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ORIGINAL ARTICLE

High remnant cholesterol is prevalent among type 2 diabetes mellitus patients in the New Juaben Municipality: A cross-sectional study

Selina Quarshie[1] · Aziz Abdul Abdulai Maikaino[1] · Tahiru Alidu[1] · Sampson K. Djonor[2] · George Nkrumah Osei[1] · Richard K D Ephraim[1,3]

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Abstract

Objective Diabetes mellitus (DM) is a global metabolic disorder with high cardiovascular risk. Information on remnant cholesterol (RC) among type 2 DM patients is insufficient in Ghana despite the cardiovascular risk it poses. This study assessed the prevalence, pattern, and correlation of remnant cholesterol levels with other lipid parameters among patients with type 2 DM in the New Juaben Municipality of Ghana.

Methods A cross-sectional study was conducted among type 2 DM patients receiving treatment at St. Joseph Hospital and the Eastern Regional Hospital from January 2022 to May 2022. The sociodemographic details of participants were obtained with a structured questionnaire. Venous blood samples were collected, and analyzed for fasting blood glucose (FBG), total cholesterol (TC), HDL-cholesterol (HDL-C), and triglycerides. These lipid parameters were then used to calculate low density lipoprotein cholesterol (LDL-C), non-HDL-C, and remnant cholesterol (RC) levels. Data were analyzed accordingly using the IBM SPSS and GraphPad Prism.

Results A total of 398 participants were recruited (median age of 50), of whom 265(66.6%) were females. The majority of participants had no family history of DM (78.89%) and were aged 46-65 years (42.21%). The prevalence of high remnant cholesterol was found to be 60.3%. Controlling for all significant factors including HDL-C and sex, having high RC was found to be associated with 51% increased odds of having high non-HDL cholesterol ($p=0.001$). A subgroup analysis on LDL-C and RC indicated that high LDL-C/high RC was most prevalent among participants 156(39.2%). Total cholesterol (TC), triglycerides (TG), non-HDL cholesterol, and LDL- cholesterol were all substantially correlated with discordant/concordant LDL-C and RC.

Conclusion The findings of this study indicate an increased prevalence of high RC among type 2 DM patients projecting a possible increased risk of developing cardiovascular complications in the future. Much attention should therefore be paid to RC and its correlated non-HDL cholesterol in the treatment and management of type 2 DM.

Keywords Remnant cholesterol · Type 2 diabetes mellitus · Non-HDL cholesterol · LDL-cholesterol · Ghana

✉ George Nkrumah Osei
gosei003@stu.ucc.edu.gh

Selina Quarshie
sqwilson1984@gmail.com

Aziz Abdul Abdulai Maikaino
maikanoabdul4@gmail.com

Tahiru Alidu
belgiumboy2011@gmail.com

Sampson K. Djonor
kadjnrsampson@gmail.com

Richard K D Ephraim
rephraim@ucc.edu.gh

[1] Department of Medical Laboratory Science, School of Allied Health Sciences, University of Cape Coast, Cape Coast, Ghana

[2] Department of Immunology, Laboratory Sub-BMC, Korle Bu Teaching Hospital, Accra, Ghana

[3] Kidney Research Initiative, Cape Coast, Ghana

Introduction

Diabetes mellitus (DM) is a metabolic disorder with high prevalence worldwide, causing a significant burden on society and premature mortality [1–5]. DM is caused by high blood glucose levels and disrupted metabolism of carbohydrates, fats, and proteins [6]. Type 2 DM accounts for 85–95% of DM cases in low-income countries [7]. Despite 12% of global health expenditures spent on treating DM and its complications (including both microvascular and macrovascular problems) in 2005, it still caused 5 million deaths worldwide [8, 9].

Remnant cholesterol (RC) refers to the cholesterol component of triglyceride-rich lipoproteins including very low-density lipoprotein and intermediate-density lipoprotein, postprandial chylomicrons, and their remnants [10]. Although plasma triglyceride (TG) can be used in clinical settings as a surrogate measure for triglyceride-rich lipoproteins (TRLs) or RC, they represent different lipid disorders [11]. Cholesterol content in TRLs contributed more directly to cardiovascular disease (CVD) rather than TG, thus, highlighting RC in the lipids management recently [12]. High serum RC concentrations increase arterial wall penetration, leading to faster foam cell formation and inflammation. This can also trigger cytokines, interleukins, and proatherogenic adhesion molecules, potentially leading to plaque rupture and consequently, cardiovascular mortality [13–15]. As a result, it is hypothesized that excessive levels of RC may be a predictive marker of future cardiovascular disease including coronary artery disease (CAD), atherosclerosis development, and a great risk of stroke [16–18].

