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Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

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ABSTRACT

Objective: To measure knowledge, attitude and practice of antibiotics and antibiotic resistance and their determinants in the Eritrean urban population.

Design: Population-based, nation-wide cross-sectional study with quantitative approach.

Setting: Urban settings of Eritrea

Participants: Members of the general public aged 18 years and above and living in thirteen urban places of Eritrea. Three stage stratified cluster sampling was used to select the study participants.

Data collection and analysis: Face-to-face interview was conducted using a structured questionnaire to collect data. Data collection was conducted from July to September 2019. Data was double entered and analyzed using CSPro (Version 7.0) and SPSS (Version 23) respectively. Descriptive statistics, chi-square test, t-tests, analysis of variance and multivariate logistic regression was performed. All analyses were weighted and $p<0.05$ was considered significant.

Primary and secondary outcome measures: Main outcome variables were knowledge, attitude and practice of antibiotics and antibiotic resistance. Secondary outcome measures were the determinants of knowledge, attitude and practice.

Results: A total of 2477 adults, dominated by females (74.7%), were interviewed. The knowledge and attitude of antibiotics and antibiotics resistance (ABR) mean score was 10.36/20 (SD= 3.51, minimum=0 and maximum=20) and 22.34/30 (SD= 3.59, minimum= 6 and maximum =30) respectively. The proportion of at least one risky practice in all those participants who used antibiotics was 23.8%. Young age <24 years (AOR=1.59, 95% CI: 1.06 to 2.38), male sex (AOR=1.48, 95% CI: 1.15 to 1.92), higher level of education (AOR=1.77, 95% CI: 1.05 to 2.90), and negative attitude on antibiotic use ($p<0.001$) were found to be the significant determinants of risky practice of antibiotics.

Conclusion: The gap in knowledge and risky practice of antibiotics in the Eritrean urban population was widespread, requiring immediate attention from policymakers and healthcare professionals.

Keywords: Antibiotic; antibiotics resistance; knowledge; attitude; practice; Eritrea.

Article summary

Strengths and limitations of this study

- This was a population-based study covering nation-wide representative of all urban residents with high response rate.
- It is the first of its kind in Eritrea.
- The results were self-reported and thus, findings might be under- or over-estimated, which could introduce information bias or recall bias.

INTRODUCTION

Antibiotics, one of the subsets of antimicrobials, have the ability to cure bacterial infections. Their emergence was a breakthrough in medical care and has ended the dark ages of medicine, when simple infections were fatal and due to the risk of contamination, medical interventions like assisted delivery and surgical procedures were not safe. However, such advances are being threatened by the emergence of resistant strains rendering many of the previously novel antibiotics ineffective. With the quest to achieve universal health coverage, access to essential medicines, like antibiotics, to the general public has been highly advocated. On the other hand, the excess use of antibiotics, in addition to wastage of resources, poses a great health risks that would escalate bacterial resistance [1-4].

Resistant infections are now estimated to cost at least 50,000 lives each year in Europe and the US alone [5]. From this, one can speculate that the burden of antimicrobial resistance would be much higher in resource-constrained countries in which the inappropriate use of antibiotics by healthcare professionals and consumers could be rampant. This in part is due to poor regulation, weak health systems, surveillance, knowledge and higher infectious diseases [1 6 7]. If left unimpeded, by 2050, deaths attributable to antimicrobial resistance are estimated to be 10 million per year globally [1].

Nowadays, antibiotic resistance is recognized as one of the biggest threats to global health and is becoming a medical emergency that would limit the advances of healthcare delivery services. This endangers the achievements of the Millennium Development Goals and also Sustainable Development Goals [8]. Thus, antimicrobial resistance in general and antibiotic resistance in particular is transforming to be a political agenda.

As estimated by the WHO, 80% of antibiotics is used in the community, of which 20-50% is used inappropriately [9]. Use of antibiotics without prescription [10-13], physicians' perception of patient expectation for antibiotics [14 15], patient demand [16-18], unrestricted use of antibiotics [7 19] and poor healthcare system [20] have been reported as among the main factors for the inappropriate use of antibiotics. To tackle this, at the 68th World Health Assembly, a global action plan was endorsed [21]. One of the five global strategic objectives was to improve awareness and understanding about antimicrobial resistance [21], thus; all member states were recommended by the WHO to annually conduct antibiotic awareness week campaigns in a one-health approach [21].

As part of this initiative, Eritrea started conducting massive antibiotic awareness week campaigns, in a one health approach, since 2017. Due to lack of baseline data, the impact of the continuous campaigns could not be assessed against pre-established parameters. This study is therefore conducted to measure knowledge, attitude and practice of antibiotic usage and identify key determinants for knowledge, attitude and practice in the Eritrean urban population.

METHODS

Study Design

A cross-sectional study design, with a quantitative approach, was used.

Study Area and Period

Eritrea is a country with an estimated population of 3.4 million [22]. It has six administrative zones comprising 58 subzones in total. The country has five administrative levels namely: National, Zonal, Sub-zonal, Local Administration (Kebabi administration) and Village/Block (village in rural or block in urban settings) levels.

The survey was conducted between July and September 2019 in all urban sites of the country. In Eritrea, there are a total of 13 cities and/or towns. The urban sites included in this study were three from Gash Barka, five from Debub, two from Semenawi Keih-Bahri (SKB) and one city or town from each of the three zones, namely Anseba, Debubawi Keih-Bahri (DKB), and Maekel (Table

1). A total of 25 sub-zones and 72 local administrations (Kebabi administration) located in the above-mentioned towns and/or cities were involved in the survey.

Table 1: Number of households in the urban places of Eritrea (July 2019).

Zone	City/Town	HH Size
Gash Barka	Akordat	3,822
	Barentu	10,935
	Tessenei	15,205
	Subtotal	**29,962**
Debub	Mendefera	8,023
	Adiquala	3,419
	Dekemhare	9,769
	AdiKeih	5,335
	Senafe	6,574
	Subtotal	**33,120**
SKB	Ghindae	5,832
	Massawa	9,512
	Subtotal	**15,344**
Anseba	Keren	19,343
	Subtotal	**19,346**
DKB	Assab	3,106
	Subtotal	**3,106**
Maekel	Asmara	116,146
	Subtotal	**116,146**
Total		**217,024**

SKB: Semienawi Keih Barhri; DKB: Debubawi Keih Barhri; HH: Household

Target Population

The target population of the study includes all members of the general public aged 18 years or above and living in the thirteen urban places in which the survey was conducted.

Sample Size and Sampling Technique

Sample size

Sample size for the study was computed after considering the necessary parameters, namely: sampling techniques, expected proportion, precision, and level of significance. Calculation of the sample size for stratified random sampling was done using the following formula [23]:

$$n \geq \frac{NV1.96^2}{V * 1.96^2 + (N-1) * 0.05^2};$$

Where; 1.96 refers to the standard normal score of the 95% confidence level of the estimation, 0.05 to the precision, N=overall population size (of the urban places), and V=$\frac{SD^2}{Pooled\ proportion^2}$

SD was computed to be 0.5, using the household sizes of each zone (Table 1) and assuming p=0.5 since no other nation-wide studies were conducted in the past. Using the same data, the pooled proportion was 0.25. Hence, the sample size for all the six strata became 1524.5 and after adjusting for 10% non-response rate, it was increased to 1694.4. Finally, the design effect (deff=1.5) adjusted sample size was 2542 individuals.

Sampling Technique

The awareness, knowledge, attitude, and practice towards antibiotics and antibiotic resistance varies across the zones in Eritrea. For this reason, each zone was considered as a stratum having unique level of awareness, knowledge and attitude. There was homogeneity of awareness, knowledge, attitude, and practice within each zone, which allowed us to cluster urban places and take representative samples. Hence, it was presumed that the sample design that led to the selection of a legible person was a stratified three-stage cluster sample with some recognized geo-political area unit of variable size as the primary sampling unit, an approximately equal-sized area, segment, consisting of roughly 200 households as the secondary sampling unit, and individual households selected within sampled segments [24].

Sampling Frame

A new frame was constructed based on recognized administrative and geo-political organization of the urban places in Eritrea. All urban places eligible for the study were requested to supply the

list of households by subzones, local administration and blocks. According to the listing received, majority of the blocks had households size ranging from 200 to 1000. Hence, the frame used in this survey during the first stage of the selection comprised the blocks in each local administration of the subzone.

Determination of number of households in each cluster

Theoretically, the number of clusters to be selected depends on the design effect and the inter-cluster correlation. With decrease in inter-cluster correlation, more clusters need to be taken, keeping the design effect constant [25]. Considering the economic and administrative issues, a household size of 25 was used to form each cluster and thus; there was a demand of 102 clusters in total to achieve the desired sample size.

Allocation of Households/Clusters

Sampling guidelines suggest proportional allocation as the best one because it assigns equal weights to the zones/urban places. However, the sample size allocated for DKB using proportional allocation to the population was too small to bring zonal/urban level reliable estimates. On the other hand, equal allocation would generate too large sample, which would seriously affect the variance of country estimates. Hence, a proportional to square root of the population was used to bring about the overall and zonal level reliable estimates.

Data collection tools and approach

A structured questionnaire was prepared by reviewing questionnaires of similar studies [26-28]. The questionnaire (see online supplementary file) was customized in such a way to reflect issues relevant to Eritrea whilst keeping certain necessary variables that are essential for international comparison. Modifications were made after a series of consultative meetings. The questionnaire was initially prepared in English and then translated into the common local language, Tigrigna. The questionnaire had four sections namely: personal characteristics of the respondent; awareness, knowledge regarding antibiotics and antimicrobial resistance; attitude regarding antibiotics and antimicrobial resistance, and practice of the general public on antibiotics usage.

Efforts were made to recruit pharmacy professionals who had prior experience of data collection in surveys as enumerators (n=16). Very close, however, inspiring supervision was made by two principal investigators. Orientation was provided to data collectors and supervisors in order to

familiarize them with the survey objectives, questionnaire, principles of conducting an interview, data collection procedures, standards of practice, procedures for listing the households, and the second as well as third stage sample selection of the households.

Prior to the main fieldwork, the questionnaire was pre-tested on five different clusters, which were not included in the main survey. These clusters are found in two local administrations of Asmara. Twenty-five households were interviewed from each selected cluster. The pre-test aided in assessing the accuracy of translation, the ability of the questions to elicit appropriate information, the ability of enumerators to administer the questionnaire and record the response given, and to estimate the time required to complete a questionnaire. Based on the observations, interviewers' comments and review of the findings from the pre-test, the questionnaire was revised and adjusted for the main study.

Actual data collection was conducted from July to September 2019. Two teams were formed and each team was composed of a supervisor, 8 interviewers, and a driver. Each team was allocated 51 clusters. Information on selected clusters was provided to the supervisor and communicated to the respective sub-zone administrative office before the field work. Households were sampled with the assistance of the administration office after listing them in selected blocks. When eligible respondents were absent from their homes, at least three visits were made to offer respondents the opportunity to participate in the survey. If the selected candidate was found to be unavailable in a successive of three to four attempts, it was considered as a 'no response'.

Data quality and management

Orientation training, pre-test, close supportive supervision and daily field editing of the completed questionnaires were carried out to achieve high response and maximize data quality. Completed questionnaires were submitted from the field to the data manager on a daily to weekly basis. Data was processed by the data manager on frequent intervals to check for quality and reporting completeness. Processing the data concurrently with data collection allowed for regular monitoring of team performance and data quality. Data was also checked for consistency, completeness and feedback/corrective actions were provided to field supervisors on spot to improve data quality. Additionally, rigorous editing and cleaning of the entered data was made throughout the process of data entry.

Data Analysis

Data was double entered using Census and Survey processing system (CSPro, Version 7.0) software package and exported to statistical package for social sciences (SPSS) Version 23. Data was summarized by using weighted percentages and counts. Cross-tabulations and further analysis were also done whenever relevant.

Kolmogorov-Smirnov test was used to check on the normality of the knowledge and attitude scores. Frequencies, percentages, mean (with standard deviation), median (with interquartile range) were used to describe the data, as appropriate. Independent samples t-test and analysis of variance (ANOVA) were also applied to find out the potential differences in mean scores of the knowledge and attitude towards antibiotic usage and resistance among the six zones. Scheffe adjustment and Duncan's test were used in pair-wise and group wise comparison of the post-hoc test, respectively. To compare the mean attitude and knowledge scores, among various categories of the demographic characteristics, an independent sample t-test and ANOVA was computed. To explore the association between the risky practice of antibiotic and the categorical demographic characteristics, chi-square test was performed and to control potential confounders, variables that were found to be significant or slightly higher than the cut point were subjected to multivariate analysis. In this study, *p*-value less than 0.05, in all the analyses, is considered as significant.

RESULTS

Demographic characteristics of the study participants

A total of 2542 individuals were selected for the survey. Among the selected individuals, 2,477 successfully interviewed; making an overall response rate of 97.44%. Demographic characteristics of the respondents are summarized in table1. The unweighted numbers reflect the actual observations at the time of survey, whereas the weighted numbers reflect figures that have been adjusted by the probability of selection of the respondents. A total of 2477 respondents, 18 years and above, were interviewed in the survey. The survey participants were mostly females (74.7%), Christians (77.4%), Tigrigna ethnic group (82.3%), and household size of four or more (73.6%) (Table 2).

Table 2: Percent distribution of respondents, 18 years and above, on the knowledge, attitude and practice survey of antibiotics and antibiotic resistance by background characteristics, 2019, Eritrea

Background Characteristics		Weighted Percent	Weighted Number	Unweighted Number
Age				
	24 or less	18.2	451	433
	25 to 34	25.9	643	644
	35 to 44	22.3	552	567
	45 to 54	15.0	372	396
	55 and above	18.5	459	437
Sex				
	Male	24.7	611	605
	Female	74.7	1851	1857
	Missing	0.6	15	15
Religion				
	Christian	77.4	1918	1749
	Moslem	22.5	558	726
	Other	0.1	2	2
Zone				
	Anseba	8.4	209	352
	Debub	15.9	393	410
	Gash Barka	12.1	301	397
	Maekel	55.7	1380	865
	SKB	6.3	155	322
	DKB	1.6	39	131
Educational Level				
	Illiterate	12.0	298	342
	Elementary	15.9	394	452
	Junior	18.6	462	510
	Secondary	35.7	884	801
	Higher	17.1	425	358
	Missing	0.6	15	14
Household Size				
	One	4.4	108	104
	Two to three	22.0	545	533
	Four or more	73.6	1824	1840
Occupation				
	Governmental	22.8	566	529
	Private employee	4.9	121	115
	House wife	38.3	949	980
	Self employed	8.2	202	209
	Unemployed	14.8	366	361
	Student	7.2	179	166
	Farmer/Fisher	2.2	55	77
	Other*	1.2	30	33
	Missing	0.4	10	7
	Total	100	2477	2477

SKB: Semenawi KeihBahri, DKB: Debubawi Keih Bahri

Awareness and Knowledge on Antibiotics and Antibiotic Resistance

About three-fourth (73.3%) of the survey participants were aware of the term 'antibiotics' and 39% aware of the term 'antibiotics resistance'. A quarter (23.8%) of respondents knew at least one commonly used antibiotic. The sources of information about antibiotics and antibiotic resistance (ABR) were mainly health facilities (39.6%), television (31.5%) and other people (10.1%).

Distinguishing antibiotics from non-antibiotics, identification of common illnesses that can require antibiotics and those that do not need antibiotics, when to stop antibiotics once started, definition of ABR, and potential impact and transmission of ABR were the main indicators used to measure the level of knowledge of the respondents on antibiotics and antibiotic resistance. Of the list of medicines provided, 59.4% of the respondents correctly identified penicillin while only 44.8% and 11.9% correctly identified cotrimoxazole and ciprofloxacin respectively. Besides, Ibuprofen, ORS and paracetamol were correctly identified as non-antibiotics by 58.5% to 70.6% of the respondents.

Less than half (36.6%-49.5%) of the respondents correctly reported about indication of antibiotics for common illnesses. Majority of the respondents reported that antibiotics can be used to treat viral infection (63.4%), watery diarrhea (61.8%), common cold (58.9%), dry cough (54.2%) and dengue fever (50.5%). Sixty-one per cent of the respondents also reported that antibiotics are not indicated for tuberculosis. Majority (83.3%) of the respondents know when to stop taking antibiotics once they had begun treatment.

Over three-fourth (78.2%) of the respondents correctly reported that ABR is an issue that could affect them and their family and about two-third (63.6%) correctly answered the definition of ABR. About 59% know that bacteria resistant to antibiotics can spread from person to person and another 59% reported that ABR is an issue in other countries but not in Eritrea.

The overall mean knowledge score on antibiotics and ABR was found to be 10.36/20 (SD= 3.51, min=0 and max=20). Males ($p<0.001$), Christians ($p<0.001$), respondents aged between 25 and 54 years ($p<0.001$), those who had higher educational level ($p<0.001$) and big family size ($p<0.001$) and government employee status ($p<0.001$) were more likely to have better knowledge score.

Besides, study participants residing in Maekel and Anseba Zones had better knowledge score ($p<0.001$) on antibiotics and ABR compared to those living in other Zones (Table 3).

Respondents' attitude on antibiotics and ABR

The overall mean attitude score was 22.34/30 (SD= 3.59, minimum=6 and maximum=30). A negative attitude towards appropriate disposal of antibiotics was documented in over 50% of the study participants (Table 4). Males ($p<0.001$), respondents aged between 25 and 54 years ($p<0.019$), those who had higher educational level ($p<0.001$), and government employees ($p<0.001$) had better attitude score compared to their counterparts (Table 5).

Table 3: Comparison of knowledge scores across the categories of demographic characteristics

Characteristics	Mean (SD)	F/t Value	p-value	p-value trend (Type of trend)	Post Hoc Test	
					Pair wise comparison	Group wise comparison
Age						
24 or less **A**	9.57 (3.24)					
25 to 34 **B**	10.53 (3.25)					
35 to 44 **C**	11.02 (3.36)	16.03**	<0.0001	<0.0001 (Quadratic)	A<B, A<C, A<D, A=E, B=C=D, B>E, C>E, D>E	Group 1: A and E Group 2: B, C, and D
45 to 54 **D**	10.77 (3.70)					
55 and above **E**	9.73 (3.91)					
Gender						
Male	10.98 (3.61)	5.08	<0.0001	-	M>F	-
Female	10.15 (3.44)					
Religion						
Christian	10.57 (3.53)	5.93	<0.0001	-	C>M	-
Muslim	9.60 (3.30)					
Educational Level						
Illiterate	7.99 (3.28)					
Primary	9.49 ((3.38)					Group 1: I Group 2: P and M Group 3: M and S Group 4: H
Middle	10.16 (3.31)	66.78	<0.0001	<0.0001 (Linear)	I<P, I<M, I<S, I<H, P=M, P<S, P<H, M=S, M<H, S<H	
Secondary	10.72 (3.38)					
Higher	11.97 (3.23)					
Family Size						
One	8.84 (4.19)					
Two to three	10.08 (3.45)	12.62	<0.0001	<0.0001 (Linear)	O<T, O<F, T<F	Group 1: O Group 2: T and F
Four or more	10.52 (3.46)					
Occupation						
Governmental	11.76 (3.40)					
Private employee	10.85 (3.57)					
House wife	10.10 (3.27)					
Self-employed	10.13 (3.54)	22.05	<0.0001	-	G=P, G>H, G>Se, G>U, G>St, G>F, G=O, P=H, P=Se, P>U, P=U, P=St, P=O, H=Se, H=U, H=St, H=F, H=O, Se=U, Se=St, Se=F, Se=O, U=St, U=F, U=O, St=F, St=O, F=O	Group 1:F, U, St, O, H and Se, Group 2:U, St, O, H, Se and P Group 3: H, Se, P and G
Unemployed	9.40 (3.67)					
Student	9.54 (3.40)					
Farmer/Fisher	8.71 (3.32)					
Other*	9.62 (3.30)					
Zone						
Anseba	10.53 (3.36)					
Debub	8.85 (3.65)					
Gash Barka	9.54 (3.18)	28.45	<0.0001	-	A>De, A=G, A=M, A=S, A=D, De<M, De=G, De=S, De=D, G<M, G=S, G=D, M>S, M=D,	Group 1: De, S, and G, Group 2: S, G, D and A Group 3: G,D,A and M
Maekel	11.00 (3.39)					
SKB	9.44 (3.51)					
DKB	10.27 (3.09)					

Other: Day laborer, soldier, sheik/priest etc; ** Welch test statistic was used to obtain robust result; SKB: Semenawi Keih Bahri; DKB: Debubawi Keih Bahri*

Table 4: Respondents response on the attitude of antibiotics and Antibiotic Resistance (ABR), Eritrea, 2019 (N=2477)

Attitude questions on antibiotics and ABR	% agreed/ strongly agreed
Hand washing decreases ABR	92.7
Taking antibiotics when it is not required can facilitate ABR	89.7
You have a role to fight ABR	85.8
It is not okay to share antibiotics with others	90.1
We cannot use antibiotics without prescription	88
Farmers should not give antibiotics without consulting veterinarian	82.1
It is not okay to keep leftover antibiotics and use them later	82
Leftover antibiotics should not be disposed with regular garbage	46
Leftover antibiotics should not be disposed at toilets	35.7

Table 5: Comparison of attitude scores on antibiotics and antibiotic resistance across the categories of demographic characteristics, Eritrea, 2019.

