IJPSR (2024), Volume 15, Issue 12 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 25 June 2024; received in revised form, 09 July 2024; accepted, 19 July 2024; published 01 December 2024

ASSESSING HYPERLIPIDEMIA ROLE IN THE ETIOLOGY OF CARDIAC ARREST: CASE-CONTROL STUDY

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Keywords:

Hyperlipidemia, Coronary artery disease, Cardiac arrest, Cholesterol, Lipid, Meta-Analysis

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ABSTRACT: Introduction: Hyperlipidemia, characterized by elevated lipid levels, is linked to increased cardiovascular disease risk. This study explores whether hyperlipidemia heightens the likelihood of cardiac arrest, stemming from its role in atherosclerosis and coronary artery disease. The objective was to determine if individuals with hyperlipidemia face a higher risk of cardiac arrest, underscoring the importance of managing lipid levels for cardiovascular health. **Materials and Methods:** A systematic review and meta-analysis were conducted following PRISMA guidelines. 20 randomized controlled trials (RCTs) were included, totaling 12,146 participants with hyperlipidemia and comorbidities such as atherosclerosis and coronary artery disease. Quality assessment utilized the Newcastle-Ottawa Scale (NOS). Odds ratios (OR) and risk ratios (RR) were computed for meta-analyses, assessing the association between hyperlipidemia and cardiac arrest risk. Publication bias was evaluated through funnel plots. **Results:** The meta-analysis revealed a significant association between hyperlipidemia and cardiac arrest risk. Both OR (0.51) and RR (0.77) indicated odds of slight cardiac arrest among individuals with hyperlipidemia as per forest plot analytical data is OR (Chi^2 of 31.14 and df of 19, P = 0.04); I^2 = 39%0 and RR (Chi2=23.61, df=13, P=0.03; I2=45%). Moderate heterogeneity was observed and also was no publication bias as per analysis from funnel plot readings. **Conclusion:** Hyperlipidemia may exhibit an associative relationship with cardiac arrest risk. This challenges conventional understanding and emphasizes the need for better approaches to cardiovascular risk assessment. Future research should delve into underlying mechanisms and explore personalized interventions to mitigate cardiac arrest risk in hyperlipidemic individuals.

INTRODUCTION: Hyperlipidemia involves elevated lipid levels, increasing heart disease risk. Key lipids include cholesterol, triglycerides, and lipoproteins like very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL). Maintaining lipid balance is crucial for cardiovascular health. Understanding their roles clarifies hyperlipidemia's ties to atherosclerosis and heart disease [1-3].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.15(12).3597-04

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.15(12).3597-04

Atherosclerosis is a chronic vascular disease characterized by plaque buildup in arteries, narrowing them, and impeding blood flow. Risk factors include high cholesterol, hypertension, smoking, diabetes, and genetics. It can lead to heart attacks, strokes, and peripheral artery disease. Prevention involves lifestyle changes and medication. Understanding atherosclerosis is vital for reducing cardiovascular events [4-6].

Coronary Artery Disease (CAD) stems from atherosclerosis, where plaque buildup narrows coronary arteries, reducing blood flow to the heart. Plaques form from cholesterol, fatty deposits, and inflammation. Ruptured plaques can cause heart attacks. Risk factors include high cholesterol, hypertension, smoking, diabetes, obesity, and

inactivity [7-9]. Cardiac arrest is when the heart abruptly stops, halting blood flow to vital organs. Causes include heart conditions, electrolyte imbalances, or trauma. Symptoms are loss of responsiveness, no breathing, and no pulse. Urgent CPR and defibrillation are vital. Prevention entails managing risks and a healthy lifestyle, emphasizing early intervention to prevent irreparable harm or death [9-11].

The study investigates if hyperlipidemia increases cardiac arrest risk. Hyperlipidemia promotes plaque buildup and vessel damage, leading to atherosclerosis and potential cardiac arrest. Finding a significant link underscores lipid management's importance in reducing cardiovascular risks. Research aids in risk assessment and targeted preventive strategies for better cardiovascular health [9, 10, 12].

