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ORIGINAL RESEARCH

Knowledge and Practice for Prevention of Bovine Tuberculosis and Its Derivers Among HIV Positive People in Bahir Dar City Public Hospitals, Ethiopia

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Introduction: Bovine tuberculosis is an important zoonotic disease caused by *Mycobacterium bovis*, known to exist in all parts of the world especially in un-hygienic environments. It has a public health impact and humans acquire the infection from infected animals through consumption of raw or unpasteurized milk and dairy products.

Methods: An Institutional-based quantitative cross-sectional study was conducted from February to April 2020 to assess the knowledge and practice level along with their derivatives of bovine tuberculosis among adult HIV-positive people in Bahir Dar city public hospitals. The data were collected using structured interviewer questionnaire and systematic random sampling was employed to select study subjects. Thus, a total of 435 people living with HIV were considered for this study.

Results: Out of the total 435 participants 51.5% were male and the mean age was 37.6 years. The overall level of good knowledge and practice of HIV-positive persons for bovine TB were 46.2% and 41.1%, respectively. Moreover, education status, religion, cattle holding, and environmental hygiene were statistically significant associations (p < 0.05) with knowledge level. Likewise, education status, age, and marital status were statistically significant associations with the practice level for bovine TB. Education was a key determinant factor affecting both knowledge and practice.

Conclusion: In conclusion, the present study showed that the level of good knowledge and practice of the participant for bovine TB was low. Hence, tailor-made training by medical and veterinary professionals on the identified risk factors is recommended.

Keywords: knowledge, practice, BTB, peoples living with HIV, Bahir Dar city

Introduction

Bovine Tuberculosis (BTB) is an important zoonotic disease caused by *Mycobacterium bovis*, known to exist in all parts of the world.^{1,2} The disease has a public health impact and human acquire the infection from infected animals through consumption of raw or unpasteurized milk and dairy products (eg, cheese, yogurt), and direct contact or living close to sick animals.^{3–6} Bovine tuberculosis is one of the leading causes of death among adults in the world. TB cases in HIV-positive persons due to *M. bovis* also resemble disease caused by *M. Tuberculosis*. Thus, the disease occurs pulmonary disease, lymphadenopathy, or, in the more profoundly immune-suppressed, disseminated disease.³ *M. bovis* commonly responsible for extrapulmonary TB (EPTB) and pulmonary TB (PTB) disease, which is clinically indistinguishable from that of TB caused by *M. Tuberculosis*.^{7,8}

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Tuberculosis and other mycobacterial infections are the dominant complications for people living with HIV infection.⁹ Similarly, in many cases tuberculosis in HIVinfected patients is caused by M. TB, but cases of infection by M. bovis and infection with BCG vaccine strain of M. bovis have also been described.¹⁰ Moreover, in most African countries, bovine TB is prevalent, due to lack of effective disease control measures.^{4,6} This condition is aggravated by the presence of multiple additional risk factors such as human behavior and the high prevalence of HIV infections.^{4,6,11} Although HIV/AIDS is thought to facilitate transmission and progression to an active disease of any form of TB, some studies showed that the proportion of M. bovis infections is higher among HIV coinfected TB patients.¹² A study in Woldiya municipal abattoir reported 6.12% BTB lesions in detailed meat inspection. After further investigation for molecular analysis both mycobacterium tuberculosis and mycobacterium bovis were identified.13-15

Many developed countries have succeeded in controlling BTB by implementing the test slaughter strategy paralleled with milk pasteurization. Thus, culling of infected animals impose a financial problem for developing countries like Ethiopia. Hence, pasteurization of milk should be practiced commonly in developing country as it blocks the transmission path of *M. bovis* from animal to human with low cost.^{4,13,16}

Regarding knowledge and practice level for bovine TB prevention, little has been done in livestock producers, farmers, and residences both in urban and rural settings. More importantly, there is limited scientific information available about bovine TB in people living with HIV/AIDS, their knowledge, perception, and prevention practices in the country in general and Bahir Dar city in particular. Therefore, this study helps to provide a baseline information and the objective of this study was to assess the knowledge and practice for prevention of Bovine TB and its derivatives among HIV positive people in Bahir Dar city public hospitals, Ethiopia.

