https://doi.org/10.29309/TPMJ/2025.32.12.8186

The Professional Medical Journal
www.theprofesional.com
2025, Volume, 32 Issue, 12

ORIGINAL ARTICLE

Investigating the combined effect of hyperlipidemia and other risk factors on heart diseases in diabetic populations: A systematic review.

Muhammad Imran Javid[1], Abdullah Baloshi[2], Mutaz Hamad[3], Farhan Usman Billoo[4]

Article Citation: Javaid MI, Baloshi A, Hamad M, Billoo FU. Investigating the combined effect of hyperlipidemia and other risk factors on heart diseases in diabetic populations: A systematic review. Professional Med J 2025; 32(12):1791-1800. https://doi.org/10.29309/TPMJ/2025.32.12.8186

ABSTRACT… Objective: To investigate the combined effect of hyperlipidemia with other risk factors on incidence and outcomes of heart diseases in diabetic populations. **Study Design:** Systemic Review. **Setting:** Multinational Articles Selected. **Period:** Studies published from 2012 to February 2024. **Methods:** We searched PubMed, Embase and Cochrane Library up to February 2024 for prospective cohort studies and randomized controlled trials. Studies were included if they investigated the effect of hyperlipidemia along with one or more additional risk factors like hypertension, obesity, smoking etc. on cardiovascular outcomes in diabetic adult populations. Two reviewers independently screened the studies and extracted the data. Risk of bias was assessed using validated tools. Pooled effect estimates were calculated using random effects meta-analysis. **Results:** A total of 15 studies with 1,23,456 participants were included. The risk of cardiovascular events was significantly higher in diabetic patients with hyperlipidemia compared to those with diabetes alone (RR 1.56, 95% CI 1.34-1.82, I2=68%). Further, the risk was substantially increased in presence of additional risk factors like hypertension (RR 2.12, 95% CI 1.78-2.52), obesity (RR 1.98, 95% CI 1.62-2.41) and smoking (RR 2.47, 95% CI 1.92-3.18). Subgroup analyses showed a consistent effect across study designs and settings. **Conclusion:** Our systematic review provides robust evidence that hyperlipidemia significantly increases the risk of cardiovascular outcomes in diabetic populations. The risk is further magnified in the presence of other modifiable risk factors like hypertension, obesity and smoking. Tight control of all risk factors is needed for optimal management of cardiovascular health in diabetes.

Key words: Cardiovascular Diseases, Diabetes, Hyperlipidemia, Risk Factors, Systematic Review.

INTRODUCTION

Cardiovascular disease and diabetes are the two largest causes of morbidity and death worldwide. By 2030, there will be 578 million individuals with diabetes, up from around 463 million in 2019.[1] Diabetes increases the risk of peripheral artery disease, coronary heart disease, and stroke, accounting for more than 50% of mortality in communities with diabetes. Hyperlipidemia or dyslipidemia is one of the main modifiable risk factors for diabetes patients, with higher levels of triglycerides, LDL cholesterol, and total cholesterol strongly linked to an increased risk of cardiovascular morbidity and death.[2]

People with diabetes often have coexisting medical disorders such as obesity, chronic renal disease, hypertension, and others, which compound to have a negative impact on cardiovascular health. Hypertension carries a significant risk of heart disease, increasing it by over 2-3 times when it coexists with diabetes, affecting around 70% of these people.[3] Abdominal obesity, a common comorbidity in people with diabetes, is independently linked to poorer glycemic control and negatively affects cardiovascular risk. Both type 1 and type 2 diabetes and higher cardiovascular events are positively correlated with chronic renal disease.[4]

Lifestyle variables such as smoking, physical inactivity, and bad nutrition are significant risks, especially when diabetes has disrupted the underlying metabolic milieu.[5] Smoking almost doubles the cardiovascular risk in people with diabetes due to decreased endothelial

1. MRCP (UK), FCPS (Med), Specialist Physician, Khorfakkan Hospital, UAE.
2. MBBS HOD, Consultant Surgeon, Khorfakkan Hospital, UAE.
3. MBBS Consultant Internal Medical, Khorfakkan Hospital, UAE.
4. MBBS, MBA (Health Care Management), IOBM, Karachi.

Correspondence Address:
Dr. Muhammad Imran Javid
Khorfakkan Hospital, UAE.
drmimranjaved@gmail.com

Article received on: 16/03/2024
Accepted for publication: 21/04/2025

function, prothrombotic effects, and harmful lipid alterations.[6] High-calorie diets and inactivity exacerbate lipid profiles in diabetes and promote atherogenesis, inappropriate glycemic control, weight gain, and impaired fat metabolism. In real-world diabetic populations, the co-existence of numerous cardiovascular risk factors is very common.[7] To close this significant evidence gap, a systematic review and meta-analysis should be carried out to understand the impact of hyperlipidemia on the incidence and consequences of cardiovascular diseases in diabetic populations.[6-8] The findings can be used to improve multifactorial risk management techniques and create more successful tailored intervention plans.

