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Insulin resistance in type 2 diabetes mellitus and correlation with atherogenic index

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Abstract
Background: Insulin resistance is a hallmark of type 2 diabetes mellitus (T2DM), it is associated with an increased risk of cardiovascular disease (CVD). The atherogenic index (AI) reflects the balance between athero-promoting and anti-atherogenic lipoproteins and may be a marker for CVD risk assessment. In the current review, we examine the correlation between insulin resistance and AI inpatients with T2DM.
Methods: A comprehensive review was performed on the relevant literature on insulin resistance, AI, and their association with T2DM; PubMed, EMBASE, and other databases were searched to investigate the association of these factors.
Results: Studies suggest a positive relationship between insulin resistance and AI in T2DM patients. Patients with high insulin resistance often exhibit an atherosclerotic lipid profile characterized by elevated triglycerides and small, dense LDL particles, along with decreased levels of HDL cholesterol. This imbalance increases AI, indicating a higher risk of atherosclerosis and CVD development.
Conclusion: This review highlights the potential association between insulin resistance and AI in T2DM and suggests that AI may be a useful tool to identify patients at high risk for CVD. To explore the potential of AI as a therapeutic target or prognostic marker in T2DM management, further studies are needed.

Keywords: Atherogenic index, cardiovascular disease, insulin resistance, low density lipoprotein, type 2 diabetes mellitus

1. Introduction
Insulin resistance (IR) is a fundamental metabolic disease characterized with the aid of way of a reduced responsiveness of body tissues, mainly muscle, fat, and liver, to the blood sugar-reducing hormone insulin. Under everyday conditions, insulin acts as a key, unlocking the door for glucose to go into within the cell and be used for strength. In IR, this key becomes lots less powerful, ensuing in a buildup of glucose inside the bloodstream (Zhao *et al*., 2023) [65].

In T2DM, persistent hyperglycemia arises due to a dysregulation of glucose homeostasis. This is in widespread pushed via a combined sickness in insulin movement (resistance) at intention tissues and a faded ability of pancreatic β-cells to secrete insulin (American Diabetes Association. 2023) [4]. This impaired capability of insulin to correctly alter blood sugar degrees has full-size downstream consequences, which include an extended threat of cardiovascular disorder (CVD) (Alberti *et al*., 2018) [1].

A critical link between T2DM and CVD is the emergence of atherogenic dyslipidemia. This precise lipid profile fosters atherosclerotic plaque improvement within arteries. It is characterized with the aid of the use of extended triglycerides, extended diploma of small, dense LDL-C (atherogenic LDL), and a lower in HDL-C (defensive HDL). (Stefanutti *et al*., 2020) [57].

The atherogenic index (AI) serves as a concise mathematical tool that integrates vital blood lipid measurements. This composite fee reflects a man or woman's susceptibility to atherogenesis, the underlying technique of atherosclerotic plaque formation (Razizadeh *et al*., 2018) [50]. Emerging evidence suggests a robust correlation between T2DM-associated IR and a heightened atherogenic index. This finding underscores the ability software of AI as a scientific metric for figuring out patients susceptible to CVD headaches (Li *et al*., 2018) [33].

2. Insulin Resistance in T2DM
Impaired Response of Muscular tissues, fats cells, and liver to Insulin is a metabolic disease

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which involves the muscle, fats and liver tissues inability to respond to insulin hormones appropriately resulting in impaired transport of glucose fuel into the cells and the cells systemic use of glucose through the whole body which leads to hyperglycemia and compensatory hyperinsulinemia. IR is the major problem of centrality in developing T2DM or CVD or other metabolic problems. An expanding trends of IR is being discovered in a sphere of international relations. This might be attributable to the comorbid or simultaneous outbreaks of weightlessness and sedentary nature among human beings. Dietary patterns include the use of ready to eat or delicious carbohydrate-rich processed food and a decreased physical activity level, which are presumed to be the major contributors to obesity (Freeman & Pennings 2023) [20].