Characteristics	Mean (SD)	F/t Value	p-value	p-value trend (Type of trend)	Post Hoc Test	
					Pair wise comparison	Group wise comparison
Age						
24 or less **A**	22.10 (3.81)					
25 to 34 **B**	22.50 (3.31)					
35 to 44 **C**	22.25 (3.66)	2.97*	0.019	0.034 (quadratic)	A=B=C=D=E,	Group 1: A, B, C, D and E
45 to 54 **D**	22.80 (3.47)					
55 and above **E**	22.07 (3.76)					
Gender						
Male	23.0 (3.86)	4.92	<0.0001	-	M>F	-
Female	22.13 (3.48)					
Religion						
Christian	22.37 (3.54)	0.7	0.488	-	-	-
Muslim	22.24 (3.80)					
Educational Level						
Illiterate	21.36 (3.64)					
Primary	22.14 (3.46)				I=P, I<M, I<S, I<H, P=M, P=S, P<H, M=S, M<H, S<H	Group 1: I Group 2: P, S and M Group 3:H
Middle	22.34 (3.65)	10.76	<0.0001	<0.0001 (linear)		
Secondary	22.32 (3.52)					
Higher	23.16 (3.62)					
Family Size						
One	21.86 (3.42)					
Two to three	22.25 (3.46)	1.2	0.300	-	-	-
Four or more	22.39 (3.64)					
Occupation						
Governmental	22.93 (3.73)					
Private employee	22.04 (3.32)					
House wife	22.30 (3.51)					
Self-employed	22.62 (3.48)					
Unemployed	21.69 (3.38)				G=P, G=H, G=Se, G>U, G=St, G=F, G=O, P=H, P=Se, P=U, P=U, P=St, P=O, H=Se, H=U, H=St, H=F, H=O, Se=U, Se=St, Se=F, Se=O, U=St, U=F, U=O, St=F, St=O, F=O	Group1:F, U, St, O, H, G, and Se
Student	21.82 (3.85)	4.95	<0.0001	-		
Farmer/Fisher	21.65 (3.92)					
Zone						
Anseba	23.19 (3.43)					
Debub	22.27 (3.35)					
Gash Barka	23.24 (3.73)				A=De, A=G, A>M, A=S, A=D, De=M, De<G, De=S, De=D, G>M, G=S, G=D, M=S, M=D, S=D	Group 1: A, De, M, S, and D Group 2: A, De, M, S, and G
Maekel	22.01 (3.62)	8.87	<0.0001	-		
SKB	22.76 (3.20)					
DKB	21.73 (4.32)					

** Welch test statistic was used to obtain robust result; SKB: Semenawi Keih Bahri; DKB: Debubawi Keih Bahri.*

Respondents practice on usage of antibiotics

Majority (84.5%) of the respondents had used antibiotics at least once in their life time. Over half (55%) of the study participants had history of intake of antibiotics in the last one year and 12.3% in the last one month prior to commencement of this study. Of those who ever used antibiotics (N=2407), 88.1% reported that their last intake of antibiotic(s) was prescribed by authorized healthcare professionals while the rest 12% were rather on self-medication. The non-seriousness of the disease (39.0%), need to get quick relief (33.9%), previous own successful experiences (16.1%), having no time to visit a health facility (15.0%) and a long queue existing in health facilities (14%) were the top five reasons reported for self-medication with antibiotics. For those who used antibiotics without prescription, the main sources of their last course of antibiotics were drug retail outlets (83.6%) (Figure 1).

One fifth (18.8%) of those who had ever used antibiotics interrupted taking antibiotics before completing the full course. The main reason for interruption of antibiotics intake was improved illness condition (63.4%) followed by the experience of adverse effects (12.9%) (Figure 2). A small number (2.7%) of the respondents reported they had used antibiotics on their own at least once, though healthcare professionals advised them not to do so.

Overall, risky practice of antibiotics (use of antibiotics without prescription and/or discontinuation of prescribed antibiotics before completing the full course) was reported in 23.8% of the respondents. The chi-square analyses found that age ($p<0.001$), gender ($p=0.01$), educational level ($p<0.001$), occupation ($p<0.001$) and zonal location ($p<0.001$) were the significant associates of risky practice of antibiotics. On multivariate model, young age - 24 years or less (AOR=1.59, 95% CI: 1.06 to 2.38), males (AOR=1.48, 95% CI: 1.15 to 1.92), and higher level of education (AOR=1.77, 95% CI: 1.05 to 2.90) were more likely to be determinants of risk practice of antibiotics. Having positive attitude on antibiotics (AOR=0.95, 95% CI: 0.92 to 0.97) showed a protective effect for risky practice of antibiotics while knowledge had no association (Table 6).

Table 6: Multivariable predictors of risky practice of antibiotics across the categories of demographic characteristics and attitude score, Eritrea, 2019.

Background characteristic	Multivariable analysis		
	AOR	95% CI	*p*-value
Age			
24 or less	1.59	1.06 to 2.38	0.026
25 to 34	1.25	0.88 to 1.78	0.217
35 to 44	1.05	0.74 to 1.49	0.790
45 to 54	0.89	0.61 to 1.29	0.533
55 and above	*Ref.*		
Gender			
Male	1.48	1.15 to 1.92	0.003
Female	*Ref.*		
Educational Level			
Illiterate	*Ref.*		
Elementary	1.02	0.66 to 1.57	0.920
Junior	1.20	0.77 to 1.84	0.421
Secondary	1.32	0.86 to 2.02	0.207
Higher	1.77	1.05 to 2.90	0.023
Family Size			
One	0.79	0.44 to 1.43	0.436
Two to three	1.15	0.90 to 1.46	0.255
Four or more	*Ref.*		
Occupation			
Governmental	2.27	0.67 to 7.68	0.189
Private employee	2.58	0.72 to 9.25	0.146
House wife	3.01	0.89 to 10.22	0.077
Self-employed	3.43	0.99 to 11.90	0.052
Unemployed	2.59	0.75 to 8.93	0.132
Student	3.28	0.93 to 11.60	0.066
Farmer/Fisher	3.35	0.84 to 13.38	0.088
Other*	*Ref.*		
Zone			
Anseba	0.47	0.21 to 1.04	0.077
Debub	0.72	0.33 to 1.58	0.416
Gash Barka	0.70	0.31 to 1.55	0.375
Maekel	0.88	0.42 to 1.86	0.740
SKB	0.81	0.35 to 1.87	0.622
DKB	*Ref.*		
Attitude	0.95	0.92 to 0.97	<0.001

A total of 1473 of the respondents had animals and about 14% reported that they have treated their animals with antibiotics at least once. Of those who used antibiotics for their animals, 62% purchased at least once in the last year, prior to the study period. The commonly used antibiotics for animals were amoxicillin (44.1%), oxytetracycline (36.2%) and penicillin (16.3%). About 51%

of antibiotics used for animals was prescribed by veterinarians (50.7%) whereas the rest were supplied by non-veterinarians, mainly from pharmacy retail outlets (20.8%) (Figure 3).

DISCUSSION

This nation-wide urban population-based survey revealed a significant risky practice of antibiotics, in Eritrea. One in five of the respondents, who had ever used antibiotics, reported that their last intake of antibiotic(s) was terminated for many reasons. Discontinuation of antibiotics when the consumer felt better was the most frequently reported reason. This reflects lack of awareness on the appropriate use of antibiotics and risk of antibiotic resistance. Majority of the antibiotics most recently consumed by the respondents were reported to have been prescribed by qualified healthcare professionals. This is encouraging and the nation-wide, massive antibiotic awareness week campaigns conducted in the last three years, prior to the study, might have had positive contributions. Yet, due to lack of a national baseline data, the authors could not infer causation.

The disease condition being non-serious, intention to get a quick relief, previous successful experience, shortage of time to visit health facilities and long queues were the main triggering factors reported for self-medication with antibiotics. The first three reasons mentioned above for self-medication of antibiotics reflect lack of awareness on the risks of inappropriate use of antibiotics. In Eritrea, guided by 'health for all policy and social justice', healthcare services are provided at a highly subsidized or nominal cost through public health facilities. To further improve patient's satisfaction, accessibility and engagement in visiting health facilities and health seeking behavior, the existing healthcare delivery services need to be optimized. Moreover, the one-week annual antibiotic awareness week campaign in place should be augmented by other continuous and regular similar activities throughout the year.

In this study, drug retail outlets were reported as the main sources for the sales of antibiotics without prescription. A recently conducted study to determine the sales of antibiotics without prescription in all drug retail outlets in Eritrea also revealed an alarming picture (87%) [10] which requires immediate attention of regulators and policy makers. Continued refresher courses on appropriate use of antibiotics and antibiotic resistance as well as further enforcement of regulations

would have an impact in bridging these gaps. Cognizant of this, the National Medicines and Food Administration of the Ministry of Health developed medicines schedule in 2019 and all antibiotics are put under the 'prescription only medicine' category. To ensure implementation and adherence to scheduling terms, the National Medicines and Food Administration is recommended to conduct strict and continuous inspection on drug retail outlets.

Use of antibiotics without prescription, in this study was more or less consistent with findings of similar studies conducted in many European countries, where this practice is reported to occur in a proportions of 7% (ranging from 1% to 16%). It was however much lower than that reported in Italy [29], Jordan [30 31], United Arab Emirates [32], Palestine [33], Lebanon [34], Iraq [35], Indonesia [36], Yemen [37], Saudi Arabia [38], Haiti [39], Kuwait [40], and Ethiopia [41 42], where proportions ranged between 31% and 79%. The variation in results, however, could be due to differences in study designs, study area, study population, type of questions, level of awareness of the study participants and soon.

Respondents of young age (24 years or less), male sex, high level of education and poor attitude score were identified as determinants of risk practice of antibiotics. It is unknown why those who had higher level of education and those who were young (relatively with greater educational opportunities) were more involved in the risky practice of antibiotics. This might be explained as knowing more or being educated would predispose people to the tendency to take self-made decisions more casually with the assumption that they have the knowledge. But qualitative studies are required to further identify the determinants of risky practice of antibiotics.

In this study, an appreciably high mean attitude score towards antibiotics and antibiotic resistance was reported. Those who scored poor attitude were more likely to be involved in risky practice of antibiotics, whereas protective effect was noted in those with higher attitude scores. Male sex, age between 45 and 54 years, high educational level, being a government employee, and residing in Anseba and Gash Barka zones were associated with better attitude scores. It is, however, important to note that the poor attitude reported on the appropriate disposal of leftover antibiotics, requiring immediate attention from policy makers.

Unlike the relatively good attitude score, the mean knowledge score of respondents on antibiotics and antibiotic resistance was not satisfactory. This study revealed that majority of the respondents

had no clear picture on what an antibiotic is and were unable to recognize, by name, the most commonly used antibiotics (penicillin, cotrimoxazole and ciprofloxacin) in the country. Additionally, categorizing ibuprofen, ORS and paracetamol as antibiotics by a large number of respondents was concerning. A significant proportion of the respondents also had the misunderstanding that antibiotics could treat viral infections like common cold and acute watery diarrhea. Hence, continued awareness raising programs should target such misconceptions and familiarize the public with the commonly used antibiotics, their proper indications and potential for resistance. The assumption that antibiotic resistance is a threat elsewhere, but not in Eritrea, as reported in this study, reflects how oblivious people are on the issue of antibiotic resistance and might limit the public from taking appropriate actions at their levels.

Regarding the use of antibiotics to treat animals, oxytetracycline and two other antibiotics we use for humans namely: amoxicillin and penicillin, were the most frequently reported ones in this study. About half of the antibiotics used in animals were supplied by non-veterinarians including drug retail outlets and open markets, indicating poor regulation of antibiotics in animal and human health.

The study has benefited many strengths, including: being the first of its kind in Eritrea; covering nation-wide representation of all urban population; excellent data quality and management, and high response rates. On the other hand, one of the main limitations of this study is that results were self-reported and thus, findings might be under- or over-estimated, which could introduce information bias or recall bias.

Conclusion

The risky practice of antibiotics in Eritrea was prevalent and inversely proportional to the mean attitude score of the respondents. Young respondents, males, and those who had higher level of education and poor attitude score were identified as having greater tendency for risky practices associated with antibiotics. The inability of many of the respondents to distinguish antibiotics from other medicines and the reported misunderstanding that viral infections can be treated with antibiotics, indicates limited knowledge of respondents on antibiotics and ABR. Continuous awareness raising programs on the rational use of antibiotics (mainly on the risks of self-medication, treatment interruption, and use of antibiotics for viral infections) and familiarizing the

public with the commonly used antibiotics are recommended. As drug retail outlets were identified to be the main sources for the supply of antibiotics without prescription, both in humans and animals, medicines schedule and regulatory inspections should be enforced. Besides, the huge gap in attitude towards appropriate disposal of antibiotics requires immediate attention from policy makers and the establishment of an appropriate disposal system of leftover antibiotics for the community.

DECLARATIONS

Ethics approval and informed consent

Ethical approval to conduct the study was obtained from the Ministry of Health, Eritrea and further approval was also obtained from the Ministry of Local Government. Besides, informed consent was obtained from all study participants to take part in the study.

Patient consent for publication: Not required.

Conflict of interests

The authors declare that they have no competing interests.

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Author contributions

The idea was conceived by MR and IB and designed by MB, MD, MR, AK, AA, YF, IB, SK, JN and EHT. Data was collected by MD, AK, AA and YF and supervised by MR and MB. EHT analyzed the data and all the co-authors participated in the interpretation of the results. The manuscript was drafted by MB, MR and EHT and critically reviewed and edited by all of the authors. Finally, all the co-authors agreed that the article be published in an international journal and to take responsibility and be accountable for its content.

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Availability of data

All data related to the study are included in the manuscript. The complete dataset used for this study can be obtained from the corresponding author upon request.

Acronyms

ABR: Antibiotic Resistance; DKB: Debubawi Keih Bahri; SKB: Semenawi Keih Bahri; WHO: World Health Organization.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

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Figure 1: Source of antibiotics used without prescription among urban residents, Eritrea, 2019 (n=242)

Figure 2: Reasons for stopping the intake of antibiotics among urban residents, Eritrea, 2019 (n=357)

Figure 3: Source of antibiotics for animals among urban residents, Eritrea, 2019 (n=245)

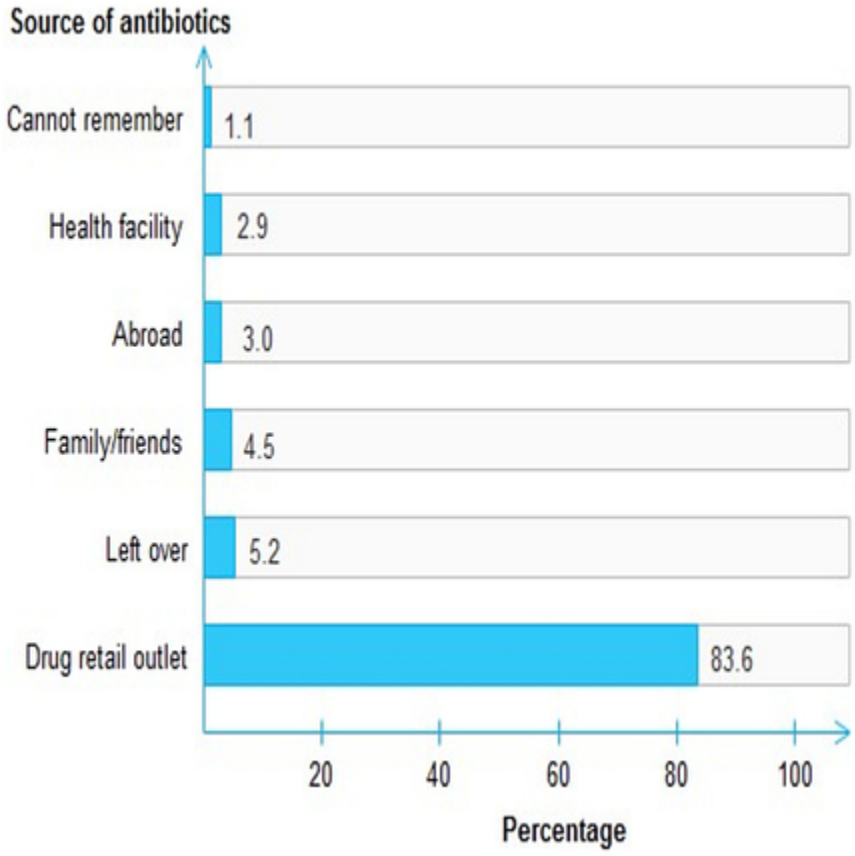

Figure 1: Source of antibiotics used without prescription among urban residents, Eritrea, 2019 (n=242)

38x38mm (300 x 300 DPI)

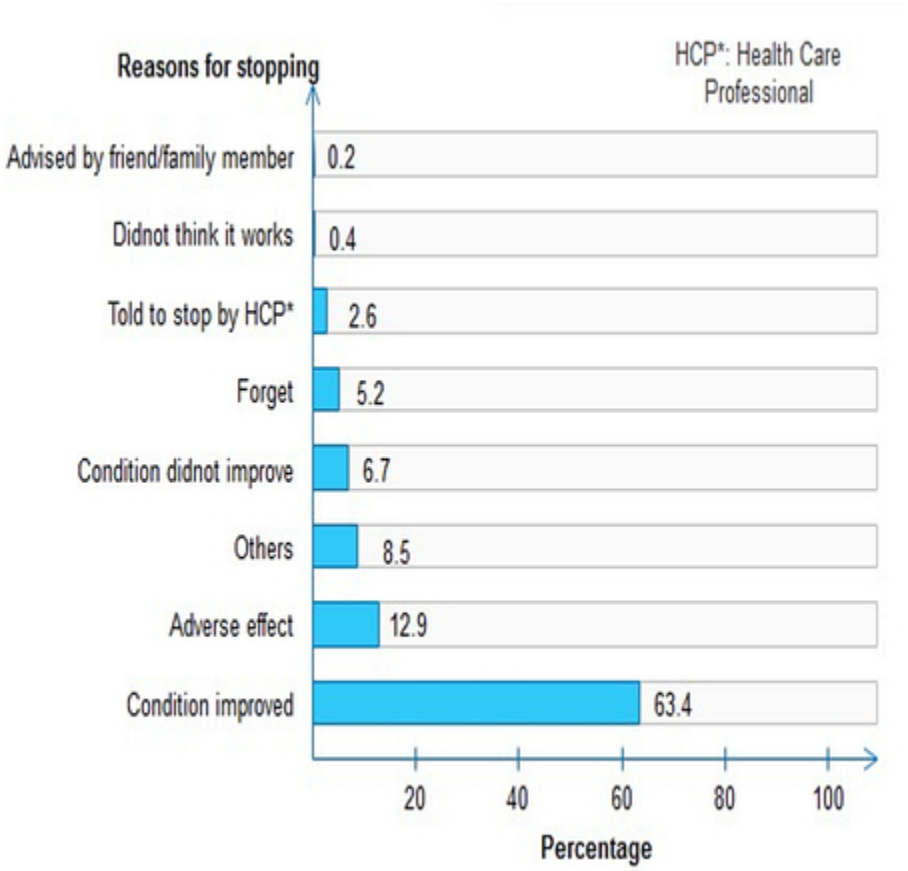

Figure 2: Reasons for stopping the intake of antibiotics among urban residents, Eritrea, 2019 (n=357)