According to studies by Sugden and Holness (2017), elevated remnant lipoprotein-cholesterol levels are associated with insulin resistance and an independent risk of CAD in type 2 diabetes mellitus patients [17]. In type 2 DM, an increased cardiovascular risk often exists for many years before the onset of biochemical hyperglycemia [19]. However, there is limited information on the prevalence and pattern of remnant cholesterol among type 2 DM in Ghana and sub-Saharan Africa. To help address the issue of increased risk of cardiovascular diseases and arteriosclerosis incidence among type 2 DM patients in Ghana, this study assessed the prevalence and pattern of remnant cholesterol levels, and its association with total cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol, and non-HDL-cholesterol among patients with type 2 diabetes mellitus in the New Juaben Municipality of Ghana. The findings in this study will aid efforts to develop strategies to manage and prevent cardiovascular complications in type 2 DM patients.

Methods and Materials

Study design

A cross-sectional study was conducted at St. Joseph Hospital and the Eastern Regional Hospital in the New Juaben Municipality among type 2 DM patients. The study period was from January 2022 to May 2022. A non-randomized sampling approach was used to select and collect data from the consented participants. A total of 398 participants were recruited for the study.

Eligibility criteria

Individuals diagnosed with type 2 DM regardless of age and gender were eligible for the study. Type 1 DM and non-diabetic patients were excluded. Also, individuals with a history of cardiovascular events or lipid-lowering therapy were excluded.

Sampling collection procedure

Socio-demographic details

The age, sex, marital status, level of education, occupation, and history of type 2 DM in the family were collected from all participants using a structured questionnaire.

Assessment of biochemical parameters

About 5 ml of blood samples were taken from participants after 9–12 h of overnight fasting into a gel tube. The collected blood samples stood for about 10 min to allow for complete clotting and were centrifuged at 4000 rpm for 5 min to obtain serum. The serums were then analyzed for their fasting blood glucose level (FBG), total cholesterol (TC), HDL-cholesterol, and triglycerides using a BIOBASE automatic chemistry analyzer. The Friedewald formula, LDL-c (mg/dL) = TC (mg/dL) − HDL-c (mg/dL) − TG (mg/dL)/5, was then used to calculate for LDL-cholesterol concentration [20, 21]. Remnant cholesterol was calculated by subtracting HDL-C and LDL-C from non-fasting total cholesterol (RC = TC − HDL-C − LDL-C) [22]. Non-HDL-C was also calculated by subtracting HDL-C from total cholesterol [23, 24].

Data analysis

Initial entry and organization of data were done using Microsoft Excel. The data were cleaned and imported into IBM SPSS and GraphPad Prism for analysis. The normality of the variables was assessed using the Kolmogorov–Smirnov test.

Comparison of variables was done with Kruskal–Wallis test for continuous variables with a non-normal distribution and results were shown as median (Q1–Q3), while for variables following normal distribution, student *t*-test statistics were used and results shown as mean with standard deviations. All analyses were done at a 95% confidence interval, and *p*-values less than or equal to 0.05 were considered statistically significant.

Results

The study involved 398 participants [median age 50]. Table 1 summarizes the sociodemographic characteristics of participants. The majority of participants were female 265 (66.6%), married 239 (60.1%), and hold a high school education certificate (JHS/O'Level/SHS/A'Level) 254 (63.8%) (Table 1). The majority of participants (42.21%) were also aged from 46 to 65 years with the least number of participants (9.55%) aged less than 25 years. Three hundred and fourteen participants (78.89%) had no family history of DM (Table 1). The majority of participants were traders (37.94%) followed by those who were either students or unemployed (31.66%).

The prevalence of high remnant cholesterol (RC) was 60.3% ($n = 240$) [cut-off of 0.62 mmol/L (24 mg/dL)]. Table 1 also shows the association between RC (low and high) and various socio-demographics of participants. Participants aged 26 to 45 [68.18% (75 out of 110)], as well as farmers/fashion designers and retirees (64.00% and 64.29%, respectively), were found to have high levels of RC. High RC was however equally distributed among males and females as well as participants with and without a family history of DM (Table 1).