IR is the key metabolic dysfunction that is mainly caused this disorder developing into T2DM that is illustratively shown in Figure 1. DM type 2 is a very common co-morbid complication that involves weight problems, high blood pressure or bad cholesterol. This is what is called insulin resistance, when cells no longer have the ability to move glucose molecules in and out of their cell membrane, causing disruption in their glucose uptake. Genetic factors are the bases, while environmental triggers and life style behaviors are all interact extensively to work together. The deposition of fat occurs at the visceral fat, skeletal muscle and liver which is the main culprits of IR (Andrey Santos et al., 2021) [6]. The adipose tissue within the body is where multiplied lipolysis take place where in turn their free fatty acids (FFAs) molecules are released in large amounts, thus holding the potential of disrupting insulin signaling cascades. IR in skeletal muscle results in the irrespective and the subsequent breakdown of the cells which normally accomplish the diet intake and storing of glucose. In hepatic process raise, it then gains insulin resistance, thereby becoming the path of overproduction and liberation of glucose to the bloodstream (Andrey Santos et al., 2021) [6]. Based on the knowledge about the collaboration between these factors contribute enormously to the development of successful approaches to combat changing environment. Representing a major factor in the process of applicant of T2DM, IR can be linked with a bunch of different reasons and risk factors for the illness. Another great has risk is obesity, especially the central adiposity - which is highly linked to the reduced function of insulin. Low-grade inflammation with the rise in levels of inflammatory markers like interleukin-6 and hs-CRP is another triggering factor for IR. Alongside this, genetics also have magnificent role in IR improvement as mutations in particular genes that contribute to the disregulation of insulin signaling pathways have been reported by Mohammed Al-Beltagi et al., in 2022 [41]. Chance factors apart from these miserable psychological conditions include body constitutional conditions of no interest, aging, proper medications (like glucocorticoids), bad behavioral patterns such as over consumption of carbohydrates and fats. This thesis is also concerned with the impaired glucose uptake which is the essence of the whole issue and also the health concern of the impaired regulation of glucose. Studies have shown that some studies have a link with IR that increases the risk of T2DM, high blood pressure, heart disease and non-alcoholic fatty liver disease. These factors might be considered the driving force, since they can cause a lot of complexities regarding home care, thereby resulting to increase of the mortality rate, the death rate among the patients, immensely.

On top of that, IR creates a multiple of the risk towards many different types of cancers such as breast, colon, pancreatic cancer's. The following piece of writing centers on how critical the right and severe positions to the general health of different body parts is, and if this is not attended to, several body problems will ensue. Moreover, the role of inflammasome, TNF-α and the underlying molecular mechanisms involving FFAs and adipokines are the subject of intensive research advancing the understanding of IHD.

Inflammasome: The existence of data on an intricate protein called the inflammasome, which is critical to the body's immune system response, has been found to correlate with the development of bookmark T2DM and IR. It could be working on the insulin signaling pathway and take part in the growth imperfections and development of T2DM (Lu et al., 2023) [35].

TNF-α: The studies suggest the cytokine (adipo-cytokine) tumor necrosis factor-α and the insulin resistance relations. This correlation is observed vividly in patients with T2DM, which was proved by research (Koliaki & Katsilambros, 2022) [31], expecting TNF- α levels and IR.

Molecular Mechanisms: The pathways linked to FFA, adipokines, insulin receptor substrate-2, Foxo 1a and Akt are enlisted among the biological factors suspected to be behind IR. Impairments in the building blocks of life- the ones dna- could give rise to Iwr in vivo (Sayed et al., 2022) [53].

IR is a key element in the T2DM pathogenesis, affecting how cells reply to insulin and major to multiplied blood sugar degrees. Understanding the ones mechanisms is crucial for growing powerful remedies for T2DM.
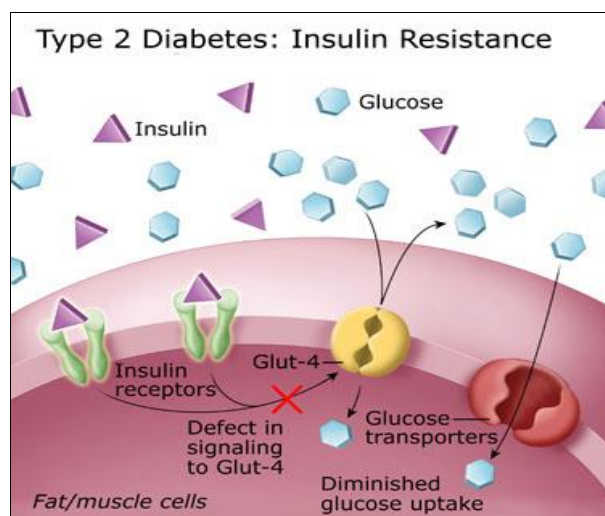
Fig 1: Role of insulin resistance in the pathophysiology of T2DM