38x38mm (300 x 300 DPI)

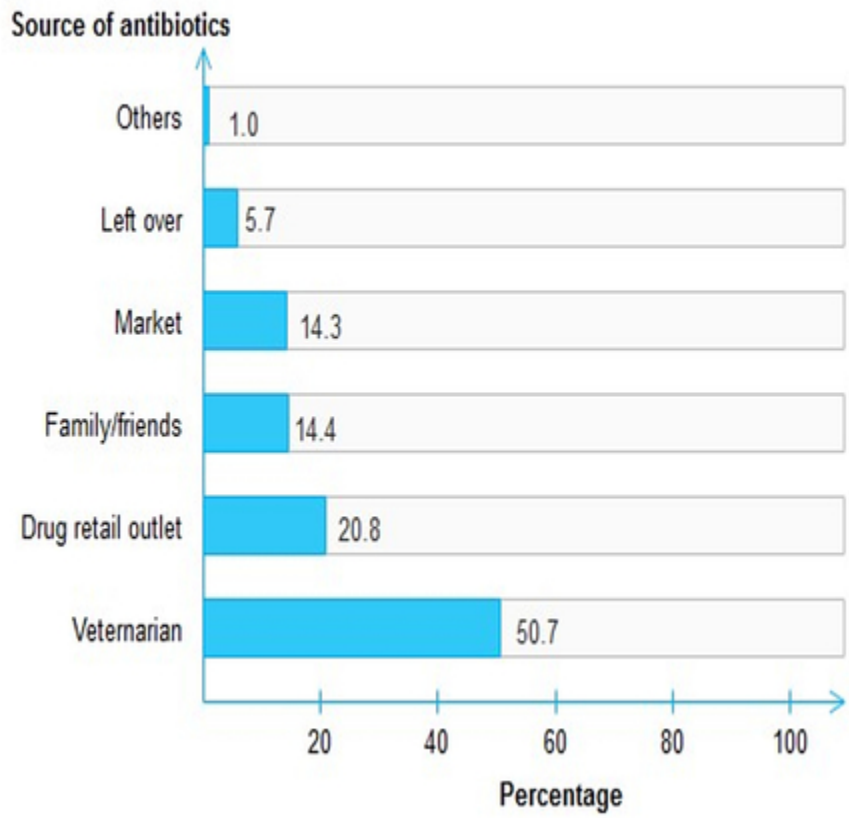

Figure 3: Source of antibiotics for animals among urban residents, Eritrea, 2019 (n=245)

38x38mm (300 x 300 DPI)

MINISTRY OF HEALTH
National Medicines and Food Administration

Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

Household Questionnaire

Part I: Identification Particulars

Zoba	
Subzoba	
City/Town	
Kebabi	
Respondent number	

Interviewer Visits

	1	2	3	Final Visit
Date				Day / Month / Year (2019)
Interviewer's Name				Int. No.
Result*				Result*
Next visit: Date				Total number of visits
Time				

*Result codes:

1 Completed
2 Not completed
3 Not willing
4 Other _____ (Specify)

Total persons In household

Total eligible persons (>18)

Supervisor	Field editor	Keyed by
Name / Number	Name / Number	Name / Number

Part II: Demographic Information

No.	Indicators	Coding categories	Skip
101	Age (in completed years)	☐☐	
102	Sex	Male ..... 1 Female 2	
103	Ethnicity	Tigrina ..... 1 Afar ..... 2 Tigre ..... 3 Saho ..... 4 Rashida ..... 5 Kunama ..... 6 Blien ..... 7 Hidarb ..... 8 Nara ..... 9 Other (please specify) _____ #	
104	Religion	Christian ..... 1 Muslim ..... 2 Other (please specify) _____ 3	
105	Level of education (Highest level of education)	Illiterate ..... 1 Primary school ..... 2 Middle school ..... 3 Secondary school ..... 4 Higher education 5	
106	Main occupation	Farmer ..... 1 Government employee ..... 2 Private employee ..... 3 Housewife ..... 4 Self-employed ..... 5 Unemployed ..... 6 Student ..... 7 Fisher man ..... 8 Other (please specify) _____ 9	

Part III: Knowledge

No.	Questions	Coding categories	Skip
201	Have you ever heard about antibiotics?	Yes . . . . . 1 →	203
		No 2	
202	Have you ever heard of any one of the following medications? ASK FOR EACH MEDICATION.	Amoxicillin . . . . . A Tetracycline . . . . . B Oxytetracycline . . . . . C I haven't heard all of them . . . . . D →	**End**
203	Which of the following do you think are antibiotics? ASK FOR EACH MEDICATION. If the response in 201 is No and heard of any one of the examples of antibiotics, explain that the term Antibiotics refers to these drugs before continuing to 204 .	Y N DK Ibuprofen . . . . . 1 2 3 Tetracycline . . . . . 1 2 3 Bactrium . . . . . 1 2 3 ORS . . . . . 1 2 3 Amoxicillin . . . . . 1 2 3 Paracetamol . . . . . 1 2 3 Ciprofloxacin . . . . . 1 2 3 Penicillin 1 2 3	
204	Which of these diseases do you think are treated with antibiotics? ASK FOR EACH ILLNESS.	Common cold . . . . . 1 2 3 Watery diarrhea . . . . . 1 2 3 TB . . . . . 1 2 3 Dengue fever . . . . . 1 2 3 Pneumonia . . . . . 1 2 3 Dry cough 1 2 3	
205	Do antibiotics treat viral infections?	Yes . . . . . 1 No . . . . . 2 Don't know 3	
206	When do you think you should stop taking antibiotics once you've begun treatment? MULTIPLE RESPONSES ARE POSSIBLE. PROBE: Are there any other reasons	When I feel better . . . . . A When I do not see improvements . . . . . B When I encounter adverse drug reactions C It should not be stopped . . . . . D Don't know . . . . . E	
207	Have you ever heard of the term antibiotic resistance (ABR)?	Yes . . . . . 1 No 2	
208	Antibiotic resistance occurs when your becomes resistant to antibiotics and they no work.	Yes . . . . . 1 No . . . . . 2 Don't know 3	**216**
209	Where did you hear about antibiotic resistanc MULTIPLE RESPONSES ARE POSSIBL PROBE: Are there any other sources	Health facility . . . . . A Pharmacy . . . . . B Radio . . . . . C TV . . . . . D Newspaper . . . . . E Campaign/Seminar . . . . . F Other (please specify) _____ G	

210	Antibiotic resistance is an issue that could affect me or my family.	Yes . . . . . 1 No . . . . . 2 Don't know 3	
211	Antibiotic resistance is an issue in other countries but not here.	Yes . . . . . 1 No . . . . . 2 Don't know 3	
212	Bacteria which are resistant to antibiotics can spread from person to person.	Yes . . . . . 1 No . . . . . 2 Don't know 3	

Part IV: Attitude

No.	Questions		Skip
213	Proper handwashing play a role in ABR.	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
214	Taking antibiotics when it is not required can facilitate ABR.	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
215	You have a role to fight ABR	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
216	We can use antibiotics without prescription	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
217	It is okay to share antibiotics with family members or friends for similar illness	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
218	It is okay to keep leftover antibiotics and use them later	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	

219	Farmers can give antibiotic without consulting veterinarian	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
220	Leftover antibiotics should be disposed with regular garbage	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
221	Leftover antibiotics should be disposed at toilets	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	

Part V: Practice

No.	Questions	Coding categories	Skip
222	Have you ever used antibiotics?	Yes . . . . . 1 No . . . . . 2 Don't remember 3	**230**
223	When was the last time you took antibiotics?	Now . . . . . 1 Last month . . . . . 2 Last six months . . . . . 3 Last year . . . . . 4 More than a year ago . . . . . 5 Don't remember 6	
224	Source of the last course of antibiotic MULTIPLE RESPONSES ARE POSSIBLE.	Health facility . . . . . A Drug retail outlet . . . . . B Friend or family member . . . . . C Saved up from a previous time . . . . . D From abroad . . . . . E Don't remember . . . . . F	
225	On that occasion, did you get a prescription for the antibiotics from a doctor/nurse?	Yes . . . . . 1 No . . . . . 2 Don't remember 3	→**227**
226	What was (were) your reason(s) of self-medication with antibiotics? MULTIPLE RESPONSES ARE POSSIBLE.	Long queue . . . . . A Had no time to visit a health facility . . . B To get a quick relief . . . . . C Disease was not serious . . . . . D To save expenses . . . . . E Own previous successful experience . . . F Other (please specify) _____ G	

227	Did you ever stop taking antibiotics before completing the full course?	Yes . . . . . 1 No . . . . . 2 Don't remember 3	**229**
228	Why did you stop taking the antibiotics?	Condition didn't improve . . . . . 1 Condition improved . . . . . 2 Due to adverse effects . . . . . 3 Advised by a friend or family member 4 I didn't think it works . . . . . 5 Told to stop by a healthcare profession . 6 Other (please specify) _____ 7	
229	Ever used antibiotics on your own, though health care professionals advice you not to take	Yes . . . . . 1 No . . . . . 2 Don't remember 3	
230	Have you ever given antibiotics to your animals?	Yes . . . . . 1 No . . . . . 2 Don't remember . . . . . 3 Don't have an animal 4	**301**
231	Which antibiotic did you use for your animal? ASK FOR EACH MEDICATION.	Amoxicillin . . . . . A Erythromycin . . . . . B Oxytetracycline . . . . . C Penicillin . . . . . D Tylosin . . . . . E Didn't use all of these antibiotics . . . . . F Other (please specify) _____ G	
232	Source of the antibiotics	Bought from the market . . . . . A Bought from Drug retail outlet . . . . . B Veterenarian . . . . . C Friends/family membe . . . . . D Other (please specify) _____ E	
233	How many times did you buy antibiotics for your animal in the last one year ?	Once . . . . . 1 Twice . . . . . 2 Three times . . . . . 3 More than three times . . . . . 4 Never 5	

INTERVIEWER'S OBSERVATIONS

TO BE FILLED IN AFTER COMPLETING THE INTERVIEW
COMMENTS ABOUT THE INTERVIEW
COMMENTS ON SPECIFIC QUESTIONS
ANY OTHER COMMENTS
SUPERVISOR'S OBSERVATIONS
EDITOR'S OBSERVATIONS

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-8*
Bias	9	Describe any efforts to address potential sources of bias	5-8
Study size	10	Explain how the study size was arrived at	6-7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	9-10
		(*c*) Explain how missing data were addressed	9-10
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	7-8
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6,7,10
		(b) Give reasons for non-participation at each stage	10
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-10
		(b) Indicate number of participants with missing data for each variable of interest	9-10
Outcome data	15*	Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-19

		(*b*) Report category boundaries when continuous variables were categorized	10-19
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	21
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19-21
Generalisability	21	Discuss the generalisability (external validity) of the study results	21-22
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

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ABSTRACT

Objective: To measure knowledge, attitude and practice of antibiotics and antibiotic resistance and their determinants in the Eritrean urban population.

Design: Population-based, nation-wide, cross-sectional study.

Setting: Urban settings of Eritrea.

Participants: Members of the general public aged ≥18 years and living in thirteen urban places of Eritrea. Three stage stratified cluster sampling was used to select the study participants.

Data collection and analysis: Date was collected from July to September 2019 in a face-to-face interview using a structured questionnaire. The collected data was double entered and analyzed using CSPro (Version 7.0) and SPSS (Version 23) respectively. Descriptive statistics, chi-square test, t-tests, analysis of variance, factorial analysis and multivariable logistic regression were performed. All analyses were weighted and $p<0.05$ was considered significant.

Primary and secondary outcome measures: Main outcome variables were knowledge, attitude and practice of antibiotics and antibiotic resistance. Secondary outcome measure was the determinants of knowledge, attitude and practice.

Results: A total of 2477 adults were interviewed. The knowledge and attitude of antibiotics and antibiotic resistance (ABR) mean score was 10.36/20 (SD=3.51, minimum=0 and maximum=20) and 22.34/30 (SD=3.59, minimum=6 and maximum=30) respectively. The proportion of at least one risky practice (use of antibiotics without prescription and/or discontinuation of prescribed antibiotics before completing the full course) in all those study population who used antibiotics was 23.8%. Young age <24 years (AOR=1.59, 95% CI: 1.06 to 2.38), male sex (AOR=1.48, 95% CI: 1.15 to 1.92), higher level of education (AOR=1.77, 95% CI: 1.05 to 2.90), and negative attitude on antibiotic use (p<0.001) were found to be the significant determinants of risky practice of antibiotics.

Conclusion: The gap in knowledge and risky practice of antibiotics in the Eritrean urban population was widespread, requiring immediate attention from policymakers and healthcare professionals.

Keywords: Public health, infectious diseases, epidemiology

ARTICLE SUMMARY

Strengths and limitations of this study

- This is among the few globally reported population-based surveys covering nation-wide representative of all urban residents of Eritrea.
- The study employed rigorous data quality and management approaches and had high percentage of response.
- Results of this study were self-reported and thus, findings might be under- or over-estimated which might in-turn have introduced information or recall bias.
- During data collection, the information regarding family size and available members was gathered, without verification using administrative list, from the household members who were present at the time of visit and this might have introduced respondents' selection bias.
- The reliability and validity of the scales for knowledge and attitude on antibiotics usage were not checked using statistical tools.

INTRODUCTION

The excess use of antibiotics, in addition to wastage of resources, poses a great health risks that would escalate bacterial resistance [1-4]. Resistant infections are now estimated to cost at least 50,000 lives each year in Europe and the US alone [5]. From this, one can speculate that the burden of antimicrobial resistance (AMR) would be much higher in resource-constrained countries in which the inappropriate use of antibiotics by healthcare professionals and consumers could be rampant. This in part is due to poor regulation, weak health systems, surveillance, knowledge and higher infectious diseases [1 6 7]. If left unimpeded, by 2050, deaths attributable to AMR are estimated to be 10 million per year globally [1].

Nowadays, antibiotic resistance (ABR) is recognized as one of the biggest threats to global health and is becoming a medical emergency that would limit the advances of healthcare delivery services. This endangers the achievements of the millennium development goals and also

sustainable development goals [8]. Thus, AMR in general and ABR in particular is transforming into a political agenda.

As estimated by the WHO, 80% of antibiotics is used in the community, 20-50% of which is used inappropriately [9]. Use of antibiotics without prescription [10-13], physician perception of patients expectation for antibiotics [14 15], patient demand [16-18], unrestricted use of antibiotics [7 19] and poor healthcare system [20] have been reported among the main factors for the inappropriate use of antibiotics. To tackle this, at the 68th World Health Assembly, a global action plan was endorsed [21]. One of the five global strategic objectives was to improve awareness and understanding about AMR [21], thus; all member states were recommended by the WHO to annually conduct antibiotic awareness week campaigns in a one-health approach [21].

With these recommendations, Eritrea has been in a process of establishing an antimicrobial stewardship program. Through a multisectoral approach, Eritrea has developed a national action plan for combating AMR that is expected to be effective in 2021. One of the four strategic objectives of the national action plan is 'raise awareness through education and training'. Moreover, the National Medicines and Food Administration of the State of Eritrea has published a medicines schedule that is expected to contribute towards the antimicrobial stewardship. Prior to implementation, knowing the current status and weakest links are important for policy decisions and to identify areas of intervention on tackling AMR. This study is conducted to measure knowledge, attitude and practice of antibiotic usage and identify key determinants for knowledge, attitude and practice in the Eritrean urban population. As there is no baseline data to start with and assess the effectiveness of the annually conducted antibiotic awareness weeks, the findings of this study could also be taken as a point of reference to assess relative changes in the determinants of change in practice.

METHODS

Study Design and area

A cross-sectional study design, with a quantitative approach, was used. Eritrea is a country with an estimated population of 3.4 million [22]. It has six administrative zones comprising 58 subzones in total. The country has five administrative levels namely: National, Zonal, Sub-zonal, Local

Administration (Kebabi administration) and Village/Block (village in rural or block in urban settings) levels.

The survey was conducted between July and September 2019 in all urban sites of the country. In Eritrea, there are a total of 13 cities and/or towns. The urban sites included in this study were three from Gash Barka, five from Debub, two from Semenawi Keih-Bahri (SKB) and one city or town from each of the remaining three zones, namely Anseba, Debubawi Keih-Bahri (DKB), and Maekel (supplementary File 1). A total of 25 sub-zones and 72 local administrations (Kebabi administration) located in the above-mentioned towns and/or cities were involved in the survey.

Target Population

The target population of the study includes all members of the general public aged 18 years or above and living in the thirteen urban places in which the survey was conducted.

Sample Size and Sampling Technique

Sample size

Sample size was computed mainly for an estimation of proportion of safe practice taking 95% confidence level, 0.05 precision; using the formula [23]: $n \geq \frac{NV1.96^2}{V * 1.96^2 + (N-1) * 0.05^2}$, where V= $\frac{SD^2}{Pooled\ proportion^2}$=0.5 and N=size of the target population. Upon consideration of the aforementioned parameters, the initial sample size was 1525. After an adjustment of non-response percent (10%) and design effect (deff=1.5), the final sample size was 2542 individuals.

Sampling Technique

Local data, conducted by Ateshim et al. 2019 [11] and other unpublished studies, implies that the awareness, knowledge, attitude, and practice towards antibiotics and ABR varies across the zones in Eritrea. Hence, it was presumed that the sample design that led to the selection of a legible person was a stratified three-stage cluster sample. During the first stage of the sampling, a total of 102 primary sampling units referred to as blocks (having households ranging from 200 to 1000) were selected from the 13 urban sites. During the second stage, 25 households were selected from each block taking into consideration the design effect, inter-cluster correlation, economic and administrative issues [24]. Finally, samples were selected from each household. To bring about reliable zonal and overall estimates, square root allocation of households was undertaken.

Data collection tools and approach

A structured questionnaire (Supplementary file 2) was prepared by reviewing questionnaires of similar studies [25-27] and was customized in such a way to reflect issues relevant to Eritrea. It was initially prepared in English and then translated into the common local language, Tigrigna. The questionnaire had four sections namely: personal characteristics of the respondent; awareness, knowledge regarding antibiotics and AMR; attitude regarding antibiotics and AMR, and practice of the general public on antibiotic usage.

Sixteen pharmacy professionals who had prior experience were recruited as data collectors. Close supervision was made by two principal investigators. Orientation was provided to data collectors in order to familiarize them with the survey objectives, questionnaire, principles of conducting an interview, data collection procedures, standards of practice, procedures for listing the households, and the second as well as third stage sample selection of the households.

Prior to the main fieldwork, the questionnaire was pre-tested on five different clusters, which were not included in the main survey. These blocks are found in two local administrations of Asmara. Twenty-five households were interviewed from each selected block. The pre-test aided in assessing accuracy of translation, ability of the questions to elicit appropriate information, and ability of enumerators to administer the questionnaire. Moreover, it was helpful in estimating the time required to complete the questionnaire. The questionnaire was finally modified based on the results of the pre-test.

Households were sampled with the assistance of the administration office after listing them in selected blocks. When eligible respondents were absent from their homes, at least three visits were made to increase the opportunity of participation in the survey. If the selected candidate was found to be unavailable in a successive of three to four attempts, it was considered as a 'no response'.

Outcome measures: The primary outcome measures were knowledge, attitude and practice of antibiotics and ABR in the urban setting of Eritrea. The secondary outcome measure was the determinants of knowledge, attitude and practice of antibiotics and ABR.

Data Analysis

Data was double entered using Census and Survey processing system (CSPro, Version 7.0) software package and exported to statistical package for social sciences (SPSS) Version 23. It was summarized by using weighted percentages and counts. Cross-tabulations and further analysis were also done whenever relevant.