Figure 1 shows the distribution of various biomedical markers such as remnant cholesterol (RC), low-density lipoprotein cholesterol (LDL-C), and fasting blood glucose (FBG) among participants in graphs. None of the variables

Table 1 Socio-demographic characteristics and the association between remnant cholesterol and socio-demographic characteristics of participants

Variable	Overall	Low RC ($n = 158$)	High RC ($n = 240$)	*p*-value
Age category (years) [50 (37–64)]				0.200*
< 25	38 (9.55)	15 (39.47)	23 (60.53)	
26–45	110 (27.64)	35 (31.82)	75 (68.18)	
46–65	168 (42.21)	70 (41.67)	98 (58.33)	
> 65	82 (20.60)	38 (46.34)	44 (53.66)	
Sex				
Female	265 (66.58)	105 (39.62)	160 (60.38)	0.965*
Male	133 (33.42)	53 (39.85)	80 (60.15)	
Marital status				
Single	55 (13.82)	21 (38.18)	34 (61.82)	0.735*
Married	239 (60.05)	93 (38.91)	146 (61.09)	
Divorced	35 (8.79)	17 (48.57)	18 (51.43)	
Widowed	69 (17.34)	27 (39.13)	42 (60.87)	
Level of education				0.856#
None	16 (4.02)	7 (43.75)	9 (56.25)	
Elementary/primary	14 (3.52)	4 (28.57)	10 (71.43)	
JHS/O'Level/SHS/A'Level	254 (63.82)	102 (40.16)	152 (59.84)	
Tertiary	114 (28.64)	45 (39.47)	69 (60.53)	
Occupation				0.965#
Unemployed/student	126 (31.66)	53 (42.06)	73 (57.94)	
Trading	151 (37.94)	60 (39.74)	91 (60.26)	
Farming/fashion design	25 (6.28)	9 (36.00)	16 (64.00)	
Civil servant/teaching/security	82 (20.60)	31 (37.80)	51 (62.20)	
Retired	14 (3.52)	5 (35.71)	9 (64.29)	
Family history of diabetes				
No	314 (78.89)	125 (39.81)	189 (60.19)	0.931*
Yes	84 (21.11)	33 (39.29	51 (60.71)	

Data were expressed as mean ± SD, median (25th and 75th percentile), or *n* (%)

*Chi square *p*-value; #Fisher's exact *p*-value

appears to have a perfectly normal distribution among participants.

In assessing the association between RC and other lipid parameters, RC was found to be significantly associated with total cholesterol (TC), triglycerides (TG), and non-high density lipoprotein cholesterol (non-HDL-C) (Table 2). However, the association between these significant parameters in earlier analyses was explored in logistic regression. Controlling all significant factors including HDL-C and sex, having high RC was associated with increased odds of having high non-HDL cholesterol (aOR = 1.51, 95% CI 1.19–1.91, $p = 0.001$) (Table 3). To better understand the association, scatter diagrams with best-fitted lines at a 95% confidence interval (95% CI) were constructed for RC against non-HDL cholesterol (Fig. 2). Increasing non-HDL cholesterol was associated with increasing RC as well.

To assess the impact of RC and the LDL-C in type 2 DM patients as employed in studies by Hu et al. (2022), study participants were categorized into four groups (group 1: low LDL-C/low RC, group 2: low LDL-C/high RC, group 3: high LDL-C/ low RC, and group 4: high LDL-C/high RC) based on LDL-C and RC cut-off points of 2.6 mmol/L (100 mg/dL) and 0.62 mmol/L (24 mg/dL) respectively [11]. The prevalence of concordant low LDL-C and low RC was 15.3% ($n = 61$), that of discordant low LDL-C and high RC was 21.1% ($n = 84$), that of discordant high LDL-C and low RC was 24.4% ($n = 97$), and that of concordant high LDL-C and high RC was 39.2% ($n = 156$) (Table 4). Discordant/