3. Atherogenic Dyslipidemia and Atherogenic Index

Atherogenic dyslipidemia is seen in the form of unusual blood lipid profiles whose lipoproteins are more likely to get trapped in the inner lining of the arteries, depositing as 'fatty plaques' next to the blood cells. This metabolite is almost exclusively expressed in association with low HDL-C and high triglycerides. This lipid profile partly mirrors IR. Obesity and diabetes however follow the trends of the lipid profile. An elevated dyslipidemia, characteristic of atherogenesis, has been identified as being closely correlated with a host of other health issues, including T2DM and liver fibrosis in patients with NAFLD (Halcox et al., 2017) [22]. Whereas, though this highly is not show itself in any detectable way, the atherogenic dyslipidemia is, however, a serious risk factor for CVD. Patients with dark blood pressure disorders such as atherogenic dyslipidemia will not notice anything abnormal,

but their non-typical lipid profile increases the chance for serious health problems like heart diseases, strokes, and the others. Subclinical manifestations of CVD, such as angina pectoris, dyspnea, and weakness of muscles may be exhibited among atherogenic dyslipidemia patients since chances of getting complications like atherosclerosis and CVD also increase (Kutkiene et al., 2018) [32].

Atherogenic dyslipidemia being a combination of high triglycerides of low HDL cholesterol ("beneficial" cholesterol), or regular / elevated LDL cholesterol ("harmful" cholesterol). The research shows that there are direct connections between this (Atherogenic dyslipidemia) and metabolic syndrome in T2D (Alloubani et al. 2021) [2].

The AI stands for Artificial Intelligence and it is the risk assessment means that used to analyze the lipid profile parameters to estimated the potential risk of cardiovascular disease. It is done by an exponential math job that extrapolation the ratio of triglyceride (TG) to HDL-C is a viewpoint. Several particular studies have proved that the plasma atherogenic index (AIP) is a reliable risk point of the CVD event and can be used in predicting and diagnosing the CVD; AIP correlates with the size of the lipoprotein particles and has been demonstrated to be better than the LDL, HDL ratio or TG in predicting the total length of the lipoprotein particles (Lütf et al., 2023) [37]. AIP values are better in overweight youth, especially those with fatty liver. It has a nice correlation with frame mass index, IR, and insulin ranges (see parent 2) (Hüseyin et al., 2023) [26].

There are some of atherogenic indices used for assessing the risk of CVD via evaluating lipid profiles and other related factors. These indices help predict the probability of growing atherosclerosis and cardiovascular events. Common atherogenic indices include the following.

3.1 Atherogenic Index of Plasma (AIP)
Increased AIP values indicate a higher incidence of atherosclerosis (Amirkhizi et al., 2023) [5].

3.2 Castelli's Risk Index I and II
These indices are calculated as total cholesterol divided by HDL-C or HDL-C divided by LDL-C, respectively. The higher these indices are, the higher the risk of CVD (Dai et al., 2023) [13].

3.3 Atherogenic Coefficient
This index is calculated as (total cholesterol - HDL-C)/HDL-C. A higher atherogenic coefficient indicates a higher risk of atherosclerosis (Amirkhizi et al., 2023) [5].

3.4 Non-HDL Cholesterol
Non-HDL-C is calculated as universal ldl ldl cholesterol minus HDL-C. This size is concept to be a stronger indicator of your possibilities of developing CVD in comparison to LDL-C ranges on my own (Fernández et al., 2023) [18].

Monitoring of AIP is especially crucial in sufferers withT2DM due to the accelerated threat of CVD related to diabetes. Patients with T2DM are recommended to have a better AIP with a multiplied hazard of atherosclerosis, coronary artery disorder, and other cardiovascular headaches (Gebreyesus et al., 2022) [21].

