

ORIGINAL ARTICLE

The adherence gap: Rural dwelling, low level of education, and missed opportunities for optimal hepatitis B control

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ABSTRACT

Background and Objectives: Long-term antiviral use can suppress hepatitis B virus (HBV) DNA, normalize liver function tests, reverse fibrosis and cirrhosis, and improve histological changes. Understanding adherence and the factors affecting it is crucial for managing chronic hepatitis B virus (CHB) patients, achieving sustained suppression with low drug resistance risk, and developing strategies to address poor adherence. This study aims to assess antiviral medication adherence and factors associated with adherence among HBV patients on treatment at the gastroenterology clinic in Tikur Anbessa Specialized Hospital (TASH). **Methods:** A cross-sectional study was conducted in 149 HBV patients undergoing therapy at TASH from May 2023 to February 2024. The medication adherence level was assessed using Morisky's 8-item medication adherence questionnaire. Data was entered into Epi Info 7 for database construction and exported to SPSS version 26. Different statistical analyses were used, including frequencies of variables and descriptive statistics. An ordinal logistic regression analysis was used to identify factors associated with medication adherence levels. The proportional odds model (POM) assumptions were checked using chi-square and parallel line tests. **Results:** The study found that only 32.2% participants had high adherence, 39.6% had medium adherence, and 28.2% had low adherence. Rural dweller (a POR: 2.4; 95%CI: 1.09 to 5.20), low educational level (a POR: 3; 95%CI: 1.27 to 7.13), being unmarried (a POR: 2.52; 95%CI: 1.15 to 5.50), not being counseled about medication adherence by treating physicians (a POR: 3.2; 95%CI: 1.61 to 6.50), and an abnormal liver function tests (a POR: 2.31; 95%CI: 1.08 to 4.92) were significantly associated with medium or low medication adherence level. **Conclusion:** The study reveals low medication adherence rates among participants, with only a minority demonstrating high adherence. Factors such as rural dwellings, low educational level, being unmarried, lack of counseling, and abnormal liver function tests were significantly associated with medium or low adherence. Targeted interventions are needed to improve adherence, especially for individuals in rural areas with lower education levels and who are unmarried. Efforts should be made to integrate medication adherence discussions into routine healthcare visits and raise physician awareness about counseling patients on adherence are crucial.

Key words: chronic hepatitis B virus infection, adherence, rural residency, education level, counseling

INTRODUCTION

Chronic infection with the Hepatitis B virus (HBV) is a

major global public health problem and a significant cause of morbidity and mortality.^[1] Hepatic decompensation, liver cirrhosis, and hepatocellular


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carcinoma (HCC) develop as a complication of chronic hepatitis B (CHB) virus infection.^[1] The estimated worldwide prevalence of CHB is 3.6%, ranging from 0.5% in European countries to more than 8% in sub-Saharan Africa.^[2] World Health Organization (WHO) estimated that in 2019, 296 million people were chronic HBV carriers worldwide, and approximately 2 billion people have been infected worldwide, and about 820,000 die from it annually (mostly from complications of cirrhosis and hepatocellular carcinoma).^[3]

According to WHO, countries in Africa, Asia, and South America have carrier rates as high as 8%, with sub-Saharan Africa accounting for 20% of the global burden.^[4] The overall HBV pooled prevalence in East Africa and Ethiopia was 6.025%^[5] and 7.4%,^[6] respectively. Hepatitis B accounts for 17 percent of chronic liver disease in Ethiopia.^[7]

Long-term use of antivirals in eligible patients among chronic HBV patients resulted in the potent suppression of HBV DNA, normalization of alanine aminotransferase (ALT) reversal of fibrosis/cirrhosis, and continued histological improvement.^[8] Adherence to antiviral medication is essential for the management of chronic HBV patients to achieve the goal of therapy, which is achieving a high rate of sustained or maintained HBV suppression with a low risk of drug resistance.^[9–12]

Medication adherence is the cornerstone in the management of chronic illness.^[13] Several studies have shown that, in developed countries, patients with chronic conditions have adherence rates of 50% to 60%.^[14–16] In CHB patients, low medication adherence was demonstrated in 33% of patients, which is also associated with increased mortality.^[17] Suboptimal adherence was also associated with virologic failure.^[18]

In Ethiopia, antiviral medications are available at specific government centers and in private settings for chronic HBV patients who fulfill the eligibility criteria for treatment. However, very few studies explored the level of adherence to antiviral therapy among chronic HBV patients and factors associated with poor adherence in our setup.

