

Lipid Profiles of Nigerians Living with type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis

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Abstract

Introduction: Dyslipidemia is often associated with type 2 diabetes (T2D), with both having an additive effect on cardiovascular risk. The objective of the meta-analysis was to determine the prevalence of dyslipidemia in individuals living with T2D mellitus in Nigerian and to examine the pattern of their dyslipidemia. **Methods:** The study followed the preferred reporting items for systematic reviews and meta-analyses guidelines. Medical databases such as PubMed, Google Scholar, African Journals Online, and SCOPUS as well as the gray literature were systematically searched. MetaXL was used for statistical analysis adopting the random effect model. Heterogeneity was determined using the I^2 statistic, while publication bias was assessed with the funnel plot. **Results:** Twenty-two studies met the eligibility criteria for the meta-analysis. The total sample size was 3575. The prevalence of dyslipidemia among Nigerians living with diabetes ranges from 25% to 97.1%. The pooled prevalence of dyslipidemia among Nigerians living with T2D was 63% (95% confidence interval [CI]: 52%–72%). I^2 statistic was 97%. The funnel plot implied minimal publication bias. The pooled prevalence of elevated low-density lipoprotein cholesterol was 33% (95% CI: 18%–49%). The pooled prevalence of elevated hypertriglyceridemia was 88% (95% CI: 84%–91%). The pooled prevalence of low high-density lipoprotein cholesterol (HDL-C) was 47% (95% CI: 32%–62%). The pooled prevalence of elevated hypercholesterolemia was 33% (95% CI: 23%–43%). **Conclusions:** The prevalence of dyslipidemia among Nigerians with T2D mellitus is very high. The most common abnormalities are hypertriglyceridemia and low HDL-C.

Keywords: Dyslipidemia, hypercholesterolemia, lipid profile, Nigeria, prevalence, type 2 diabetes

INTRODUCTION

Diabetes mellitus is the most common metabolic disorder globally.^[1] It is characterized by chronic hyperglycemia caused by a deficiency of insulin secretion or action or both.^[2] The global prevalence of diabetes is about 9.3% which translates to over 400 million people living with diabetes worldwide.^[3] There are over 15 million individuals who live with diabetes in Africa.^[4] In a meta-analysis, the prevalence of diabetes in Nigeria was estimated as 5.8%, although the age-adjusted prevalence of diabetes in Nigeria was reported as 3.1% by the International Diabetes Federation.^[5,6] Diabetes increases the risk of cardiovascular mortality by 2–4 times.^[7] Dyslipidemia further increases the incidence and mortality from cardiovascular disease among individuals living with diabetes.^[8] Nigeria has the largest number of people living with diabetes in Africa; hence, it^[8] becomes imperative to highlight the factors predisposing to increased cardiovascular death among this cohort of Nigerians.^[9]

Abnormalities of the lipid profile are one of the constellations of clinical presentations that accompany type 2 diabetes (T2D) in a disorder termed metabolic syndrome. Insulin resistance has been proposed as the key concept behind metabolic syndrome. Therefore, metabolic syndrome is sometimes called insulin resistance syndrome.^[10] Dyslipidemia is generally defined as one or more of the following abnormalities – elevated low-density lipoprotein cholesterol (LDL-C), elevated total cholesterol (TC), elevated fasting triglyceride (TG), and reduced high-density lipoprotein cholesterol (HDL-C).^[11]

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Dyslipidemia has been richly documented in the literature to be a major risk factor for cardiovascular disease.^[12] According to the National Cholesterol Education Program Adult Treatment Panel III, dyslipidemia was defined as elevated LDL-C >130 mg/dl, TC >200 mg/dl mmol/L, fasting TG >150 mg/dl, and/or HDL-C lower than 40 mg/dl in men or 50 mg/dl in women.^[11]

A peculiar pattern of dyslipidemia in diabetes, characterized by low HDL-C, elevated triglycerides, and elevated small dense LDL-C, is termed diabetic dyslipidemia.^[13] Diabetic dyslipidemia has been associated with a high risk of cardiovascular disease.^[14] This calls for a special attention to this deleterious phenomenon. Even among individuals with diabetic dyslipidemia who are on statins and lifestyle therapy, there remains a residual increased cardiovascular risk and this implies that extensive researches are still needed to unravel this complicated observation.^[15] An important peculiarity of diabetic dyslipidemia is the increase in the highly atherogenic small dense LDL rather than the absolute LDL level (which is comparable with that of nondiabetic controls).^[16] Insulin resistance is the main culprit in the pathophysiology of diabetic dyslipidemia.^[17]

