*Cardiology and Angiology: An International Journal*

*10(4): 31-39, 2021; Article no.CA.74472*
*ISSN: 2347-520X, NLM ID: 101658392*

# Correlation of Triglyceride with Coronary Artery Disease Severity in Pre-Diabetic Chronic Stable Angina Patients

**Mahmoud Mohammed Tolba[1*], Mohamed Khalfallah[1], Sameh Samir Khalel[1] and Hanan Kamel Kassem[1]**

*[1]Cardiovascular Department, Faculty of Medicine, Tanta University, Tanta, Egypt.*

***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

***Article Information***

DOI: 10.9734/CA/2021/v10i430176
Editor(s):
(1) Prof. Francesco Pelliccia, University La Sapienza, Italy.
Reviewers:
(1) Elsa de La Chesnaye, National Medical Center, Mexican Social Security Institute, Mexico.
(2) Laxmikant Chavan, AIMST University, Malaysia.
Complete Peer review History: http://www.sdiarticle4.com/review-history/74472

***Original Research Article***

***Received 01 August 2021***
***Accepted 03 October 2021***
***Published 02 November 2021***

## ABSTRACT

**Background:** Individuals with prediabetes have multiple disturbances in lipoprotein metabolism resulting from multiple combinations of insulin deficiency, insulin resistance and hyperglycemia. Dyslipidemia is the commonest complication of prediabetes and diabetes, and it predispose to premature atherosclerosis causing cardiovascular complication. The aim of this study was to assess correlation of triglyceride (TG) with coronary artery disease (CAD) severity in pre-diabetic chronic stable angina patients.

**Methods:** Our cross-sectional observational study was conducted on 100 pre-diabetic patients (HbA1c 5.7% to 6.4%) with different levels of TG and stable CAD, referred to Tanta university hospitals. Each patient had been subjected to adequate history taking, complete clinical examination and laboratory investigations and electrocardiogram with transthoracic echocardiography. SYNTAX score was calculated.

**Results:** There were significant positive correlations between TG and LDL, ratio and TLC respectively while there was a significant negative correlation between TG and HDL. There was significant positive correlation between SYNTAX and LDL, ratio and urea respectively while there was high significant negative correlation between TG and HDL. TG level was

**Corresponding author: E-mail: mahmoudtolba888@gmail.com;*

significantly higher in male than female (p= 0.028). There was no significant difference in SYNTAX regarding gender. For the multivariate analysis, only LDL was a significant independent predictor for CAD.
**Conclusions:** There was a positive correlation between the TG and the severity of coronary lesions in pre-diabetic stable angina pectoris patients.

*Keywords: Triglyceride; coronary artery disease; pre-diabetic; stable angina.*

## 1. INTRODUCTION

The American Diabetes Association defines prediabetes as an intermediate condition of individuals whose fasting blood sugar is 100–125 mg/dl, after a 2 hour Glucose Tolerance Test (GTT) of 140 mg/dl–199 mg/dl and HbA1c 5.7% to 6.4%) [1]. Prediabetes has been associated with other coronary vascular risk factors and with an increased total cardiovascular risk [2].

The prognostic impact of high levels of HbA1c in ischemic heart disease was verified in a meta-analysis of more than 11.000 patients and its association with mortality was much more significant in patients with no established diagnosis of diabetes [3]. Data has also been reported for approximately 900 patients followed up for 14 years suggesting that apparently healthy individuals with prediabetes, diagnosis based on HbA1c levels, are at greater risk of developing ischemic heart disease [4].

Individuals with prediabetes have multiple disturbances in lipoprotein metabolism resulting from the combinations of insulin deficiency, insulin resistance and hyperglycemia [5]. Dyslipidemia is the commonest complication of prediabetes and diabetes, and it predisposes to premature atherosclerosis causing cardiovascular complications [6]. Adipose tissue produce pro-inflammatory mediators involving atherosclerosis in patients [7].

Substantial data suggest that elevated triglycerides (TG) are associated with increased coronary risk and may be an independent coronary risk factor [8].

The aim of this study was to assess a correlation between high levels of TG with coronary artery disease (CAD) severity in pre-diabetic chronic stable angina patients.