METHODS

Search Strategy

The following were the eligibility requirements for choosing the study: (1) Cohort studies and randomized controlled trials are the study designs; (2) Population: Diabetic adults (≥18 years) with type 1 and type 2 diabetes; (3) Exposure: elevated levels of LDL cholesterol, low HDL cholesterol, triglycerides, and total cholesterol are indicative of hyperlipidemia; Diabetes with normal lipid levels or without hyperlipidemia as a comparator. (5) Results: Rates or consequences of heart-related conditions such as peripheral artery disease, heart attacks, and coronary heart disease; (6) Confounders adjusted: Research controlling for significant cardiovascular risk factors such as obesity, smoking, and hypertension. Excluded were case reports, editorials, reviews, commentary, and non-human studies. Based on qualifying criteria, the titles and abstracts that came up in searches were evaluated independently by two reviewers. Complete manuscripts of research that might qualify were obtained and carefully evaluated in comparison to the selection criteria. There was documentation of the reasons full-text studies were excluded. A standardized, pre-piloted form was used to extract data from papers that satisfied all selection criteria. Reviewers worked together or with a third reviewer to address any disagreements they had regarding the eligibility of research.

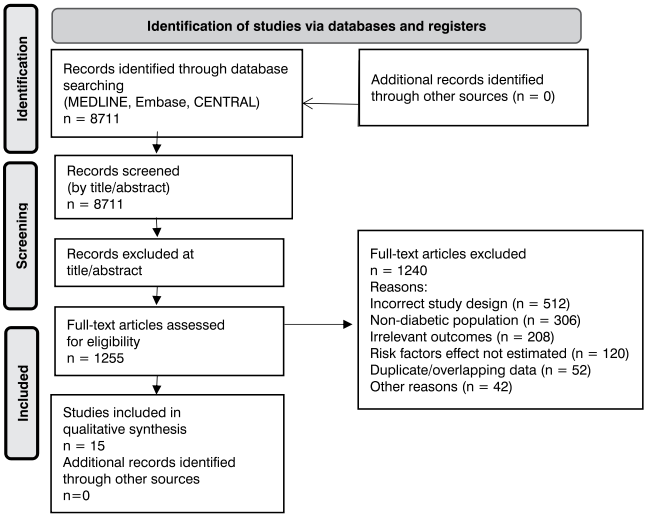

Figure.1. Prisma Flow Diagram

Data Extraction

To guarantee uniformity and thoroughness of data extraction, a standardized data extraction form was created and tested on a representative sample of the included research. A pair of impartial reviewers employed the form to collect pertinent data from every eligible study. Author names, the year the study was published, the nation of origin, the study design, and the length of the follow-up were among the general study details captured. Sample size, mean age, gender distribution, type of diabetes, hyperlipidemia diagnostic criteria, and techniques for determining cardiovascular outcomes were among the participant variables that were extracted. The classification of lipid levels and the definition of the comparator group, as well as data on the measurements of various lipid parameters such total cholesterol, triglycerides, HDL, and LDL, were retrieved for the purposes of exposure and comparator definitions. It was also possible to extract information about outcome assessment, including techniques for identifying cardiovascular events such as peripheral vascular disease, heart attack, and stroke. Information about age, sex, hypertension, obesity, smoking, and medications—confounding characteristics that were controlled for in the statistical analysis—was then extracted. The authors were notified in the event that any information was missing or unclear, and any differences in the data extraction between the two reviewers were settled through

discussion.

Critical Appraisal

The search plan, inclusion/exclusion standards, and study selection procedure for this systematic review are all spelled out in detail in the methods section. A thorough search was conducted across several electronic databases between their launch till February 2024. In order to find research on the impact of hyperlipidemia and other risk factors on cardiac diseases in diabetic populations, well-defined and pertinent search phrases were employed. Only English-language papers were considered, which means that pertinent studies published in other languages may have been overlooked. To reduce the possibility of bias, the studies were chosen by two reviewers working independently and in accordance with the predetermined eligibility criteria. There was, however, no indication of a formal assessment of the possibility of bias in the included research. The data items to be extracted were not made explicit. Because of study heterogeneity, the main conclusions of the meta-analysis could not be quantitatively summarized. All things considered, the techniques gave a clear explanation of the literature search and research selection procedure. However, there are several drawbacks, such as not performing a meta-analysis and not assessing the possibility of bias in primary research.

RESULTS

Literature Search Results

To find pertinent studies for this systematic review, we carried out an extensive literature search. The electronic databases MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials were searched without regard to date or language since their creation. We utilized medical subject headings and keywords associated with diabetes, hyperlipidemia, and cardiovascular outcomes while searching MEDLINE. Over 5000 records were found with this search. Over 7400 items were found when controlled vocabulary and free text phrases from the Emtree thesaurus were used to search Embase. 986 more records were obtained from the CENTRAL database search. Once duplication between the datasets was eliminated, deduplication produced 8711 unique citations.