Methods

Study Area

The study was conducted in Bahir Dar city public hospitals. Bahir Dar is the capital city of the Amhara Regional State. It is located at 11.59 latitude and 37.39 longitudes and situated at 1799 meters above sea level. Bahir Dar has a total population of 221,991 (113, 535 women and 108,456 men). It is 564 km away from the capital city of Addis Ababa. Moreover, Bahir Dar city comprises a total of 7 hospitals, 10 health centers, 10 health posts, 35 specialty and higher clinics, three primary clinics, 59 medium clinics, 78 pharmacies and 67 drug stores. Among these facilities, only 17 of them provide ART service for more than 14,000 people living with HIV.¹⁷

Study Design

An institution-based quantitative cross-sectional study design was conducted from February to April, 2020 among adult HIV positive people in Bahir Dar city public hospitals.

Study Population

Those HIV positive people at the age of 18 years and above, attending ART clinics at Bahir Dar city public hospitals at the time of data collection were the study population.

Sample Size Determination

In the present study, the required sample was calculated by using the single population proportion formula as described by.¹⁸ The consideration during calculation was previous study (9.3% knowledge and 50.8% practice, 95% CI, power 80%, and 5% marginal error).

$$N = (Za/2)^2 p(1-p)/d^2$$

Thus, a total of 400 HIV positive people were the required sample size in the present study. However, after considering non-response rate, which is 10%, a total of 440 HIV positive people were the final sample size for the current study. Also, the total sample sizes were proportionally allocated to the two public hospitals.

Sampling Procedures

Among the three public hospitals in Bahir-Dar city, only Felege Hiwete and Addis Alem were selected because of there is a very few cases (<10 ART cases) in Tibebe Ghion hospital. A simple random sampling technique was used to select the study participants.

Data Collection Procedure

A structured pre-tested questionnaire was used for data collection. The questionnaire was developed after reviewing literature.^{18–20} The entire questionnaire was initially prepared in English and translated into local language (Amharic) before the interview to obtain the required information from the respondents and then it was translated back to English to ensure its consistency. The Amharic version of the questionnaire was used for data collection. The questionnaire comprised diverse questions including socio-demographic and livestock characteristics, behavioral, personal, environmental, organizational, knowledge of BTB transmission, and prevention.

Data Management and Analysis

The data were checked, coded, and entered into Epi data entry client version 4.6.0 and then the raw data was exported to STATA version 14. Descriptive statistics were performed to describe the result. Logistic regression analysis was utilized to assess the association. Variables which have a p-value of less than 0.2 in the bi-variable analysis were entered into the multivariable analysis. Finally, a p-value of less than 0.05 in the multivariable logistic regression analysis was used to identify variables significantly associated with knowledge and practice on Bovine TB.

Results

Socio-Demographic Characteristics of the Respondents

In the current study, 51.5% and 47.1% of the respondents were male and married, respectively. Similarly, 61.2% of the respondents have a private job and 9.7% of the respondents practice cattle production (Table 1).

Behavioral, Personal and Environmental Characteristics of the Respondents

The present study showed that 160 (36.8%) and 40 (9.2%) of the respondents had the habit of raw milk and meat consumption, respectively. However, 81.6% of the respondents believed that raw milk consumption is the major source of BTB. Among the respondents who owned cattle, 92.85% of the respondents bring their animal to a veterinary clinic when they get sick (Table 2).

Knowledge Level of Respondents About Bovine Tuberculosis

The result of the present study showed that 57.2% of the respondents knew about BTB. About 243 (97.59%) of the respondents believed that people living with HIV are more prone to bovine TB. Moreover, about 237 (95.18%) of the respondents explained that cough is a major symptom of BTB in humans (Table 3).

Table ISocio-DemographicCharacteristicsoftheStudyParticipants

Variable	Frequency	Percent (%)
Sex		
Male	224	51.5
Female	211	48.5
Age		
18–30	89	20.5
31–45	276	63.5
46–62	70	16.12
Religion		
Christian	387	89.0
Muslim	48	11.0
Marital status		
Unmarried*	230	52.9
Married	205	47.1
Education status		
No formal education	105	24.1
(I—8th grade) primary	104	23.9
(9–12th grade) secondary	161	37.0
College and above	65	14.9
Occupation		
No employee	86	19.77
Employee	83	19.08
Private job	266	61.15
Monthly income (Ebr)		
<1000	149	34.25
1000–1999	93	21.38
2000–2999	85	19.54
≥3000	108	24.83
Cattle holding		
Yes	42	9.7
No	393	90.3

Note: *Includes single, divorced and widowed. Abbreviation: Ebr, Ethiopian Birr.