## 2. PATIENTS AND METHODS

Our controlled observational study was conducted on 100 pre-diabetic patients (HbA1c 5.7% to 6.4%) with different levels of TG and stable CAD, referred to Tanta University Hospitals in Egypt.

The exclusion criteria were patients with heart failure, cardiomyopathy, unstable CAD, familial dyslipidemia, patients who previously underwent coronary artery bypass graft, patients with prior myocardial infarction, thyroid abnormalities, chronic kidney disease and recent major surgical procedure or trauma.

Each pre-diabetic patients with different levels of TG and stable CAD, referred to Tanta University Hospitals had been subjected to an adequate clinical history of patient, complete clinical examination, laboratory tests and an electrocardiogram (standard 12-lead electrocardiogram) with transthoracic echocardiography done on admission.

### 2.1 Technique

Examination involves the use of an echo probe at various windows to obtain views of the heart and capturing images/videos for later playback while formally "reading" the study to come up with findings of the study. Examination is usually done while lying flat and tilted onto the left side to bring the heart into better view. Ultrasound gel is used to improve the acoustic windows and increase quality of the captured images.

### 2.2 Coronary Angiography

The SYNTAX Score (SS) has an important role in grading the complexity of CAD in patients undergoing revascularization [9].

### 2.3 Statistical Analysis

The data was analyzed with (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Quantitative parametric variables were presented as mean, standard deviation (SD) and range while qualitative data presented in the form as numbers and percentages. Data was analyzed using unpaired student t-test, linear correlation coefficient [r] and

logistic level of significance was adopted at p < 0.05.

## 3. RESULTS

Baseline demographic, medical and clinical characteristics are shown in Table 1.

There was a significant positive correlation between TG levels and SYNTAX score Fig. 1.

There were significant positive correlations among SS, and TG and LDL (r= 0.48, p= <0.001), ratio (r= 0.49, p= <0.001) and TLC (r= 0.204, p= <0.041) respectively while there was high significant negative correlation between TG and HDL (r=-0.467, p= <0.001). there was no statistically significant correlation between TG levels and other laboratory parameters (Table 2). There were significant positive correlations between SYNTAX score and LDL (r= 0.607, p= <0.001), ratio (r= -0.696, p= <0.001), SYNTAX score and urea (r= 0.253, p= = 0.12) respectively while there was high significant negative correlation between TG and HDL (r=-0.656, p= <0.001). (Capital T) there was no statistically significant correlation between TG levels and other laboratory parameters (Table 3).

TG levels were significantly higher in male than female (p= 0.028). (Capital T) there was no significant difference in SYNTAX score regarding gender. There was no significant difference between TG and SYNTAX regarding gender (Table 4).

For the multivariate analysis, only LDL was a significant independent predictor for CAD. Others (gender, HDL, Ratio, Hb, urea and creatinine) were not significant independent predictors for CAD. LDL had a coefficient β of 1.013 which means that every increase in the LDL of 1 will increase risk of CAD of 1% Table 5.

In our cohort, 53% were males. Their age ranged from 29 to 77 years with a mean of 56.36 years. HbA1C level had a mean of 6.08 with a range of (5.7 – 6.4) %. LDL, HDL and TG levels had a mean of 127.9 (range of 50 - 182) mg/dL, 43.62 (30 - 62) mg/dL and 155.83 (53 - 249) mg/dL respectively, with total cholesterol having an average of 202.72 ± 31.82. The Syntax (all letters must be in capital) score has a mean of 13.58± 13.71. Hb, TLC and platelet levels had a mean of 12.3 range of (9.6 - 16) g/dL, 7.51 (3.2 – 11.5) 10*3/mm$^3$ and 284 (156 - 446) 10*3/mm$^3$ respectively.