Peripheral insulin resistance leads to increased adipose tissue lipolysis and free fatty acid production.^[13] Enhanced flux of free fatty acids to the liver causes increased hepatic synthesis of triglyceride-rich very low-density lipoprotein (VLDL). A rise in VLDL synthesis as well as a fall in chylomicron clearance results in increased levels of triglyceride-rich lipoprotein (TGRL). Through the action of cholesteryl ester transfer protein, triglyceride (TG) is passed on to LDL and HDL in exchange for cholesterol. Triglyceride-rich LDL is catabolized to a smaller but denser LDL (otherwise called small dense LDL) by lipoprotein lipase and hepatic lipase. In the same vein, triglyceride-rich HDL is rapidly catabolized to a smaller but denser HDL which is quickly cleared from the circulation, ultimately resulting in a lower measured HDL.

The objective of the meta-analysis was to determine the prevalence of dyslipidemia in individuals living with T2D mellitus in Nigerian and to examine the pattern of the dyslipidemia. To the best of the authors' knowledge, this is the first meta-analysis addressing the prevalence and pattern of dyslipidemia among Nigerians with diabetes. This is quite important because Nigeria has the largest number of people living with T2D in Africa.^[18]

METHODS

This study is a meta-analysis. Therefore, the data used for the analysis were obtained from a detailed search of the electronic database as well as the gray literature. These data bases included PubMed, Google Scholar, African Journals Online and SCOPUS. The pre-print databases, medRxiv and Research Square, were also systematically searched. The gray literature was also considered by communicating with the relevant experts who might have

done or supervised works on the subject matter which are yet to be published although this did not yield any additional work. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines were strictly adhered to in this meta-analysis.

The eligibility criteria for selection of studies included studies on the prevalence and/or pattern of dyslipidemia among individuals living with T2D. Only studies done in Nigeria were included. In addition, the studies must have been done between January 1, 2000, and June 30, 2021. Therefore, studies on dyslipidemia in T2D carried out outside Nigeria were excluded. Similarly, studies that did not report the prevalence and/or pattern of dyslipidemia were excluded. The search terms included "dyslipidemia," "lipid disorder," "lipid abnormalities," "prevalence," "patterns," "diabetes," "diabetes mellitus," "type 2 diabetes," and "Nigeria." The Boolean operators "AND," "OR" as well as "NOT" were utilized as deemed appropriate to improve the depth, quality, and specificity of the search output.

The abstracts and the full texts of the studies were independently scrutinized by the authors. The decision to include the relevant studies was based on the eligibility criteria and independent endorsement by the majority of the authors. All the authors screened the records independently. The risk of bias in the individual studies was assessed using the National Institute of Health (NIH) quality assessment tool for observational studies. A study that answered "YES" to 0–4 questions out of 14 was rated as "poor," while a study that answered "YES" to 5–10 questions out of 14 was rated as "fair" and a study that answered "YES" in 11–14 questions out of 14 was rated as "good." This was done independently by the authors, and any inconsistent rating was adjudged by consensus.

The Excel spreadsheet was employed for the initial data extraction, collation, and scrutiny. The meta-analysis was done by using Meta XL version 5.3 (EpiGear International Ltd, Sunrise Beach, Queensland, Australia). Meta XL version 5.3 is an add-in software for Microsoft Excel. The variables of interest were the year of study, the type of study, the region where the study was conducted, and the sample size. The DerSimonian–Laird random effect model was utilized in the meta-analysis. Heterogeneity was determined using the I^2 statistic and Cochran's q -test. Publication bias was assessed with the LFK index and funnel plot.

RESULTS

Twenty-two studies met the eligibility criteria for the meta-analysis.^[18-38] The study selection algorithm is illustrated in the PRISMA flow diagram, as shown in Figure 1. Using the NIH quality assessment tool for observational studies, 87% of the studies were adjudged "good," while 13% were considered to be "fair." None of the studies were "poor." The study characteristics are shown in Table 1. The majority (86%) of the selected studies were cross-sectional in design. Similarly,

most of the studies (86%) were carried out in southern Nigeria. This implies a lack of uniform distribution in the studies across the country and this might be a limitation to generalizability of the meta-analysis.

