amongst farmers in Vietnam reported that waste water contact poses a significant risk of skin-related illnesses.<sup>54</sup>

## Limitations

Despite this being a multicentre study encompassing three major cities, the cross-sectional study design made it difficult to pinpoint the precise cause for self-medication. Additionally, the study was conducted only in the Amhara region of Ethiopia. Therefore, we recommend future studies with prospective follow-up designs to address the gaps of the current study. Nevertheless, a study strength was the provision of health education to the participants once the outcome had been determined, with the hopes of reducing self-medication, particularly of antimicrobials, thus reducing the worldwide threat of antimicrobial resistance.

## Conclusion

Our findings indicated that street dwellers have a high rate of self-medication use. Residing near sewage areas and having a low level of income are factors increasing self-medication use. Gastrointestinal diseases, respiratory ailments and dermatological conditions were the most frequently reported complaints, whereas antimicrobials and anthelmintics were the most commonly used medications. Therefore, we recommend that public healthcare services enhance outreach to the most vulnerable people such as street dwellers, especially for those with lower monthly incomes and who live near sewage areas. Moreover, community drug outlets should educate marginalized individuals, such as street dwellers, about the negative aspects of self-medication in order to promote appropriate self-medication use. Finally, decisive action must be taken with regard to the accessibility of medications, such as antimicrobials, without a valid prescription.

## Declarations

### Availability of data and materials

The manuscript contains all the necessary data. On request, you can obtain additional data that has been used to support the study findings from the corresponding author.

**Contributions:** TKZ, RBA and ZAB conceptualized the study. TKZ, MAA and BDA curated the data. TKZ, RBA and AGJ conducted the formal analysis. TKZ, BDA and ZAB conducted the investigation and TKZ, RBA and MAA defined the methodology. TKZ, MAA and AGJ conducted Project administration. TKZ, RBA and BDA supervised the project. TKZ, MAA and AGJ wrote the original draft and TKZ, RBA and AGJ edited the manuscript. Table preparation: TKZ, RBA and ZAB. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

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