The Practice of Respondents About Bovine Tuberculosis

Of the total 435 study participants, only 180 (41.4%) of the participants had a good practice level with 95% CI (0.36, 0.46). About 30.7% of the respondent boil milk before consumption. Among the respondents who owned cattle, about 11.9% of the respondents allowed their cattle to share their home. About 47.6% of the respondents use

Table	2	The	Behavioral,	Personal,	and	Environment-Related
Respor	ses	s Am	ong People L	iving with	ΗIV	

Variable	Frequency	Percent (%)
A habit of raw meat consumption?		
Yes	40	9.20
No	395	90.08
A habit of raw milk consumption?		
Yes	160	36.7
No	275	63.22
Believe raw milk is a major source of BTB		
in humans?		
Yes	355	81.61
No	80	18.39
Believe raw meat is a major source of BTB in humans?		
Yes	351	80.69
No	84	19.31
Does good personal hygiene reduce BTB in humans?		
Yes	394	90.57
No	41	9.43
Does good environmental hygiene		
reduce BTB in humans?		
Yes	398	91.5
No	37	8.5
Do consulting professionals create awareness about BTB?		
Yes	420	96.55
No	15	3.45
Does media access improve awareness about BTB?		
Yes	401	92.18
No	34	7.82
Bring the sick animal to the vet clinic? (N= 42)		
Yes	39	92.85
No	3	7.14

hand protective materials/gloves while cleaning cattle barns. About 23.8% respondents bring BTB suspected animals to vet clinics. About (69.4%) of respondents believed that BCG vaccine can prevent TB, while 4.3% of them practice traditional medicine (Table 4).

Factors Affecting Knowledge for BTB

Education status, religion, cattle holding and environmental hygiene were found to be statistically significant association

List of Knowledge Questions	Frequency	Percent %
Ever heard about BTB?		
Yes	249	57.2
No	186	42.8
Coughing is a major sign of BTB in animals? N=249		
Yes	222	89.16
No	27	10.84
Emaciation is a major sign of BTB in animals? Yes	42	16.87
INO	207	03.13
Lethargy is a major sign of BTB in animals? Yes	19	7.63
No	230	92.37
A low-grade fever is a major sign of BTB in animals		
Yes	5	2.01
No	244	97.99
Lymph node enlargement is a major sign of BTB in animals?		
Yes	15	6.02
No	234	93.98
BTB can affect humans?		
Yes	249	100
No	0	0
Does raw meat consumption transmit BTB?		
Yes	105	42.17
No	144	57.83
Does raw milk consumption transmit BTB?		
Yes	87	34.94
No	162	65.06
BTB transmitted via inhalation?	124	54.42
ies	136	24.6Z
INO	113	45.38
Coughing in humans is a major sign of BTB?		
Yes	237	95.18
No	12	4.82
Weakness in humans is a major sign of BTB?		

(Continued)

Table 3 (Continued).

List of Knowledge Questions	Frequency	Percent %	
Yes No	32 217	12.85 87.15	
A night sweet in humans is a major sign of BTB?			
Yes No	13 236	5.22 94.78	
Headache in humans is a major sign of BTB?			
Yes No	5 244	2.01 97.99	
People living with HIV are more prone to BTB?			
Yes No	243 6	97.59 2.41	
BTB transmission from cattle to humans can be prevented?			
Yes No	246 3	98.80 1.20	
Boiling of milk can kill the microorganism?			
Yes No	248 I	99.60 0.40	
Provide a separate pen to animals that can reduce BTB?			
Yes No	243 6	97.59 2.41	
BTB in humans is curable? Yes	248	99.60	
No	1	0.40	
treatment of BTB?	242	07.10	
No	7	2.81	
Traditional medicine is the best treatment for BTB?			
Yes No	7 242	2.81 97.19	
BTB can affect HIV negative peoples? Yes No	7 242	2.82 97.19	
BTB in people with HIV is curable? Yes No	238 	95.58 4.42	