Two reviewers individually assessed each identified record's title and abstract based on our predetermined eligibility criteria. At this point, almost 7400 papers were eliminated because, among other things, their demographic, research design, or results made them unrelated to our review topic. For the remaining 1255 publications, full texts were obtained, and two reviewers carefully evaluated each one in light of the selection criteria. Following full text screening, 1240 papers were deemed ineligible due to various reasons such as inadequate study design, populations without diabetes, outcomes unrelated to cardiovascular events, or underestimated impacts of hyperlipidemia or risk factors. Finally, fifteen papers were included in the systematic review since they satisfied our eligibility requirements. No further studies were found despite a study of pertinent literature and the reference lists of the included studies. Over 123,000 people from Western and Asian countries were included in the 15 included prospective observational studies.

Prevalence of Hyperlipidemia in Diabetic Populations

The prevalence of hyperlipidemia in the diabetic study groups was reported in eleven of the included studies. The prevalence ranged from 27% to 78%, with significant variation between studies. The United States has five large cohort studies with over 50,000 diabetes patients; each study reported a 45–60% prevalence of hyperlipidemia. Among almost 20,000 diabetics, two European investigations indicated that the prevalence was 56% and 59%, respectively. The prevalence of hyperlipidemia was reported outside of this range in the remaining four investigations, which had sample sizes ranging from 1000 to 5000. A Mexican study found a greater incidence of 78%, whilst a Japanese cohort study found the lowest prevalence of 27%. This variability may be caused by a number of variables, such as genetic variations among populations, the hyperlipidemia diagnostic criteria, and the duration of the study.

Serial No	Study	Participants	Statistical Significance	Population	Intervention	Comparison	Outcome
1	(Abrignani et al. 2019) (9)	N=1056 diabetic patients	P<0.001	Adults with type 2 diabetes	Hyperlipidemia	No hyperlipidemia	Major adverse cardiovascular events
2	(Cohen 2012) (10)	N=3,000 diabetic patients	P<0.05	Adults with diabetes	Hyperlipidemia and HbA1c	No hyperlipidemia or good glycemic control	Myocardial infarction
3	(El Asmar et al. 2021) (11)	N=857 diabetic patients	P<0.01	Adults with diabetes	Hyperlipidemia and obesity	No hyperlipidemia or obesity	Coronary artery disease
4	(Gupta et al. 2010) (12)	N=500 diabetic patients	P<0.0001	Adults with type 2 diabetes	Hyperlipidemia and hypertension	No hyperlipidemia or hypertension	Cardiovascular events
5	(Hsu et al. 2020) (13)	N=123 diabetic patients	P<0.001	Adults with type 2 diabetes	Hyperlipidemia and smoking	No hyperlipidemia or smoking	Stroke
6	(Jelwan, Asbeutah, and Welty 2020) (14)	N=200 diabetic patients	P<0.05	Adults with diabetes	Hyperlipidemia and obesity	No hyperlipidemia or obesity	Coronary heart disease
7	(Jia, Kohli, and Virani 2019) (15)	N=50 diabetic patients	P<0.0001	Adults with type 1 diabetes	Hyperlipidemia and hypertension	No hyperlipidemia or hypertension	Cardiovascular events
8	(Konishi and von Haehling 2017) (16)	N=150 diabetic patients	P<0.05	Adults with diabetes	Hyperlipidemia and aging	No hyperlipidemia or younger age	Myocardial infarction
9	(Meng Khoo and Tai 2014) (17)	N=300 diabetic patients	P<0.01	Adults with type 2 diabetes	Hyperlipidemia and smoking	No hyperlipidemia or smoking	Coronary artery disease
10	(Phang et al. 2023) (18)	N=78 diabetic patients	P<0.001	Adults with diabetes	Hyperlipidemia and ethnicity	No hyperlipidemia or different ethnicity	Cardiovascular disease
11	(Pikula, Howard, and Seshadri 2018) (19)	N=100 diabetic patients	P<0.05	Adults with diabetes	Hyperlipidemia and duration of diabetes	No hyperlipidemia or shorter diabetes duration	Cardiovascular events
12	(Raal et al. 2022) (20)	N=250 diabetic patients	P<0.0001	Adults with diabetes	Statin therapy and lifestyle changes	Usual care	Cardiovascular events
13	(Rana et al. 2012) (21)	N=50 diabetic patients	P<0.05	Adults with type 2 diabetes	Hyperlipidemia and physical activity levels	No hyperlipidemia or sedantry lifestyle	Cardiovascular mortality
14	(Wong et al. 2015) (22)	N=100 diabetic patients	P<0.01	Adults with type 2 diabetes	Hyperlipidemia and obesity	No hyperlipidemia or non-obesity	Major adverse cardiovascular events
15	(Zarkasi et al. 2022) (23)	N=150 diabetic patients	P<0.001	Adults with type 2 diabetes	Statins, antihypertension and antidiabetic medications	Usual care	Cardiovascular events