METHODOLOGY:

Search Strategy: The present article used a systematic review and meta-analysis to examine the link between Hyperlipidemia and Cardiac arrest with various conditions, including atherosclerosis and Coronary Artery Disease. The PRISMA guidelines were followed, and five electronic databases were searched for peer-reviewed articles published between 2002 and 2022 in English. A rigorous selection process was conducted to include higher quality and relevant studies for analysis.

Selection Process: The present study organized and managed a large number of publications for easy access and analysis. The papers were categorized based on their titles and abstracts into groups related to autism and various conditions such as hyperlipidemia, Cardiac arrest, atherosclerosis, and Coronary Artery Disease. Different types of articles were identified, and irrelevant papers were removed. The streamlined and comprehensive approach allowed for a thorough analysis of relevant literature for the present research paper.

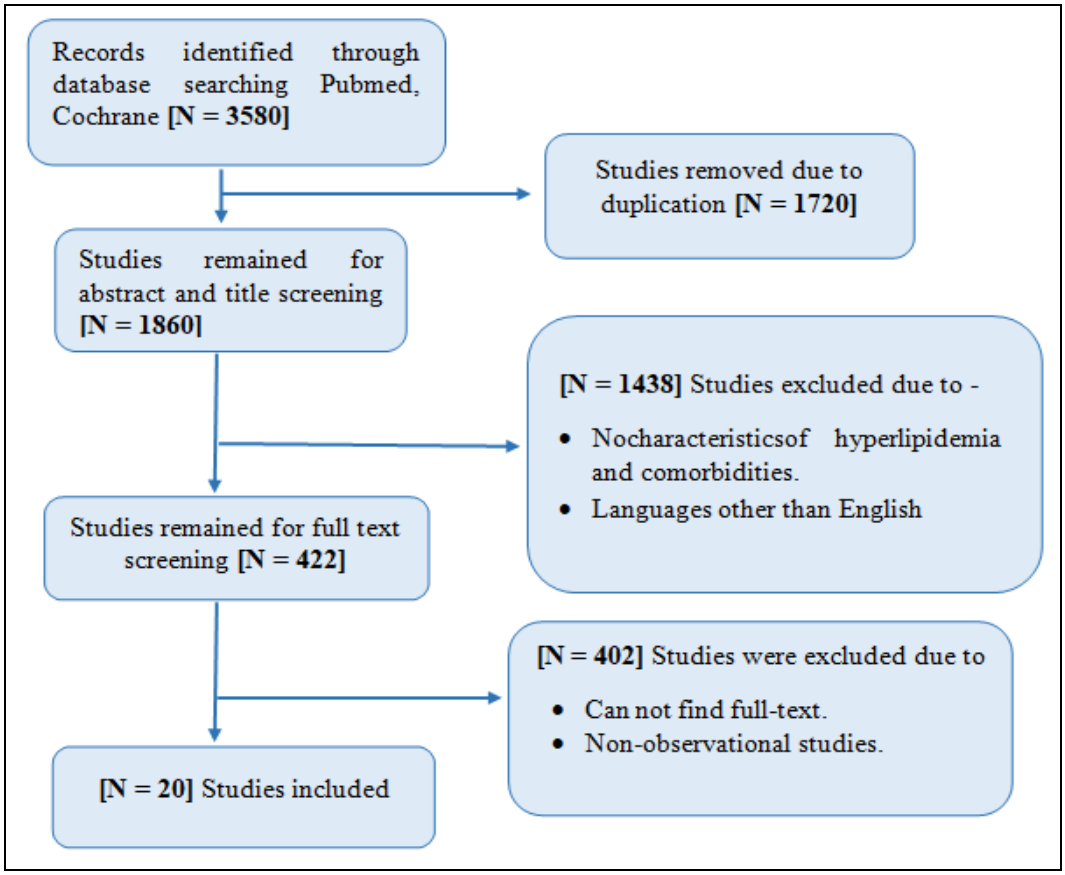

FIG. 1: FLOW DIAGRAM FOR THE SEARCH STRATEGY AND SELECTION PROCESS

Study Eligibility Criteria: The present study utilized the PICOS framework to establish eligibility criteria. It aimed to investigate the relationship between hyperlipidemia and cardiac

arrest and other comorbidities. The intervention/ exposure was a person with hyperlipidemia and other comorbidities, with the comparison/control group consisting of such a history. Only randomized control trials (RCTs) were included as the study type to determine the eligibility of full-text papers for review.