**Table 1. Baseline demographic and laboratory characteristics in the studied patients**

| | Range | | | Mean | ± | SD |
|---|---|---|---|---|---|---|
| Age (years) | 29 | - | 77 | 56.36 | ± | 9.78 |
| | N | | | % | | |
| Gender | | | | | | |
| Female | 47 | | | 47 | | |
| Male | 53 | | | 53 | | |
| Smoker | 34 | | | 34 | | |
| Hypertension | 53 | | | 53 | | |
| Family history | 1 | | | 1 | | |
| HbA1C (%) | 5.7 | - | 6.4 | 6.08 | ± | 0.22 |
| LDL (mg/dl) | 50 | - | 182 | 127.90 | ± | 31.50 |
| HDL (mg/dl) | 30 | - | 62 | 43.62 | ± | 8.99 |
| Triglyceride (mg/dl) | 53 | - | 249 | 155.83 | ± | 51.56 |
| Cholesterol (mg/dl) | 131 | - | 260 | 202.72 | ± | 31.82 |
| SYNTAX score | 0 | - | 49 | 13.58 | ± | 13.71 |
| EF (%) | 45 | - | 74 | 57.96 | ± | 7 |
| Hb(gm/dl) | 9.6 | - | 16 | 12.30 | ± | 1.33 |
| TLC ($10^3$/mm$^{3)}$ | 3.2 | - | 11.5 | 7.51 | ± | 2.07 |
| Platelet ($10^3$/mm$^3$) | 156 | - | 446 | 284.00 | ± | 69.25 |
| TSHmIU/L | 0.7 | - | 4.1 | 2.33 | ± | 0.48 |
| Urea (mg/dl) | 18 | - | 87 | 32.78 | ± | 10.81 |
| Creatinine (mg/dl) | 0.5 | - | 1.4 | 0.97 | ± | 0.21 |

*CA: coronary angiography, PCI: percutaneous coronary intervention, LAD: left anterior descending artery, RCA: right circumflex artery, LCX: left circumflex artery, CABG: coronary artery bypass graft, HbA1C: hemoglobin A1C, LDL: low density lipoprotein, HDL: high density lipoprotein, EF: ejection fraction, Hb: hemoglobin, TLC: total leucocytic count, TSH: thyroid stimulating hormone*