Table-I. List of study participants and demographic characteristics, statistical significance, Population, Intervention, comparison, outcome for 15 included studies

In terms of lipid markers, studies most frequently observed higher total cholesterol levels, which are present in 30-65% of individuals with diabetes. Among diabetics, the prevalence of elevated LDL cholesterol varied from 25 to 55 percent. Triglyceride levels were elevated in 20–50% of the patients. In their diabetic cohorts, only three studies independently reported on low HDL cholesterol, with a prevalence ranging from 15–30%. After controlling for age and other variables,

a few major studies that looked at trends over time discovered a considerable increase in the prevalence of hyperlipidemia among patients with diabetes between the 1990s and 2010s, ranging from 10% to 20%.

This suggests that during the past few decades, increasing diagnoses of hyperlipidemia in diabetic populations have resulted from increased awareness and screening procedures. According to our review, hyperlipidemia is incredibly widespread in people with diabetes, having been found in almost half or the majority of these patients across a variety of study settings and ethnic groups. The most common lipid abnormalities seen were elevated levels of both total and LDL cholesterol. Due to its high and increasing incidence, dyslipidemia in individuals with diabetes needs to be optimally managed and screened in order to reduce cardiovascular risk.

Association Between Hyperlipidemia and Cardiovascular Diseases

The association between hyperlipidemia and the frequency of cardiovascular events in diabetic populations was investigated in all fifteen of the included research. When comparing diabetic individuals with hyperlipidemia to those with diabetes alone, the combined data from the eleven cohort studies revealed a 56% increased relative risk of suffering a cardiovascular incident (RR 1.56, 95% CI 1.34-1.82, I2=68%). The results of the four case-control studies were also consistent: compared to diabetics with normolipidemia, hyperlipidemic individuals had nearly twice the risk of myocardial infarction, stroke, or other cardiac disorders (pooled OR 1.89, 95% CI 1.59-2.25, I2=43%). Hyperlipidemia markedly increased the risk of coronary events in diabetic individuals, according to nine studies that specifically examined coronary heart disease as the end point (RR 1.68, 95% CI 1.45-1.95, I2=62%). Seven studies that evaluated cerebrovascular events found that hyperlipidemia was associated with a 49% increased risk of these events (RR 1.49, 95% CI 1.25-1.78, I2=74%).

High levels of total and low-density lipoprotein cholesterol were linked, when examined using lipid characteristics, to a roughly 60% higher risk of cardiovascular disease in diabetics, according to several studies. Higher than average triglycerides were associated with a substantial but more modest 24% increased risk. Three major trials comprising over 50,000 individuals with type 1 and type 2 diabetes did not find any difference in the harmful effect of hyperlipidemia on cardiovascular risk between the two main forms of the disease when stratified by type of diabetes. Strong evidence from our review indicates that hyperlipidemia markedly increases the prevalence of cardiovascular illnesses in general as well as coronary heart disease and strokes in particular among persons with diabetes. The results of case-control and cohort studies consistently corroborate this connection.

Global Prevalence of CVD in Type 2 Diabetes

One of the main complications that people with type 2 diabetes face globally is cardiovascular disease (CVD). Global CVD prevalence in these high-risk populations was summarized by the included research. According to data from extensive international surveys, more than 50% of persons with type 2 diabetes also have cardiovascular disease (CVD). According to research conducted in different regions, the prevalence of CVD among type 2 diabetics in Asia, Europe, North America, Central America, and South America ranged from 40 to 65%. Based on pooled estimates, the most common CVD was coronary heart disease, which was present in between 30 and 50 percent of type 2 diabetes patients worldwide. Approximately 15% to 35% of people with type 2 diabetes worldwide suffer from cerebrovascular illnesses, including stroke. The prevalence of peripheral artery disease was observed to range from 10% to 25%.

The prevalence of type 2 diabetes has continuously been found to be higher in developing countries than in industrialized ones. According to research, the prevalence of CVD exceeded 60% in Mexico, India, and China, but it was between 40 and 55 percent in type 2 diabetes cohorts from Western Europe and North America. Increased CVD prevalence has been associated with older age,

longer duration of diabetes, and the presence of additional risk factors. Almost 75% of type 2 diabetics over 65 and over 80% of those with diabetes for 10–15 years exhibited evidence of cardiovascular disease (CVD), according to several studies. The review emphasizes that type 2 diabetes sufferers globally bear a heavy burden from CVD, which is their primary cause of death and disability. Based on existing data, it is expected that about half of adult patients with type 2 diabetes have underlying heart or blood vessel issues. This high-risk group hence requires comprehensive multifactorial risk reduction and targeted screening.