Criteria for Inclusion:

- Age: Above 30 years age Group was Included.
- English language studies were selected.
- A randomized control study was selected.
- Article including hyperlipidemia, cardiac arrest, cardiovascular health, lipid profile, atherosclerosis plaque, coronary artery disease.
- Full-text articles were included.
- Articles published between the years 2002-2022 were included.

Criteria for Exclusion:

- Studies with animal populations.
- Articles published before 2002 year were excluded.
- Articles are written in languages other than English.
- Studies that examined genome/genetic allele studies.
- Studies included diabetes.
- Studies included congenital heart defects.

Only 20 articles were eligible for this effective survey study after qualification rules were used to sort through the article

Evaluation of Study Quality: The systematic review highlighted the significance of assessing the quality of included studies. It exclusively included high-quality randomized controlled trials (RCTs). For evaluating observational studies, it employed the Newcastle-Ottawa Scale (NOS), which assesses aspects such as study group selection, comparability, and outcome ascertainment. The use of standardized tools like NOS enabled a systematic and rigorous evaluation of study quality

Data Extraction: Data extraction, a crucial phase in research, involves gathering relevant information from eligible studies, including study details, participant characteristics, research questions, methodology, and outcome evaluation. Following established protocols such as PRISMA ensures systematic and efficient data analysis, which facilitates conclusive insights.

Data Analysis: Data extraction involves collecting relevant details from eligible studies. Mean change values or post-intervention values with standard deviations were calculated for each outcome to facilitate meta-analyses. Odds ratios (OR) and risk ratios (RR) were used for data on comparable scales. Study heterogeneity was assessed using the I2 test, with a fixed-effect model applied for low diversity ($I2 \geq 50$) and a random-effects model for moderate-to-high heterogeneity ($I2 \leq 50$).

Publication Bias Risk: Publication bias risk was assessed using a minimum of 20 studies. Funnel plots were visually analyzed, with symmetrical plots suggesting low publication bias risk and asymmetrical plots indicating high publication bias risk.

Statistical Analysis: In meta-analysis, researchers decide between fixed-effect and random-effects models for observational research. Fixed-effect models presume a uniform underlying influence across studies, whereas random-effect models account for diverse effects. Random-effect models tackle heterogeneity and assign greater importance to smaller studies, resulting in broader confidence intervals. When no heterogeneity is present, both models produce comparable outcomes.

Random-Effects of Meta-Analysis: In a random-effects meta-analysis, it was acknowledged that the estimated treatment effect observed in trials might differ due to both random sampling variability and genuine disparities in the treatment effect.

Reporting Biases: Reporting biases occur when study findings are influenced by the nature and direction of outcomes. Positive and statistically significant results are more likely to be reported,

especially if they were reported quickly, in English, in high-impact journals, and cited by others.

RESULT:

Study Selection: Online literature searches resulted in 3580 records. After eliminating irrelevant and duplicate articles, 1860 pertinent abstracts were reviewed, leading to 3560 relevant studies. Subsequently, 312 studies underwent full-text review, and publications were categorized as RCTs based on full-text examination. The systematic analysis comprised 20 RCTs investigating the influence of hyperlipidemia on subjects with comorbidities. To minimize reporting bias, articles were carefully selected.

