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Dyslipidemia in Patients with Type 2 Diabetes Mellitus (DM2) According to Ethnicity: A Systematic Review

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Abstract **Original Research Article**

Background: The role of dyslipidemia as a significant risk factor for cardiovascular disease (CVD) in patients diagnosed with type 2 diabetes mellitus (DM2) is well established. There are few studies examining the prevalence of dyslipidemia among different ethnic groups. This review aims to analyze literature that has studied dyslipidemia and ethnicity. Should treatment guidelines reflect ethnicity? ***Method:*** Systemic narrative synthesis and data extraction was performed using the Preferred Reporting Items for Systematic Review (PRISMA) guidelines. Studies were selected between January 2010 and January 2022 using PubMed, Medline, and Google Scholar. The quality of the studies was assessed through Joanna Briggs Institute (JBI) checklist. ***Results:*** Four relevant studies were retrieved from different countries. Asians, mainly Indians and Filipinos, have high triglycerides (TG) levels and low High-Density Lipoproteins (HDL) levels which can partially explain the high incidence of coronary heart disease (CHD) in this group. Indians have high concentrations of small LDL particles, which are more atherogenic than large LDL particles (25). Asians are more sensitive to statin treatment, and lower doses can achieve the same therapeutic target as white Caucasian individuals. Proprotein convertase subtilisin/Kexin type 9 (PCSK9) injectable therapies effectively lower cholesterol among all ethnic groups and may be a suitable alternative when statins are not tolerated. ***Conclusions*** - There are differences in dyslipidemia patterns among various ethnic groups compared to white Caucasians. *South Asians have more atherogenic dyslipidemia than other ethnic minorities. Such differences might require tailored guidelines to address these ethnic differences*.

Keywords: Type 2 Diabetes Mellitus (DM2), Dyslipidemia, cardiovascular disease (CVD), injectable therapies.

1. INTRODUCTION

The incidence of type 2 diabetes mellitus (DM-2) is on the rise [1]. In 2014 the International Diabetes Federation (IDF) estimated that 8.2% of the global adult population (387 million) are affected by diabetes [2]. The number of people living with diabetes is projected to increase to 592 million by 2035 [2]. The annual global health expenditure on diabetes is estimated to be 850 billion USD [3].

Dyslipidemia is a major risk factor for the development of macrovascular complications in diabetes [4]. The American Diabetes Association (ADA) advises lipid profile checks to be performed at the diagnosis of diabetes [5]. Lipid profile includes total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides (TG). It is well established that reducing LDL can reduce the risk of Atherosclerotic Cardiovascular Disease (ASCVD) [6].

Among patients diagnosed with diabetes, cardiovascular disease prevalence varies among ethnic groups [7]. Dyslipidemia and hypertension, as risk factors for ASCVD, are distributed differently among people of different ancestry. Also, the response to drug treatment differs among those groups. Caucasians require higher doses of statins to achieve the desired therapeutic goal compared to people of Asian descent [8]. African Americans have less TG and lower LDL than other minorities in the United States, such as Asian Indians, Filipinos, Japanese and Vietnamese [9].

They studied the impact of ethnicity on different chronic conditions and revealed exciting findings. DM2 is more prevalent among Mexican

Americans, but they have less dyslipidemia than Caucasians [10]. Lipid management can be achieved by using several medications such as statins, fibrates [11] and PCSK9 injectables. The first choice in the medical management of lipid profiles in patients with diabetes is statins. The drug and the dose selection are based on risk evaluation before initiation of treatment. Primary prevention requires a moderate dose of statins. Secondary prevention requires a higher dose of statins or combination therapy of statins and fibrates when statins fail to achieve the treatment target [12]. PCSK-9 are reserved for patients who fail to achieve treatment targets because of their high cost. In a recent study about PCSK9 concentration in blood, African Americans have higher plasma levels of PCSK9 compared to Caucasians [13]. PCSK9 levels are protective in lowering the lifetime risk for cardiovascular disease [14]. Ample data is studying the patterns of dyslipidemia among different ethnic groups. Dyslipidemia is a modifiable risk factor for diabetes. It is known that diabetes forms a high risk for cardiovascular disease (CVD). Patients with diabetes develop congestive heart failure and have a higher mortality rate than those without diabetes [15].