METHODS

Study design

A hospital-based cross-sectional study was conducted at Tikur Anbessa Specialized Hospital from May 2023 to February 2024. Eligible patients were CHB adults (> 18 years) on antiviral medication for more than six months. Patients on antiviral medication for less than six months and those who started on antiviral for the prevention of HBV flare were excluded from the study.

Sample size determination

All eligible patients during the study period were included; therefore, sample size determination and sampling techniques were not used.

Data collection tools and procedures

Data was collected by face-to-face interviews and electronic medical records using structured questionnaires. The questionnaire comprised four components: sociodemographic factors, disease-related factors, health education, medications, and adherence.

Operational definitions

Chronic hepatitis B virus: CHB is defined as persistence of hepatitis B surface antigen (HBsAg) for six months or more after acute infection with HBV or from the time it was documented by lab investigation). On Morisky 8-item medication adherence questionnaire: Yes = 1, No = 0 for the yes, no questions, and A = 0, and B–E = 1, for the 8th question.

High medication adherence is when the sum of Morisky's 8-item medication adherence questionnaire is 0.

Medium medication adherence is when the sum of Morisky's 8-item medication adherence questionnaire is 1 or 2.

Low medication adherence is when the sum of Morisky's 8-item medication adherence questionnaire is greater than 2.

Comorbidities: any chronic medical condition attributed other than CHB and its complication.

Antiviral medication: any recommended antiviral medication given for the treatment of CHB.

Abnormal liver enzyme test: aspartate aminotransferase (AST) or/and ALT above the upper unit of normal.

Statistical analysis

Descriptive statistics, including frequency distributions, measures of central tendency, and dispersion, were employed to characterize the variables. Medication adherence was categorized as high, medium, or low, and an ordinal logistic regression model was used to identify factors associated with adherence levels. We assessed the proportional odds (PO) model assumptions using chi-square and parallel line tests. Bivariate analyses evaluated the association between potential explanatory variables and adherence level. Variables with a *P* value < 0.25 in the bivariate analyses were included in the multivariable PO model to control possible confounding factors.

Adjusted proportional odds ratios (ORs) with 95% confidence intervals (CIs) were estimated to determine the strength and significance (P value < 0.05) of the associations between explanatory variables and medication adherence.

RESULTS

Sociodemographic characteristics

A total of 149 HBV patients participated in the study. More than half (55.7%) of patients were over 40 years old, and about three-fourths (72.5%) were males. Fifty-five (36.9%) had completed college and were above the educational level. About three-fourths (73.2%) were urban dwellers, and 98 (65.7%) of those who participated were married. Nearly a third (29.5%) were government employees, and about half (47.6%) of participants' total family income was from 5000 to 10,000 Ethiopian birr per month (Table 1).

Clinical characteristics

About two-thirds (64.4%) of patients have had the hepatitis B virus for one to five years, and 53 (35.6%) have a comorbidity. About 22.6% of patients have multiple comorbidities (Figure 1), and 15.1% have diabetes. Nearly half (48.3%) had cirrhosis at the initiation of treatment, and 89 (59.7%) have cirrhosis currently. Fifty-four (29.5%) had elevated AST in the past three months, and 18 (12.1%) had elevated ALT (Table 2).

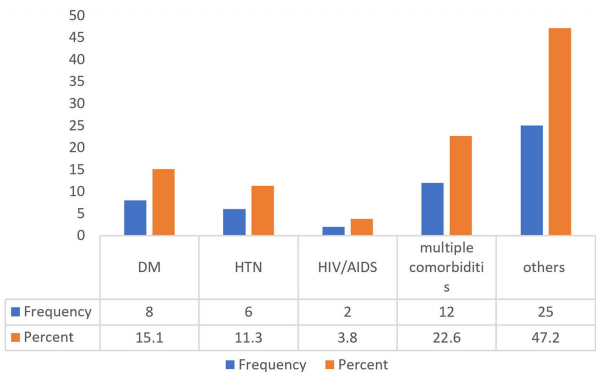


Figure 1. The common comorbidity among hepatitis B virus patients at Tikur Anbessa Specialized Hospital, Addis Ababa, 2024.

