**INTRODUCTION**

Diabetes mellitus (DM) is a rising global metabolic disease that is instigating other complications in the human body leading to major consequences. It is characterized by elevated glucose levels resulting from defects in insulin secretion or action.\(^1,^2\) DM is a major global health problem affecting approximately 537 million people according to International Diabetes Federation (2021). By 2045, this number is expected to increase to 784 million. Approximately 90–95% of these cases are Type 2 DM (T2DM).\(^3,^4\) DM is a devastating disease. The estimated 5-year mortality rate in patients with T2DM is calculated as 18.9%. Diabetic complications, mainly cardiovascular diseases,\(^5,^6\) neuropathy,\(^7,^8\) retinopathy,\(^9,^10\) and nephropathy,\(^11,^12\) with subsequent amputation,\(^13,^14\) usually lead to death.\(^15-20\)

CRP is a representative acute phase inflammation response protein. It is mainly synthesized in the liver, stimulated by inflammatory cytokines such as interleukin-6, and has a half-life of up to 19 h.\(^21\) With the advancement of technology, a high sensitivity (Hs)-CRP assessment method was developed, enabling the measurement of
C-reactive protein (CRP) with high precision even at low concentration, or mild elevation such as that seen in chronic inflammation. CRP is linked to a higher risk of getting Type 2 diabetes (T2D), according to a number of prospective cohort research investigations and nested case–control research. Inconclusive findings were found in certain investigations that looked at the connection between HbA1c and Hs-CRP in diabetic patients. Chronic CRP increase could additionally have biological impacts on atherosclerotic plaque stability, low-density lipoprotein (LDL) oxidation, fibrinolysis, coagulation, and endothelial function. According to numerous investigations, elevated levels of CRP are linked to a greater risk of cardiovascular incidents, including CHD. The American Heart Association has determined that Hs-CRP amounts influence cardiovascular risk. According to the study, CRP in the human body is highly related with the cardiovascular risks is also tested for understanding the insulin level in blood which causes major harm to the heart. The total relative risk of T2D was 1.26 (95% confidence interval 1.16–1.37) per increase of 1 log mg/L in CRP levels, according to a meta-analysis of 18 prospective research investigations. However, to the best of our knowledge, there is no single study that discusses the effect of hsCRP on cardiovascular risk of T2DM adults. In terms of dietary regulations, this study is highly significant to aware people about the nutrition aspect of diabetes patients.

Aims and objectives
To evaluate association of glycated albumin, hs-CRP with risk of developing cardiovascular complications among type 2 DM patients.

MATERIALS AND METHODS

Search strategy
This systematic review was prepared in accordance with the preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines. For data extraction, data synthesis, and meta-analysis, standard techniques should be taken into account. In addition, the participants, interventions, comparisons, and outcomes strategy was modified according to the review’s population, exposure, and outcome.

Study design
The review contains studies using observation that concentrate on the extremely responsive CRP on cardiovascular risk of T2DM, which include cross-sectional research and subsequent research. In the study selection process for research, the inclusion and exclusion criteria play an important role. The study for the systemic review has been selected based on some criteria. Those studies are selected for the systematic reviews which are written in English. Those studies are also selected for the systematic review in the present study which are available in the proper PDF format and which has page and volume number. On the other hand, some scholarly articles are also selected which have relevant information related to the subject matter of the present study. The following were excluded from the study: opinions, case reports/series, systematic reviews, proceedings from conferences, narrative reviews, commentaries, and letters to the editor.

Population (P): Adults with T2DM

Intervention (I): hs-CRP measurement

Comparison (C): Participants who had high levels of hs-CRP in comparison to those who had low levels

Result (O): Risk factors for cardiovascular disease, including mortality, myocardial infarction, stroke, and peripheral artery disease, can be used to quantify this risk.

Study selection
The information was found through searches of digital sources such as EBSCO, EMBASE, PubMed, Scopus, and Web of Science. The investigator separately reviewed each abstract and title in comparison to predetermined inclusion and exclusion standards. Google Scholar was used for further research. Using terms, a thorough search plan was created. The terms “hs-CRP,” “Type 2 diabetes mellitus,” and “cardiovascular disease” have been utilized. To translate the results for other databases, the original search was done in PubMed. To find additional pertinent papers, reference lists of the research included and previously released reviews were also examined.