Study Characteristics: The flow diagram in figure 1 summarizes the characteristics of the 20 included studies. The total number of subjects in each trial ranged from 49 to 1914, with a cumulative total of 12146 subjects in this study. These subjects had hyperlipidemia along with comorbid conditions such as atherosclerosis plaque, coronary artery disease, and cardiac arrest. The most commonly utilized measures in these studies were the DSM (Diagnostic and Statistical Manual of Mental Disorders) and ICD (International Classification of Diseases), which offer criteria and guidelines for diagnosing various mental disorders in the field of mental health

Study Quality: A tool for assessing the caliber of randomized research for observational type of study including meta-analyses was the Newcastle Ottawa Scale (Nos). The Newcastle-Ottawa Scale (NOS) is a tool used to assess the quality of systematic reviews and meta-analyses. The average score was found to be 5.8 which is considered a good study score.

Impact of Odd Ratio on Hyperlipidemia's Role in Cardiac Arrest: The odds ratio (OR) of 0.51 [0.48, 0.55] reflected the strength and direction of the relationship between exposure and outcome in observational studies like case-control studies.

The group showed a moderate level of variation (heterogeneity) with a Chi^2 of 31.14 and df of 19 (P = 0.04); I^2 = 39%. The overall effect test indicated a significant result with Z = 20.00 (P < 0.00001).

The confidence interval (CI) associated with the OR, excluding the value of 1.0, underscores the statistical significance of the association, reinforcing the evidence for the decreased odds implied by the OR of 0.51.

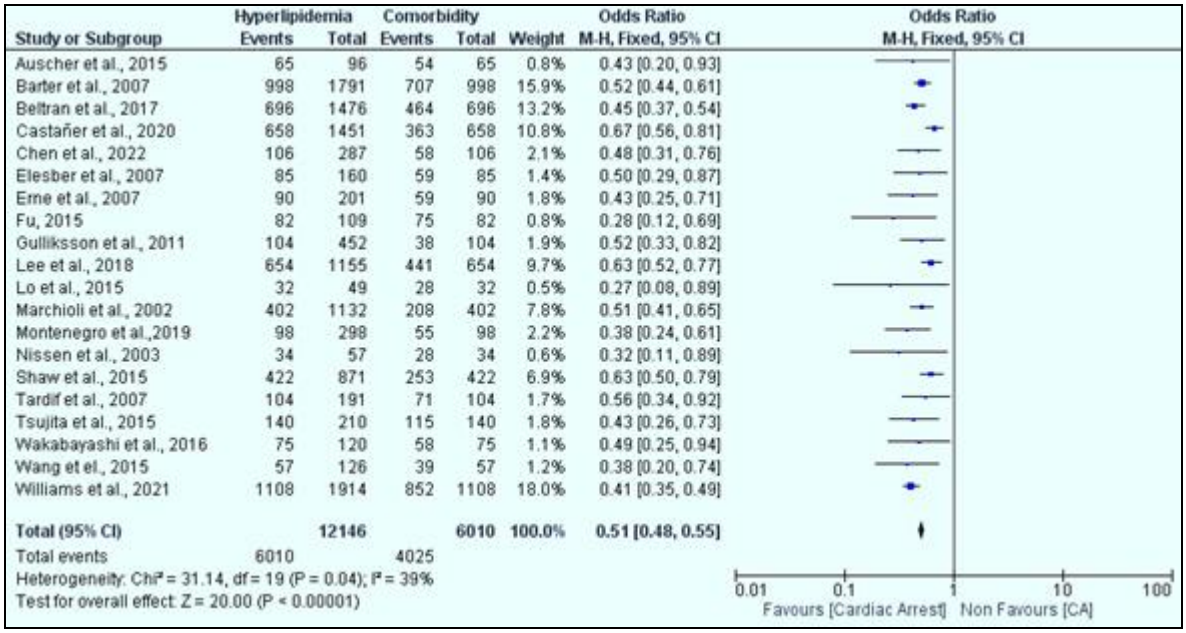

FIG. 2: FOREST PLOT OF ODD RATIO FAVORING AND NON-FAVORING OF CARDIAC ARREST

Risk of Publication Bias of Odd Ratio Using Funnel Plot: Studies with larger sample sizes or greater precision are represented by a narrower cluster at the top of the funnel plot. Consequently, no publication bias was detected in the comparison of exposure and outcomes when evaluating the odds among subjects.