Dyslipidemia in patients with diabetes increases the risk of (CVD) for various reasons. The lipoprotein profile has elevated triglycerides, low HDL and small dense LDL particles. This pattern of small LDL particles is highly atherogenic. The lipoprotein pattern is also a reason for insulin resistance which is one of the mechanisms of diabetes and metabolic syndrome. It is proven that triglycerides level >132 mg/dl can form small LDL particles. Therefore lowering lipoproteins to the treatment goals is very important in lowering (CVD) among patients diagnosed with diabetes. Studying patterns of dyslipidemia among different ethnic groups may lead to modification of guidelines to address those differences.

2. METHODOLOGY

2.1 Aim

Assessment of dyslipidemia patterns LDL, HDL and triglycerides among patients with diabetes according to their ethnicity.

2.2 Objectives:

- To investigate the correlation between DM2, LDL levels and HDL/Cholesterol ratio in different ethnic groups.
- To evaluate the prevalence of dyslipidemia among different ethnicities.

2.3 Study design

A systematic review was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines, and the quality of findings was reported using the Joanna Briggs Institute (JBI) checklist (critical-appraisal-tools - Critical Appraisal Tools Joanna Briggs Institute, n.d.; Moher *et al*., 2015) [16].

P. Population, patients with diabetes.

I. Interest, dyslipidemia.

Co. Context ethnic groups. (We have the modified PICo framework to produce a qualitative article).

2.4 Key search words:

Diabetes – diabetic patient.

Dyslipidemia – dyslipidemia, hypercholesterolemia, hyperlipidemia.

Ethnicity – ethnic groups, minorities, race.

2.5 Search strategy:

- Diabet* OR hyperglyc*.
- AND dyslipid* OR Hyperlipid* OR hypercholesterol*.
- AND ethnic* OR race OR minority.
- Limits years of conducted research 12 years.
- Database Cochrane, PubMed and Google scholar.

2.6 Data Extraction:

The reviewers have conducted research to find related studies. Zotero tool is used to organize search results which were 216 articles. Of those articles, only 4 matched the inclusion criteria. The extracted data contained patterns of dyslipidemia among different ethnic groups. Effects of lipid-lowering medication on individuals with different ethnicity. Relevant studies are examined to match the search question. Information regarding dyslipidemia patterns and their relation to ethnicity is extracted and organized using a similar template.

2.7 Inclusion Criteria:

- Randomized and observational studies.
- Adult population with DM2 and dyslipidemia 20-65 years old.
- Studies published between 2010 to 2020
- Patients of different ethnic backgrounds.
- Studies must be written in English.

2.8 Exclusion Criteria:

- Type 1 diabetes mellitus (DM1).
- Studies published before the year 2010.
- Studies that included children and adolescents.
- Studies with includes < 200 participants.
- Studies without primary data.

2.9 Assessment of methodological quality:

The authors of this review critically reviewed the eligible studies for methodological quality using the standard JBI Critical Appraisal Checklist (Critical Appraisal Tools JBI, 2022).

Four studies were methodologically appraised using the JBI checklist for analytical cross-sectional studies. The studies demonstrated clear inclusion

criteria, a clear description of the study population and settings, and a reliable way of measuring the study condition and the outcome.

2.9.1 Data extraction and analysis:

The quality of collected data was assessed using the Joanna Briggs Institute (JBI) checklist [17]. The four studies have addressed the prevalence and the patterns of dyslipidemia among various ethnic groups. Risk factors which affect dyslipidemia were identified and discussed. Gender differences in dyslipidemia among the same ethnic group and other ethnic groups were studied and compared. The extracted data included countries where the studies were conducted, the study objectives, the ethnic groups, the intervention used, and the outcomes. The measurements of dyslipidemia were critically reviewed to exclude any ambiguous outcomes.