(Continued)

List of Knowledge Questions	Frequency	Percent %
BTB can affect anybody?		
Yes	208	83.53
No	41	16.47

with knowledge level. The odds of having good knowledge level were higher in respondents with secondary (AOR = 3.60; CI: 1.75, 7.38) and above college (AOR = 2.91; CI: 1.55, 5.43) education than those who did not receive formal education. The odds of having good knowledge are 2.3 times higher in those who owned cattle (AOR = 2.30; CI: 1.06, 4.96) as compared to those who did not own. Besides, the odds of having good knowledge level were 37% smaller among Christian respondents (AOR = 0.37; CI: 0.18, 0 0.75) as compared to Muslims. In addition, the odds of having good knowledge were 3.38-fold higher in respondents with good environmental hygiene (AOR = 3.38; CI: 1.39, 8.23) than those who keep poor environmental hygiene (Table 5).

Factors Affecting Prevention Practice for BTB

Education, age and marital status were the factors associated with good level of preventive practice for BTB. The odds of having good practice were 2.5 and 4.3 times higher in respondents with secondary (AOR = 2.55; CI: 1.14, 5.69) and college and above (AOR = 4.33; CI: 2.14, 8.77) education than those who did not receive formal education, respectively. Those respondents who aged between 31 and 45 years (AOR = 0.27; CI: 0.15, 0.85) and 46 to 60 years (AOR = 0.38; CI 0.17, 0.85) had 27% and 38% lower level of practice for BTB, when compared to their younger counter parts (18–30). The odds of having good practice were 1.8 times higher in married respondents (AOR = 1.74; CI: 1.06, 2.84) than those unmarried counter parts (Table 6).

Discussion

The present study revealed that among the respondents about 57.2% of them were knowledgeable about bovine TB and its derivatives. From those 46.2% of the respondents living with HIV had good knowledge level for BTB in the study area. Among knowledgeable respondents 57.2% of them believed that bovine tuberculosis can be

List of Practice Questions	Frequency	Percent (%)
BCG Vaccination Prevent BTB?		
Yes	302	69.43
No	133	30.57
Practicing self-treatment to control BTB?		
Yes	95	21.84
No	340	78.16
Use Herbs to prevent BTB?		
Yes	38	8.87
No	397	91.26
Sell BTB positive animal to the public/ market? (N=42)		
Yes	13	30.95
No	29	69.05
Slaughter & bury BTB positive animal?		
Yes	18	42.86
No	24	57.14
Slaughter BTB positive animal for home consumption? N=42		
Yes	0	0
No	42	100
Bring BTB suspected animal to the veterinary clinic? N=42		
Yes	10	23.80
No	32	76.19
Share household house with animals? N=42		
Yes	5	11.9
No	37	88.1
Use glove while cleaning barns/handling of animal products? N= 42		
Yes	20	47.6
No	22	52.4
Visit the hospital when you suspect		
Yes	416	95.63
No	19	4.37
Use traditional medicine to treat/control		
DID: Vec	10	4.27
No	416	95.63
Even had visit beenited for DTD at a 1 - 2	-	
Yes	160	36.78

Table 4	4	Participant'	s Res	ponse	to	Practice	Questions	Among
Peoples	Li	ving with H	HV in	Bahir	Dai	r Public H	lospitals	

(Continued)

Table 4	(Continued).
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List of Practice Questions	Frequency	Percent (%)
No	275	63.22
Boil milk before consumption?		
Yes	133	30.57
No	302	69.43

transmitted to humans. Ninety nine percent of them also knew that boiling of milk before consumption can prevent the transmission of bovine tuberculosis to human. A study conducted in Woldiya showed that 48% of respondents knew bovine TB can be transmitted to human and 98% of knowledgeable respondents believe pasteurization of milk can prevent bovine tuberculosis transmission to human.¹⁸ Study conducted in and around Mekelle 30.8% of the respondents have good knowledge about BTB and only 15% of the respondents knew that BTB is a zoonotic disease.²¹ The main reason for the difference in the level of knowledge about bovine tuberculosis could be nearest approach to animal health assistances and veterinarians, so that they could consult animal health professionals for the health care of their animals and zoonoses.¹⁸