Institutional and other related characteristics

More than half, 85 (57%), were medication adherence by treating physicians, while only 30 (20.1%) had received health education. About one-fourth (21.5%) were used as reminders to take medication, and 116 (77.9%) were community-based health insurance members. More than a third of patients had missed their appointments, and 99 (66.4%) had attendants accompanying them during

their health visits (Table 3).

Level of adherence

The MMAS's mean (SD) score in this study was 2.86 ± 1.87 . Among the participants, 32.2% demonstrated high adherence, 39.6% showed medium adherence, and 28.2% had low adherence levels (Figure 2).

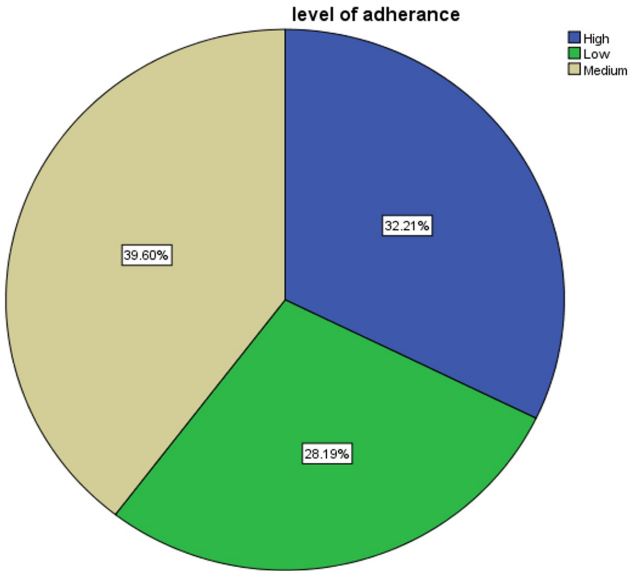


Figure 2. Level of adherence to antivirals in hepatitis B virus patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia 2024.

Factors associated with adherence

Medication adherence-related questions were asked in hepatitis B virus patients (Table 4). In the bivariable proportional odds model, age, sex, marital status, monthly income, educational status, rural residency, elevated liver function test, and counseling by treating physician were found to have a P value < 0.25. While in the final POM, marital status, educational status, rural residency, liver function test (LFT), and counseling by the doctor were independent risk factors for medication adherence level. The chi-squared test of parallelism showed that the ORs were constant across all medication adherence level cutoff points for the final model at a 5% level ($P = 0.474$). Accordingly, the results of POM revealed that the likelihood of low or medium medication adherence was 2.4 times (a POR: 2.4; 95%CI: 1.09 to 5.20) higher for rural patients than urban patients. Likewise, unmarried participants were 2.5(a POR: 2.52; 95%CI: 1.15 to 5.50) times more likely to be low- or medium-level adherents than married participants. The odds of being in the lower order of adherence level (low or medium) were three times (a POR: 3.0; 95%CI: 1.27 to 7.13) higher among those with low educational status than participants who had completed college and above.

Table 1: Sociodemographic characteristics of hepatitis B virus patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia 2024

| Variables | | Frequency (n) | Percentage (%) |
|--|----------------------|---------------|----------------|
| Age (years) | 18–40 | 83 | 55.7 |
| | 41–60 | 62 | 41.6 |
| | > 60 | 4 | 2.7 |
| Gender | Male | 108 | 72.5 |
| | Female | 41 | 27.5 |
| Educational status | No formal education | 9 | 6.0 |
| | Primary | 37 | 24.8 |
| | Secondary | 48 | 32.2 |
| | College and above | 55 | 36.9 |
| Residency | Rural | 40 | 26.8 |
| | Urban | 109 | 73.2 |
| Marital status | Single | 41 | 27.5 |
| | Married | 98 | 65.8 |
| | Divorced and widowed | 10 | 6.7 |
| Occupation | Government employee | 44 | 29.5 |
| | Private employe | 54 | 36.2 |
| | Farmer | 4 | 2.7 |
| | Marchant | 4 | 2.7 |
| | Unemployed | 33 | 22.1 |
| | Retired | 6 | 4.0 |
| | Student | 4 | 2.7 |
| | | | |
| Average family income (Ethiopian Birr) | < 5000 | 53 | 35.6 |
| | 5000–10000 | 71 | 47.6 |
| | > 10000 | 25 | 16.8 |