Kolmogorov-Smirnov test was used to check on the normality of the knowledge and attitude scores. Frequencies, percentages, mean (with standard deviation), median (with interquartile range) were used to describe the data, as appropriate. After using independent samples t-test and analysis of variance (ANOVA) at bivariate level of analysis, factorial analysis was employed to assess the predictors of knowledge and attitude at multivariable level. To explore the association between the risky practice of antibiotic and the categorical demographic characteristics, chi-square test was performed and to control potential confounders, variables that were found to have a p-value less than 0.055 were subjected to multivariable analysis using logistic regression. In this study, *p*-value less than 0.05, in all the analyses, is considered as significant.

Operational definition

Risky practice: Refers to the act of self-medication with antibiotics and/or discontinuation of a regimen of antibiotics. It was determined by assessing whether the last used antibiotics were prescribed by authorized health professionals and/or those who had ever used antibiotics interrupted taking antibiotics before completing the full course.

RESULTS

Demographic characteristics of the study participants

A total of 2542 individuals were selected for the survey. Among the selected individuals, 2,477 were successfully interviewed; making an overall response of 97.44%. Demographic characteristics of the respondents are summarized in table 1. The unweighted numbers reflect the actual observations at the time of survey, whereas the weighted numbers reflect figures that have been adjusted by the probability of selection of the respondents (Table 1).

Table 1: Distribution of the study population, 18 years and above, on the knowledge, attitude and practice survey of antibiotics and antibiotic resistance by background characteristics, 2019, Eritrea.

Background Characteristics		Weighted Percent	Weighted Number	Unweighted Number
Age				
	24 or less	18.2	451	433
	25 to 34	25.9	643	644
	35 to 44	22.3	552	567
	45 to 54	15.0	372	396
	55 and above	18.5	459	437
Sex				
	Male	24.7	611	605
	Female	74.7	1851	1857
	Missing	0.6	15	15
Religion				
	Christian	77.4	1918	1749
	Moslem	22.5	558	726
	Other	0.1	2	2
Zone				
	Anseba	8.4	209	352
	Debub	15.9	393	410
	Gash Barka	12.1	301	397
	Maekel	55.7	1380	865
	SKB	6.3	155	322
	DKB	1.6	39	131
Educational Level				
	Illiterate	12.0	298	342
	Elementary	15.9	394	452
	Junior	18.6	462	510
	Secondary	35.7	884	801
	Higher	17.1	425	358
	Missing	0.6	15	14
Household Size				
	One	4.4	108	104
	Two to three	22.0	545	533
	Four or more	73.6	1824	1840
Occupation				
	Governmental	22.8	566	529
	Private employee	4.9	121	115
	House wife	38.3	949	980
	Self employed	8.2	202	209
	Unemployed	14.8	366	361
	Student	7.2	179	166
	Farmer/Fisher	2.2	55	77
	Other*	1.2	30	33
	Missing	0.4	10	7
Total		100	2477	2477

*SKB: Semenawi Keih Bahri, DKB: Debubawi Keih Bahri, * Day laborer, soldier, sheik/priest etc*

205

Awareness and Knowledge on Antibiotics and ABR

Based on participants' response, 73.3% and 39% of the study population were aware of the term 'antibiotic' and 'antibiotic resistance' respectively. The sources of information about antibiotics and ABR were mainly from health facilities (39.6%), television (31.5%) and other people (10.1%).

Distinguishing antibiotics from non-antibiotics, identification of common illnesses that require antibiotics and those that do not need antibiotics, when to stop antibiotics once started, definition of ABR, and potential impact and transmission of ABR were the main indicators used to measure the level of knowledge of the study population on antibiotics and ABR. Of the list of medicines provided, 59.4% of the study population correctly identified penicillin while only 44.8% and 11.9% correctly identified cotrimoxazole and ciprofloxacin respectively. Besides, Ibuprofen, ORS and paracetamol were correctly identified as non-antibiotics by 58.5%, 60.7%, and 70.6% of the population respectively.

Less than half (36.6 - 49.5%) of the study population correctly reported the indication of antibiotics for common illnesses. Majority of them reported that antibiotics can be used to treat viral infection (63.4%), watery diarrhea (61.8%), common cold (58.9%), dry cough (54.2%) and dengue fever (50.5%). Sixty-one per cent of the study population also reported that antibiotics are not indicated for tuberculosis. Correct knowledge on when to stop taking antibiotics once they had begun treatment was in majority (83.3%) of the study population.

Over three-fourth (78.2%) of the study population correctly reported that ABR is an issue that could affect them and their family and about two-third (63.6%) correctly answered the definition of ABR. The proportion of the study population who knew that bacteria resistant to antibiotics can spread from person to person and those who reported that ABR is an issue in other countries but not in Eritrea was about 59% in both cases.

The overall mean knowledge score on antibiotics and ABR was found to be 10.36/20 (SD= 3.51, min=0 and max=20). At bivariate level, males ($p<0.001$), Christians ($p<0.001$), those who were aged between 25 and 54 years ($p<0.001$), those who had higher educational level ($p<0.001$), those having big family size ($p<0.001$) and who were government employees ($p<0.001$) were more likely to have better knowledge score. Besides, study population residing in Maekel and Anseba Zones had better knowledge score ($p<0.001$) on antibiotics and ABR compared to those living in other Zones (Supplementary file 3). At multivariable level, age ($p<0.001$), religion ($p=0.003$),

educational level (p<0.001), family size (p=0.015), occupation (p<0.001), and zone (p<0.001) maintained their association with knowledge score (Table 2). Educational level has the largest partial eta squared (6.8%), showing its prime role in prediction of the knowledge score (Table 2).

Table 2: Predictors of knowledge and attitude towards antibiotics and ABR at multivariable level, Eritrea, 2019.

Knowledge				
Predictor	F	p-value	Partial Eta Squared	Observed Power
Age	28.5	<0.001	0.04	1.000
Gender	0.4	0.536	<0.001	0.095
Religion	9	0.003	0.003	0.849
Educational Level	49.7	<0.001	0.068	1.000
Family size	4.2	0.015	0.003	0.738
Occupation	6.3	<0.001	0.014	0.999
Zone	18.4	<0.001	0.033	1.000
Attitude				
Predictor	F	p-value	Partial Eta Squared	Observed Power
Age	4.5	0.001	0.007	0.944
Gender	11.6	0.001	0.004	0.926
Educational Level	22	<0.001	0.031	1.000
Occupation	3.4	0.003	0.007	0.942
Zone	21.6	<0.001	0.038	1.000

Attitude on antibiotics and ABR

A positive attitude to the majority of the attitude items (82- 92.7%) was reported (Table 3). However, a positive attitude towards appropriate disposal of antibiotics was documented in less than 50% of the study population (Table 3). The overall mean attitude score was 22.34/30 (SD= 3.59, minimum=6 and maximum=30). At bivariate level, males (p<0.001), those aged between 25 and 54 years (p<0.019), those who had higher educational level (p<0.001), and government employees (p<0.001) had better attitude score compared to their counterparts (Supplementary file 4). At the multivariable level, age (p=0.001), gender (p=0.001), educational level (p<0.001), occupation (p=0.003) and zone (p<0.001) maintained their significance as predictors of attitude

score. Zone has largest explanatory (partial eta squared=3.8%) capability for the attitude towards antibiotics (Table 2).

Table 3: Agree/strongly agree response on the attitude of antibiotics and antibiotic resistance (ABR), Eritrea, 2019 (N=2477)

Attitude questions on antibiotics and ABR	% (95% CI)
Hand washing decreases ABR	92.7 (91.6-94.1)
Taking antibiotics when it is not required can facilitate ABR	89.7 (88.2-91.1)
You have a role to fight ABR	85.8 (84.5-87.8)
It is not okay to share antibiotics with others	90.1 (89.4-91.6)
We cannot use antibiotics without prescription	88 (87.5-89.8)
Farmers should not give antibiotics without consulting veterinarian	82.1 (80.9-83.7)
It is not okay to keep leftover antibiotics and use them later	82 (80.7-83.5)
Leftover antibiotics should not be disposed with regular garbage	46 (45.4-49.1)
Leftover antibiotics should not be disposed at toilets	35.7 (34.3-37.9)

Practice on usage of antibiotics

Majority (84.5%) of the study population had used antibiotics at least once in their life time and 55% had history of intake of antibiotics in the last one year and 12.3% in the last one month prior to commencement of this study. Of those who ever used antibiotics (N=2407), 88.1% reported that their last intake of antibiotic(s) was prescribed by an authorized healthcare professional. Non-seriousness of the disease (39.0%), need to get quick relief (33.9%), previous own successful experiences (16.1%), having no time to visit a health facility (15.0%) and long queues existing in health facilities (14%) were the top five reasons reported for self-medication with antibiotics. For those who used antibiotics without prescription, the main sources of their last course of antibiotics were drug retail outlets (83.6%) (Figure 1).

One fifth (18.8%) of those who had ever used antibiotics interrupted their regimen before completing the full course. The main reason for interruption of antibiotics was improved illness condition (63.4%) (Figure 2). About 3% of the study population reported that they had used

antibiotics on their own at least once, though they were advised by healthcare professionals not to do so.

Overall, risky practice of antibiotics (use of antibiotics without prescription and/or discontinuation of prescribed antibiotics before completing the full course) was reported in 23.8% of the study population. The chi-square analyses found that age (p<0.001), gender (p=0.01), educational level (p<0.001), occupation (p<0.001) and zonal location (p<0.001) were the significant associates of risky practice of antibiotics. On multivariable level, those who were young - 24 years or less (AOR=1.59, 95% CI: 1.06 to 2.38), males (AOR=1.48, 95% CI: 1.15 to 1.92), those who had higher level of education (AOR=1.77, 95% CI: 1.05 to 2.90) and those with higher attitude score (AOR=0.95, 95% CI: 0.92 to 0.97) were more likely to involve in risky practice of antibiotics (Table 4).

Table 4: Predictors of risky practice of antibiotics across the categories of demographic characteristics and attitude score at multivariable level, Eritrea, 2019.

Background characteristic	Multivariable analysis		
	AOR	95% CI	*p*-value
Age			0.046
24 or less	1.59	1.06 to 2.38	
25 to 34	1.25	0.88 to 1.78	
35 to 44	1.05	0.74 to 1.49	
45 to 54	0.89	0.61 to 1.29	
55 and above	*Ref.*		
Gender			
Male	1.48	1.15 to 1.92	0.003
Female	*Ref.*		
Educational Level			0.098
Illiterate	*Ref.*		
Elementary	1.02	0.66 to 1.57	
Junior	1.20	0.77 to 1.84	
Secondary	1.32	0.86 to 2.02	
Higher	1.77	1.05 to 2.90	
Family Size			0.332
One	0.79	0.44 to 1.43	
Two to three	1.15	0.90 to 1.46	
Four or more	*Ref.*		
Occupation			0.177
Governmental	Ref.		
Private employee	1.13	0.70 to 1.82	
House wife	1.33	0.96 to 1.83	
Self-employed	1.52	1.02 to 2.25	

Unemployed	1.14	0.79 to 1.66	
Student	1.45	0.94 to 2.22	
Farmer/Fisher	1.48	0.70 to 3.13	
Other*	0.44	0.13 to 1.50	
Zone			0.071
Anseba	0.47	0.21 to 1.04	
Debub	0.72	0.33 to 1.58	
Gash Barka	0.70	0.31 to 1.55	
Maekel	0.88	0.42 to 1.86	
SKB	0.81	0.35 to 1.87	
DKB	*Ref.*		
Attitude score	0.95	0.92 to 0.97	<0.001

**Day laborer, soldier, sheik/priest etc*

A total of 1473 of the study population had animals and about 14% reported that they have treated their animals with antibiotics at least once. Of those who used antibiotics for their animals, 62% purchased at least once in the last year, prior to the study period. The commonly used antibiotics for animals were amoxicillin (44.1%), oxytetracycline (36.2%) and penicillin (16.3%). About 51% of antibiotics used for animals were obtained from veterinarians whereas the rest were mainly from pharmacy retail outlets (20.8%), family/friends (14.4%) and open markets (14.3%) (Figure 3).

DISCUSSION

This nation-wide urban population-based survey revealed a significant risky practice of antibiotics in Eritrea. One in five of the study population, who had ever used antibiotics, reported that their last intake of antibiotic(s) was interrupted for many reasons. Discontinuation of antibiotics when the consumer felt better was the most frequently reported reason. This reflects lack of awareness on the appropriate use of antibiotics and risk of ABR. Majority of the antibiotics most recently consumed by the study population were reported to have been prescribed by qualified healthcare professionals. This is encouraging and the nation-wide, massive antibiotic awareness week campaigns conducted in the last three years, prior to the study, might have had positive contributions. However, due to lack of a national baseline data, the authors could not come up with a definitive conclusion regarding the effectiveness of the previously conducted campaigns.

The disease condition being non-serious, intention to get a quick relief, previous successful experience, shortage of time to visit health facilities and long queues were the main triggering factors reported for self-medication with antibiotics. The first three reasons mentioned above for self-medication with antibiotics reflect lack of awareness on the risks of inappropriate use of antibiotics. In Eritrea, guided by 'health for all policy' and 'social justice', healthcare services are provided at a highly subsidized or nominal cost through public health facilities. To further improve patients' satisfaction, accessibility to health services and health seeking behavior, the existing healthcare delivery services need to be optimized. Moreover, the annual antibiotic awareness week campaign should be augmented by additional continuous and regular health promotional activities.

In this study, drug retail outlets were reported as the main sources for the sales of antibiotics without prescription. A recently conducted study also revealed an alarming picture of 87% of retail outlets dispensing antibiotics without prescription in Eritrea [10] and that requires immediate attention from regulators and policy makers. Continued refresher courses on appropriate use of antibiotics and ABR as well as further enforcement of regulations would have an impact in bridging these gaps. Cognizant of this, the National Medicines and Food Administration of the Ministry of Health developed medicines schedule in 2019 and all antibiotics are put under the 'prescription only medicine' category. To ensure implementation and adherence to scheduling terms, the National Medicines and Food Administration is recommended to conduct strict and continuous inspection on drug retail outlets.

Use of antibiotics without prescription, in this study was more or less consistent with findings of similar studies conducted in European countries, where this practice is reported to occur in a proportion of 7% (ranging from 0% to 20%) [28]. It was however much lower than that reported in Italy [29], Jordan [30 31], United Arab Emirates [32], Palestine [33], Lebanon [34], Iraq [35], Indonesia [36], Yemen [37], Saudi Arabia [38], Haiti [39], Kuwait [40], and Ethiopia [41 42], where proportions ranged between 31% and 79%. The variation in results, however, could be due to differences in study designs, study area, study population, type of questions and level of awareness of the study population. Following the WHO recommendation (2015) for all member states to start annual awareness raising programs on AMR, Eritrea started to implement it since 2016. This study was conducted after a few years of massive public campaigns and might have influenced the current findings. It is also possible that in other countries that have made similar initiatives, the existing profile might have been influenced in the same way despite no current studies are available.

Factors such as young age (24 years or less), male sex, high level of education and poor attitude score were identified as determinants of risky practice of antibiotics. It is unknown why those who had higher level of education and those who were young (relatively with greater educational opportunities) were more involved in the risky practice of antibiotics. This might to some extent be explained by the fact that knowing more or being educated predisposes people to the tendency to take self-made decisions more casually with the assumption that they have the knowledge. Qualitative studies are required to further identify the determinants of risky practice of antibiotics.

In this study, an appreciably high mean attitude score towards antibiotics and ABR was reported. It is however important to note that the poor attitude reported on the appropriate disposal of leftover antibiotics requires immediate attention from policy makers. Studies on awareness and disposal practices of unused and expired medicines by consumers in India and Nigeria also reported that improper practices such as the disposal of medicines in domestic trash, toilets and sinks is prevalent [43 44].

Unlike the relatively good attitude score, the mean knowledge score of the study population on antibiotics and ABR was not satisfactory. This study revealed that majority of the study population had no clear picture on what an antibiotic is and were unable to recognize, by name, the most commonly used antibiotics (penicillin, cotrimoxazole and ciprofloxacin) in the country. Categorizing ibuprofen, ORS and paracetamol as antibiotics by a large number of the study population was another concern. A significant proportion of the study population also had the misunderstanding that antibiotics could treat viral infections like common cold and acute watery diarrhea. Hence, continued awareness raising programs should target such misconceptions and familiarize the public with the commonly used antibiotics, their proper indications and the potential for resistance. The assumption that ABR is a threat elsewhere, but not in Eritrea, as reported in this study, reflects how oblivious people are on the issue of ABR and this may limit the public from taking appropriate actions. Several of the variables (age, religion, educational level, family size, occupation, and zone) identified as factors associated with knowledge and attitude do not seem to be clinically meaningful as small difference in results could give statistically significant difference. Thus, readers should cautiously interpret the results.

Regarding the use of antibiotics to treat animals, in this study, oxytetracycline, amoxicillin and penicillin were the most frequently reported ones. About half of the antibiotics used in animals

were supplied by non-veterinarians such as drug retail outlets and open markets. This indicates poor regulation of antibiotics in animal health.

Because parasites and infections do not respect borders, combating ABR has since long ago been a global agenda. A problem identified in one country could have direct or indirect implication on the containment of ABR by other countries. The significance of this nationwide survey and the results it comes up with are all expected to be of a particular interest for countries with similar socioeconomic statuses as Eritrea. Many of these countries share the common problems of poor quality, inequitable, overstretched, unregulated and poorly accessible health services which could trigger the general public to be involved in risky practice of antibiotics. Moreover, they lack the systems to control antibiotic consumption and the initiative to tackle the issue of resistance. If Eritrea's profile with regard to the prevalence of risky practices such as self-medication with antibiotics has been relatively good while there is a long way to go to improve the healthcare infrastructure, it is not hard to imagine the progress the country could assume if the existing policies such as the national action plan on AMR and regulations such as medicines scheduling are enforced.

This is among the few globally reported nation-wide population-based surveys that measure knowledge, attitude and practice of antibiotic and ABR. The study employed a rigorous data quality and management approaches and had high percentage of response. On the other hand, one of the main limitations of this study is that the results were self-reported and thus, findings might be under- or over-estimated. This could introduce information or recall bias. Another limitation is that during data collection, the information regarding family size and available members was gathered from the present household members and no verification was done using administrative list. This may have in-turn introduced respondents selection bias. Moreover, the reliability and validity of the scales for knowledge and attitude on antibiotics usage were not checked using statistical tools.

Conclusion

The risky practice of antibiotics in Eritrea was prevalent and inversely proportional to the mean attitude score. Being young, male, and those who had higher level of education and poor attitude score were identified as having greater tendency for risky practices associated with antibiotics. The inability of high proportion of the study population to distinguish antibiotics from other

medicines and the reported misunderstanding that viral infections can be treated with antibiotics, indicates limited knowledge on antibiotics and ABR. Continuous awareness raising programs on the rational use of antibiotics (mainly on the risks of self-medication, treatment interruption, and use of antibiotics for viral infections) and familiarizing the public with the commonly used antibiotics are recommended. As drug retail outlets were identified to be the main sources for the supply of antibiotics without prescription, both in humans and animals, enforcement of medicines schedule and strengthening of regulatory inspections is vital. Besides, the huge gap in attitude towards appropriate disposal of antibiotics requires immediate attention from policy makers and establishment of an appropriate disposal system of leftover antibiotics for the community. Last but not least, it is high time to expedite the implementation of the strategies stipulated under the national action plan on AMR which was released in February 2021.

DECLARATIONS

Ethics approval and informed consent

Ethical approval to conduct the study was obtained from the Ministry of Health, Eritrea and further approval was also obtained from the Ministry of Local Government. Besides, informed consent was obtained from all study participants to take part in the study.

Patient consent for publication: Not required.

Conflict of interests

The authors declare that they have no competing interests.

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Author contributions

The idea was conceived by MR and IB and designed by all authors (MB, MD, MR, AK, AA, YF, IB, SK, JN and EHT). Data was collected by MD, AK, AA and YF and supervised by MR and MB. EHT edited and analyzed the collected data and all the co-authors participated in the interpretation of the results. The manuscript was drafted by MB, MR and EHT and critically reviewed and edited by all of the authors. Finally, all the co-authors agreed that the article be published in an international journal and to take responsibility and be accountable for its content.

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Availability of data

All data related to the study are included in the manuscript. The complete dataset used for this study can be obtained from the corresponding author upon request.