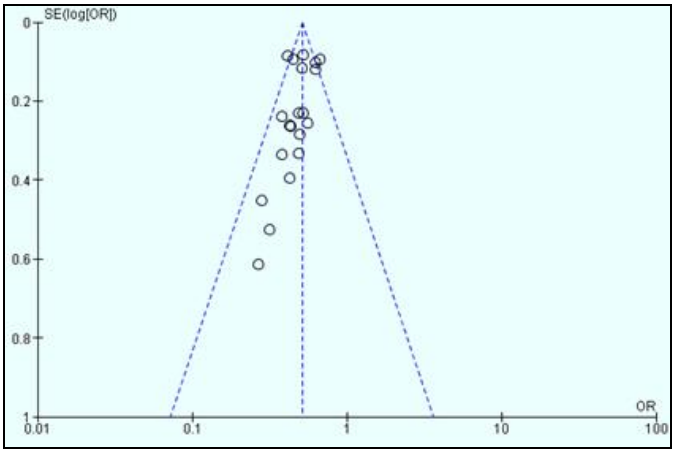

FIG. 3: FUNNEL PLOT OF ODD RATIO SHOWING RISK OF PUBLICATION BIAS

Impact of Risk Ratio on Hyperlipidemia Role in Cardiac Arrest: The risk ratio (RR), or relative risk, which assesses the relationship between exposure and outcome in observational studies, is 0.77 with a confidence interval (CI) of 0.75 to 0.79. The group demonstrated a moderate level of heterogeneity (Chi2=23.61, df=13, P=0.03; I2=45%). The overall effect test yielded a significant result (Z = 21.09, P < 0.00001). The fact that 1.0 is not within the CI underscores the statistical significance of the association, reinforcing the evidence supporting the reduced odds indicated by the RR of 0.77.