Data extraction and quality assessment
For the extraction of data, the research papers that had been selected at the full-text step were carried over. Data are gathered, and the details pertaining to the topic are interpreted. The research papers were carefully chosen to ensure the caliber of the study. From the papers that are specifically focused on the topic, only pertinent information is taken. Existing journals that contain peer-reviewed articles about medical issues are gathered as secondary data for this research. A systematic evaluation is carried out to assess the results. The criteria for choosing and the number of papers utilized in this research are presented in a flow chart using the PRISMA table. The following information was taken out of the research: (a) creator and article information, (b) region or country, (c) objective of the study, (d) methodology employed, (e) participant and population sub-group demographic information, (f) additional primary results, and (g) conclusion.
<table>
<thead>
<tr>
<th>Author</th>
<th>Study design</th>
<th>country</th>
<th>Findings</th>
<th>Significance</th>
<th>Participants</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kamath et al.</td>
<td>Parallel</td>
<td>India</td>
<td>CVD are common among diabetes patients who have a past history of hs-CRP. Inflammation in the blood causes acute coronary syndrome, peripheral artery disease, and stroke. CRP levels in the human body are stable as they do not react to the intake of food. hsCRP has some properties that influence the endothelial dysfunction in the human body, which causes cardiovascular disease among diabetes mellitus patients in India.</td>
<td>This study aims to evaluate the significance of hsCRP in the occurrence of CVD among diabetes mellitus patients. The relevance of hsCRP and CRP among different regional people is also investigated, indicating the accuracy of the cardiovascular disease chances making humans prone to get inflammation in the blood.</td>
<td>Patients with low grade of systematic inflammation and normal cholesterol level.</td>
<td>Past two decades.</td>
</tr>
<tr>
<td>Mohan et al.</td>
<td>Cross-sectional and longitudinal Asia-India</td>
<td>Glycated albumin is triggered by the dietetic factors of humans, and cardiovascular disorders among diabetes patients are directly relevant to dietary factors. The dietary factors of Asian people include carbohydrates in different forms that increase the chances of diabetes. Inclusion of refined substances in the daily diet triggers inflammation in blood, which is the main reason for diabetes as basal stability gets interrupted from higher intake of glucose and carbohydrate. Higher glucose level or blood sugar in blood limits the functions of blood vessels.</td>
<td>This study aims to identify the relevance of albumin in measuring the fructose level in the human body, which generates from glucose intake. Carbohydrate is a major source of glucose in the human body; hence the dietary factors were found to be extremely relevant and impactful on CVD control.</td>
<td>Patients with MS and cardiovascular disease</td>
<td>Not specified</td>
<td></td>
</tr>
<tr>
<td>Khare et al.</td>
<td>Parallel</td>
<td>India</td>
<td>Diabetes mellitus can cause chronic COPD. COPD restricts the blood flow in the heart leading to major consequences for people. Inflammation in the lungs is caused mainly from smoking and inhalation of harmful substances which restrict the flow of blood in the heart. Increasing blood sugar level in the human body limits the normal function of the lungs, which causes COPD among diabetes patients. Endothelial function among COPD patients causes major issues in the lungs which causes damage in the vasodilatory function leading to major cardiovascular risk among the patients.</td>
<td>This study aims to develop the relativity between the lungs' condition and the CVD by identifying the underlying causes of COPD, which is an inflammatory disease in the lungs that restricts the normal functions of lungs.</td>
<td>16 COPD patients</td>
<td>3 min</td>
</tr>
<tr>
<td>Indumathy et al.</td>
<td>Parallel</td>
<td>India</td>
<td>Insulin resistance is a major concern among diabetes patients who possess a higher risk of cardiovascular disease as cardiometabolic risks increase with an imbalance in the insulin level in the human body. Cardiovascular risk among insulin-resistance groups is higher compared to non-insulin-resistant people. Obesity among diabetic patients determines the insulin resistance level.</td>
<td>This study aims to evaluate the relationship between insulin resistance and cardiovascular risk among diabetic patients.</td>
<td>Obese individuals</td>
<td>2012–2015</td>
</tr>
</tbody>
</table>

(Contd...)
Data analysis and synthesis
Obtained data are analyzed using a systematic review method where each article was discussed with their core findings. Each article is contributing to generating a critical analysis on the relevant factors. Using the systematic review method each article was thoroughly explored and only factual information was selected including survey results and descriptive knowledge.

Outcome measures
Increasing rate of DM and cardiovascular disease is becoming a global concern, hence, through this study a clear understanding of cardiovascular diseases among diabetes patients is expected. Outcome of this study is to determine the hsCRP role in controlling the cardiovascular risk in DM patients.

RESULTS
Flow of studies
The researcher of the present study has selected 50 articles for the systematic reviews and entire data analysis. Only five studies among those are selected because others are not meeting the inclusion criteria. Two studies among 50 articles were not in the English language and others were not informative enough regarding the subject matter of the present research. Scanning of abstracts removed 20 articles and their meaning 28 articles were tested for eligibility and only 10 articles were found to be appropriate. Based on relevance and accuracy, three more articles were removed. Two articles are used which are published in 2013 and 2015 and the rest in 2018.

DISCUSSION
Carbohydrate quality matters in cardiovascular diseases as the study results suggest that chronic complications of diabetes are the main reason for cerebrovascular and macroangiopathy disease. Glycemic index, protein, and carbohydrate type in the diet of the participants are tested which indicates that Type 2 diabetes is triggered by the level of the glycaemic index in the body. The inclusion of whole grains provides fibre in the body which reduces systolic
blood pressure leading to a low risk of CHD. glycaemic properties are improved with a high-fiber wheat diet which eliminates the risk of T2D patients getting heart diseases. Whereas energy generated from fat decreases the chances of mortality among T2D patients. Cardiovascular diseases among T2DM patients require a proper test of CRP to determine the level of inflammation in the lungs. The function of endothelium and inflammation can increase the risk of cardiovascular disease among COPD patients. The body mass index (BMI) of a diabetes patient is highly impactful on the vascular system and COPD patients have higher chances of heart disease if their BMI is high. Obese people suffer from improper BMI rates which increases their chances of being affected in the lungs, leading to major heart conditions. T2DM patients who are obese have shown a higher rate of COPD. Cardiovascular diseases are frequent in insulin resistance (IR) people as the blood flow in their heart is highly unstable as the blood sugar is high in the blood which is not being used by the cells. The high blood sugar level in blood facilitates IR among people which limits the blood flow in the heart causing major heart diseases which can be fatal in obese people.