Acronyms

ABR: Antibiotic Resistance; AMR: Antimicrobial resistance; DKB: Debubawi Keih Bahri; SKB: Semenawi Keih Bahri; WHO: World Health Organization.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication: Not required.

Provenance and peer review: Not commissioned; externally peer reviewed.

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Figure 1: Source of antibiotics used without prescription among urban residents, Eritrea, 2019 (n=242)

Figure 2: Reasons for stopping the intake of antibiotics among urban residents, Eritrea, 2019 (n=357)

Figure 3: Source of antibiotics for animals among urban residents, Eritrea, 2019 (n=245)

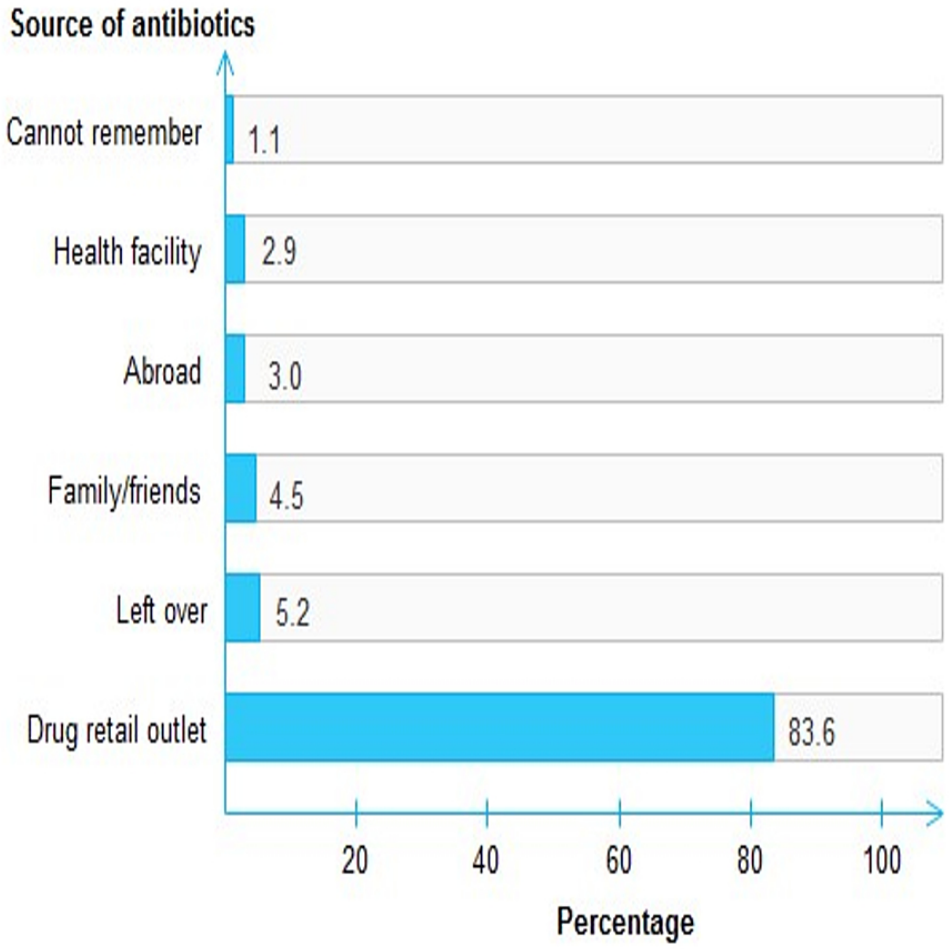

Figure 1: Source of antibiotics used without prescription among urban residents, Eritrea, 2019 (n=242)

38x38mm (600 x 600 DPI)

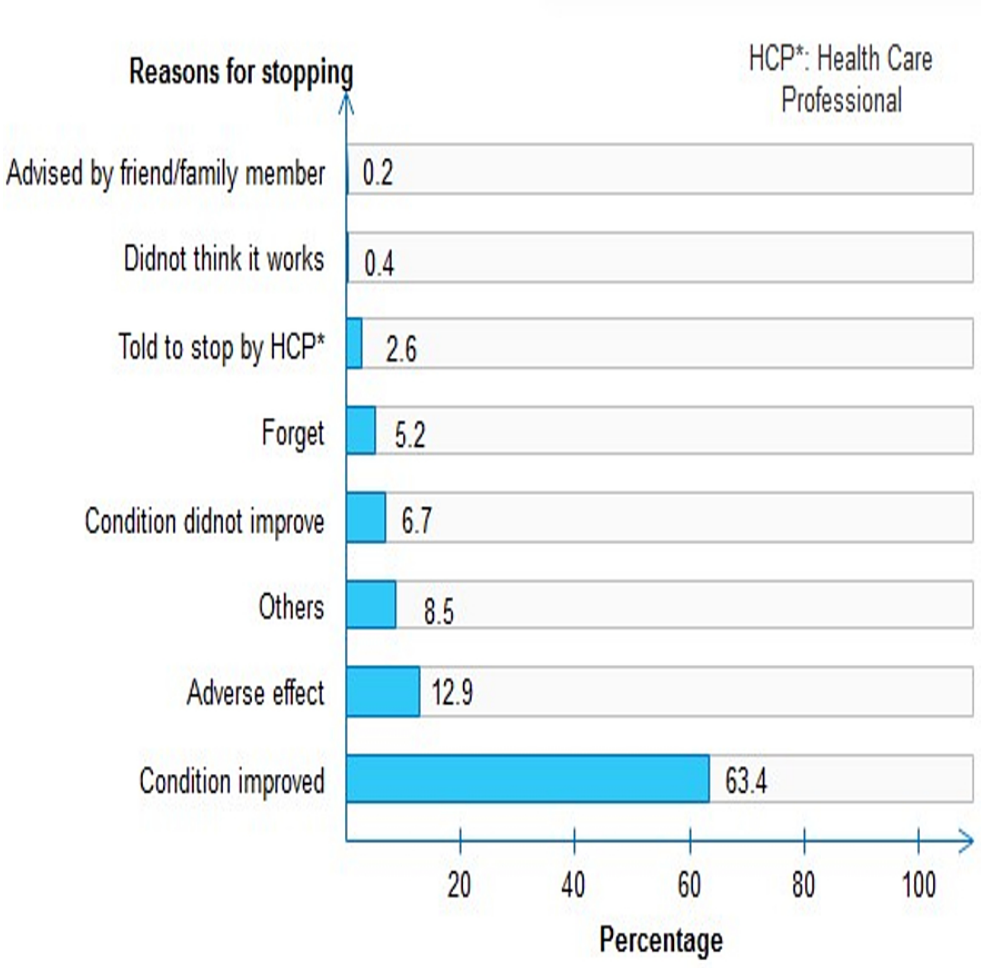

Figure 2: Reasons for stopping the intake of antibiotics among urban residents, Eritrea, 2019 (n=357)

38x38mm (600 x 600 DPI)

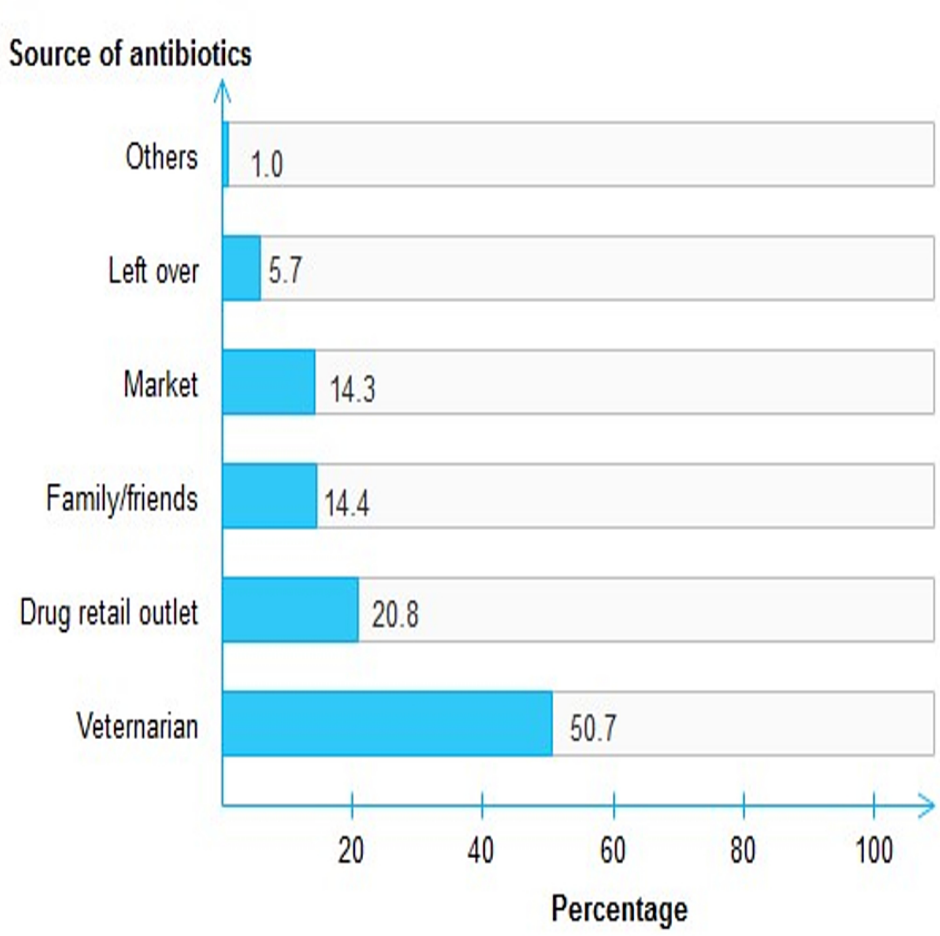

Figure 3: Source of antibiotics for animals among urban residents, Eritrea, 2019 (n=245)

38x38mm (600 x 600 DPI)

Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

Mulugeta Russom[1], Merhawi Bahta[1*], Merhawi Debesai[1], Iyassu Bahta[1], Abrahalei Kessete[1], Aziza Afendi[1], Yodit Fitsum[1], Josephina Nambozi[2], Soliana Kidane[2], Eyasu H. Tesfamariam[3]

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Supplementary file 1: Number of households in the urban places of Eritrea (July 2019)

Zone	City/Town	Number of Households
Gash Barka	Akordat	3,822
	Barentu	10,935
	Tessenei	15,205
	Subtotal	**29,962**
Debub	Mendefera	8,023
	Adiquala	3,419
	Dekemhare	9,769
	AdiKeih	5,335
	Senafe	6,574
	Subtotal	**33,120**
SKB	Ghindae	5,832
	Massawa	9,512
	Subtotal	**15,344**
Anseba	Keren	19,343
	Subtotal	**19,346**
DKB	Assab	3,106
	Subtotal	**3,106**
Maekel	Asmara	116,146
	Subtotal	**116,146**
Total		**217,024**

SKB: Semienawi Keih Barhri; DKB: Debubawi Keih Barhri; HH: Household

Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

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Part I: Identification Particulars

Zoba	
Subzoba	
City/Town	
Kebabi	
Respondent number	

Interviewer Visits

	1	2	3	Final Visit
Date				Day / Month / Year: 2019
Interviewer's Name				Int. No.
Result*				Result*
Next visit: Date				Total number of visits
Time				

*Result codes:

Completed
Not completed
Not willing
Other _____ (Specify)

Total persons In household

Total eligible persons (≥18)

Supervisor	Field editor	Keyed by
Name _____ Number	Name _____ Number	Name _____ Number

Part II: Demographic Information

No.	Indicators	Coding categories	Skip
201	Age (in completed years)	☐☐	
202	Sex	Male ..... 1 Female 2	
203	Ethnicity	Tigrina ..... 1 Afar ..... 2 Tigre ..... 3 Saho ..... 4 Rashida ..... 5 Kunama ..... 6 Blien ..... 7 Hidarb ..... 8 Nara ..... 9 Other (please specify) _____ 10	
204	Religion	Christian ..... 1 Muslim ..... 2 Other (please specify) _____ 3	
205	Level of education (Highest level of education)	Illiterate ..... 1 Primary school ..... 2 Middle school ..... 3 Secondary school ..... 4 Higher education 5	
206	Main occupation	Farmer ..... 1 Government employee ..... 2 Private employee ..... 3 Housewife ..... 4 Self-employed ..... 5 Unemployed ..... 6 Student ..... 7 Fisher man ..... 8 Other (please specify) _____ 9	

Part III: Knowledge

No.	Questions	Coding categories	Skip
301	Have you ever heard about antibiotics?	Yes . . . . . 1 →	303
		No 2	
302	Have you ever heard of any one of the following medications? ASK FOR EACH MEDICATION.	Amoxicillin . . . . . A Tetracycline . . . . . B Oxytetracycline . . . . . C I haven't heard all of them . . . . . D →	**END**
303	Which of the following do you think are antibiotics? ASK FOR EACH MEDICATION. If the response in 201 is No and heard of any one of the examples of antibiotics, explain that the term Antibiotics refers to these drugs before continuing to 204 .	Y N DK Ibuprofen . . . . . 1 2 3 Tetracycline . . . . . 1 2 3 Bactrium . . . . . 1 2 3 ORS . . . . . 1 2 3 Amoxicillin . . . . . 1 2 3 Paracetamol . . . . . 1 2 3 Ciprofloxacin . . . . . 1 2 3 Penicillin 1 2 3	
304	Which of these diseases do you think are treated with antibiotics? ASK FOR EACH ILLNESS.	Common cold . . . . . 1 2 3 Watery diarrhea . . . . . 1 2 3 TB . . . . . 1 2 3 Dengue fever . . . . . 1 2 3 Pneumonia . . . . . 1 2 3 Dry cough 1 2 3	
305	Do antibiotics treat viral infections?	Yes . . . . . 1 No . . . . . 2 Don't know 3	
306	When do you think you should stop taking antibiotics once you've begun treatment? MULTIPLE RESPONSES ARE POSSIBLE. PROBE: Are there any other reasons	When I feel better . . . . . A When I do not see improvements . . . . . B When I encounter adverse drug reactions C It should not be stopped . . . . . D Don't know . . . . . E	
307	Have you ever heard of the term antibiotic resistance (ABR)?	Yes . . . . . 1 No 2	
308	Antibiotic resistance occurs when your becomes resistant to antibiotics and they no work.	Yes . . . . . 1 No . . . . . 2 Don't know 3	**404**
309	Where did you hear about antibiotic resistanc MULTIPLE RESPONSES ARE POSSIBL PROBE: Are there any other sources	Health facility . . . . . A Pharmacy . . . . . B Radio . . . . . C TV . . . . . D Newspaper . . . . . E Campaign/Seminar . . . . . F Other (please specify) _____ G	

310	Antibiotic resistance is an issue that could affect me or my family.	Yes . . . . . 1 No . . . . . 2 Don't know 3	
311	Antibiotic resistance is an issue in other countries but not here.	Yes . . . . . 1 No . . . . . 2 Don't know 3	
312	Bacteria which are resistant to antibiotics can spread from person to person.	Yes . . . . . 1 No . . . . . 2 Don't know 3	

Part IV: Attitude

No.	Questions		Skip
401	Proper handwashing play a role in ABR.	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
402	Taking antibiotics when it is not required can facilitate ABR.	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
403	You have a role to fight ABR	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
404	We can use antibiotics without prescription	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
405	It is okay to share antibiotics with family members or friends for similar illness	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
406	It is okay to keep leftover antibiotics and use them later	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	

407	Farmers can give antibiotic without consulting veterinarian	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
408	Leftover antibiotics should be disposed with regular garbage	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
409	Leftover antibiotics should be disposed at toilets	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	

Part V: Practice

No.	Questions	Coding categories	Skip
501	Have you ever used antibiotics?	Yes . . . . . 1 No . . . . . 2 Don't remember 3	**509**
502	When was the last time you took antibiotics?	Now . . . . . 1 Last month . . . . . 2 Last six months . . . . . 3 Last year . . . . . 4 More than a year ago . . . . . 5 Don't remember 6	
503	Source of the last course of antibiotic MULTIPLE RESPONSES ARE POSSIBLE.	Health facility . . . . . A Drug retail outlet . . . . . B Friend or family member . . . . . C Saved up from a previous time . . . . . D From abroad . . . . . E Don't remember . . . . . F	
504	On that occasion, did you get a prescription for the antibiotics from a doctor/nurse?	Yes . . . . . 1 Don't remember . . . . . 2 No 3	**506**
505	What was (were) your reason(s) of self-medication with antibiotics? MULTIPLE RESPONSES ARE POSSIBLE.	Long queue A Had no time to visit a health facility . . . B To get a quick relief . . . . . C Disease was not serious . . . . . D To save expenses . . . . . E Own previous successful experience . . . F Other (please specify) _____ G	

506	Did you ever stop taking antibiotics before completing the full course?	Yes . . . . . 1 No . . . . . 2 Don't remember 3	**508**
507	Why did you stop taking the antibiotics?	Condition didn't improve . . . . . 1 Condition improved . . . . . 2 Due to adverse effects . . . . . 3 Advised by a friend or family member 4 I didn't think it works . . . . . 5 Told to stop by a healthcare profession . 6 Other (please specify) _____ 7	
508	Ever used antibiotics on your own, though health care professionals advice you not to take	Yes . . . . . 1 No . . . . . 2 Don't remember 3	
509	Have you ever given antibiotics to your animals?	Yes . . . . . 1 No . . . . . 2 Don't remember . . . . . 3 Don't have an animal 4	**END**
510	Which antibiotic did you use for your animal? ASK FOR EACH MEDICATION.	Amoxicillin . . . . . A Erythromycin . . . . . B Oxytetracycline . . . . . C Penicillin . . . . . D Tylosin . . . . . E Didn't use all of these antibiotics . . . . . F Other (please specify) _____ G	
511	Source of the antibiotics	Bought from the market . . . . . A Bought from Drug retail outlet . . . . . B Veterenarian . . . . . C Friends/family membe . . . . . D Other (please specify) _____ E	
512	How many times did you buy antibiotics for your animal in the last one year ?	Once . . . . . 1 Twice . . . . . 2 Three times . . . . . 3 More than three times . . . . . 4 Never 5	

END OF INTERVIEW

INTERVIEWER'S OBSERVATIONS

TO BE FILLED IN AFTER COMPLETING THE INTERVIEW
COMMENTS ABOUT THE INTERVIEW
COMMENTS ON SPECIFIC QUESTIONS
ANY OTHER COMMENTS
SUPERVISOR'S OBSERVATIONS
EDITOR'S OBSERVATIONS

Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

Mulugeta Russom[1], Merhawi Bahta[1*], Merhawi Debesai[1], Iyassu Bahta[1], Abrahalei Kessete[1], Aziza Afendi[1], Yodit Fitsum[1], Josephina Nambozi[2], Soliana Kidane[2], Eyasu H. Tesfamariam[3]

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Supplementary Table 2: Comparison of knowledge scores across the categories of demographic characteristics at bivariate level, Eritrea, 2019

Characteristics	Mean (SD)	F/t Value	p-value	p-value trend (Type of trend)	Post Hoc Test	
					Pair wise comparison	Group wise comparison
Age						
24 or less **A**	9.57 (3.24)					
25 to 34 **B**	10.53 (3.25)					
35 to 44 **C**	11.02 (3.36)	16.03**	<0.0001	<0.0001 (Quadratic)	A<B, A<C, A<D, A=E, B=C=D, B>E, C>E, D>E	Group 1: A and E Group 2: B, C, and D
45 to 54 **D**	10.77 (3.70)					
55 and above **E**	9.73 (3.91)					
Gender						
Male	10.98 (3.61)	5.08	<0.0001	-	M>F	-
Female	10.15 (3.44)					
Religion						
Christian	10.57 (3.53)	5.93	<0.0001	-	C>M	-
Muslim	9.60 (3.30)					
Educational Level						
Illiterate	7.99 (3.28)					
Primary	9.49 ((3.38)					Group 1: I Group 2: P and M Group 3: M and S Group 4: H
Middle	10.16 (3.31)	66.78	<0.0001	<0.0001 (Linear)	I<P, I<M, I<S, I<H, P=M, P<S, P<H, M=S, M<H, S<H	
Secondary	10.72 (3.38)					
Higher	11.97 (3.23)					
Family Size						
One	8.84 (4.19)					
Two to three	10.08 (3.45)	12.62	<0.0001	<0.0001 (Linear)	O<T, O<F, T<F	Group 1: O Group 2: T and F
Four or more	10.52 (3.46)					
Occupation						
Governmental	11.76 (3.40)					
Private employee	10.85 (3.57)					
House wife	10.10 (3.27)					
Self-employed	10.13 (3.54)	22.05	<0.0001	-	G=P, G>H, G>Se, G>U, G>St, G>F, G=O, P=H, P=Se, P>U, P=U, P=St, P=O, H=Se, H=U, H=St, H=F, H=O, Se=U, Se=St, Se=F, Se=O, U=St, U=F, U=O, St=F, St=O, F=O	Group 1:F, U, St, O, H and Se, Group 2:U, St, O, H, Se and P Group 3: H, Se, P and G
Unemployed	9.40 (3.67)					
Student	9.54 (3.40)					
Farmer/Fisher	8.71 (3.32)					
Other*	9.62 (3.30)					
Zone						
Anseba	10.53 (3.36)					
Debub	8.85 (3.65)					
Gash Barka	9.54 (3.18)	28.45	<0.0001	-	A>De, A=G, A=M, A=S, A=D, De<M, De=G, De=S, De=D, G<M, G=S, G=D, M>S, M=D,	Group 1: De, S, and G, Group 2: S, G, D and A Group 3: G,D,A and M
Maekel	11.00 (3.39)					
SKB	9.44 (3.51)					
DKB	10.27 (3.09)					

Other: Day laborer, soldier, sheik/priest etc; ** Welch test statistic was used to obtain robust result; SKB: Semenawi Keih Bahri; DKB: Debubawi Keih Bahri*

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Supplementary Table 3: Comparison of attitude scores on antibiotics and antibiotic resistance across the categories of demographic characteristics at bivariate level, Eritrea, 2019.