Similarly, the odds of low or medium medication adherence level for not being counseled by the treating physician were 3.2 times (a POR: 3.2; 95%CI: 1.61 to 6.50) higher than those advised by the treating physician. Moreover, patients with an abnormal LFT had 2.3 times (a POR: 2.31; 95%CI: 1.08 to 4.92) higher odds of low or medium medication adherence than those with a normal liver function test (Table 5).

DISCUSSION

Our study revealed that 28.2% of participants had low adherence levels to their antiviral therapy. The finding was higher than a study done in India, with 10.5%,^[19] Pakistan (15.7%)^[20] and Australia (23.8%).^[21] The discrepancy in patient adherence may be due to factors like socioeconomic differences, comorbidity, participant age, 40% of our patients were from different regions, and cost of transportation, which may affect their follow-up. However, it is lower than a study done in China, with 32.2%,^[16] Israel (33%),^[17] Chinese and Vietnamese Americans (34%),^[22] Brazil (43%),^[23] and Australia (53.89%).^[24] The possible reason for this is a variation in adherence measurement tools, a higher prevalence of substance abuse, daily free treatment

availability, and proper patient counseling by the treating team. The efficacy of these drugs boosts patient confidence, promoting regular drug intake and adequate follow-up, thereby promoting early virological decline and promoting regular drug intake.

Most of our participants reside in rural areas, affecting their medication adherence due to various factors. Rural patients had 2.4 times higher odds of poor medication adherence. This is consistent with a study done in China, which reported that patients residing in urban regions were 4.88 times more likely to have high adherence.^[16] On the contrary, in another study done in Pakistan, residents of rural areas showed better compliance rates.^[20] This may be due to factors such as limited access to healthcare resources, lower socioeconomic status, and a lack of education regarding the importance of medication adherence.

The study found that education level significantly impacts medication adherence, with patients with lower education levels experiencing threefold higher rates of non-adherence. The finding was similar to a study done at North Shewa Zone, Amhara Regional State, Ethiopia^[25] and China.^[16] This could be because the literacy level of individuals is one of the strongest

Table 2: Clinical characteristics of hepatitis B virus patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia 2024

| Variables | | Frequency (n) | Percentage (%) |
|------------------------------------|----------------|---------------|----------------|
| Duration of illness | below one year | 6 | 4.0 |
| | 1 to 5 years | 96 | 64.4 |
| | 5 to 10 years | 38 | 25.5 |
| | > 10 years | 9 | 6.0 |
| Duration since starting medication | below one year | 14 | 9.4 |
| | 1 to 5 years | 105 | 70.5 |
| | 5 to 10 years | 30 | 20.1 |
| Viral load in the past 12 months | Undetectable | 27 | 18.1 |
| | Detectable | 42 | 28.2 |
| | not determined | 80 | 53.7 |
| AST in the past three months | Normal | 105 | 70.5 |
| | High | 44 | 29.5 |
| ALT | Normal | 131 | 87.9 |
| | High | 18 | 12.1 |
| Cirrhosis at the initiation of Rx | Yes | 72 | 48.3 |
| | No | 77 | 51.7 |
| Cirrhosis currently | Yes | 89 | 59.7 |
| | No | 60 | 40.3 |
| Other medication to be taken | Yes | 68 | 45.6 |
| | No | 81 | 54.4 |
| Comorbidity | Yes | 53 | 35.6 |
| | No | 96 | 64.4 |

ALT: alanine aminotransferase; AST: aspartate aminotransferase

determinants of healthcare-seeking behavior. Educated people are more knowledgeable about the complications of hepatitis, and they adhere to their medications.

Marital status significantly impacts adherence to antiretroviral therapy (ART), with unmarried patients 2.5 times more likely to not adhere to medication than married individuals, as supported by a study in East Gojjam Zone, Northwest Ethiopia.^[15] This might be because married individuals often have a spouse who provides emotional and practical support, reminding them to take their medication and accompanying them to medical appointments. In contrast, unmarried individuals may lack this support system, making it more challenging for them to adhere to their medication consistently. This underscores the importance of social support in promoting medication adherence among hepatitis B patients.