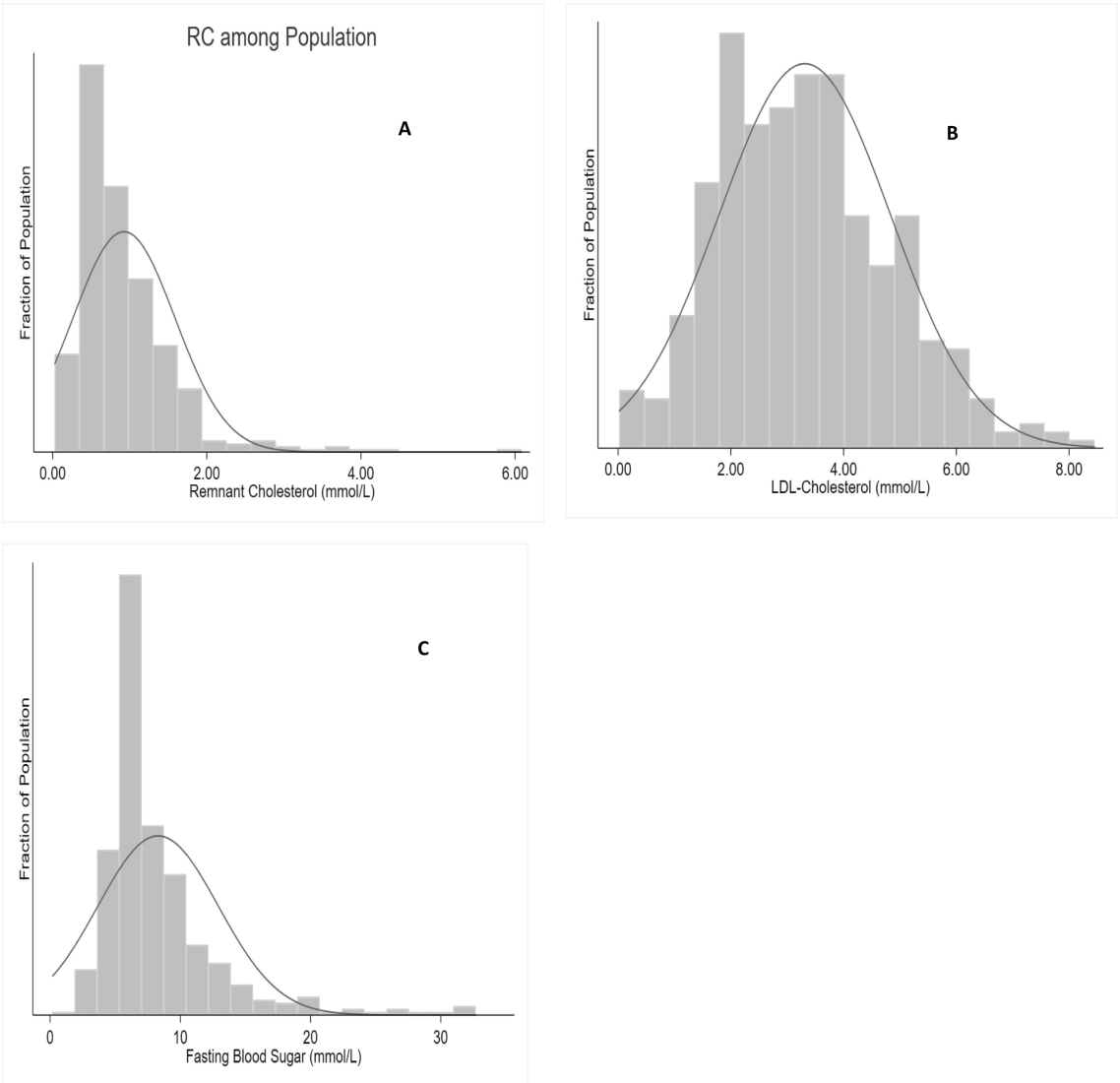

Fig. 1 Distribution of various biochemical parameters among participants by graphs. **A** Remnant cholesterol. **B** Low-density lipoprotein cholesterol. **C** Fasting blood glucose

Table 2 Association between remnant cholesterol and other lipid parameters and FBG

Variable	Overall	Low RC (n = 158)	High RC (n = 240)	*p*-value
HDL-C	1.11 (0.79–1.54)	1.14 (0.77–1.56)	1.10 (0.80–1.54)	0.821†
Total cholesterol (TC)	5.35 (4.15–6.55)	4.97 (3.81–6.16)	5.54 (4.55–6.75)	0.0001†
Triglycerides (TG)	1.60 (1.12–2.54)	1.05 (0.81–1.19)	2.30 (1.79–3.20)	< 0.0001†
Non-HDL-C	3.81 (2.73–4.89)	3.02 (2.03–4.44)	4.12 (3.15–5.09)	< 0.0001†
LDL-C	3.20 (2.17–4.26)	3.29 (2.17–4.35)	3.19 (2.17–4.19)	0.695†
LDL-C category				0.464*
Low [≤ 2.60 mmol/L (100 mg/dL)]	145 (36.43)	61 (42.07)	84 (57.93)	
High [> 2.60 mmol/L (100 mg/dL)]	253 (63.57)	97 (38.34)	156 (61.66)	
FBG (mmol/L)	6.86 (5.74–9.80)	6.86 (5.74–9.88)	6.83 (5.73–9.54)	0.613†