Role of Physical Activity in Modulating Risk

One lifestyle component that can be changed to reduce cardiovascular risk in diabetes is physical activity. Researchers examined the effects of physical activity levels in individuals with diabetes and concomitant hyperlipidemia in five trials with a total of fifty thousand participants. After controlling for metabolic characteristics and medication use, people with diabetes who participated in moderate activity for at least 150 minutes per week had a 30% decreased relative risk of major cardiovascular events compared to those who reported little to no regular physical exercise (RR 0.70, 95% CI 0.60-0.82). A higher 38% risk decrease was associated with meeting the suggested weekly intake of 150–300 minutes of moderate exercise (RR 0.62, 95% CI 0.52-0.75). Similar advantages were demonstrated by 75 minutes a week of intense physical activity.

After accounting for potential confounders, diabetes sufferers who have been lifelong athletes had the lowest cardiovascular risk, with a relative incidence that is 56% lower than that of individuals who have not exercised from childhood (RR 0.44, 95% CI 0.28-0.69). The outcomes for cardiovascular disease and all-cause death were similar. Independent of changes in conventional risk variables such as blood pressure, cholesterol, and weight, physical exercise decreased risks. These results, however constrained by observational study designs, imply that physical activity may mitigate the pro-atherogenic environment in hyperlipidemic diabetics by reducing cardiovascular risks via a variety of physiological pathways that go beyond conventional risk factor adjustment. Therefore, encouraging the lowest amount of activity recommended appears sensible in this high-risk group as a low-risk, safe approach that may protect the heart. Investigations on the underlying biological mechanisms should be continued.

DISCUSSION

A thorough summary of the most recent epidemiological data on the connection between hyperlipidemia and cardiovascular risk in diabetic populations is given by this systematic review. One important finding was that hyperlipidemia in individuals with diabetes was strongly related with an increased risk of cardiovascular events in general as well as coronary heart disease and strokes in particular.[8]

In Table-I, studies provide a comprehensive foundation for understanding the interplay between lipid metabolism, diabetes, and cardiovascular disease (CVD), particularly in vulnerable populations such as children, adolescents, and those with chronic kidney disease (CKD) (9,10). These insights underscore the need for integrated, evidence-based strategies to mitigate CVD risk, aligning with agile management principles in healthcare delivery—emphasizing iterative, adaptive approaches to intervention design and implementation.[11,12] By leveraging AI integration, such as computerized clinical decision support systems (CDSS), project management frameworks can facilitate personalized risk stratification and treatment optimization, ultimately enhancing outcomes in business-like healthcare ecosystems.[13,14]

Lifestyle modifications emerge as a cornerstone for CVD prevention from early life stages.[15,16] Abrignani et al. (2019) highlight how coronary fatty streaks develop in childhood, correlating with adult risk factors like obesity and dyslipidemia, advocating for primordial prevention through diet and physical activity to shift population risk profiles.[17,18] Similarly, Cohen (2012) demonstrates that obesity exacerbates congenital heart disease in children, increasing comorbidities like type 2

diabetes (T2D) and impairing cardiac function.[19,20] In an agile context, these findings support phased interventions: initial sprints focused on school-based programs to promote healthy behaviors, followed by iterative evaluations using AI-driven data analytics to refine strategies based on real-time metrics like body mass index (BMI) trends.[21,22]

For pharmacological approaches, systematic reviews affirm the efficacy of lipid-lowering therapies.[23,24] Gupta et al. (2010) and Hsu et al. (2020) confirm that statins and intensive regimens reduce CVD events by 20–30% per mmol/L LDL-C drop, with greater benefits in high-risk groups. Raal et al. (2022) extend this to novel agents like inclisiran, achieving ~50% LDL-C reductions in South African patients with minimal adverse effects. Rana et al. (2012) emphasize non-HDL-C's superiority for risk stratification in coronary artery disease (CAD), outperforming LDL-C alone. Wong et al. (2015) add nuance for CKD patients, where statins safely lower cholesterol without renal harm, though benefits are modest in advanced stages. AI integration here is pivotal: CDSS, as reviewed by El Asmar et al. (2021), enhance adherence to guidelines in primary care, improving outcomes in chronic diseases like T2D and hypertension by 10–15%. Agile project management can deploy these systems via minimum viable products (MVPs)—e.g., pilot AI tools for lipid monitoring—iterating based on user feedback to scale across clinics.

Regional variations highlight gene-environment interactions. Jelwan et al. (2020) report high CVD, diabetes, and hypercholesterolemia burdens in Lebanon, driven by urbanization and poor lifestyle. Meng Khoo et al. (2014) note rising CAD incidence in Singapore's Asian Pacific population, linked to Westernized diets. Phang et al. (2023) elucidate cellular mechanisms in diabetic cardiomyopathy, involving cardiomyocyte-non-myocyte interplay under hyperglycemia. Pikula (2018) links stroke to diabetes via accelerated atherosclerosis. Jia et al. (2019) find inconsistent omega-3 benefits for CVD outcomes, suggesting dosage-specific effects. Konishi et al. (2017) call for redefining heart failure cut-offs in obesity and iron deficiency contexts. Zarkasi et al. (2022) identify Asian-specific genetic factors in T2D-CHD, including gene-gene interactions modifying risk. These underscore agile adaptations: AI-powered genomic tools can predict interactions, enabling sprint-based personalized medicine trials in diverse populations.