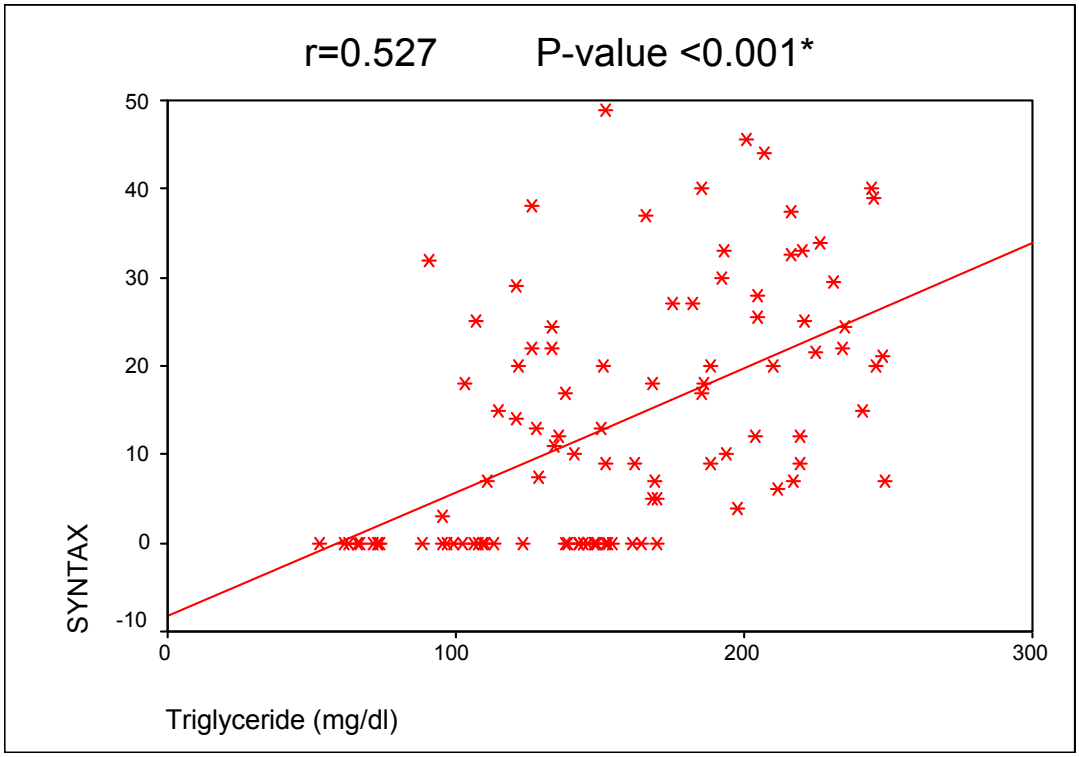


**Fig. 1. Correlation between triglyceride levels and SYNTAX score**

**Table 2. Correlation among TG, age and other laboratory parameters**

| | TG | |
|---|---|---|
| | **r** | **P-value** |
| Age | 0.160 | 0.113 |
| HbA1C | 0.009 | 0.932 |
| LDL | 0.480 | <0.001* |
| HDL | -0.467 | <0.001* |
| LDL/HDL Ratio | 0.490 | <0.001* |
| Hb | -0.055 | 0.588 |
| TLC | 0.204 | 0.041* |
| Platelet | 0.062 | 0.537 |
| TSH | 0.057 | 0.571 |
| Urea | 0.111 | 0.278 |
| Creatinine | 0.089 | 0.382 |

*HbA1C: hemoglobin A1C, LDL: low density lipoprotein, HDL: high density lipoprotein, Hb: hemoglobin, TLC: total leucocytic count, TSH: thyroid stimulating hormone*

## 4. DISCUSSION

Our results are in agreement with the study of Sudjana et al., [10] as they reported that the study sample comprised 80 patients (mean (SD) age: 60±8 years, 71.1% male). TG and HDL levels had a median and a range of 114 (48 - 283) mg/dL and 47 (27 - 85) mg/dL with a TG/HDL ratio having an average of 2.56 ± 1.04. Gensini score has a mean of 51 ± 36.

In the study of Thai et al., [11], 62% male, mean age 58.9 ± 10.8 years, BMI 24.8 ± 2.6 kg/m2, HbA1c 7.9 ± 1.0%. TyG index mean value was 9.64 ± 0.63 (range: 7.80–10.96).

Our results were supported by study of Klempfner et al., [12] as they reported that 32% of their studied group had hypertension and 1.9% of them had cerebrovascular accidents.

**Table 3. Correlation between SYNTAX and age and other laboratory parameters**

| | SYNTAX | |
|---|---|---|
| | **r** | **P-value** |
| Age | 0.080 | 0.432 |
| HbA1C | 0.103 | 0.306 |
| LDL | 0.607 | <0.001* |
| HDL | -0.656 | <0.001* |
| LDL/HDL Ratio | 0.696 | <0.001* |
| Hb | 0.012 | 0.905 |
| TLC | 0.140 | 0.166 |
| Platelet | -0.034 | 0.738 |
| TSH | -0.029 | 0.773 |
| Urea | 0.253 | 0.012* |
| Creatinine | 0.146 | 0.152 |

*HbA1C: hemoglobin A1C, LDL: low density lipoprotein, HDL: high density lipoprotein, Hb: hemoglobin, TLC: total leucocytic count, TSH: thyroid stimulating hormone*

**Table 4. Relation between TG and SYNTAX regarding gender and smoking**

| | GENDER | | | |
|---|---|---|---|---|
| | **Female** | **Male** | **T-test** | |
| | **Mean ± SD** | **Mean ± SD** | **t** | **P-value** |
| **TG** | 143.83 ± 51.97 | 166.47 ± 49.25 | 2.236 | 0.028* |
| **SYNTAX** | 11.94 ± 14.09 | 15.03 ± 13.33 | 1.127 | 0.263 |
| | **SMOKER** | | | |
| | **Yes** | **No** | **T-test** | |
| | **Mean ± SD** | **Mean ± SD** | **t** | **P-value** |
| **TG** | 158.38± 50.38 | 154.52 ±52.48 | 0.354 | 0.724 |
| **SYNTAX** | 15.62± 13.61 | 12.52 ±13.75 | 1.070 | 0.287 |