Among the insulin non-resistance group, the chances of cardiovascular diseases have been observed to be less compared to the IR group as the blood sugar is properly being utilized by body cells. Thus, it is clear that to reduce the chances of cardiovascular diseases it is important to control the insulin level, lipid profile, and BMI. Adiponectin can be used to treat obesity and insulin imbalance. However, a lack of circulating adiponectin in the body imposes a greater risk of cardiovascular diseases among IR patients and a surge of serum neopterin can make the cardiovascular system unfavorable for diabetic patients. Baroreceptor sensitivity must be controlled in Insulin-resistant patients to reduce the chances of morbidity of cardiovascular conditions. IR is the major driver of cardiovascular diseases in obese and non-obese groups which refers to the fact that diabetic patients have higher chances of being affected by cardiovascular disease. Pre-obese period and post-obese period both include the risks of cardiovascular conditions among diabetes patients if the Insulin level is not within the desired level.

Hence, precautionary measures must be taken to remove the vulnerabilities of cardiovascular diseases among T2DM patients. In addition, Asian people especially the Indian population have excessive IR which makes them more exposed to cardiovascular diseases. In addition, Elevated triglycerides are controlled by statin therapies which are caused by IR and obesity. Fatality rates of cardiovascular diseases are mostly found among individuals who have DM. Asian Indians have a higher rate of DM and low tolerance to glucose even after maintaining their obesity level. High lipid profile among young Asian Indians is the main reason for early cardiac arrest and by reducing the LDL, Statin therapy aims to reduce the risk of cardiovascular diseases among young people. Early adoption of Statin therapy has represented a lower mortality rate from coronary artery disease (CAD). Atherosclerosis in children is developed from high cholesterol which affects Indians as they grow old. Cardiovascular disease is observed to affect these kinds of individuals at an early age as their LDL develops atherosclerotic leading to early death.

Children with diabetes must be intervened at earliest as possible to reduce their chances of cardiovascular diseases as reduction of LDL is more effective at an early age compared to the later period when atherosclerosis develops strongly. Global CAD burden can be reduced by treating diabetes patients at the right time with statin therapy. Asian Indians are genetically prone to have higher lipid levels in their blood and the adaptability of unhealthy lifestyles among them increases their vulnerability to diabetes at an early age. Statin therapy can have adverse effects if diabetes patients have other health conditions such as cancer. Medication can interfere with the treatment of an individual by interrupting the functions of different organs. Despite this, statin therapy eliminates the chances of mortality risk among DM patients as a primary preventive measure. Reduction of LDL is the main aim of statin therapy as higher CRP levels and cholesterol can infuse the risk of diabetes patients having cardiovascular diseases at an early age.

CONCLUSION

It has been observed from the systematic review that DM patients have higher chances of being affected from cardiovascular diseases. Asian Indians are at high risk of cardiovascular disease and DM due to their high carbohydrate intake, unhealthy lifestyle, and genetic factors. IR is the major determinant of the cardiovascular risk among diabetes patients which can be tested through hsCRP and tumor necrosis factor-α. Lipid profile matters in cardiovascular diseases as obese diabetic patients have higher chances of heart failure as cholesterol blocks the arteries and high levels of glucose in blood support cholesterol development in the body.

ACKNOWLEDGMENT

Acknowledge and thank Department of Biotechnology, Government of India for funding this thesis (vide reference number TU/DBT-NC/Med/14-15/31.
RECOMMENDATIONS

In future systematic reviews, a diverse range of data sources should be selected to gather optimum knowledge regarding the subject area, restrictions of data collection from specific sources limit the abundance of information. Hence, integrating different medical research sources can expand the quantitative analysis with large samples. Diverse range of sources can provide region-based information, unlike this study where a specific focus has been given to the Asian region.

REFERENCES


Authors Contributions:
BU- Carried out the experiment and collected the data and analyzed the data; MLS- Conceived and presented the idea, developed the theory and computations verified the analytical methods, and encouraged and supervised the findings of this work, and guided the entire work; KLB- Drafted the manuscript and aided in designing and writing the manuscript.

Work attributed to:
Sikkim Manipal Institute of Medical Sciences, Gangtok, Sikkim, India.

Orcid ID:
Dr. Benoy Upreti- https://orcid.org/0009-0000-5528-1565
Dr. Mingma Lhamu Sherpa- https://orcid.org/0000-0002-5905-6127
Dr. Karma Lakhi Bhutia- https://orcid.org/0000-0003-1069-8775