The total sample size was 3575. The prevalence of dyslipidemia among Nigerians living with diabetes ranged from 25% to 97.1%. The pooled prevalence of dyslipidemia among Nigerians living with T2D was 63% (95% confidence interval [CI]: 52%–72%). The forest plot of the meta-analysis is shown in Figure 2. Heterogeneity was determined using the I^2 statistic and the Cochran's Q. I^2 statistic was 97%, while Cochran's Q was 780 ($P < 0.001$). These imply that there was a significant heterogeneity in the studies selected for this meta-analysis. Publication bias was tested using the LFK index which was -1.78 . This implies minimal publication bias. This was further corroborated by the funnel plot which is shown in Figure 3.

Table 2 below shows the pattern of dyslipidemia among the selected studies. The prevalence of elevated LDL-C among individuals with T2D is 0%–92.3%. The pooled prevalence of elevated LDL-C is 33% (95% CI: 18%–49%). The prevalence of hypertriglyceridemia among individuals with T2D is 7.9%–87.7%. The pooled prevalence of elevated hypertriglyceridemia was 88% (95% CI: 84%–91%). The prevalence of low HDL-C among individuals with T2D was 13%–100%. The pooled prevalence of low HDL-C is 47% (95% CI: 32%–62%). The prevalence of hypercholesterolemia among individuals with T2D was 12.3%–92.3%. The pooled prevalence of elevated hypercholesterolemia was 33% (95% CI: 23%–43%). The

summary of the pattern of dyslipidemia among Nigerian living with T2D is shown in Figure 4. It shows that the most common pattern of dyslipidemia in T2D is hypertriglyceridemia with low HDL-C.

DISCUSSION

This study reports the prevalence of dyslipidemia among Nigerians living with T2D as 63%. In Ethiopia, another developing sub-Saharan African country, the prevalence of dyslipidemia in T2D was found to be 66.7% which is similar to the results of the present study.^[40] However, the prevalence of dyslipidemia in this study is lower than what was reported from South Africa (86.7%), another developing sub-Saharan African nation.^[41] In contrast to this, based on a study done in Ghana, which is also a developing sub-Saharan African country, the prevalence of dyslipidemia in T2D was lower compared to what was found in this meta-analysis (53% vs. 63%).^[42] These differences might be due to the differences in the sociodemographic characteristics of the populations involved in the various studies. However; this may also be due to the methods used to assess prevalence between the various studies in the different countries.

Therefore, whichever perspective it is looked at, the prevalence of dyslipidemia among Nigerians living with T2D is high. Insulin resistance has been a key concept propounded behind the high prevalence of dyslipidemia in T2D.^[43,44] This is corroborated by the fact that a high prevalence of insulin resistance (95.5%) has been documented among Nigerians with T2D.^[45] Increasing adoption of western lifestyle and diet has also been put forward as a factor contributing to the high prevalence of dyslipidemia among Nigerians with T2D.^[46] It has also been reported that the prescription and adherence to statin usage among Nigerians with T2D is relatively low although this meta-analysis did not examine the frequency and effectiveness of statin usage among individuals with T2D which is a limitation of the study.^[47]

In terms of pattern of dyslipidemia, the study shows that the most common lipid disorders among patients living with T2D in Nigeria are hypertriglyceridemia and low HDL-C. The pooled prevalence of hypertriglyceridemia among individuals with T2D was 88%. In a study done in Ethiopia, the prevalence of hypertriglyceridemia among individuals with T2D was also reported to be very high (72.4%), although not as high as the present study.^[48] However, this is markedly different from the findings of Omodanisi *et al.* who reported the prevalence of 64% in their study done in South Africa.^[49] Differences in study design and demographics may be partly responsible for these differences. Insulin resistance and hyperglycemia cause increased production of TG-rich lipoproteins (TRLs), reduced clearance of TRLs, and suboptimal metabolism of postprandial triglyceride spike.^[17]

Another common observation in the lipid profile of people living with T2D in this study was low HDL-C. The pooled prevalence of low HDL-C among patients with T2D was 47%.