The study reveals that medication adherence counseling at each visit by a treating physician has significantly impacts their medication adherence, with those not counseled by a treating physician at every visit being 3.2 times more likely to be poor adherents. Patient health literacy significantly influences medication adherence, and counseling was a strategy to enhance health literacy

and medication adherence. A study from Australia reported that patients with inadequate health literacy levels had 2.7-fold increased odds of being non-adherent to medication.^[21] The possible justification for this is that it is true that patients' health literacy can influence medication adherence; there may be other factors involved in poor adherence, such as the complexity of the medication regimen or side effects. Moreover, an abnormal liver enzyme test significantly influenced patients' adherence to medication, with patients with an elevated test being 2.3-fold more likely to be non-adherent to their medication. Abnormal liver enzyme tests may indicate liver cirrhosis and other underlying medical conditions, which can lead to medication-related issues such as non-adherence, adverse drug reactions, drug-drug and disease interactions, and indication, dosing, and monitoring issues.^[26]

To the best of our knowledge, this is the first study to compressively assess the level of antiviral therapy adherence and its related factors among hepatitis B patients in Ethiopia. Limited literature exists on antiviral therapy and its factors among patients with CHB virus in similar settings. It is valuable to provide an overview of findings from studies on antiviral therapy adherence. However, the study has some significant limitations that

Table 3: Institutional and other related characteristics of hepatitis B virus patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia 2024

| Variables | | Frequency (n) | Percentage (%) |
|---|--------------------------------|---------------|----------------|
| Health education | Yes | 30 | 20.1 |
| | No | 119 | 79.9 |
| Frequency of health education (<i>n</i> = 30) | During each visit | 4 | 13.3 |
| | Only when I started antivirals | 14 | 46.7 |
| | Sometimes | 12 | 40 |
| Medication adherence counseling by a treating physician | During each visit | 85 | 57.0 |
| | Only when I started medication | 2 | 1.3 |
| | Sometimes | 31 | 20.8 |
| | Never | 31 | 20.8 |
| Do you use reminder | Yes | 32 | 21.5 |
| | No | 117 | 78.5 |
| Attendants accompany during health visit | Yes | 50 | 33.6 |
| | No | 99 | 66.4 |
| Where do you get your antivirals? usually | Government | 101 | 67.8 |
| | Private | 44 | 29.5 |
| | Both | 4 | 2.7 |
| Is the antiviral medication available in the TSH pharmacy | Always | 8 | 5.4 |
| | Sometimes | 137 | 91.9 |
| | Never | 4 | 2.7 |
| Health insurance | Yes | 116 | 77.9 |
| | No | 33 | 22.1 |
| Miss appointment | Never | 99 | 66.4 |
| | Rarely | 4 | 2.7 |
| | Sometimes | 46 | 30.9 |

Table 4: Responses to medication adherence-related questions among hepatitis B virus patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia 2024

| Questions | Responses <i>n</i> (%) | |
|--|------------------------|------------|
| | Yes | No |
| Do you sometimes forget to take your medicine? | 65 (43.6) | 84 (56.4) |
| People sometimes miss taking their medicines for reasons other than forgetting. Over the past two weeks, were there any days you did not take your medicine? | 49 (32.9) | 100 (67.1) |
| Have you ever cut back or stopped taking your medicine without telling your doctor because you feel worse when you take it? | 16 (10.7) | 133 (89.3) |
| When you travel or leave home, do you sometimes forget to bring your medicine? | 40 (26.8) | 109 (73.2) |
| Did you take your medicine yesterday (reverse coded)? | 14 (9.4) | 135 (90.6) |
| When you feel your symptoms are under control, do you sometimes stop taking your medicine? | 18 (12.1) | 131 (87.9) |
| Taking medicine every day is a real inconvenience for some people. Do you ever feel hassled about sticking to your treatment plan? | 24 (16.1) | 125 (83.9) |
| How often do you have difficulty remembering to take all your medicine (A(NO) = 0; B-E (yes) = 1 where A. Never/rarely; B. Once in a while; C. Sometimes, D. Usually; E. All the time) ? | 50 (33.6) | 99 (66.4) |

should be considered cautiously while interpreting the results. First, there is no single best medication adherence level measure. The study is single-centered, and it may limit its generalizability. Due to the nature of the study design, the cause-and-effect relationship

between the dependent and independent variables cannot be established.