Characteristics	Mean (SD)	F/t Value	p-value	p-value trend (Type of trend)	Post Hoc Test	
					Pair wise comparison	Group wise comparison
Age						
24 or less **A**	22.10 (3.81)					
25 to 34 **B**	22.50 (3.31)					
35 to 44 **C**	22.25 (3.66)	2.97*	0.019	0.034 (quadratic)	A=B=C=D=E,	Group 1: A, B, C, D and E
45 to 54 **D**	22.80 (3.47)					
55 and above **E**	22.07 (3.76)					
Gender						
Male	23.0 (3.86)	4.92	<0.0001	-	M>F	-
Female	22.13 (3.48)					
Religion						
Christian	22.37 (3.54)	0.7	0.488	-	-	-
Muslim	22.24 (3.80)					
Educational Level						
Illiterate	21.36 (3.64)					
Primary	22.14 (3.46)				I=P, I<M, I<S, I<H, P=M, P=S, P<H, M=S, M<H, S<H	Group 1: I Group 2: P, S and M Group 3:H
Middle	22.34 (3.65)	10.76	<0.0001	<0.0001 (linear)		
Secondary	22.32 (3.52)					
Higher	23.16 (3.62)					
Family Size						
One	21.86 (3.42)					
Two to three	22.25 (3.46)	1.2	0.300	-	-	-
Four or more	22.39 (3.64)					
Occupation						
Governmental	22.93 (3.73)					
Private employee	22.04 (3.32)					
House wife	22.30 (3.51)					
Self-employed	22.62 (3.48)					
Unemployed	21.69 (3.38)				G=P, G=H, G=Se, G>U, G=St, G=F, G=O, P=H, P=Se, P=U, P=U, P=St, P=O, H=Se, H=U, H=St, H=F, H=O, Se=U, Se=St, Se=F, Se=O, U=St, U=F, U=O, St=F, St=O, F=O	Group1:F, U, St, O, H, G, and Se
Student	21.82 (3.85)	4.95	<0.0001	-		
Farmer/Fisher	21.65 (3.92)					
Zone						
Anseba	23.19 (3.43)					
Debub	22.27 (3.35)					
Gash Barka	23.24 (3.73)				A=De, A=G, A>M, A=S, A=D, De=M, De<G, De=S, De=D, G>M, G=S, G=D, M=S, M=D, S=D	Group 1: A, De, M, S, and D Group 2: A, De, M, S, and G
Maekel	22.01 (3.62)	8.87	<0.0001	-		
SKB	22.76 (3.20)					
DKB	21.73 (4.32)					

** Welch test statistic was used to obtain robust result; SKB: Semenawi Keih Bahri; DKB: Debubawi Keih Bahri.*

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-7*
Bias	9	Describe any efforts to address potential sources of bias	6-7
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	7
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5-6
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	8-9
Outcome data	15*	Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-14

		(*b*) Report category boundaries when continuous variables were categorized	10-14
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	19
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15-18
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

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Word count: 3963

ABSTRACT

Objective: To measure knowledge, attitude and practice of antibiotics and antibiotic resistance and their determinants in the Eritrean urban population.

Design: Population-based, nation-wide, cross-sectional study.

Setting: Urban settings of Eritrea.

Participants: Members of the general public aged ≥18 years and living in thirteen urban places of Eritrea. Three stage stratified cluster sampling was used to select the study participants.

Data collection and analysis: Date was collected from July to September 2019 in a face-to-face interview using a structured questionnaire. The collected data was double entered and analyzed using CSPro (Version 7.0) and SPSS (Version 23) respectively. Descriptive statistics, chi-square test, t-tests, analysis of variance, factorial analysis and multivariable logistic regression were performed. All analyses were weighted and $p<0.05$ was considered significant.

Primary and secondary outcome measures: Main outcome variables were knowledge, attitude and practice of antibiotics and antibiotic resistance. Secondary outcome measure was the determinants of knowledge, attitude and practice.

Results: A total of 2477 adults were interviewed. The mean score of knowledge and attitude of antibiotics and antibiotic resistance (ABR) was 10.36/20 (SD=3.51, minimum=0 and maximum=20) and 22.34/30 (SD=3.59, minimum=6 and maximum=30) respectively. Of those who used antibiotics, the proportion of at least one inappropriate practice (use of antibiotics without prescription and/or discontinuation of prescribed antibiotics before completing the full course) was 23.8%. Young age <24 years (AOR=1.61, 95% CI: 1.08 - 2.41), male sex (AOR=1.48, 95% CI: 1.14 - 1.91), higher level of education (AOR=1.76, 95% CI: 1.08 - 2.88), and negative attitude on antibiotic use (AOR=0.95, 95% CI: 0.92 - 0.97) were found to be the significant determinants of inappropriate practice of antibiotics.

Conclusion: The gap in knowledge and inappropriate practice of antibiotics in the Eritrean urban population was widespread, requiring immediate attention from policymakers and healthcare professionals.

Keywords: Public health, infectious diseases, epidemiology

ARTICLE SUMMARY

Strengths and limitations of this study

- This is among the few globally reported population-based surveys covering nation-wide representative of all urban residents of Eritrea.
- The study employed rigorous data quality and management approaches and had a high percentage of response.
- Results of this study were self-reported and thus, findings might be under- or over-estimated which might in-turn have introduced information or recall bias.
- During data collection, though efforts were made to provide an equal chance of selection for every household member, there might be selection bias as about three-fourth of the respondents were found to be females. This sex-imbalance might be explained by the fact that the information regarding family size and available members during data collection was gathered without verification with an administrative list.
- The reliability and validity of the scales for knowledge and attitude on antibiotics usage were not checked using statistical tools.

INTRODUCTION

The excess use of antibiotics, poses great health risks that would escalate bacterial resistance [1-4]. Resistant infections are now estimated to cost at least 50,000 lives each year in Europe and the US alone [5]. From this, one can speculate that the burden of antimicrobial resistance (AMR) would be much higher in resource-constrained countries in which the inappropriate use of antibiotics by healthcare professionals and consumers could be rampant. This in part is due to poor regulation, weak health systems, surveillance, knowledge and higher infectious diseases [1 6 7]. If left unimpeded, by 2050, deaths attributable to AMR are estimated to be 10 million per year globally [1].

Nowadays, antibiotic resistance (ABR) is recognized as one of the biggest threats to global health and is becoming a medical emergency that would limit the advances of healthcare delivery

services. This endangers the achievements of the millennium development goals and also sustainable development goals [8]. Thus, AMR in general and ABR in particular is transforming into a political agenda.

As estimated by the World Health Organization (WHO), 80% of antibiotics are used in the community and 20-50% of which are used inappropriately [9]. Use of antibiotics without prescription [10-13], physician perception of patients expectation for antibiotics [14 15], patient demand [16-18], unrestricted use of antibiotics [7 19] and poor healthcare system [20] have been reported among the main factors for the inappropriate use of antibiotics. To tackle this, at the 68th World Health Assembly, a global action plan was endorsed [21]. One of the five global strategic objectives was to improve awareness and understanding about AMR [21], thus all member states were recommended by the WHO to annually conduct antibiotic awareness week campaigns in a one-health approach [21].

With these recommendations, Eritrea has been in a process of establishing an antimicrobial stewardship program. Through a multisectoral approach, Eritrea has developed a national action plan for combating AMR that is expected to be effective in 2021. One of the four strategic objectives of the national action plan is 'raise awareness through education and training'. Moreover, the National Medicines and Food Administration of the State of Eritrea has published a medicines schedule that is expected to contribute towards the antimicrobial stewardship. Prior to implementation, knowing the current status and weakest links are important for policy decisions and to identify areas of intervention on tackling AMR. Even though there is existing evidence of poor knowledge and inappropriate practice of antibiotics in many countries, there is paucity of nation-wide data in Eritrea and other countries with similar socio-economic profile. This study was therefore conducted to measure knowledge, attitude and practice of antibiotic usage and identify their key determinants in the Eritrean urban population. As there is no baseline data to start with and assess the effectiveness of the annually conducted antibiotic awareness weeks, the findings of this study could also be taken as a point of reference to assess relative changes in the determinants of change in practice.

METHODS

Study design and area

A cross-sectional study design, with a quantitative approach, was used. Eritrea is a country with an estimated population of 3.4 million [22]. It has six administrative zones comprising 58 subzones in total. The country has five administrative levels namely: National, Zonal, Sub-zonal, Local Administration (Kebabi administration) and Village/Block (village in rural or block in urban settings) levels.

The survey was conducted between July and September 2019 in all urban sites of the country. In Eritrea, there are a total of 13 cities and/or towns. The urban sites included in this study were three from Gash Barka, five from Debub, two from Semenawi Keih-Bahri (SKB) and one city or town from each of the remaining three zones, namely Anseba, Debubawi Keih-Bahri (DKB), and Maekel (supplementary file 1). A total of 25 sub-zones and 72 local administrations (Kebabi administration) located in the above-mentioned towns and/or cities were involved in the survey.

Target population

The target population of the study includes all members of the general public aged 18 years or above and living in the thirteen urban places in which the survey was conducted.

Sample size and sampling technique

The sample size computational formula [23] and procedures accommodating the multi-stage sampling technique [24] is provided as supplementary material (Supplementary file 2).

Data collection tools and approach

A structured questionnaire (Supplementary file 3) was prepared by reviewing questionnaires of similar studies [25-27] and was customized in such a way to reflect issues relevant to Eritrea. It was initially prepared in English and then translated into the common local language, Tigrigna. The questionnaire had four sections namely: personal characteristics of the respondent; awareness and knowledge regarding antibiotics and ABR; attitude regarding antibiotics and ABR, and practice of the general public on antibiotic usage.

Sixteen pharmacy professionals who had prior experience were recruited as data collectors. Close supervision was made by two principal investigators (MR and MB). Orientation was provided to data collectors in order to familiarize them with the survey objectives, questionnaire, principles of conducting an interview, data collection procedures, standards of practice, procedures for listing the households, and the second as well as third stage sample selection of the households.

Prior to the main fieldwork, the questionnaire was pre-tested on five different clusters, which were not included in the main survey. These blocks are found in two local administrations of Asmara. Twenty-five households were interviewed from each selected block. The pre-test aided in assessing accuracy of translation, ability of the questions to elicit appropriate information, and ability of enumerators to administer the questionnaire. Moreover, it was helpful in estimating the time required to complete the questionnaire. The questionnaire was finally modified based on the results of the pre-test.

Households were sampled with the assistance of the administration office after listing them in selected blocks. When eligible respondents were absent from their homes, at least three visits were made to increase the opportunity of participation in the survey. If the selected candidate was found to be unavailable in a successive of three to four attempts, it was considered as a 'no response'.

Outcome measures

The primary outcome measures were knowledge, attitude and practice of antibiotics and ABR in the urban setting of Eritrea. The secondary outcome measure was the determinants of knowledge, attitude and practice of antibiotics and ABR.

Data analysis

Data was double entered using Census and Survey processing system (CSPro, Version 7.0) software package and exported to statistical package for social sciences (SPSS) Version 23. It was summarized by using weighted percentages and counts. Cross-tabulations and further analysis were also computed whenever relevant.

Kolmogorov-Smirnov test was used to check on the normality of the knowledge and attitude scores. Frequencies, percentages, mean (with standard deviation), median (with interquartile range) were used to describe the data, as appropriate. After using independent samples t-test and analysis of variance (ANOVA) at bivariate level of analysis, factorial analysis was employed to assess the predictors of knowledge and attitude at multivariable level. To explore the association between the inappropriate practice of antibiotic and the categorical demographic characteristics, chi-square test was performed and to control potential confounders, variables that were found to have a p-value less than 0.05 were subjected to multivariable analysis using logistic regression. In this study, *p*-value less than 0.05, in all the analyses, is considered as significant.

Operational definition

Inappropriate practice: Refers to the act of self-medication with antibiotics and/or discontinuation of a regimen of antibiotics. It was determined by assessing whether the last used antibiotics were prescribed by an authorized health professional and/or those who used antibiotics interrupted their treatment regimen before completing the full course.

RESULTS

Demographic characteristics of the study participants

A total of 2542 individuals were selected for the survey. Among the selected individuals, 2,477 were successfully interviewed; making an overall response of 97.44%. The demographic characteristics of the respondents are summarized in table 1. The unweighted numbers reflect the actual observations at the time of the survey, whereas the weighted numbers reflect figures that have been adjusted by the probability of selection of the respondents (Table 1).

Table 1: Distribution of the study population, 18 years and above, on the knowledge, attitude and practice survey of antibiotics and antibiotic resistance by background characteristics, 2019, Eritrea.

Background Characteristics		Weighted Percent	Weighted Number	Unweighted Number
Age				
	24 or less	18.2	451	433
	25 to 34	25.9	643	644
	35 to 44	22.3	552	567
	45 to 54	15.0	372	396
	55 and above	18.5	459	437
Sex				
	Male	24.7	611	605
	Female	74.7	1851	1857
	Missing	0.6	15	15
Religion				
	Christian	77.4	1918	1749
	Moslem	22.5	558	726
	Other	0.1	2	2
Zone				
	Anseba	8.4	209	352
	Debub	15.9	393	410
	Gash Barka	12.1	301	397
	Maekel	55.7	1380	865
	SKB	6.3	155	322
	DKB	1.6	39	131
Educational Level				
	Illiterate	12.0	298	342
	Elementary	15.9	394	452
	Junior	18.6	462	510
	Secondary	35.7	884	801
	Higher	17.1	425	358
	Missing	0.6	15	14
Household Size				
	One	4.4	108	104
	Two to three	22.0	545	533

	Four or more	73.6	1824	1840
Occupation				
	Governmental	22.8	566	529
	Private employee	4.9	121	115
	House wife	38.3	949	980
	Self employed	8.2	202	209
	Unemployed	14.8	366	361
	Student	7.2	179	166
	Farmer/Fisher	2.2	55	77
	Other*	1.2	30	33
	Missing	0.4	10	7
Total		100	2477	2477

*SKB: Semenawi Keih Bahri, DKB: Debubawi Keih Bahri, * Day laborer, soldier, sheik/priest etc*

Awareness, knowledge and attitude on antibiotics and ABR

Based on participants' response, 73.3% and 39% of the study population were aware of the term 'antibiotic' and 'antibiotic resistance' respectively. The sources of information about antibiotics and ABR were mainly from health facilities (39.6%), television (31.5%) and other people (10.1%).

Of the list of medicines provided to assess distinguishing antibiotics from non-antibiotics, 59.4% of the study population correctly identified penicillin while only 44.8% and 11.9% correctly identified cotrimoxazole and ciprofloxacin respectively. Besides, Ibuprofen, ORS and paracetamol were correctly identified as non-antibiotics by 58.5%, 60.7%, and 70.6% of the population respectively.

Less than half (36.6 - 49.5%) of the study population correctly reported the indication of antibiotics for common illnesses. Majority of them reported that antibiotics can be used to treat viral infection (63.4%), watery diarrhea (61.8%), common cold (58.9%), dry cough (54.2%) and dengue fever (50.5%). Sixty-one per cent of the study population also reported that antibiotics are not indicated for tuberculosis. Correct knowledge on when to stop taking antibiotics once they had begun treatment was in the majority (83.3%) of the study population.

Over three-fourth (78.2%) of the study population correctly reported that ABR is an issue that could affect them and their family and about two-third (63.6%) correctly answered the definition of ABR. The proportion of the study population who knew that bacteria resistant to antibiotics can spread from person to person and those who reported that ABR is an issue in other countries but not in Eritrea was about 59% in both cases.

The overall mean knowledge score on antibiotics and ABR was found to be 10.36/20 (SD= 3.51, min=0 and max=20). At bivariate level, males, Christians, those who were aged between 25 and 54 years, those who had higher educational level, those having big family size and who were government employees were more likely to have better knowledge score. Besides, the study population residing in Maekel and Anseba zones had better knowledge score on antibiotics and ABR compared to those living in other Zones (Supplementary file 4). At multivariable level, age (p<0.001), religion (p=0.003), educational level (p<0.001), family size (p=0.015), occupation (p<0.001), and zone (p<0.001) maintained their association with knowledge score (Table 2). Educational level has the largest partial eta squared (6.8%), showing its prime role in prediction of the knowledge score (Table 2).

A positive attitude to the majority of the attitude items (82- 92.7%) was reported (Table 3). However, a positive attitude towards appropriate disposal of antibiotics was documented in less than 50% of the study population (Table 3). The overall mean attitude score was 22.34/30 (SD= 3.59, minimum=6 and maximum=30). At bivariate level, males, those aged between 25 and 54 years, those who had higher educational level, government employees and study population residing in Maekel and Anseba zones had better attitude score compared to their counterparts (Supplementary file 5). At the multivariable level, age (p=0.001), gender (p=0.001), educational level (p<0.001), occupation (p=0.003) and zone (p<0.001) maintained their significance as predictors of attitude score. Zone has the largest explanatory (partial eta squared=3.8%) capability for the attitude towards antibiotics (Table 2). Additionally, the distribution of literacy with the significant determinants of knowledge and attitude scores are summarized in a supplementary material (Supplementary file 6).

Table 2: Predictors of knowledge and attitude towards antibiotics and ABR at multivariable level, Eritrea, 2019.

	Knowledge			
Predictor	F	p-value	Partial Eta Squared	Observed Power
Age	28.5	<0.001	0.04	1.000
Gender	0.4	0.536	<0.001	0.095
Religion	9	0.003	0.003	0.849
Educational Level	49.7	<0.001	0.068	1.000

Family size	4.2	0.015	0.003	0.738
Occupation	6.3	<0.001	0.014	0.999
Zone	18.4	<0.001	0.033	1.000
	Attitude			
Predictor	F	p-value	Partial Eta Squared	Observed Power
Age	4.5	0.001	0.007	0.944
Gender	11.6	0.001	0.004	0.926
Educational Level	22	<0.001	0.031	1.000
Occupation	3.4	0.003	0.007	0.942
Zone	21.6	<0.001	0.038	1.000

Table 3: Agree/strongly agree response on the attitude of antibiotics and antibiotic resistance (ABR), Eritrea, 2019 (N=2477)

Attitude questions on antibiotics and ABR	% (95% CI)
Hand washing decreases ABR	92.7 (91.6-94.1)
Taking antibiotics when it is not required can facilitate ABR	89.7 (88.2-91.1)
You have a role to fight ABR	85.8 (84.5-87.8)
It is not okay to share antibiotics with others	90.1 (89.4-91.6)
We cannot use antibiotics without prescription	88 (87.5-89.8)
Farmers should not give antibiotics without consulting veterinarian	82.1 (80.9-83.7)
It is not okay to keep leftover antibiotics and use them later	82 (80.7-83.5)
Leftover antibiotics should not be disposed with regular garbage	46 (45.4-49.1)
Leftover antibiotics should not be disposed at toilets	35.7 (34.3-37.9)

Practice on usage of antibiotics

Majority (84.5%) of the study population had used antibiotics at least once in their life time and 55% had history of intake of antibiotics in the last one year and 12.3% in the last one month prior to commencement of this study. Of those who ever used antibiotics (n=2407), 88.1% reported that their last intake of antibiotic (s) was prescribed by an authorized healthcare professional. Non-seriousness of the disease (39.0%), need to get quick relief (33.9%), previous own

successful experiences (16.1%), having no time to visit a health facility (15.0%) and long queues existing in health facilities (14%) were the top five reasons reported for self-medication with antibiotics. For those who used antibiotics without prescription, the main sources of their last course of antibiotics were drug retail outlets (83.6%) (Figure 1).