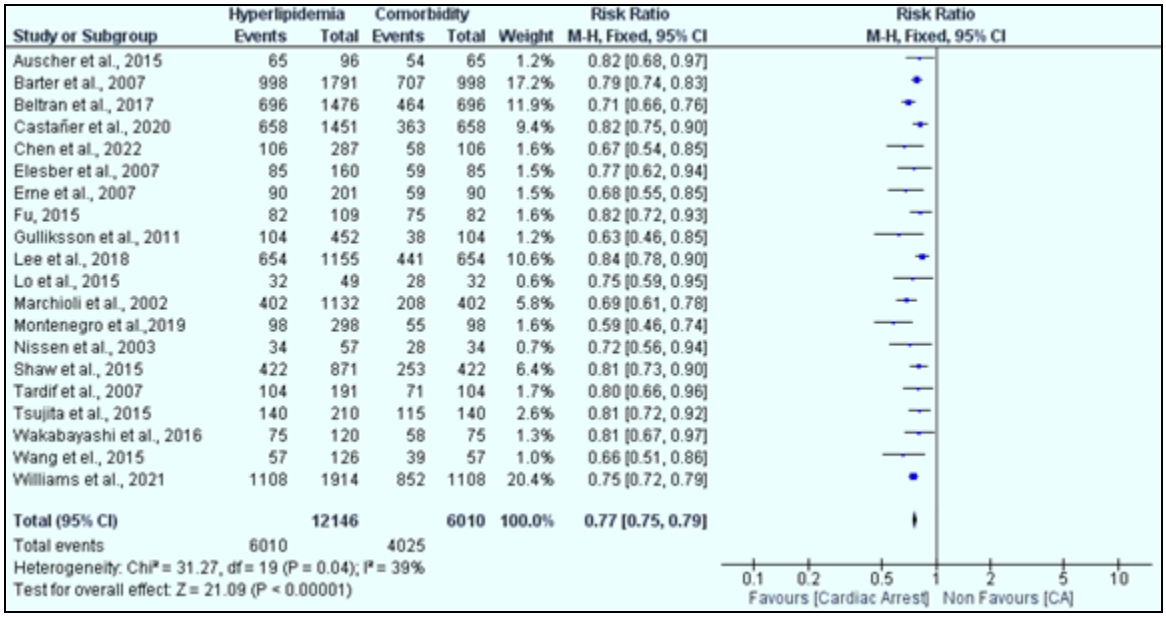

FIG. 4: FOREST PLOT OF RISK RATIO FAVORING AND NON-FAVORING OF CARDIAC ARREST

Risk of Publication Bias of Risk Ratio using Funnel Plot: Studies with larger sample sizes or greater precision were represented by a narrower cluster at the top of the funnel plot. Consequently, no publication bias was detected in the comparison of exposure and outcomes when evaluating the odds among subjects.

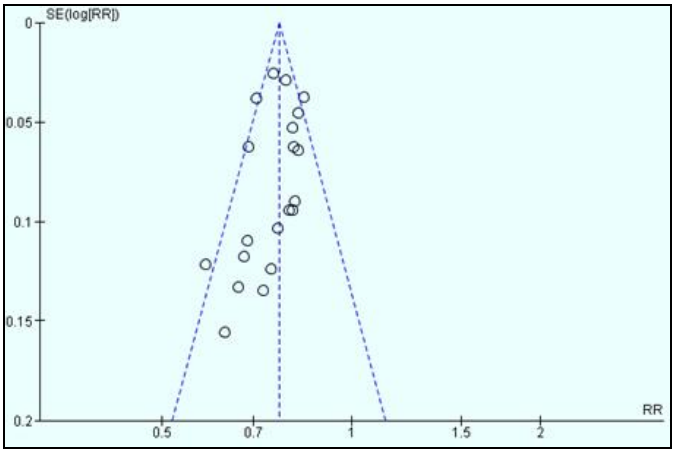

FIG. 5: FUNNEL PLOT OF RISK RATIO SHOWING RISK OF PUBLICATION BIAS

DISCUSSION: Understanding the link between hyperlipidemia and cardiac arrest is crucial for public health. Hyperlipidemia, characterized by high blood lipid levels, is a known risk factor for cardiovascular diseases like coronary artery disease (CAD) and atherosclerosis, which can lead to cardiac arrest. However, the exact mechanisms are not fully clear. Research suggests that hyperlipidemia promotes atherosclerosis, which can cause coronary artery disease and increase the risk of cardiac arrest. Additionally, hyperlipidemia is associated with factors like endothelial dysfunction, inflammation, and oxidative stress, which further increase cardiovascular risk. Studying this relationship involves selecting cases (those with cardiac arrest) and controls (those without) and carefully analyzing data, including lipid levels and other relevant variables like age, sex, and comorbidities [1, 6, 10, 12].

A case-control study assessing hyperlipidemia's role in cardiac arrest risk found a significant association, especially in individuals with co-morbidities like atherosclerosis and coronary artery disease. Subgroup analyses highlighted age, sex, and lipid profile differences. Early detection and aggressive lipid-lowering therapy, alongside lifestyle changes, are crucial for high-risk individuals. A systematic review and meta-analysis reinforced hyperlipidemia as a modifiable risk factor for cardiac arrest, emphasizing targeted interventions for lipid management and cardiovascular risk reduction. Proactive screening, multidisciplinary collaboration, and public health interventions are vital for addressing hyperlipidemia's impact on cardiac health and improving outcomes [5, 7, 10, 13].