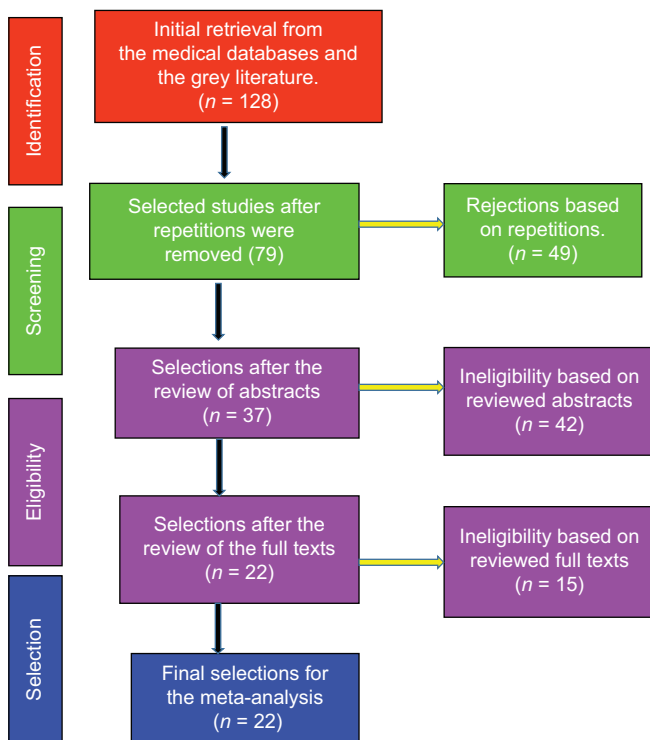


Figure 1: The preferred reporting items for systematic reviews and meta-analyses flow diagram

Table 1: Characteristics of the selected studies

Study	Year	Type	Sample size	Prevalence	Region
Isezuo <i>et al.</i> ^[19]	2003	Cross-sectional	40	25%	NW
Isezuo and Ezunu ^[20]	2005	Cross-sectional	254	72.4%	NW
Idogun <i>et al.</i> ^[21]	2007	Cross-sectional	52	30%	SS
Okafor <i>et al.</i> ^[22]	2008	Cross-sectional	192	89%	SW
Unadike <i>et al.</i> ^[23]	2008	Cross-sectional	32	68.7%	SS
Ogbera <i>et al.</i> ^[24]	2009	Cross-sectional	600	89%	SW
Kayode <i>et al.</i> ^[25]	2010	Cross-sectional	113	50.4%	SW
Edo and Adediran ^[26]	2011	Cross-sectional	52	32.7%	SS
Jisieike-Onuigbo <i>et al.</i> ^[27]	2011	Cross-sectional	108	90.7%	SE
Okafor <i>et al.</i> ^[22]	2012	Cross-sectional	233	97.1	SE
Oyelade <i>et al.</i> ^[28]	2013	Cross-sectional	219	58.5%	SW
Edo <i>et al.</i> ^[29]	2014	Retrospective	63	30.2%	SS
Ogedengbe and Ezeani ^[30]	2014	Cross-sectional	106	50.8%	SE
Edo and Edo ^[31]	2016	Retrospective	130	29.2%	SS
Enikuomehin <i>et al.</i> ^[32]	2016	Cross-sectional	300	50.4%	SW
Fasanmade <i>et al.</i> ^[33]	2016	Cross-sectional	218	80.7%	SW
Young and Onyenekwe ^[34]	2016	Cross-sectional	51	82.4%	SE
Omotoye and Fadupin ^[35]	2017	Cross-sectional	50	70%	SW
Engwa <i>et al.</i> ^[36]	2018	Cross-sectional	72	40.8%	SE
Bello-Ovosi <i>et al.</i> ^[37]	2019	Cross-sectional	322	69.3%	NW
Jaja and Yarhere ^[38]	2019	Cross-sectional	22	86.4%	SS
Amadi <i>et al.</i> ^[39]	2020	Retrospective	346	46.8%	SS