The study revealed that 28.2% and 39.6% of participants had low and medium adherence levels to their antiviral

Table 5: Factors associated with antiviral medication adherence among hepatitis B virus patients at Tikur Anbessa Specialized Hospital, Addis Abba Ethiopia, 2024

| Variables | Category | Adherence level | | | P value | a POR |
|--|---------------------|-----------------|-----------|------------|---------|----------------------|
| | | High | Low | Medium | | |
| Age (years) | < 40 | 21 (25.3) | 24 (28.9) | 38 (45.78) | 0.035 | 1.15 (0.53 to 2.49) |
| | ≥ 40 | 27 (40.9) | 18 (27.3) | 21 (31.8) | | 1 |
| Gender | Male | 31 (28.7) | 32 (29.6) | 45 (41.6) | 0.194 | 1 |
| | Female | 17 (41.5) | 10 (24.4) | 14 (34.1) | | 0.51 (0.23 to 1.13) |
| Residency | Rural | 7 (17.5) | 11 (27.5) | 22 (55.0) | 0.009 | 2.39 (1.09 to 5.20)* |
| | Urban | 41 (37.6) | 31 (28.4) | 37 (33.9) | | 1 |
| Educational status | Primary and below | 7 (15.2) | 15 (32.6) | 24 (52.2) | 0.001 | 3.0 (1.27 to 7.13)* |
| | Secondary | 15 (31.2) | 13 (27.1) | 20 (41.7) | 0.090 | 1.56 (0.70 to 3.50) |
| | Collage and above | 26 (47.3) | 14 (25.4) | 15 (27.3) | | 1 |
| Marital status ^a | Married | 39 (39.8) | 26 (26.5) | 33 (33.7) | 0.008 | 1 |
| | Currently unmarried | 9 (17.6) | 16 (31.4) | 26 (51) | | 2.52 (1.15 to 5.50)* |
| Monthly income (Ethiopian Birr) | < 5000 | 20 (37.7) | 11 (20.7) | 22 (41.5) | 0.039 | 1.61 (0.56 to 4.59) |
| | 5000–10,000 | 18 (25.4) | 22 (31) | 31 (43.6) | 0.013 | (0.90 to 6.40) |
| | > 10,000 | 10 (40.0) | 9 (36.0) | 6 (24.0) | | 1 |
| Liver function test | Normal | 40 (39.6) | 26 (25.7) | 35 (34.7) | 0.012 | 1 |
| | Abnormal | 8 (16.7) | 16 (33.3) | 24 (50.0) | | 2.31 (1.08 to 4.92)* |
| Counseling by treating physicians ^b | Yes | 37 (43.5) | 23 (27.1) | 25 (29.4) | < 0.001 | 1 |
| | No | 11 (17.2) | 19 (29.7) | 34 (53.1) | | 3.2 (1.61 to 6.50)** |

** $P < 0.001$ and * $P < 0.05$; a POR: adjusted proportional odds ratio; LFT: liver function test; ^acurrently unmarried (single and divorced); ^byes for at every visit and no for others

therapy. Educational level, rural residency, marital status, elevated level of LFT, and counseling by a treating physician were independently associated with adherence to antiviral treatment.

DECLARATIONS

Author contributions

Conceptualization, methodology, investigation, analysis, and writing of the manuscript: Dawit Habtie Tegegne, Guda Merdassa Roro, Gebeyehu Tessema Azibte; methodology, data curation, drafting, interpretation, and edition of the data and supervision: Zekarias Ayalew, Bereket Abraha Molla, Eman Omer; all authors revised the manuscript and have approved the final version of the manuscript.

Ethics approval

The study was conducted by the Declaration of Helsinki and approved by the Institutional Review Board of Addis Ababa University, College of Health Sciences protocol.

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Conflict of interest

The authors declare no conflicts of interest.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article.

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