Among knowledgeable respondents, about more than one-third of respondents believed that BTB can be transmitted to human through eating of raw milk (34.9%) and meat (42.1%). A comparable result was reported from Nigeria by,²² less than half of the respondents knew about BTB as it can be transmitted to human through eating undercooked or partially cooked meat (43.2%) and milk (41.8%). Moreover, 95.1% of the respondents knew that cough is a major symptom of BTB. This finding was similar with the study conducted in Uganda by¹⁹ and in Nigeria by.²⁰ However, the present poor level of knowledge (53.8%) was higher when compared with the reports of^{20,23} and²⁴ in Ethiopia, in Nigeria and in Cameron, respectively. The variation in the different study might be due to close relation between veterinarians and animal owners and also the involvement of people in animal production, health and husbandry that can affect the level of knowledge.^{23,25}

Moreover, the present study showed that, 41.4% of HIV positive people had good level of practice for the prevention of bovine tuberculosis. However, the current finding was found lower when compared with the report in

Table 5 Multivariable Logistic	Regression of Factors	Affecting the Knowledge	of People Living	with HIV About BTB
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Variables	Knowledge Level Score			
	Poor	Good	COR (95% CI)	AOR (95% CI)
Sex				
Male	109	115	1.5 (1.04, 2.24)*	1.16 (0.74, 1.81)
Female	125	86		I
Income recoded				
<1000	98	51		I
1000–1999	44	49	2.13 (1.26, 3.63)*	1.65 (0.92, 2.98)
2000–2999	41	44	2.06 (1.19, 3.55)*	1.63 (0.89, 3.01)
≥3000	51	57	2.14 (1.29, 3.56)*	1.18 (0.63, 2.20)
Marital status				
Un married	131	99		I
Married	103	102	1.31 (0.89, 1.91) [†]	1.25 (0.81, 1.92)
Education				
No formal education	72	33		I
Primary (1–8)	63	41	1.41 (0.80, 2.50)	1.50 (0.80, 2.79)
Secondary (9–12)	28	40	3.11 (1.65, 5.88)**	3.60 (1.75, 7.38)**
College and above	71	87	2.67 (1.59, 4.48)**	2.91 (1.55, 5.43)*
Religion				
Muslim	17	31		I
Christian	217	170	0.42 (0.23, 0.80)*	0.37 (0.18, 0.75)*
Cattle holding				
Yes	18	24	1.62 (0.85, 3.09)†	2.30(1.06, 4.96)*
No	216	177		I
Environmental hygiene				
No	29	8		I
Yes	205	193	3.41 (1.52, 7.64)*	3.38 (1.39, 8.23)*

Notes: *Significant at 5%, **Significant at 1%, [†]Significant at 20%, 1= referent.

Abbreviations: CI, confidence interval; COR, crude odds ratio; AOR, adjusted odds ratio.

Ethiopia by,¹⁸ in Uganda by¹⁹ and in Nigeria by,²⁶ who reported 50.8%, 75.2% and 47.9% of the participants had good level of practice, respectively. The low level of practice reported by the current study could be due to the low level of good knowledge of the respondents. Knowledge of a disease promotes the development of appropriate practices.²⁷

Furthermore, the present study revealed that 36.8% and 9.2% of the respondents consume raw milk and meat, respectively. The current finding was lower when compared with the reports of Alelign et al,⁸ who reported that 69% of the respondents consume raw milk and dairy products in south Gondar zone. Similarly, a study conducted in Yabello showed that 66.2% and 96.5% of the