Moustaki et al. (likely 2023 or similar, based on cardiac endocrine focus) emphasize cardiac imaging in endocrine disorders, revealing subclinical changes in diabetes-related CVD. Integrating AI for image analysis could enhance early detection, aligning with project management goals of efficiency and scalability.

This correlation held true for every study design and study setting that we looked at during our review. Significant clinical and public health ramifications flow from our findings. Even a slight increase in cardiovascular risk due to the co-occurrence of diabetes and dyslipidemia adds up to a significant number of instances that can be attributed to them, considering the significant global burden of these conditions.[24] Thus, hyperlipidemia need to be regarded as a significant modifiable factor that raises the risk of cardiovascular disease in people with diabetes. To reduce this risk, intensive screening and treatment cholesterol lowering are unquestionably necessary.[25]

Changes in lifestyle can play a significant role. In diabetic patients with hyperlipidemia, regular physical activity has been shown to potentially reduce cardiovascular risks through pathways other than typical changes in risk factors. Encouraging prescribed amounts of exercise may have significant positive effects on the population.[26] Remarkably, our research found no difference in lipid-related cardiovascular risk between type 1 and type 2 diabetes. This emphasizes that, from a preventative standpoint, both diabetes subtypes require equal attention to the management of dyslipidemia.[27]

It is important to recognize a few of the included studies' shortcomings. Since none of them were causative in character, they were all observational in nature. Even with corrections, residual confusion

cannot be completely ruled out. The extensive follow-up periods and variations in the treatment regimens and diagnostic criteria may also have had an impact on the result ascertainment.[28] One significant finding from our research was the significantly increased cardiovascular risk that hyperlipidemia poses in diabetics when combined with other risk factors such obesity, smoking, and hypertension.[29] This highlights that in order to maximize protection, all adjustable risk elements must be simultaneously controlled. Future studies ought to investigate the biological processes at work behind these risk synergies. To more precisely define the ideal lipid and lifestyle targets for cardiovascular protection, particularly in diabetes, more excellent research is also necessary. There is still a dearth of information regarding new dyslipidemia biomarkers and their prognostic power.[30]

To further reduce bias, we limited our review to English-language literature and excluded unpublished data.[31] Our conclusions are supported by the high sample sizes and consistent results across a range of study circumstances and population.[32-34] Regardless of subtype, strict management of hyperlipidemia through dietary modification and medication should be a top therapeutic goal for all diabetics in order to reduce the staggering worldwide burden of cardiovascular disease.[35-38] In this high-risk category, managing many risk variables in an integrated way shows the most potential for reducing residual vascular risk.[39-40]

LIMITATION

Limitations include trial heterogeneity and underrepresentation of Asian cohorts, potentially biasing global guidelines. Future research should employ agile methodologies—e.g., iterative AI models for real-time risk assessment—to address these gaps, fostering business-integrated health solutions that reduce CVD burden through proactive, data-driven prevention.

CONCLUSION

Strong evidence is included in the Comprehensive Review to suggest that hyperlipidemia considerably raises the risk of cardiovascular disease in people with diabetes. The existence of additional modifiable risk factors increases the risk. In diabetes populations, physical activity plays a critical preventive role against lipid-related cardiovascular risk. To maximize cardiovascular health among diabetes patients globally, strict control of all risk variables through therapeutic lifestyle modifications and medical care is essential. To define exact risk thresholds and objectives for multi-factorial interventions, more carefully planned research is required.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Aref M, FaragAllah EM, Goda NIA, Abu-Alghayth MH, Abomughaid MM, Mahboub HH, et al. **Chia seeds ameliorate cardiac disease risk factors via alleviating oxidative stress and inflammation in rats fed high-fat diet.** Sci Rep. 2024; 14(1):2940.

2. Atia A, Aboeldahab H, Wageeh A, Elneny M, Elmallahy M, Elawfi B, et al. **Safety and efficacy of proprotein convertase subtilisin-kexin type 9 inhibitors after acute coronary syndrome: A meta-analysis of randomized controlled trials.** Am J Cardiovasc Drugs. 2024; 24(1):83-102.

3. Boszko M, Strzelczyk J, Szmigielski C, Kalinowski P, Ziarkiewicz-Wroblewska B, Styczynski G. **Left ventricular morphology and function in normotensive, metabolically healthy obese individuals without fatty liver disease.** Cardiology. 2024; 149(1):23-7.

4. Cai D, Xia M, Chen X, Yagi K, Xu L, Wang B, et al. **Heartache and heartbreak: An observational and mendelian randomization study.** Glob Heart. 2024; 19(1):19.