NW: North-west, SS: South-south, SW: South-west, SE: South-east

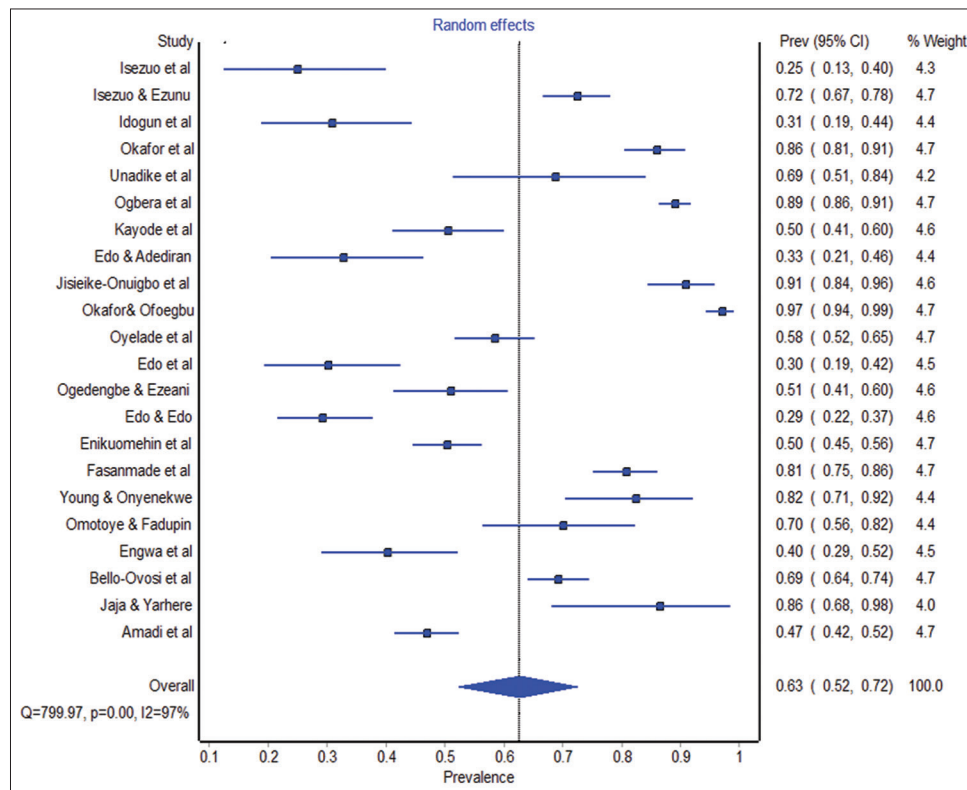


Figure 2: Forest plot of the meta-analysis

Similar findings were reported by Omodanisi *et al.*(52%) in South Africa.^[49] Similarly, in a meta-analysis done among Ethiopians living with T2D, the prevalence of low HDL-C

was reported as 44.36%, which is similar to the findings of this present meta-analysis.^[50] Insulin resistance enhances the increased production of TRLs which exchange triglyceride

Table 2: Pattern of dyslipidemia among individuals living with type 2 diabetes in Nigeria

Study	Sample size	↑LDL-C (%)	↑TG (%)	↓HDL-C (%)	↑TC (%)
Isezuo <i>et al.</i> ^[19]	40	0	10.5	28.1	12.3
Idogun <i>et al.</i> ^[21]	52	92.3	30.8	100	92.3
Okafor <i>et al.</i> ^[22]	192	58.9	25	88	55.2
Ogbera <i>et al.</i> ^[24]	600	74	53	13	42
Kayode <i>et al.</i> ^[25]	113	0	10.5	28.1	12.3
Edo and Adediran ^[26]	52	9.6	19.2	32.7	26.9
Jisieike-Onuigbo <i>et al.</i> ^[27]	108	44.4	56.5	62	53.7
Oyelade <i>et al.</i> ^[28]	219	23.7	16	44.3	12.3
Edo <i>et al.</i> ^[29]	63	30.2	7.9	25.4	17.5
Ogedengbe and Ezeani ^[30]	106	41.1	27	50.8	34.7
Edo and Edo ^[31]	130	26.9	9.2	29.2	13.1
Enikuomehin <i>et al.</i> ^[32]	187	38.3	24.7	28.3	28.3
Omotoye and Fadupin ^[35]	50	34	86.4	72	36
Engwa <i>et al.</i> ^[36]	72	27.7	40.8	NA	39.4
Jaja and Yarhere ^[38]	22	34	86.4	36.4	22.7
Amadi <i>et al.</i> ^[39]	346	NA	87.7	49.4	NA