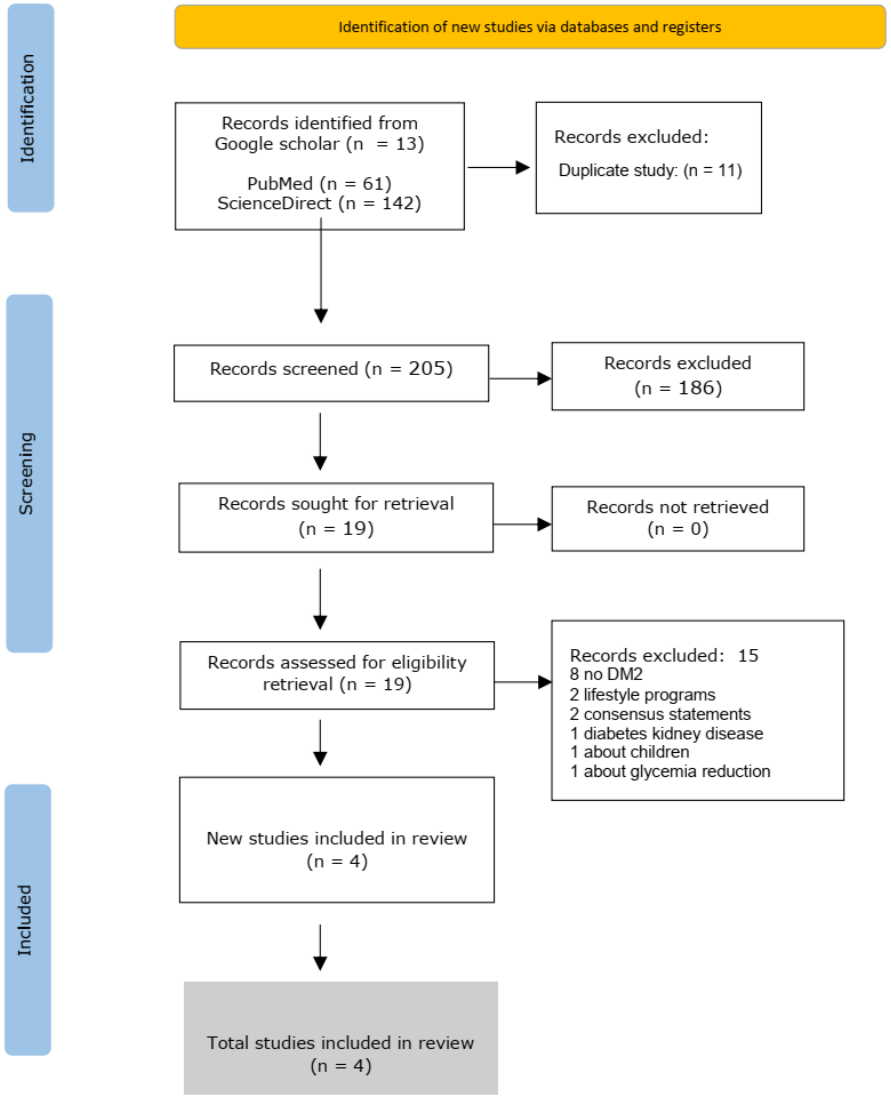
3. Ethical Issues:

Ethical approval for a systematic review is not required.

4. RESULTS

The initial search identified 216 articles (Science Direct 142, PubMed 61, Google Scholar 13). There were 11 duplicate articles. We excluded 186 articles based on the title. The reasons behind that were that some studies were conducted among children, on patients with DM1 and studies which did not contain dyslipidemia and diabetes. Nineteen articles were screened with full-text reading, and 15 articles were excluded. Eight articles were excluded because they omitted DM2. Two articles were excluded because they were about prevention programs for diabetes. Two Articles were excluded because they were consensus statements. One article was excluded because it was about children. One article was about diabetic kidney disease. One article was excluded because it discussed glycemia reduction. Four studies met the inclusion criteria and were included in the final review. Two of the excluded articles had relevant information, which was discussed in the discussion chapter.

PRISMA Flowchart



All four studies retrieved in this review were published from 2014 onward. One study was performed among ethnic minorities in California, USA. The second study was performed in Bangladesh. The third study was performed in India in 2 different regions. The fourth study was performed in southern Ethiopia. All four studies were cross-sectional reviews.