*TG: triglyceride*

**Table 5. Multivariate analysis for CAD**

| **Coefficients** | **Unstandardized coefficients** | | **Standardized coefficients** | **T-test** | | **95% confidence interval for B** | |
|---|---|---|---|---|---|---|---|
| | **B** | **SE** | **Beta** | **t** | **P-value** | **Lower bound** | **Upper bound** |
| **Gender** | 11.721 | 9.623 | 0.114 | 1.218 | 0.226 | -7.400 | 30.841 |
| **LDL** | 1.013 | 0.511 | 0.620 | 1.983 | **0.048*** | -0.002 | 2.029 |
| **HDL** | -2.660 | 1.600 | -0.468 | 1.663 | 0.100 | -5.839 | 0.519 |
| **Ratio** | -33.596 | 21.898 | -0.775 | 1.534 | 0.129 | -77.107 | 9.915 |
| **Hb** | -4.777 | 3.401 | -0.124 | 1.405 | 0.164 | -11.534 | 1.980 |
| **Urea** | 0.029 | 0.453 | 0.006 | 0.063 | 0.950 | -0.871 | 0.928 |
| **Creatinine** | -9.283 | 23.367 | -0.038 | 0.397 | 0.692 | -55.712 | 37.147 |

However, in the study of Valdivielso et al., [13], of all the patients tested, 67% of patients had coronary disease, 38% had peripheral arterial disease and 22% had cerebrovascular disease. A total of 84% had only one territory affected (13% stroke, 24% peripheral artery disease and 47% CAD), whereas 16% of the patients had two territories affected; there were no patients with three territories affected. Patients with vascular disease were older and had a higher prevalence of hypertension, Type 2 diabetes, smoking and family history of premature vascular disease.

In the study of Sudjana et al., [10], for statin consumption, 18.3% of patients took high-intensity statins, 13.3% took medium-intensity statins, 18.3% took low-intensity statins, and 50% did not take statins.

According to Bansal et al., [14] during a median 11.4 years of follow up, 1001 participants

experienced a first cardiovascular event (including 276 nonfatal myocardial infarctions, 265 ischemic strokes, 628 coronary revascularizations, and 163 cardiovascular deaths), for an overall event rate of 3.46 per 1000 person-years of follow-up.

In a study conducted by Yu et al. [15], one-vessel involvement was the most common pattern occurring in 60% (71/118) of the CAA (coronary artery atherosclerosis) positive subjects. Of the remaining subjects, 23.7% (28/118) had a two-segment disease, and 16.1% (19/118) had three or more segment disease. Additionally, the number of segments with stenotic lesions increased with plasma glucose level from 8.3% in the NGR group to 12.7% in the pre-diabetic group to 20.2% in the DM group.

Regarding Yang et al. [16], patients were divided into 2 groups: a normal fasting glucose (NFG) group (FBG <6.1 mmol/L) and an impaired fasting glucose (IFG) group (6.1 ≤FBG<7.0 mmol/L) with defined values. Baseline characteristics and angiography data of the 2 groups were compared. The prevalence of 3-vessel disease (P = .002), the GENSINI (the score is named after a professor) score (P = .002), and the SYNTAX (SYNergy between PCI with TAXUS™ and Cardiac Surgery) score (P = .002) of the IFG group was significantly higher compared to the NFG group. After multiple regression analysis, FBG was found to be independently associated with prevalence of 3-vessel disease (adjusted odds ratio: 1.62; 95% confidence interval: 1.21-2.36; P = .013), the GENSINI score (standardized β = .138, P = .008), and the SYNTAX score (standardized β = .145, P = .005). In addition, HbA1 c was independently associated with the prevalence of 3-vessel disease, the GENSINI, score, and the SYNTAX score (P < .05). Both FBG and HbA1c are independently correlated with the severity of CHD in prediabetic patients with HbA1c 5.7% to 6.4%.

Also, Mirza et al. [17], demonstrated that higher HbA1c was also associated with SYNTAX scores above 22, Left Main Stem (LMS)/Triple Vessel Disease (TVD) and increased in mean number of diseased vessel. The increase in HbA1c % level was positively correlated with SYNTAX score (r=0.594, p< 0.001). Multivariate logistic regression analysis showed that HbA1c level was an independent predictor of severity of CAD.

However, in the study of Klempfner et al., [12], patients in the higher TG's groups were significantly younger but presented with a higher BMI, and greater prevalence of diabetes mellitus and active smoking. Consistently, HDL-C levels were inversely and directly correlated, with increasing levels of TG (correlation coefficients, −0.41 and 0.20, respectively; both P<0.01). Comorbidities such as peripheral vascular disease, chronic obstructive lung disease, and past cerebrovascular accident or transient ischemic attack, as well as number of pervious MI events did not differ significantly among groups. Patients with greater TG levels were more likely to be classified as New York Heart Association functional class >1.