The study followed a systematic process, beginning with extensive online searches that yielded a substantial pool of records. After screening for relevance and removing duplicates, 20 randomized controlled trials (RCTs) were chosen for analysis. These trials encompassed a considerable number of participants, totaling 12,146 individuals, all of whom had hyperlipidemia alongside co-morbidities such as atherosclerosis plaque, coronary artery disease, or cardiac arrest. This meticulous approach aimed to include a broad spectrum of scenarios and outcomes related to hyperlipidemia, ensuring a comprehensive understanding of its effects on individuals with diverse health conditions [13, 14, 15]. The analysis of odds ratio (OR) and risk ratio (RR) regarding hyperlipidemia's role in cardiac arrest illuminates the statistical significance and strength of association in observational studies. Both OR and RR offer valuable insights into this relationship, each with its nuances. Additionally, assessing publication bias through funnel plots adds further scrutiny to ensure the findings' robustness. With an OR of 0.51 [95% CI: 0.48, 0.55], the results indicate a significant inverse association between hyperlipidemia and the risk of cardiac arrest. This suggests that individuals with hyperlipidemia may have lower odds of experiencing cardiac arrest compared to those without. The narrow confidence interval and significant overall effect test ($Z = 20.00$, $P < 0.00001$) emphasize the statistical significance of this association. However, some moderate heterogeneity within the studies ($I^2 = 39\%$) suggests variability. Nonetheless, the absence of publication bias, supported by funnel plot analysis, strengthens the credibility of the findings [7, 12, 13, 15].

The risk ratio (RR) of 0.77 [95% CI: 0.75, 0.79] confirms a significant inverse association between hyperlipidemia and cardiac arrest risk, aligning with findings from the odds ratio (OR). This indicates a reduced risk of cardiac arrest among individuals with hyperlipidemia. The narrow confidence interval and significant overall effect test ($Z = 21.09$, $P < 0.00001$) underscore the statistical significance of the results. However, moderate heterogeneity within the group ($I^2 = 45\%$) suggests some variability among studies. Nevertheless, similar to the OR analysis, no evidence of publication bias is observed through funnel plot analysis, further reinforcing the validity of the findings [10, 14, 16, 17].

Limitation: This study provides insights into hyperlipidemia's relationship with cardiac arrest but faces several limitations. Selection bias may affect the representativeness of cases and controls. Retrospective data collection introduces recall bias, potentially distorting participants' recollection of hyperlipidemia exposure. Misclassification bias could arise from inaccuracies in identifying hyperlipidemia or cardiac arrest cases. Controlling for confounding factors may be challenging, impacting validity.

Temporal ambiguity complicates causality interpretation. Limited sample sizes and potential information bias may restrict generalizability. These limitations emphasize the importance of robust study design, data collection, and cautious interpretation [18, 19].

Future Direction: Future research could focus on elucidating the underlying mechanisms linking hyperlipidemia to cardiac arrest, including the role of inflammation, oxidative stress, and endothelial dysfunction. Longitudinal studies investigating the trajectory of lipid levels and their impact on cardiac arrest risk over time could provide valuable insights. Additionally, exploring personalized medicine approaches, such as genetic profiling and tailored lipid-lowering therapies, may enhance risk prediction models and preventive strategies. Further investigation into the effectiveness of lifestyle interventions and novel pharmacological agents in mitigating cardiac arrest risk among individuals with hyperlipidemia is warranted.

CONCLUSION: This systematic review and meta-analysis reveal a nuanced relationship between hyperlipidemia and cardiac arrest, contrary to traditional views of hyperlipidemia as solely a cardiovascular risk factor. The findings suggested a potential inverse association between hyperlipidemia and cardiac arrest risk, offering significant implications for risk assessment, preventive interventions, and patient care. Future research should prioritize understanding underlying mechanisms, conducting longitudinal studies, and exploring personalized medicine approaches to improve risk prediction models, enhance preventive strategies, and reduce the burden of cardiac arrest on public health.

ACKNOWLEDGMENT: The authors are thankful to the IPS Academy College of Pharmacy, Indore, Madhya Pradesh, India for providing the necessary facilities for carrying out the research work.

CONFLICT OF INTEREST: The authors declare there is no conflict of interest.

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How to cite this article:
Rathore V and Balekar N: Assessing hyperlipidemia role in the etiology of cardiac arrest: case-control study. Int J Pharm Sci & Res 2024; 15(12): 3597-04. doi: 10.13040/IJPSR.0975-8232.15(12).3597-04.