NA: Not available, LDL-C: Low-density lipoprotein cholesterol, TG: Triglyceride, HDL-C: High-density lipoprotein cholesterol, TC: Total cholesterol

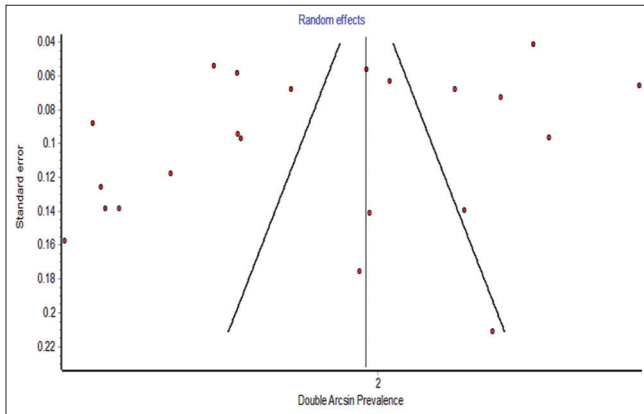


Figure 3: Funnel plot showing minor asymmetry

with cholesterol on HDL-C, making the HDL-C more susceptible to increased clearance from the bloodstream.^[51] This invariably leads to low HDL-C.

This study is highly relevant to diabetes practice in Nigeria because it is a summated substantive evidence that dyslipidemia is very common among Nigerians living with T2D. This calls for intensified testing of lipid profile among this cohort of persons and a closer attention to control the lipid abnormality so as to reduce the risk of cardiovascular morbidity and mortality. The study would also give policymakers an evidence-based reference to improve the resources allocated to the cost of care of individuals with diabetes, as the highly prevalent dyslipidemia in T2D is an additional economic burden. Having highlighted how common lipid disorders are in T2D, future research can be devoted to the treatment and possible prevention of the disease.

To the best of our knowledge, this is the first meta-analysis that estimates the prevalence of dyslipidemia among individuals with T2D in Nigeria. It not only provides the pooled prevalence

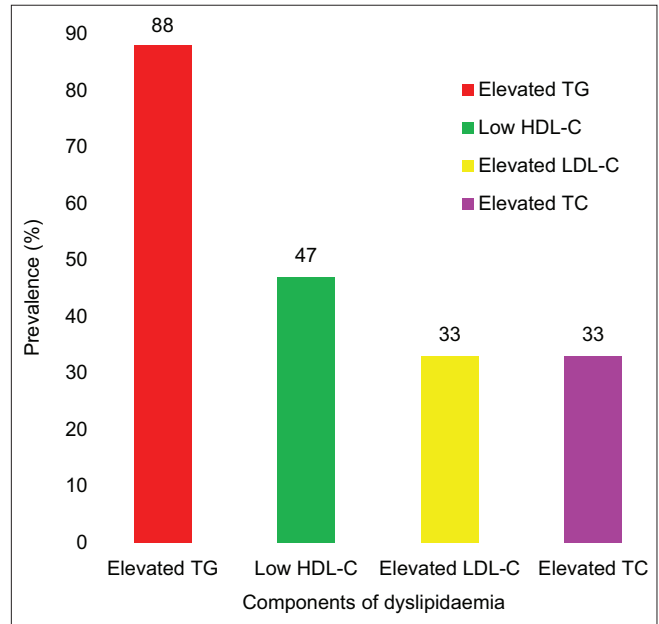


Figure 4: Pattern of dyslipidemia in type 2 diabetes mellitus

of dyslipidemia but also characterizes the pattern of lipid profiles among people living with T2D in Nigeria.

As indicated by the high I^2 statistic and the Cochran's Q score, there was a high level of heterogeneity in the studies selected for the meta-analysis. Similarly, there was an uneven distribution of the studies across the country. This may question the generalizability of the meta-analysis. Furthermore, there were no data on the level of glycemic control as well as the extent of statin usage among the participants of the study.

CONCLUSIONS

The prevalence of dyslipidemia among Nigerians with T2D is very high. The most common abnormalities are

hypertriglyceridemia and low HDL-C. Clinicians need to be aware of this so as to pay a closer attention to the lipid profiles of their patients with T2D.

Authors' contribution

All named authors confirm that they fulfill the ICMLE authorship criteria and have approved the final version of the article.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

Ethical approval is not required for systematic reviews and meta-analysis.

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