In the study of Sudjana et al., [10], TG/HDL ratio (r=0.765, p<0.001), age (r=0.321, p=0.012), hypertension (r=0.270, p=0.037, and metabolic syndrome (r=0.333, p=0.009) were found to have correlation with Gensini score. For the multivariate analysis the confounding variables included in multiple linear regression are those that have significant values (p <0.25) in the bivariate analysis of the dependent variables, namely the TG/HDL ratio, age, male sex, hypertension, obesity, and metabolic syndrome. The results of multiple linear regression analysis showed that there was a positive correlation between the TG/HDL ratio and Gensini score which was significant before being controlled by confounding variables after being controlled by confounding variables. The determinant coefficient value R2 is 0.649 which means that the TG/HDL ratio after being controlled by confounding can explain the variability of the Gensini score by 64.9% while the rest is influenced by other factors. The TG/HDL ratio has a coefficient β of 22.02 which means that every increase in the TG/HDL ratio of 1 will increase the Gensini score of 22, after being controlled by confounding factors of age, hypertension, and metabolic syndrome.

A study conducted by Da Luz et al., [18] and Conkbayir C et al., [19] showed that the TG / HDL ratio was associated with the severity of coronary lesions assessed by using Friesinger index. Da Luz et al. [18] showed TG/HDL ratio> 4 associated with the severity of coronary lesions. Both studies used stable angina pectoris patients as their study population and Conkbayir C et al. [19] excluded DM patients in their study. Ostfeld R et al., [20] include unstable angina pectoris patients as their study population. The degree of severity of coronary lesions is assessed using a

scoring system developed at the health care center where the study was conducted. Based on this study, the TG/HDL ratio ≥3.5 was associated with the severity of coronary lesions.

Yang D et al., [21] study used Gensini scores for quantifying severity of coronary lesion with a population of stable angina pectoris and acute coronary syndrome patients. The study showed an LDL/HDL ratio, total cholesterol/HDL, and TG/HDL associated with the severity of coronary lesions.

In the study of Sekimoto et al. [22], patients were divided into two groups based on the presence (n=29) or absence (n=113) of RP after 10 months. The LDL-c and sd-LDL-c (small dense low-density lipoprotein cholesterol) levels at baseline were equivalent in both the groups. However, the sd-LDL-c, TG& remnant lipoprotein cholesterol (RL-c), at follow-up were significantly higher in the RP group than in the non-RP group. The optimal threshold values of sd-LDL-c, TG for predicting RP according to receiver operating characteristics analysis were 20.9, 113, 5.5, and 9.7 mg/dL, respectively. Only the sd-LDL-c level (≥ 20.9 mg/dL) was significantly associated with incident CEs (cardiovascular events) at 31±17 months (log-rank: 4.123, p=0.043).

Our results were supported by study of Thai et al., [11], as they reported that TyG index correlated with log HOMA-IR ($p < 0.0001$). CS ≥ 50% were present in 60 participants and 32 had coronary artery stenosis ≥ 70%. TyG index and HOMA-IR were significantly higher in patients with CS ≥ 70%. The number of narrowed coronary arteries and the degree of stenosis were associated with higher TyG index levels ($p = 0.04$ and $< 0.005$ respectively). A TyG index ≥ 10 was significantly associated with an increased risk of multiple CAD and of more severe CS. After adjusting for confounding factors, including logHOMA-IR, these risks remained mostly significant. A TyG index threshold at 10 resulted in 57% sensitivity and 75% specificity for predicting the presence of CS ≥ 70%.

In the study of Sarwar et al. [23] indicate moderate and highly significant associations between TG values and coronary heart disease risk.

Furthermore, Schwartz et al. [24] reported that fasting TG levels were associated with both long-term and short-term risk after ACS.

## 5. CONCLUSION

There was a positive correlation between the TG and the severity of coronary lesions in pre-diabetic stable angina pectoris patients.

## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT AND ETHICAL APPROVAL

The study was conducted after approval from the Ethical Committee and obtaining informed written consent.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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