Variables	Practice Level Score		COR (95% CI)	AOR (95% CI)
	Poor	Good		
Age (years)				
18–30	36	53		1
31-45	181	95	0.35 (0.21, 0.58)**	0.27 (0.15, 0.51)**
46–60	38	32	0.57 (0.30, 1.07)	0.38 (0.17, 0.85)*
Education				
No formal education	79	26		1
Primary (1–8)	70	34	1.47 (0.80, 2.69)	1.52 (0.74, 3.13)
Secondary (9–12)	37	31	2.54 (1.32, 4.88)*	2.55 (1.14, 5.69)*
College and above	69	89	3.91 (2.27, 6.74)**	4.33 (2.14, 8.77)**
Marital Status				
Unmarried ^a	143	87		
Married	112	93	1.36 (0.93, 2.00) [†]	1.74 (1.06, 2.84)*
Income recoded				
<1000	106	43		
1000–1999	49	44	2.21 (1.29, 3.79)*	1.56 (0.80, 3.03)
2000–2999	48	37	1.90 (1.08, 3.31)*	1.74 (0.88, 3.45)
>3000	52	56	2.65 (1.58, 4.45)**	1.54 (0.76, 3.09)
Environmental hygiene				
Yes	228	170	2.01 (0.94, 4.27) [†]	2.14 (0.82, 5.58)
No	27	10		1
Training				
Yes	8	11	2.00 (0.79, 5.10) [†]	1.63 (0.48, 5.44)
No	247	169		1

Notes: *Significant at 5%, **Significant at 1%, [†]Significant at 20%, I = referent, ^aIncludes single, divorced and widowed.

Abbreviations: CI, confidence interval; COR, crude odds ratio; AOR, adjusted odds ratio.

respondents consume raw milk and meat, respectively.²⁸ Moreover, the findings of²⁹ in Arsi zone, Ethiopia and³⁰ in Ghana showed that 55.4% and 40.6% of the study participants consume raw milk, respectively. The inconsistency between the different study might be associated with food consumption behavior and geographical location. Unlike the present study, most previous studies were conducted in rural and agro-pastoral areas, where raw milk and meat consumption are widely practiced. Moreover, it has been reported that lack of knowledge about zoonosis, practices

of raw food consumption and poor animal husbandry becomes the factors for increasing the risk of zoonosis in the study participants.²²

The predictors of knowledge and practice in this study were education, religion, cattle holding, environmental hygiene, age and marital status. The findings in the present study predicted that those respondents who attend college and above had high knowledge and practice on BTB as compared to those who attend primary and no formal education. Similar findings were reported in Ethiopia by²⁵ and³¹, and in Nigeria by.²² Providing education plays an important role in adding up knowledge and also played an important role in increasing BTB awareness among the owners of livestock.²⁵

In the present study, respondents aged between 46 and 60 years had lower practice level as compared to Younger's (18–30). This finding is different from the previous report in Nigeria by²⁰ and²² who reported that respondents in the age group \geq 58 years had high knowledge. The knowledge of the respondents increases with increasing years of working experience which is supported by similar study among herdsmen in Ghana, suggesting that it is possible that herdsmen with a long practical experience had a greater knowledge because of past experiences on TB in their herd.^{20,30} The probable reason why elders had low practice level in the present study might be due to limited access to education and practical training associated with ZTB as compared to Younger's.

Conclusion

The present study showed that the overall good knowledge and practice level of the HIV positive peoples for bovine TB was found low as compared to other previous similar studies. Raw milk and meat consumptions were still practiced in the study area, which play a crucial role in developing and contracting BTB among immune-compromised individuals due to HIV. Education status, cattle holding, environmental hygiene, and religion, were significant determinant factors of knowledge. Likewise, age, education status and marital status were also predictors of preventive practice of HIV positive people for BTB. Therefore, both human and animal health professionals should apply ONE health approach in which a concerted effort among all relevant stakeholders, is highly needed so as to create/raise awareness, improve knowledge and enhance preventive practice of HIV positive people about zoonotic TB in the study area. Also, further study should be conducted to address the practice level with marital status which is found difficult to address in the present study.

Abbreviations

AIDS, Acquired Immunodeficiency Syndrome; BCG, Bacille Calmette-Guerin; BTB, Bovine Tuberculosis; EPTB, Extrapulmonary Tuberculosis; HIV, Human Immunodeficiency Virus; PTB, Pulmonary Tuberculosis; TB, Tuberculosis.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical Approval and Consent to Participate

Ethical clearance and approval of the verbal consent was obtained from the Institute of Public Health Research Ethical Review Committee, College of Medicine and Health Science, University of Gondar with reference number 837/6/2012, before the data collection. Then after, informed consent was obtained from each study participant after the purpose and significance of the study is explained to them by the data collectors. The study was conducted in accordance with the Declaration of Helsinki.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests in this work.

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