One fifth (18.8%) of those who had ever used antibiotics interrupted their regimen before completing the full course. The main reason for interruption of antibiotics was improved illness condition (63.4%) (Figure 2). About 3% of the study population reported that they had used antibiotics on their own at least once, though they were advised by healthcare professionals not to do so.

Overall, inappropriate practice of antibiotics (use of antibiotics without prescription and/or discontinuation of prescribed antibiotics before completing the full course) was reported in 23.8% of the study population. The chi-square analyses found that age ($p<0.001$), gender ($p=0.01$), educational level ($p<0.001$), occupation ($p<0.001$) and zonal location ($p<0.001$) were the significant associates of inappropriate practice of antibiotics. The independent sample t- test showed that the mean attitude score of those in inappropriate practice (M=21.86, SD=3.97) was significantly lower than those in safe practice (M=22.51, SD=3.45). On multivariable level, those who were young - 24 years or less (AOR=1.61, 95% CI: 1.08 - 2.41), males (AOR=1.48, 95% CI: 1.14 - 1.91), those who had higher level of education (AOR=1.76, 95% CI: 1.08 - 2.88) and those with higher attitude score (AOR=0.95, 95% CI: 0.92 - 0.97) were more likely to involve in inappropriate practice of antibiotics (Table 4).

Table 4: Predictors of inappropriate practice of antibiotics across the categories of demographic characteristics and attitude score at multivariable level, Eritrea, 2019.

Background characteristic	Multivariable analysis		
	AOR	95% CI	*p*-value
Age			0.035
24 or less	1.61	1.08 - 2.41	
25 to 34	1.26	0.89 - 1.79	
35 to 44	1.05	0.74 - 1.48	
45 to 54	0.89	0.61 - 1.29	
55 or above	*Ref.*		
Gender			
Male	1.48	1.14 - 1.91	0.003
Female	*Ref.*		
Educational Level			0.103

Illiterate	*Ref.*		
Elementary	1.02	0.66 - 1.57	
Junior	1.19	0.77 - 1.83	
Secondary	1.33	0.86 - 2.03	
Higher	1.76	1.08 - 2.88	
Occupation			0.183
Governmental	Ref.		
Private employee	1.14	0.71 - 1.85	
House wife	1.33	0.97 - 1.83	
Self-employed	1.53	1.03 - 2.27	
Unemployed	1.16	0.80 - 1.67	
Student	1.43	0.93 - 2.19	
Farmer/Fisher	1.49	0.71 - 3.15	
Other*	0.45	0.13 - 1.52	
Zone			0.069
Anseba	0.48	0.21 - 1.09	
Debub	0.73	0.34 - 1.59	
Gash Barka	0.70	0.32 - 1.57	
Maekel	0.89	0.42 - 1.88	
SKB	0.82	0.36 - 1.89	
DKB	*Ref.*		
Attitude score	0.95	0.92 - 0.97	<0.001

**Day laborer, soldier, sheik/priest etc*

A total of 1473 of the study population had animals and about 14% reported that they have treated their animals with antibiotics at least once. Of those who used antibiotics for their animals, 62% purchased at least once in the last year, prior to the study period. The commonly used antibiotics for animals were amoxicillin (44.1%), oxytetracycline (36.2%) and penicillin (16.3%). About 51% of antibiotics used for animals were obtained from veterinarians whereas the rest were mainly from pharmacy retail outlets (20.8%), family/friends (14.4%) and open markets (14.3%) (Figure 3).

DISCUSSION

This nation-wide urban population-based survey revealed a significant inappropriate practice of antibiotics in Eritrea. One in five of the study population, who had ever used antibiotics, reported that their last intake of antibiotic (s) was interrupted for many reasons. The discontinuation of antibiotics when a consumer felt better was the most frequently reported reason. This reflects

lack of awareness on the appropriate use of antibiotics and the risk of ABR. The majority of the antibiotics most recently consumed by the study population were reported to have been prescribed by qualified healthcare professionals. This is encouraging and the nation-wide, massive antibiotic awareness week campaigns conducted in the last three years, prior to the study, might have had positive contributions. However, due to the lack of a national baseline data, the authors could not come up with a definitive conclusion regarding the effectiveness of the previously conducted campaigns.

The disease condition being non-serious, intention to get quick relief, previous successful experience, shortage of time to visit health facilities and long queues were the main triggering factors reported for self-medication with antibiotics. The first three reasons mentioned above for self-medication with antibiotics reflect lack of awareness on the risks of inappropriate use of antibiotics. In Eritrea, guided by 'health for all policy' and 'social justice', healthcare services are provided at a highly subsidized or nominal cost through public health facilities. To further improve patients' satisfaction, access to health services, and health seeking behavior, the existing healthcare delivery services need to be optimized. Moreover, the annual antibiotic awareness week campaign should be augmented by additional continuous and regular health promotional activities.

In this study, drug retail outlets were reported as the main sources for the sales of antibiotics without prescription. A recently conducted study also revealed an alarming picture; 87% of retail outlets found in Eritrea were dispensing antibiotics without prescription [10] which requires immediate attention from regulators and policy makers. Continued refresher courses on the appropriate use of antibiotics and ABR as well as further enforcement of regulations would have an impact in bridging these gaps. Cognizant of this, the National Medicines and Food Administration of the Ministry of Health developed medicines schedule in 2019 and, all antibiotics are put under the category of 'prescription only medicine'. To ensure implementation and adherence to the scheduling terms, the National Medicines and Food Administration is recommended to conduct strict and continuous inspection on drug retail outlets.

Use of antibiotics without prescription in this study was more or less consistent with findings of similar studies conducted in European countries, where it was reported to occur in an average proportion of 7% (ranging from 0% to 20%) [28]. It was, however, much lower than that reported

in Italy [29], Jordan [30 31], United Arab Emirates [32], Palestine [33], Lebanon [34], Iraq [35], Indonesia [36], Yemen [37], Saudi Arabia [38], Haiti [39], Kuwait [40], and Ethiopia [41 42], where proportions ranged between 31% and 79%. The variation in results, however, could be due to differences in study designs, study area, study population, type of questions and level of awareness of the study population. Following the WHO recommendation (2015) for all member states to start annual awareness raising programs on AMR, Eritrea has started to implement it since 2016. This study was conducted after a few years of massive public campaigns and might have influenced the current findings. It is also possible that in other countries that have made similar initiatives, the existing profile might have been influenced in the same way despite no current studies are available.

Factors such as young age (24 years or less), male sex, high level of education and poor attitude score were identified as determinants of inappropriate practice of antibiotics. It is unknown why those who had higher level of education and those who were young (relatively with greater educational opportunities) were more involved in the inappropriate practice of antibiotics. This might to some extent be explained by the fact that knowing more or being educated predisposes people to a tendency to take self-made decisions more casually with the assumption that they have knowledge. Qualitative studies are required to further identify the determinants of inappropriate practice of antibiotics.

In this study, an appreciably high mean attitude score towards antibiotics and ABR was reported. It is, however, important to note that the poor attitude reported on the appropriate disposal of leftover antibiotics requires immediate attention from policy makers. Studies on awareness and disposal practices of unused and expired medicines by consumers in India and Nigeria also reported that improper practices such as the disposal of medicines in domestic trash, toilets and sinks was prevalent [43 44].

Unlike the relatively good attitude score, the mean knowledge score of the study population on antibiotics and ABR was not satisfactory. This study revealed that the majority of the study population had no clear picture on what an antibiotic is and were unable to recognize, by name, the most commonly used antibiotics (penicillin, cotrimoxazole and ciprofloxacin) in the country. Categorizing ibuprofen, ORS and paracetamol as antibiotics by a large number of the study population was another concern. A significant proportion of the study population also had the

misunderstanding that antibiotics could treat viral infections like common cold and acute watery diarrhea. Hence, continued awareness raising programs should target such misconceptions and familiarize the public with the commonly used antibiotics, their proper indications and the potential for resistance. The assumption that ABR is a threat elsewhere but not in Eritrea, as reported in this study, reflects how oblivious people were to the issue of ABR and this may limit the public from taking appropriate actions.

In this study, those who were aged between 25 and 54 years, had higher educational level, were government employees, or residing in Maekel and Anseba zones were significantly associated with higher knowledge and attitude scores. Literacy to a larger extent might explain, among others, the observed good knowledge and attitude scores in relation to the above predictors as all these categories had better educational levels (Supplementary file 6). However, more data is required to make accurate deductions with regard to these predictors. It is also important to note that the association observed with the above-mentioned variables do not seem to be clinically meaningful as a small difference in results could give statistically significant difference, and thus, readers should cautiously interpret the results. This emphasizes the need for extensive awareness raising programs for those who are illiterate and having lower level of education.

Regarding the use of antibiotics to treat animals, oxytetracycline, amoxicillin and penicillin were the most frequently reported ones. About half of the antibiotics used in animals were supplied by non-veterinarians such as drug retail outlets and open markets reflecting poor regulation of antibiotics in animal health.

Because parasites and infections do not respect borders, combating ABR has since long ago been a global agenda. A problem identified in one country could have direct or indirect implication on the containment of ABR by other countries. The significance of this nationwide survey and the results it comes up with are all expected to be of a particular interest for countries with similar socioeconomic statuses as Eritrea. Many of these countries share the common problem of poor quality, inequitable, overstretched, unregulated and poorly accessible health services which could trigger the general public to be involved in inappropriate practice of antibiotics. Moreover, they lack the systems to control antibiotic consumption and the initiative to tackle the issue of resistance. If Eritrea's profile with regard to the prevalence of inappropriate practices such as self-medication with antibiotics has been relatively good while there is a long way to go to

improve the healthcare infrastructure, it is not hard to imagine the progress the country could assume if the existing policies such as the national action plan on AMR and regulations such as medicines scheduling are enforced.

This is among the few globally reported nation-wide population-based surveys that measure knowledge, attitude and practice of antibiotics and ABR. The study employed rigorous data quality and management approaches and had a high percentage of response. On the other hand, one of the main limitations of this study was that the results were self-reported, and thus, findings might be under- or over-estimated. This could introduce information or recall bias. Additionally, though efforts were made to provide an equal chance of selection for every household member, there might be selection bias as about three-fourth of the respondents were found to be females. The sex-imbalance might be explained by the fact that the information regarding family size and available members during data collection was gathered from the present household members and, no verification was made using an administrative list. Moreover, the reliability and validity of the scales for knowledge and attitude on antibiotics usage were not checked using statistical tools.

Conclusion

The inappropriate practice of antibiotics in Eritrea was prevalent and the young age, male sex, higher level of education and poor attitude score were identified as the determinants of inappropriate practices. The inability of a high proportion of the study population to distinguish antibiotics from other medicines and the reported misunderstanding that viral infections can be treated with antibiotics indicates limited knowledge on antibiotics and ABR. Continuous awareness raising programs on the rational use of antibiotics (mainly on the risks of self-medication, treatment interruption, and use of antibiotics for viral infections) and familiarizing the public with the commonly used antibiotics are recommended. As drug retail outlets were identified to be the main sources for the supply of antibiotics without prescription, both in humans and animals, enforcement of medicines schedule and strengthening of regulatory inspections is vital. Besides, the huge gap in attitude towards appropriate disposal of antibiotics requires immediate attention from policy makers and the establishment of an appropriate disposal system of leftover antibiotics for the community. Last but not least, it is high time to

expedite the implementation of the strategies stipulated under the national action plan on AMR which was released in February 2021.

DECLARATIONS

Ethics approval and informed consent

Ethical approval to conduct the study was obtained from the Ministry of Health, Eritrea and further approval was also obtained from the Ministry of Local Government. Besides, informed consent was obtained from all study participants to take part in the study.

Patient consent for publication: Not required.

Conflict of interests

The authors declare that they have no competing interests.

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Author contributions

The idea was conceived by MR and IB and designed by all authors (MB, MD, MR, AK, AA, YF, IB, SK, JN and EHT). Data was collected by MD, AK, AA and YF and supervised by MR and MB. EHT edited and analyzed the collected data and all the co-authors participated in the interpretation of the results. The manuscript was drafted by MB, MR and EHT and critically reviewed and edited by all of the authors. Finally, all the co-authors agreed that the article be published in an international journal and to take responsibility and be accountable for its content.

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Availability of data

All data related to the study are included in the manuscript. The complete dataset used for this study can be obtained from the corresponding author upon request.

Acronyms

ABR: Antibiotic Resistance; AMR: Antimicrobial resistance; DKB: Debubawi Keih Bahri; SKB: Semenawi Keih Bahri; WHO: World Health Organization.

Patient and public involvement: Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication: Not required.

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Figure 1: Source of antibiotics used without prescription among urban residents, Eritrea, 2019 (n=242)

Figure 2: Reasons for stopping the intake of antibiotics among urban residents, Eritrea, 2019 (n=357)

Figure 3: Source of antibiotics for animals among urban residents, Eritrea, 2019 (n=245)

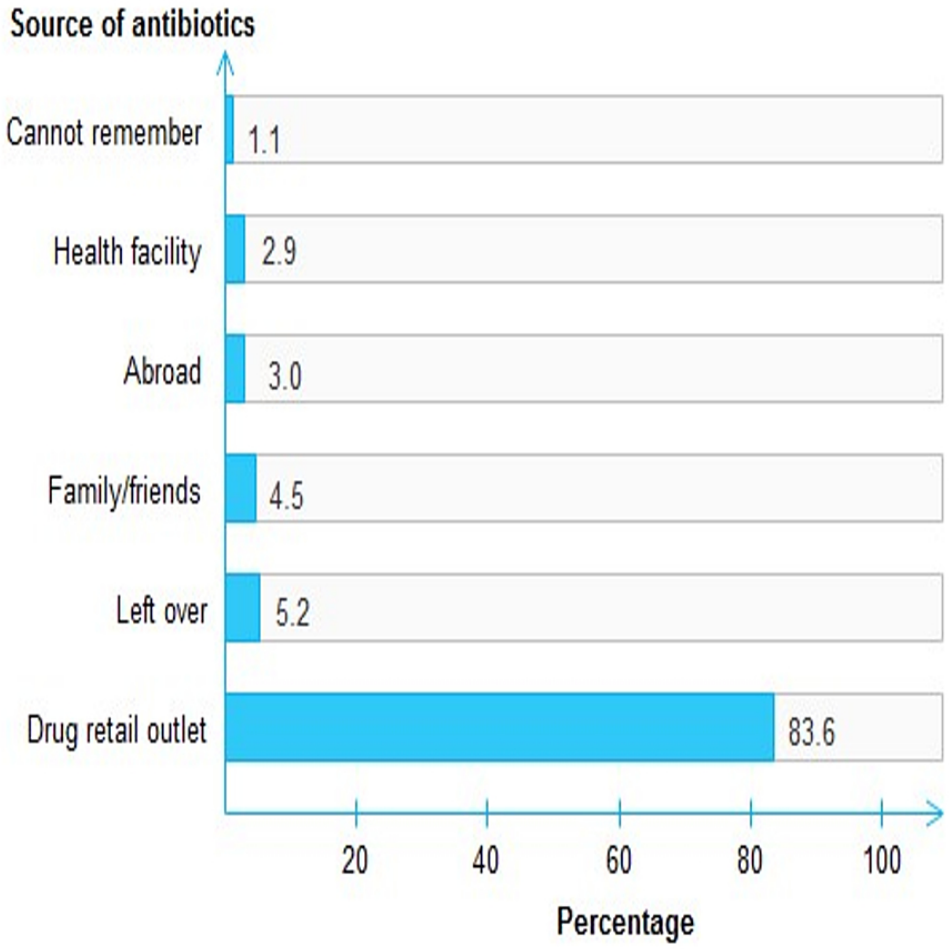

Figure 1: Source of antibiotics used without prescription among urban residents, Eritrea, 2019 (n=242)

38x38mm (600 x 600 DPI)

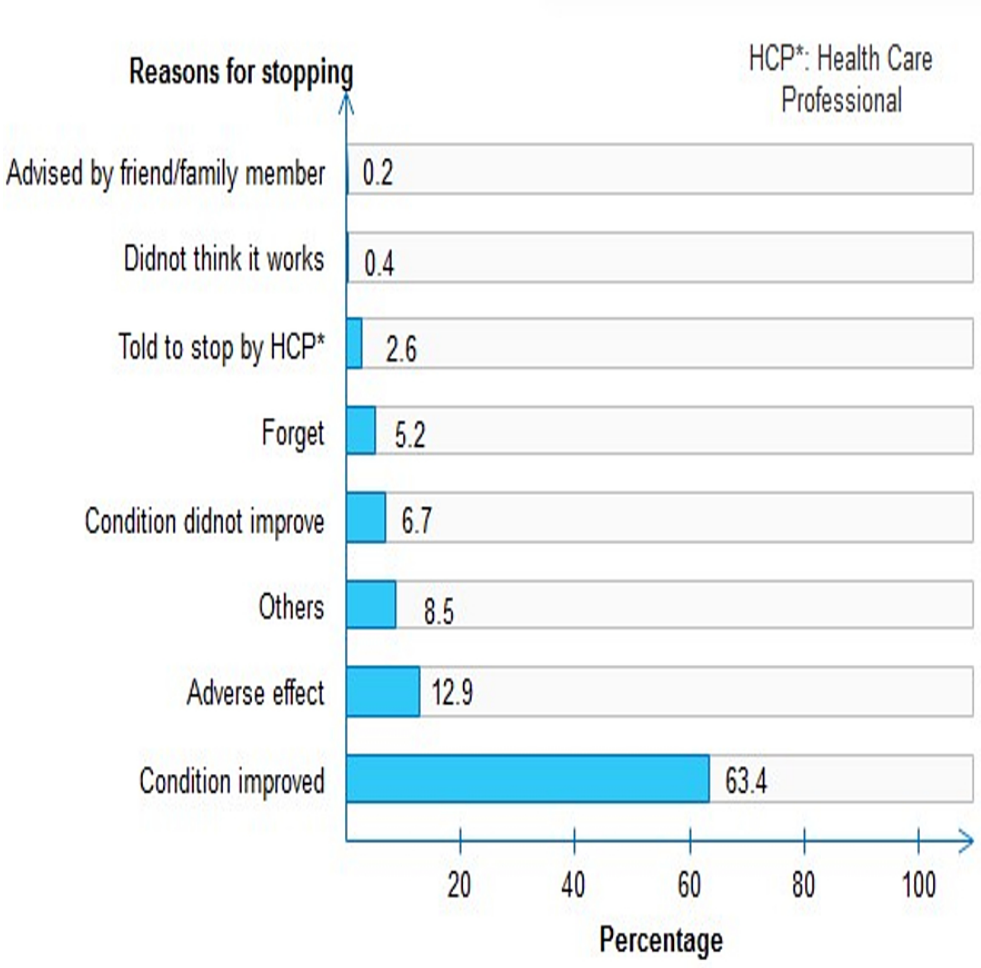

Figure 2: Reasons for stopping the intake of antibiotics among urban residents, Eritrea, 2019 (n=357)

38x38mm (600 x 600 DPI)