Ariel *et al*., assessed dyslipidemia patterns in Northern Californi among 169430 patients ≥ 35 years old. All participants had lower body mass index (BMI) except Mexicans and Blacks, who had higher BMI than non-Hispanic Whites (NHWs). In the study, most of the studied ethnic minority individuals, except Blacks and Japanese, had low HDL levels and high TG levels when compared to (NHWs). Females mainly had higher values of TG and lower HDL than males. 3 Asian subgroups had higher rates of DM2, namely Asian Indians, Filipinos and Japanese. Black and Vietnamese were more likely to have smoked in the past, while all Mexican and Asian women were less likely ever to have smoked than NHWs. Filipino and Mexican women had the highest prevalence of LDL-C and TG. When HDL-C was measured was low compared to NHWs, with the following results Asian Indians (54.9%) and Mexican (50.9%). Besides Mexican women (45.4%), almost every Asian woman had high TG compared to NHWs except Korean women and Black women, who had the lowest prevalence of TG, who had 27.6% and 18.2%, respectively. When TC, TG and LDL levels are considered, men score higher than women. LDL results were as follows: Filipino men were the highest with 73.1%, Vietnamese men scored 71.3%, Asian Indians scored 52.7%, Mexican men 47.8%, and Japanese men scored the lowest with 26.3%. Similar to results observed in women, all Asian and Mexican men had increased values of hypertriglyceridemia. In comparison with NHWs, the black men had low values. Overweight Asian women (age > 55) were likely to have combined dyslipidemia compared to Asian men. Overweight men who smoked were more likely to have combined dyslipidemia with multiple abnormal lipid profile indices.

Hrishov *et al*., evaluated dyslipidemia among 1008 diabetic patients in southern Bangladesh. 683 (67.8%) patients were females, and 325 (32.2%) were males. The prevalence of dyslipidemia among male patients was 72.92%, while among females was 71%. Among men, the levels of high serum cholesterol, high TG, low HDL and high LDL were 35.69%, 44.31%, and 50.15%, respectively, whereas the results for females were 35.29%, 40.85%, 49.49%, respectively. The study's conclusion confirms the high prevalence of dyslipidemia among the studied group. Furthermore, the dyslipidemia results were higher than those obtained in India, Sri Lanka, Saudi Arabia and other parts of Bangladesh. The study raises awareness about the importance of early screening of dyslipidemia among patients with Diabetes in Bangladesh.

Longkumer *et al*., studied two ethnic subgroups in India by comparing two Mendelian populations with different ancestry. Jats and Meiteis are two ethnic groups living separately in 2 different districts of India. The study population were recruited through a household survey. The study recruited 2371 individuals ≥ 30 years. Two groups were allocated, one for individuals with impaired fasting glucose (IFG) and the second for DM2. Although both manifested similarities regarding abnormal TC, very low-density lipoproteins (VLDL), waist circumference (WC) and BMI, there was a significant increase in DM2 among ≥ 60 years Jats in comparison with Meiteis suggesting higher morbidity. The number of recruited Jats was 1542 subjects versus 829 recruited Meitieis.

Bekele *et al*., examined the prevalence and the pattern of dyslipidemia among subjects diagnosed with diabetes in the Kembat Tembaro area in southern Ethiopia. The study involved 224 subjects the study using convenient sampling techniques. The prevalence of dyslipidemia among them was 65%. The lipid profile analysis showed elevated LDL-C in 43.8%, TC 23.7%, TG 40.6%, and HDL was reduced among 41.9%. Older age, longer duration of diabetes, sedentary lifestyle and high BMI increased the prevalence of dyslipidemia among studied subjects. The prevalence of dyslipidemia in the studied subjects, at 65%, was higher than in China at 34.64%, less than in Finland at 85%, less than in the USA at 80% and less than in Jordan at 90%. Compared to Jordan, dyslipidemia was higher among males than females in the studied subjects. The results from the study were similar to another study conducted in a different part of Ethiopia [27].

4.1 Quality assessment of the studies.

Table 1: Analytical Cross-Sectional Study

Citation	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Frank T.H. 2014	Y	Y	Y	Y	U	U	Y	Y
Shifrew Bekele 2017	Y	Y	Y	Y	Y	N	Y	Y
Das H. 2019	Y	Y	Y	Y	N	N	Y	Y
Longkumer I. 2020	Y	Y	Y	Y	Y	Y	Y	Y
%	100.0	100.0	100.0	100.0	50.0	20.0	100.0	100.0

Q1 Were the criteria for inclusion in the sample clearly defined?
Q2 Were the study subjects and the setting described in detail?
Q3 Was the exposure measured validly and reliably?
Q4 Were objective, standard criteria used for measurement of the condition?
Q5 Were confounding factors identified?
Q6 Were strategies to deal with confounding factors stated?
Q7 Were the outcomes measured in a valid and reliable way?
Q8 Was appropriate statistical analysis used?
Y: Yes N: No U: Unclear N/A: Not applicable