Data were expressed as median (25th and 75th percentile) or *n* (%). Convert TG and FBG from SI units (mmol/L) to mg/dL by multiplying by 88.57 and 18, respectively

LDL-C low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *FBG* fasting blood glucose

†Mann–Whitney *U* test *p*-value; *chi-square *p*-value

Table 3 Logistic regression of remnant cholesterol groups against significantly associated biochemical parameters of participants

Variable	OR ± SE	95% CI	*p*-value	AOR ± SE	95% CI	*p*-value
Total cholesterol (mmol/L)	1.28 ± 0.08	1.3–1.46	< 0.0001	0.98 ± 0.12	0.77–1.25	0.875
Triglycerides (mmol/L)#	-	-	-	-	-	-
Non-HDL-C (mmol/L)	1.47 ± 0.11	1.28–1.69	< 0.0001	1.51 ± 0.18	1.19–1.91	0.001

CI confidence interval, *SE* standard error, *OR* crude odds ratio, *AOR* adjusted odds ratio while controlling for all significant factors including HDL-C and sex (Varbo, Benn et al., 2013; Huh, Han, Cho, Kang 2022) in that order

#Predicts data perfectly (all those with high TG were found to belong to the high remnant cholesterol group)

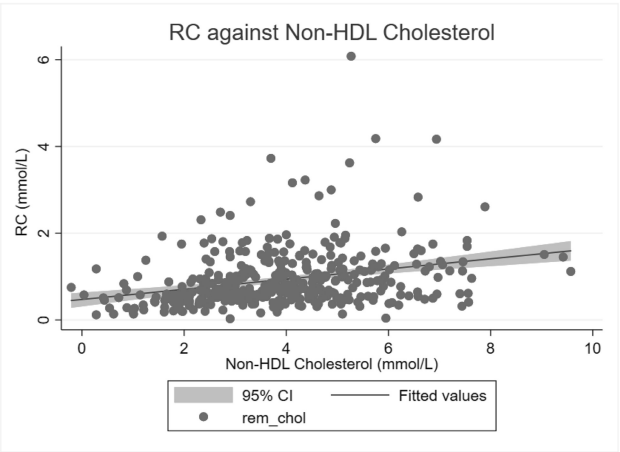

Fig. 2 Association between RC and non-high-density lipoprotein (non-HDL) cholesterol using scatter plots

concordant LDL-C and RC were significantly associated with total cholesterol (TC), triglycerides (TG), non-HDL-C, and LDL-C (Table 4).

Discussion

Elevated remnant cholesterol levels are associated with insulin resistance and an independent risk of cardiovascular disease in type 2 DM patients. This study assessed the prevalence and pattern of remnant cholesterol levels and its association with total cholesterol, triglycerides, LDL-cholesterol, HDL-cholesterol, and non-HDL-cholesterol among patients with type 2 DM in the New Juaben Municipality of Ghana.

The study involved 398 participants with the majority of participants being females 265 (66.6%), and married 239 (60.1%). This gender pattern differs from similar studies conducted by Ram et al. (2014) and Dedov et al. (2016) who found a male dominance (59%) and an equal distribution in both sexes among type 2 DM patients respectively [25, 26]. The majority of participants were aged 46–65 years (42.21%), with 78.89% having no family history of type 2 DM. This indicates that persons in their midlife age are more prone to developing type 2 DM.

Remnant cholesterol prevalence was found to be 60.3% among participants. This finding was in line with similar studies by Hu et al. (2022), Cao et al. (2020), and Shan et al.

Table 4 Association between lipid parameters and groups of discordant/concordant LDL-C and RC