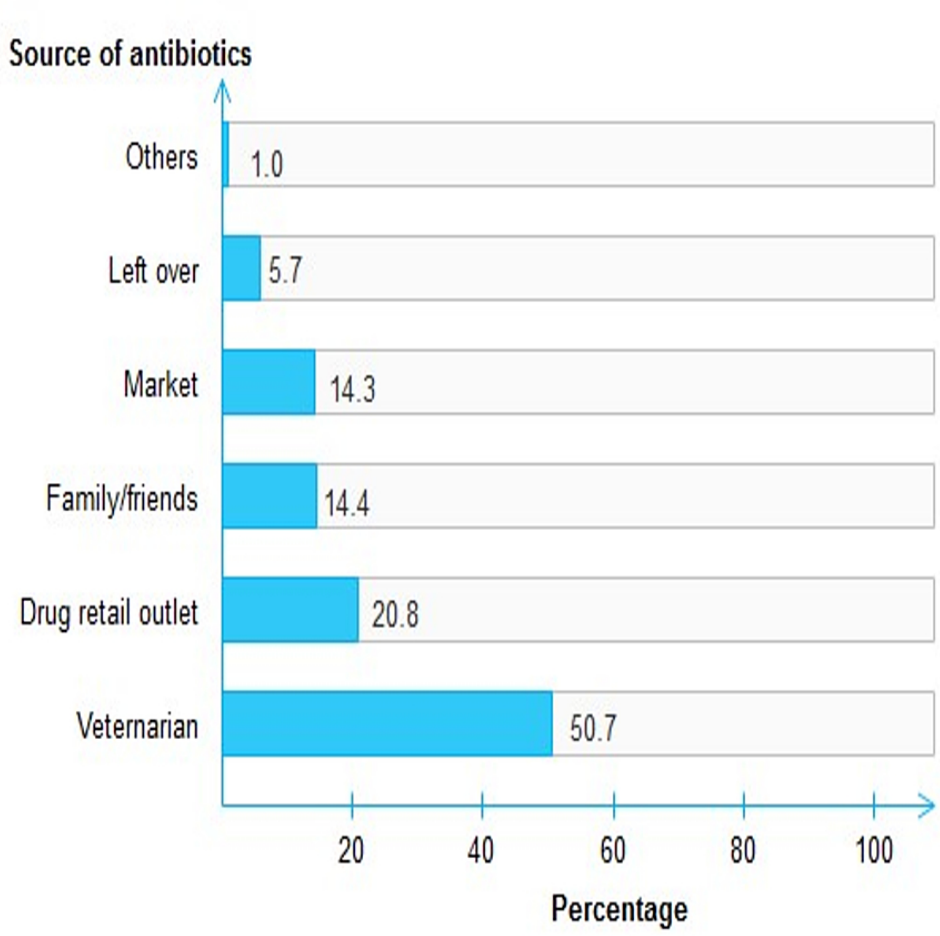

Figure 3: Source of antibiotics for animals among urban residents, Eritrea, 2019 (n=245)

38x38mm (600 x 600 DPI)

Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey

Mulugeta Russom[1], Merhawi Bahta[1*], Merhawi Debesai[1], Iyassu Bahta[1], Abrahalei Kessete[1], Aziza Afendi[1], Yodit Fitsum[1], Josephina Nambozi[2], Soliana Kidane[2], Eyasu H. Tesfamariam[3]

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Supplementary file 1: Number of households in the urban places of Eritrea (July 2019)

Zone	City/Town	Number of Households
Gash Barka	Akordat	3,822
	Barentu	10,935
	Tessenei	15,205
	Subtotal	**29,962**
Debub	Mendefera	8,023
	Adiquala	3,419
	Dekemhare	9,769
	AdiKeih	5,335
	Senafe	6,574
	Subtotal	**33,120**
SKB	Ghindae	5,832
	Massawa	9,512
	Subtotal	**15,344**
Anseba	Keren	19,343
	Subtotal	**19,346**
DKB	Assab	3,106
	Subtotal	**3,106**
Maekel	Asmara	116,146
	Subtotal	**116,146**
Total		**217,024**

SKB: Semienawi Keih Barhri; DKB: Debubawi Keih Barhri; HH: Household

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Supplementary file 2: Brief description of the sampling technique and sample size, Eritrea, 2019

Sample size

Sample size was computed mainly for an estimation of proportion of safe practice taking 95% confidence level, 0.05 precision; using the formula [23]: $n \geq \frac{NV1.96^2}{V*1.96^2+(N-1)*0.05^2}$, where $V=\frac{SD^2}{Pooled\ proportion^2}$=0.5 and N=size of the target population. Upon consideration of the aforementioned parameters, the initial sample size was 1525. After an adjustment of non-response percent (10%) and design effect (deff=1.5), the final sample size was 2542 individuals.

Sampling Technique

Local data, conducted by Ateshim et al. 2019 [11] and other unpublished studies, implies that the awareness, knowledge, attitude, and practice towards antibiotics and ABR varies across the zones in Eritrea. Hence, it was presumed that the sample design that led to the selection of a legible person was a stratified three-stage cluster sample. During the first stage of the sampling, a total of 102 primary sampling units referred to as blocks (having households ranging from 200 to 1000) were selected from the 13 urban sites. During the second stage, 25 households were selected from each block taking into consideration the design effect, inter-cluster correlation, economic and administrative issues [24]. Finally, samples were selected from each household. To bring about reliable zonal and overall estimates, square root allocation of households was undertaken.

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Supplementary file 3: Questionnaire on Knowledge, Attitude and Practice of Antibiotics and their Determinants in Eritrea: Urban Population-based Survey, 2019

Part I: Identification Particulars

Zoba				
Subzoba				
City/Town				
Kebabi				
Respondent numbe				

Interviewer Visits

	1	2	3	Final Visit
Date				Day / Month / Year (2019)
Interviewer's Name				Int. No.
Result*				Result*
Next visit: Date				Total number of visits
Time				

*Result codes:

Completed
Not completed
Not willing
Other _____ (Specify)

Total persons In household

Total eligible persons (≥18)

Supervisor		Field editor		Keyed by	
Name	Number	Name	Number	Name	Number

Part II: Demographic Information

No.	Indicators	Coding categories	Skip
201	Age (in completed years)	☐☐	
202	Sex	Male ..... 1 Female 2	
203	Ethnicity	Tigrina ..... 1 Afar ..... 2 Tigre ..... 3 Saho ..... 4 Rashida ..... 5 Kunama ..... 6 Blien ..... 7 Hidarb ..... 8 Nara ..... 9 Other (please specify) _____ 10	
204	Religion	Christian ..... 1 Muslim ..... 2 Other (please specify) _____ 3	
205	Level of education (Highest level of education)	Illiterate ..... 1 Primary school ..... 2 Middle school ..... 3 Secondary school ..... 4 Higher education 5	
206	Main occupation	Farmer ..... 1 Government employee ..... 2 Private employee ..... 3 Housewife ..... 4 Self-employed ..... 5 Unemployed ..... 6 Student ..... 7 Fisher man ..... 8 Other (please specify) _____ 9	

Part III: Knowledge

No.	Questions	Coding categories	Skip
301	Have you ever heard about antibiotics?	Yes . . . . . 1 →	303
		No 2	
302	Have you ever heard of any one of the following medications? ASK FOR EACH MEDICATION.	Amoxicillin . . . . . A Tetracycline . . . . . B Oxytetracycline . . . . . C I haven't heard all of them . . . . . D →	**END**
303	Which of the following do you think are antibiotics? ASK FOR EACH MEDICATION. If the response in 201 is No and heard of any one of the examples of antibiotics, explain that the term Antibiotics refers to these drugs before continuing to 204 .	Y N DK Ibuprofen . . . . . 1 2 3 Tetracycline . . . . . 1 2 3 Bactrium . . . . . 1 2 3 ORS . . . . . 1 2 3 Amoxicillin . . . . . 1 2 3 Paracetamol . . . . . 1 2 3 Ciprofloxacin . . . . . 1 2 3 Penicillin 1 2 3	
304	Which of these diseases do you think are treated with antibiotics? ASK FOR EACH ILLNESS.	Common cold . . . . . 1 2 3 Watery diarrhea . . . . . 1 2 3 TB . . . . . 1 2 3 Dengue fever . . . . . 1 2 3 Pneumonia . . . . . 1 2 3 Dry cough 1 2 3	
305	Do antibiotics treat viral infections?	Yes . . . . . 1 No . . . . . 2 Don't know 3	
306	When do you think you should stop taking antibiotics once you've begun treatment? MULTIPLE RESPONSES ARE POSSIBLE. PROBE: Are there any other reasons	When I feel better . . . . . A When I do not see improvements . . . . . B When I encounter adverse drug reactions C It should not be stopped . . . . . D Don't know . . . . . E	
307	Have you ever heard of the term antibiotic resistance (ABR)?	Yes . . . . . 1 No 2	
308	Antibiotic resistance occurs when your becomes resistant to antibiotics and they no work.	Yes . . . . . 1 No . . . . . 2 Don't know 3	**404**
309	Where did you hear about antibiotic resistanc MULTIPLE RESPONSES ARE POSSIBL PROBE: Are there any other sources	Health facility . . . . . A Pharmacy . . . . . B Radio . . . . . C TV . . . . . D Newspaper . . . . . E Campaign/Seminar . . . . . F Other (please specify) _____ G	

310	Antibiotic resistance is an issue that could affect me or my family.	Yes . . . . . 1 No . . . . . 2 Don't know 3	
311	Antibiotic resistance is an issue in other countries but not here.	Yes . . . . . 1 No . . . . . 2 Don't know 3	
312	Bacteria which are resistant to antibiotics can spread from person to person.	Yes . . . . . 1 No . . . . . 2 Don't know 3	

Part IV: Attitude

No.	Questions		Skip
401	Proper handwashing play a role in ABR.	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
402	Taking antibiotics when it is not required can facilitate ABR.	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
403	You have a role to fight ABR	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
404	We can use antibiotics without prescription	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
405	It is okay to share antibiotics with family members or friends for similar illness	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
406	It is okay to keep leftover antibiotics and use them later	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	

407	Farmers can give antibiotic without consulting veterinarian	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
408	Leftover antibiotics should be disposed with regular garbage	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	
409	Leftover antibiotics should be disposed at toilets	Strongly disagree . . . . . 1 Disagree . . . . . 2 Neutral . . . . . 3 Agree . . . . . 4 Strongly agree 5	

Part V: Practice

No.	Questions	Coding categories	Skip
501	Have you ever used antibiotics?	Yes . . . . . 1 No . . . . . 2 Don't remember 3	**509**
502	When was the last time you took antibiotics?	Now . . . . . 1 Last month . . . . . 2 Last six months . . . . . 3 Last year . . . . . 4 More than a year ago . . . . . 5 Don't remember 6	
503	Source of the last course of antibiotic MULTIPLE RESPONSES ARE POSSIBLE.	Health facility . . . . . A Drug retail outlet . . . . . B Friend or family member . . . . . C Saved up from a previous time . . . . . D From abroad . . . . . E Don't remember . . . . . F	
504	On that occasion, did you get a prescription for the antibiotics from a doctor/nurse?	Yes . . . . . 1 Don't remember . . . . . 2 No 3	**506**
505	What was (were) your reason(s) of self-medication with antibiotics? MULTIPLE RESPONSES ARE POSSIBLE.	Long queue A Had no time to visit a health facility . . . B To get a quick relief . . . . . C Disease was not serious . . . . . D To save expenses . . . . . E Own previous successful experience . . . F Other (please specify) _____ G	

506	Did you ever stop taking antibiotics before completing the full course?	Yes . . . . . 1 No . . . . . 2 Don't remember 3	**508**
507	Why did you stop taking the antibiotics?	Condition didn't improve . . . . . 1 Condition improved . . . . . 2 Due to adverse effects . . . . . 3 Advised by a friend or family member 4 I didn't think it works . . . . . 5 Told to stop by a healthcare profession . 6 Other (please specify) _____ 7	
508	Ever used antibiotics on your own, though health care professionals advice you not to take	Yes . . . . . 1 No . . . . . 2 Don't remember 3	
509	Have you ever given antibiotics to your animals?	Yes . . . . . 1 No . . . . . 2 Don't remember . . . . . 3 Don't have an animal 4	**END**
510	Which antibiotic did you use for your animal? ASK FOR EACH MEDICATION.	Amoxicillin . . . . . A Erythromycin . . . . . B Oxytetracycline . . . . . C Penicillin . . . . . D Tylosin . . . . . E Didn't use all of these antibiotics . . . . . F Other (please specify) _____ G	
511	Source of the antibiotics	Bought from the market . . . . . A Bought from Drug retail outlet . . . . . B Veterenarian . . . . . C Friends/family membe . . . . . D Other (please specify) _____ E	
512	How many times did you buy antibiotics for your animal in the last one year ?	Once . . . . . 1 Twice . . . . . 2 Three times . . . . . 3 More than three times . . . . . 4 Never 5	

Y: Yes; N;No; DK: Don't Know

END OF INTERVIEW

INTERVIEWER'S OBSERVATIONS

TO BE FILLED IN AFTER COMPLETING THE INTERVIEW
COMMENTS ABOUT THE INTERVIEW
COMMENTS ON SPECIFIC QUESTIONS
ANY OTHER COMMENTS
SUPERVISOR'S OBSERVATIONS
EDITOR'S OBSERVATIONS

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Supplementary file 4: Comparison of knowledge scores across the categories of demographic characteristics at bivariate level, Eritrea, 2019

Characteristics	Mean (SD)	F/t Value	p-value	p-value trend (Type of trend)	Post Hoc Test	
					Pair wise comparison	Group wise comparison
Age						
24 or less **A**	9.57 (3.24)					
25 to 34 **B**	10.53 (3.25)					
35 to 44 **C**	11.02 (3.36)	16.03**	<0.0001	<0.0001 (Quadratic)	A<B, A<C, A<D, A=E, B=C=D, B>E, C>E, D>E	Group 1: A and E Group 2: B, C, and D
45 to 54 **D**	10.77 (3.70)					
55 and above **E**	9.73 (3.91)					
Gender						
Male	10.98 (3.61)	5.08	<0.0001	-	M>F	-
Female	10.15 (3.44)					
Religion						
Christian	10.57 (3.53)	5.93	<0.0001	-	C>M	-
Muslim	9.60 (3.30)					
Educational Level						
Illiterate	7.99 (3.28)					
Primary	9.49 ((3.38)					Group 1: I Group 2: P and M Group 3: M and S Group 4: H
Middle	10.16 (3.31)	66.78	<0.0001	<0.0001 (Linear)	I<P, I<M, I<S, I<H, P=M, P<S, P<H, M=S, M<H, S<H	
Secondary	10.72 (3.38)					
Higher	11.97 (3.23)					
Family Size						
One	8.84 (4.19)					
Two to three	10.08 (3.45)	12.62	<0.0001	<0.0001 (Linear)	O<T, O<F, T<F	Group 1: O Group 2: T and F
Four or more	10.52 (3.46)					
Occupation						
Governmental	11.76 (3.40)					
Private employee	10.85 (3.57)					
House wife	10.10 (3.27)					
Self-employed	10.13 (3.54)	22.05	<0.0001	-	G=P, G>H, G>Se, G>U, G>St, G>F, G=O, P=H, P=Se, P>U, P=U, P=St, P=O, H=Se, H=U, H=St, H=F, H=O, Se=U, Se=St, Se=F, Se=O, U=St, U=F, U=O, St=F, St=O, F=O	Group 1:F, U, St, O, H and Se, Group 2:U, St, O, H, Se and P Group 3: H, Se, P and G
Unemployed	9.40 (3.67)					
Student	9.54 (3.40)					
Farmer/Fisher	8.71 (3.32)					
Other*	9.62 (3.30)					
Zone						
Anseba	10.53 (3.36)					
Debub	8.85 (3.65)					
Gash Barka	9.54 (3.18)	28.45	<0.0001	-	A>De, A=G, A=M, A=S, A=D, De<M, De=G, De=S, De=D, G<M, G=S, G=D, M>S, M=D,	Group 1: De, S, and G, Group 2: S, G, D and A Group 3: G,D,A and M
Maekel	11.00 (3.39)					
SKB	9.44 (3.51)					
DKB	10.27 (3.09)					

Other: Day laborer, soldier, sheik/priest etc; ** Welch test statistic was used to obtain robust result; SKB: Semenawi Keih Bahri; DKB: Debubawi Keih Bahri*

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Supplementary file 5: Comparison of attitude scores on antibiotics and antibiotic resistance across the categories of demographic characteristics at bivariate level, Eritrea, 2019.

Characteristics	Mean (SD)	F/t Value	p-value	p-value trend (Type of trend)	Post Hoc Test: Pair wise comparison	Post Hoc Test: Group wise comparison
Age						
24 or less **A**	22.10 (3.81)					
25 to 34 **B**	22.50 (3.31)					
35 to 44 **C**	22.25 (3.66)	2.97*	0.019	0.034 (quadratic)	A=B=C=D=E,	Group 1: A, B, C, D and E
45 to 54 **D**	22.80 (3.47)					
55 and above **E**	22.07 (3.76)					
Gender						
Male	23.0 (3.86)	4.92	<0.0001	-	M>F	-
Female	22.13 (3.48)					
Religion						
Christian	22.37 (3.54)	0.7	0.488	-	-	-
Muslim	22.24 (3.80)					
Educational Level						
Illiterate	21.36 (3.64)					
Primary	22.14 (3.46)					
Middle	22.34 (3.65)	10.76	<0.0001	<0.0001 (linear)	I=P, I<M, I<S, I<H, P=M, P=S, P<H, M=S, M<H, S<H	Group 1: I Group 2: P, S and M Group 3:H
Secondary	22.32 (3.52)					
Higher	23.16 (3.62)					
Family Size						
One	21.86 (3.42)					
Two to three	22.25 (3.46)	1.2	0.300	-	-	-
Four or more	22.39 (3.64)					
Occupation						
Governmental	22.93 (3.73)					
Private employee	22.04 (3.32)					
House wife	22.30 (3.51)					
Self-employed	22.62 (3.48)					
Unemployed	21.69 (3.38)					
Student	21.82 (3.85)	4.95	<0.0001	-	G=P, G=H, G=Se, G>U, G=St, G=F, G=O, P=H, P=Se, P=U, P=U, P=St, P=O, H=Se, H=U, H=St, H=F, H=O, Se=U, Se=St, Se=F, Se=O, U=St, U=F, U=O, St=F, St=O, F=O	Group1:F, U, St, O, H, G, and Se
Farmer/Fisher	21.65 (3.92)					
Zone						
Anseba	23.19 (3.43)					
Debub	22.27 (3.35)					
Gash Barka	23.24 (3.73)					
Maekel	22.01 (3.62)	8.87	<0.0001	-	A=De, A=G, A>M, A=S, A=D, De=M, De<G, De=S, De=D, G>M, G=S, G=D, M=S, M=D, S=D	Group 1: A, De, M, S, and D Group 2: A, De, M, S, and G
SKB	22.76 (3.20)					
DKB	21.73 (4.32)					

** Welch test statistic was used to obtain robust result; SKB: Semenawi Keih Bahri; DKB: Debubawi Keih Bahri.*

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Supplementary file 6: Distribution of the significant determinants of knowledge and attitude scores by low educational level

Variables		% low level of education
Age	25 to 54 years	25.0
	> 54 years	63.0
Employment	Government employees	7.5
	Other categories of occupation*	34.2
Family size	2 or more	13.8
	One	61.1
Sex	Males	16.0
	Females	32.0
Religion	Christians	25.6
	Muslims	38.4
Zones	Maekel	10.2
	Anseba	33.8
	Other zones**	43.2

**Other categories of occupation: Private employee, house wife, self-employed, unemployed, student and farmer/fisher;*

***Other zones: Debub, Gash Barka, Semenawi Keih Bahri, Debubawi Keih Bahri*

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5-6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-7*
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	5-6
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	6-7
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	8-9
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8-9
		(b) Indicate number of participants with missing data for each variable of interest	8-9
Outcome data	15*	Report numbers of outcome events or summary measures	NA
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-13

		(*b*) Report category boundaries when continuous variables were categorized	10-13
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	NA
Discussion			
Key results	18	Summarise key results with reference to study objectives	17-18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	13-17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.