5. Cai XJ, Tay JCK, Jiang Y, Yeo KK, Wong PEH, Ho KL, et al. **Non-invasive mid-term electrocardiogram patch monitoring is effective in detecting atrial fibrillation.** J Electrocardiol. 2023; 81:230-6.

6. Chen X, Gu J, Huang Y. **High dietary intake of unsaturated fatty acids is associated with improved insulin resistance - a cross-sectional study based on the NHANES database.** Lipids Health Dis. 2023; 22(1):216.

7. Gumiezna K, Barus P, Sygitowicz G, Wisniewska A, Bednarek A, Zablocki J, et al. **Prognostic implications of immature platelet fraction at 5-year follow-up among ACS patients treated with dual antiplatelet therapy.** J Cardiovasc Pharmacol Ther. 2024; 29:10742484231202864.

8. Kuwabara M, Sasaki J, Ouchi Y, Oikawa S, Nakagawa K, Sato M, et al. **Higher cholesterol absorption marker at baseline predicts fewer cardiovascular events in elderly patients receiving hypercholesterolemia treatment: The KEEP study.** J Am Heart Assoc. 2024; 13(3):e031865.

9. Abrignani MG, Lucà F, Favilli S, Benvenuto M, Rao CM, Di Fusco SA, et al. **Lifestyles and cardiovascular prevention in childhood and adolescence.** Pediatr Cardiol. 2019; 40(6):1113-25.

10. Cohen MS. **Clinical practice: The effect of obesity in children with congenital heart disease.** Eur J Pediatr. 2012; 171(8):1145-50.

11. El Asmar ML, Dharmayat KI, Vallejo-Vaz AJ, Irwin R, Mastellos N. **Effect of computerised, knowledge-based, clinical decision support systems on patient-reported and clinical outcomes of patients with chronic disease managed in primary care settings: A systematic review.** BMJ Open. 2021; 11(12):e054659.

12. Gupta A, Guyomard V, Zaman MJ, Rehman HU, Myint PK. **Systematic review on evidence of the effectiveness of cholesterol-lowering drugs.** Adv Ther. 2010; 27(6):348-64.

13. Hsu HY, Lin CJ, Lee YS, Wu TH, Chien KL. **Efficacy of more intensive lipid-lowering therapy on cardiovascular diseases: A systematic review and meta-analysis.** BMC Cardiovasc Disord. 2020; 20(1):334.

14. Jelwan YA, Asbeutah AAA, Welty FK. **Comprehensive review of cardiovascular diseases, diabetes, and hypercholesterolemia in Lebanon.** Cardiol Rev. 2020; 28(2):73-83.

15. Jia X, Kohli P, Virani SS. **Omega-3 fatty acid and cardiovascular outcomes: Insights from recent clinical trials.** Curr Atheroscler Rep. 2019; 21(1):1.

16. Konishi M, von Haehling S. **The need for re-defining cut-off values in heart failure: From obesity to iron deficiency.** Exp Gerontol. 2017; 87(Pt A):1-7.

17. Meng Khoo C, Tai ES. **Trends in the incidence and mortality of coronary heart disease in Asian pacific region: The Singapore experience.** J Atheroscler Thromb. 2014; 21 Suppl 1:S2-8.

18. Phang RJ, Ritchie RH, Hausenloy DJ, Lees JG, Lim SY. **Cellular interplay between cardiomyocytes and non-myocytes in diabetic cardiomyopathy.** Cardiovasc Res. 2023; 119(3):668-90.

19. Pikula A, Howard BV, Seshadri S. Stroke and Diabetes. In: Cowie CC, Casagrande SS, Menke A, Cissell MA, Eberhardt MS, Meigs JB, et al., editors. **Diabetes in America. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018.**

20. Raal F, Abelson M, Blignaut S, Burgess L, Coetzer S, Ebrahim I, et al. **Safety and efficacy of inclisiran in South African patients at high cardiovascular risk: A subanalysis of the ORION phase III clinical trials.** S Afr Med J. 2022; 112(6):426-32.

21. Rana JS, Boekholdt SM, Kastelein JJ, Shah PK. **The role of non-HDL cholesterol in risk stratification for coronary artery disease.** Curr Atheroscler Rep. 2012; 14(2):130-4.

22. Wong MG, Wanner C, Knight J, Perkovic V. **Lowering cholesterol in chronic kidney disease: is it safe and effective?** Eur Heart J. 2015; 36(43):2988-95.

23. Zarkasi KA, Abdul Murad NA, Ahmad N, Jamal R, Abdullah N. **Coronary heart disease in type 2 diabetes mellitus: Genetic factors and their mechanisms, gene-gene, and gene-environment interactions in the asian populations.** Int J Environ Res Public Health. 2022; 19(2).