Variable	Overall	Group 1 [low LDL-C and low RC] $n=61$	Group 2 [low LDL-C and high RC] $n=84$	Group 3 [high LDL-C and low RC] $n=97$	Group 4 [high LDL-C and high RC] $n=156$	p-value†
HDL-C	1.11 (0.79–1.54)	1.01 (0.72–1.25)	1.06 (0.77–1.45)	1.25 (0.80–1.70)	1.16 (0.84–1.64)	0.058
Total cholesterol (TC)	5.35 (4.15–6.55)	3.47 (2.86–3.91)	4.21 (3.74–4.74)	5.94 (5.13–6.90)	6.39 (5.44–7.17)	0.0001
Triglycerides (TG)	1.60 (1.12–2.54)	1.06 (0.81–1.23)	2.58 (1.85–3.86)	1.02 (0.81–1.18)	2.24 (1.73–2.86)	0.0001
Non-HDL-C	3.81 (2.73–4.89)	2.09 (1.72–2.65)	3.01 (2.65–3.60)	4.00 (3.19–5.07)	4.69 (4.01–5.69)	0.0001
LDL-C	3.20 (2.17–4.26)	1.98 (1.42–2.28)	1.98 (1.42–2.19)	3.99 (3.43–5.05)	3.84 (3.23–4.86)	0.0001
FBG (mmol/L)	6.86 (5.74–9.80)	7.07 (5.90–9.60)	7.05 (5.64–9.29)	6.71 (5.70–9.88)	6.79 (5.80–9.82)	0.894

Data was presented as median (Q1–Q3)

LDL-C low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *RC* remnant cholesterol, *FBG* fasting blood glucose

†Kruskal Wallis rank test p-value

(2022) in China, who found increased levels of RC among DM patients [11, 27, 28]. Studies by Hu et al. (2022) found an association between RC and the risk of type 2 DM incidence in the general population indicating RC concentration as an independent risk factor for the development of type 2 DM [29]. This can as well be observed in our study which projected a high prevalence of RC among type 2 DM patients suggesting a likely association between type 2 DM incidence and RC.

Despite the fact that female dominance and unequal distribution of participants with and without type 2 DM in their families was found, high RC was however evenly distributed among males and females as well as participants with and without a family history of type 2 DM. This indicates that RC levels in type 2 DM patients are not affected by sex as well as being genetically related to persons with type 2 DM.

Controlling all significant factors including HDL-C and sex, having high RC was also found to be associated with 51% increased odds of having high non-HDL cholesterol ($p=0.001$). This current study's finding offers novel evidence that circulating level of RC is positively correlated with non-HDL cholesterol levels. This positive correlation corresponds with studies by Lu et al. (2013) and Jiang et al. (2004) who found non-HDL cholesterol as a strong predictor of cardiovascular disease in men and women with DM [30, 31]. High RC has also been associated with the incidence of new-onset carotid plaque even in participants of lower baseline LDL-C levels after about 7 years of follow-up on people without any incidence of CVDs [32] leading to a recommendation that in people with low LDL-C, RC can be used as a marker in preventing atherosclerotic outcomes. These findings, therefore, stand to suggest that RC and non-HDL cholesterol should be measured simultaneously in assessing plausible prediction of cardiovascular disease among individuals with type 2 DM patients.

The study also found discordant/concordant LDL-C and RC to be associated with type 2 DM to varying degrees. High LDL-C/high RC subgroup was more common among participants. More importantly, this relationship was stronger in females than males. This finding however differed from that reported by Hu et al. (2022) who found subgroup low LDL-C/high RC to be more common among DM patients projecting the role of RC beyond LDL-C in DM patients [11]. These variations could be due to differences in sample size, study design, population, and duration employed in both studies.

Our study has a few limitations. This study used a cross-sectional study design and hence could not establish causal associations or risks with RC. LDL-C measurement was calculated and not obtained from the direct measurement from a chemistry analyzer which may be prone to analytical errors of TG, total cholesterol, and HDL-C.

Conclusion

The study shows an increased prevalence of high remnant cholesterol (RC) among type 2 diabetes mellitus patients with an equal distribution among males and females as well as participants with and without a family history of DM. It is therefore prudent that RC is significantly monitored and controlled for individuals with type 2 DM to prevent possible onset of micro- and macro-vascular complications that impedes adequate treatment outcomes, optimal disease control, and quality of life.

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Authors' contribution RKDE, SQ, ABAM, TA, and GNO conceived and designed this study. SQ, ABAM, TA, and SKD were responsible for data collection and analysis. SQ, ABAM, TA, GNO, and SKD were responsible for data visualization. RKDE and GNO drafted the manuscript. All authors revised the manuscript critically for important intellectual content. All authors read and agreed with the final manuscript.

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Data availability All data generated or analyzed during this study are available upon request from the corresponding author.

Declarations

Conflict of interest The authors declare no competing interests.

Ethical consideration The study was approved by the Department of Medical Laboratory Science, University of Cape Coast. Ethical clearance was sought from the institutional review board of St. Joseph Hospital. All methods were carried out following relevant guidelines and regulations. Informed consent was obtained from all participants. Confidentiality was also observed throughout the entire study.

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