5. DISCUSSION

Dyslipidemia is a significant risk factor for cardiovascular diseases among patients affected by diabetes [18]. Worldwide studies revealed differences in the prevalence of dyslipidemia among patients with diabetes. The prevalence of dyslipidemia in the USA and Finland is the highest at 70.5% and 85%, respectively [20]. In China, the prevalence of dyslipidemia is 34.64% [21], in Jordan is 90% [22], and in Ethiopia is 65% [18]. In the USA, it appears that Hispanic Mexicans have a higher prevalence of diabetes compared to other ethnicities, including Hispanics at 22.1%, non-Hispanic Black at 20.4%, non-Hispanic Asian groups at 19% and non-Hispanic whites at 12.1% [19]. African Americans have high TG and low HDL. The same pattern of dyslipidemia is present among African subjects studied in Ethiopia. The dyslipidemia patterns of southeast Asians are characterized by high TG, low HDL and high LDL levels. Besides, Southeast Asians have more atherogenic dyslipidemia characterized by very small particles of LDL [23]. In addition to other factors, this may explain the higher rate of cardiovascular mortality among Southeast Asians 285/100,000 compared to Americans 122/100,000 [24]. These disparities in mortality rates necessitate that guidelines for screening and early treatment of dyslipidemia should reflect these ethnic variations.

Indians have high cardiovascular disease (CVD) risk because of the atherogenic pattern of dyslipidemia. In South Asia, patients from Bangladesh shared a similarly high risk as Indians. It is essential to consider that minor variations in dyslipidemia distribution can occur between comparable ethnic minorities within the same country, as observed in India. The same phenomenon is observed when comparing two ethnic groups in Ethiopia, where one group showed slightly different HDL-C levels. Studies from Africa and Asia have shown different patterns of dyslipidemia in rural areas and urbanized cities. In Africa, it was observed that patients with diabetes who use vehicles as a mode of transport are 14 times more likely to develop dyslipidemia than those walking on foot [18]. The situation in India is similar, where urban dwellers have a higher prevalence of dyslipidemia than people living in rural areas [26]. This indicates the effect of an urbanized lifestyle on dyslipidemia prevalence.

Indians in urban areas of India and western countries have dyslipidemia with smaller LDL particles when compared with Indians in rural areas. Smaller LDL particles are more atherogenic. This might explain the higher CVD mortality among this ethnic group compared to Caucasians [28]. The implication of differences in dyslipidemia has encouraged physicians in India to develop guidelines to reduce morbidity and mortality caused by it.

Depending on ethnicity, there are also differences in dyslipidemia patterns between males and females. While Ethiopian females have a higher prevalence of dyslipidemia than males, we find that Jordanian males have higher dyslipidemia than Jordanian females. A study among immigrant females in the USA has established that Mexican females have different dyslipidemia patterns than female Japanese immigrants.

The drugs of choice in lowering lipids are statins. As mentioned above, Caucasians need higher doses than other minorities to achieve the treatment target. Some patients cannot tolerate statins or cannot reach the treatment target with the highest recommended doses of statins. In 2018 a study was published assessing the efficacy of evolocumab (a PCSK9) 's efficacy in treating dyslipidemia [34]. A pooled analysis of 3146 patients was studied. It showed that this drug was more potent in achieving dyslipidemia targets than statins.

ADA guidelines recommend medication treatment to achieve lowered lipid targets. A study has found that different ethnic groups have different lipid patterns and respond differently to the lipid-lowering treatment. While the South Asian population responds well to lower doses of statins, Caucasians need higher statins to achieve the same treatment target [29].

The injectable drug PCSK9 decreases LDL significantly in all ethnic groups regardless of age. These drugs are an effective alternative for patients who cannot tolerate statins or have familiar hyperlipidemia that responds poorly to statins. The high cost of PCSK9 drugs makes them out of reach for people of lower income strata.

Table 2: Dyslipidaemia prevalence per ethnic group

Ethnicity	China	Ethiopia	USA	Finland	Jordan
Dyslipidaemia %	34.64%	65%	70%	85%	90%

6. CONCLUSION

This review shows that dyslipidemia prevalence and pattern vary among different ethnicities. Compared to Caucasians, most minority ethnic groups have higher prevalence rates of dyslipidemia. South Asians often display an atherogenic dyslipidemia profile, leading to a high risk of CVD. Genetic and environmental factors can influence the pattern of dyslipidemia among different ethnic groups. Nevertheless, much research must be done among minorities in their home and migration countries to determine the optimum screening and treatment of the affected individuals.

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