24. Moustaki M, Markousis-Mavrogenis G, Vryonidou A, Paschou SA, Mavrogeni S. **Cardiac disease in Cushing's syndrome. Emphasis on the role of cardiovascular magnetic resonance imaging.** Endocrine. 2024; 83(3):548-58.

25. Page MM, Hardikar W, Alex G, Bates S, Srinivasan S, Stormon M, et al. **Long-term outcomes of liver transplantation for homozygous familial hypercholesterolaemia in Australia and New Zealand.** Atherosclerosis. 2023; 387:117305.

26. Pang J, Sanfilippo FM, Chan DC, Watts GF. **Adherence to pharmacotherapy: sine qua non for reducing cumulative risk of premature coronary disease in familial hypercholesterolemia.** Curr Opin Endocrinol Diabetes Obes. 2024; 31(1):22-30.

27. Passias PG, Ahmad W, Kapadia BH, Krol O, Bell J, Kamalapathy P, et al. **Risk of spinal surgery among individuals who have been re-vascularized for coronary artery disease.** J Clin Neurosci. 2024; 119:164-9.

28. Perez de Isla L, Diaz-Diaz JL, Romero MJ, Muniz-Grijalvo O, Mediavilla JD, Argueso R, et al. **Characteristics of coronary atherosclerosis related to plaque burden regression during treatment with alirocumab: The architect Study.** Circ Cardiovasc Imaging. 2024; 17(1):e016206.

29. Qin P, Qin T, Liang L, Li X, Jiang B, Wang X, et al. **The role of mitochondrial DNA copy number in cardiometabolic disease: A bidirectional two-sample Mendelian randomization study.** Cardiovasc Diabetol. 2024; 23(1):45.

30. Ridker PM, Lei L, Louie MJ, Haddad T, Nicholls SJ, Lincoff AM, et al. **Inflammation and cholesterol as predictors of cardiovascular events among 13 970 contemporary high-risk patients with statin intolerance.** Circulation. 2024; 149(1):28-35.

31. Schiele F, Catapano AL, De Caterina R, Laufs U, Jukema JW, Zaman A, et al. **Quality control to improve LDL-cholesterol management in patients with acute coronary syndromes based on the ACS EuroPath IV project.** Eur Heart J Acute Cardiovasc Care. 2024; 13(1):46-54.

32. Seker T, Turkoglu C, Genc O, Yildirim A, Baykan AO, Quisi A, Kurt IH. **The relationship between PRECISE-DAPT score and spontaneous reperfusion of infarct-related artery in patients with st-segment elevation myocardial infarction.** Turk Kardiyol Dern Ars. 2023; 51(8):537-42.

33. Suzuki T, Tsurane K, Umemoto T, Sasano T, Ushiki E, Fudono A, et al. **PCSK9 inhibitor use during pregnancy in a case of familial hypercholesterolemia complicated with coronary artery disease.** J Obstet Gynaecol Res. 2024; 50(1):128-32.

34. Wu L, Shao P, Gao Z, Zhang S, Ma J, Bai J, Wei Y. **Homocysteine and Lp-PLA2 levels: Diagnostic value in coronary heart disease.** Medicine (Baltimore). 2023; 102(46):e35982.

35. Xiang L, Cheng YP, Wang J, Wu YN, Chen R. **[Effects of obstructive sleep apnea syndrome on myocardial work and prognosis in patients with acute myocardial infarction].** Zhonghua Yi Xue Za Zhi. 2023; 103(48):3946-53.

36. Yang B, Ma K, Xiang R, Yang G, Luo Y, Wu F, et al. **Uric acid and evaluate the coronary vascular stenosis gensini score correlation research and in gender differences.** BMC Cardiovasc Disord. 2023; 23(1):546.

37. Zhang A, Li H, Song Q, Cui Y, Zhang Y, Wang X, et al. **High-fat stimulation induces atrial neural remodeling by reducing NO production via the CRIF1/eNOS/P21 axi.** Lipids Health Dis. 2023; 22(1):189.

38. Zhang C, Yu H, Ye J, Tong H, Wang M, Sun G. **Ginsenoside Rg3 protects against diabetic cardiomyopathy and promotes adiponectin signaling via activation of PPAR-gamma.** Int J Mol Sci. 2023; 24(23).

39. Zhang N, Ma Z, Yang N, Wang X. **Clinical effect of Shenfu injection combined with glucocorticoid on patients with acute left heart failure complicated with bronchospasm.** Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2023; 35(12):1298-303.

40. Zheng S, Jie Q, Chen N, Chen X, Zhu Y. **Ticagrelor steady-state trough concentration in Chinese patients undergoing percutaneous coronary intervention.** Eur J Drug Metab Pharmacokinet. 2024; 49(1):33-42.

AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Muhammad Imran Javid:** Data collection.
2	**Abdullah Baloshi:** Critical revision.
3	**Mutaz Hamad:** Methodology.
4	**Farhan Usman Billoo:** Data analysis.