By assessing AIP, healthcare carriers can better determine the lipid profile of T2DM patients and tailor interventions to lessen cardiovascular risk. To successfully manipulate CVD in T2DM patients, lifestyle changes collectively with multiplied bodily hobby, nutritional changes, alongside pharmacologic interventions adjustments can be encouraged based on AIP ranges (Li et al. 2018) [33].
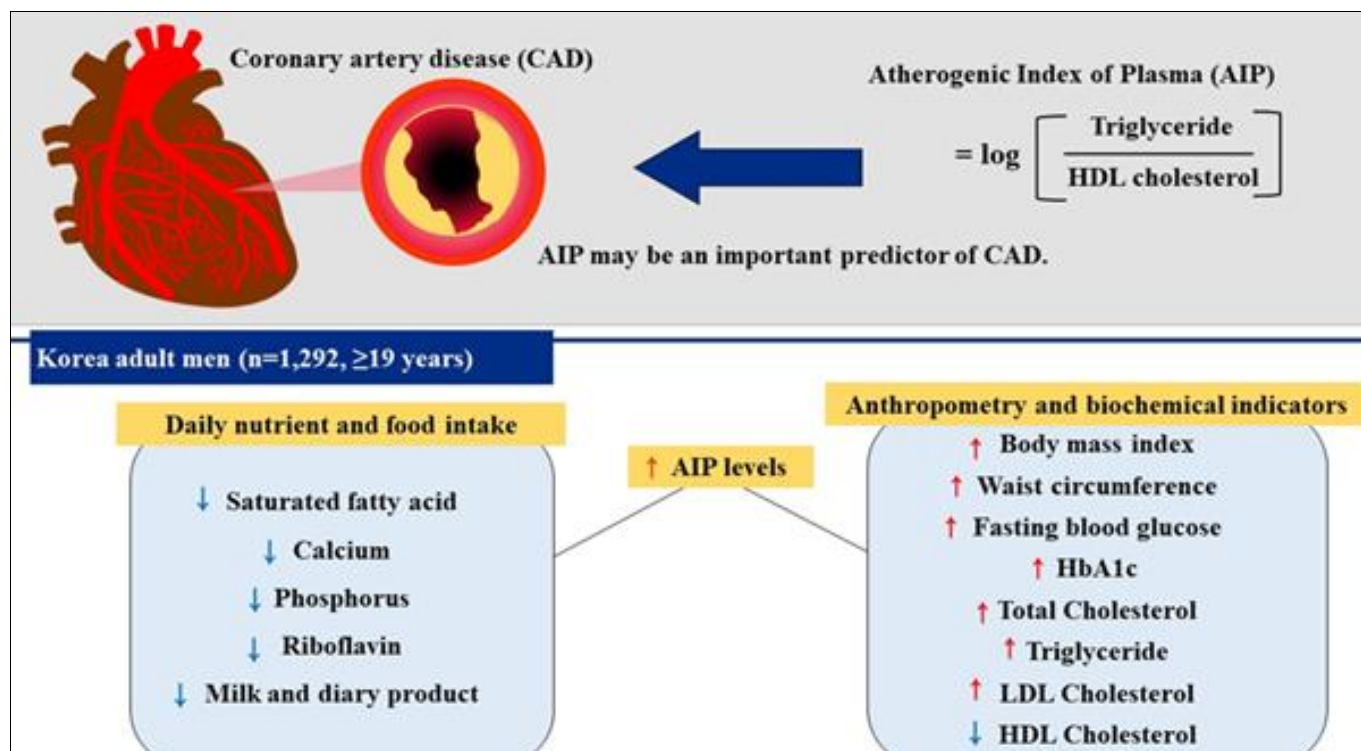
Fig 2: Factors affecting AIP.

4. Correlation between Insulin Resistance and Atherogenic Index
IR has several effects that contribute to the increase in AI and the development of atherosclerosis. The following are the

main mechanisms.

4.1 Dyslipidemia
Dyslipidemia stands for unnaturally high blood lipids level

with high cholesterol and/or triglyceride level being a common leads. IR means IR removes the regular procedure that enables cells to sense the insulin which is in blood stream and increases insulin in the blood stream. The relations between dyslipidemia and IR are inflated and complex (Jin *et al*., 2023) [28].

IR leads to abnormal lipid metabolism, which appears in elevated triglyceride formation and declined lipolysis. When the cells rebukes against insulin, body will secret more insulin to make up for the criterion. The elevation of insulin in the bloodstream that is driven by growth of insulin levels make a liver offer more triglycerides thus enlarge triglyceride levels in the blood. As well, the fat intake reduction caused by IR, giving rise to the dyslipidemia (the presence of higher levels of triglycerides and LDL cholesterol and lower levels of HDL cholesterol in the blood), in similar fashion makes its own contribution (Di Pino *et al*., 2019) [14].

Conversely, dyslipidemia exacerbates IR. Extremely high levels of fatty molecule like FFA, LDL cholesterol, and triglycerides show detrimental consequences on internal working of insulin signaling as well as a cause of IR. Thus, it builds a feedback loop where both conditions amplify one and another (Hasheminasabgorji *et al*., 2021) [23]. As for distinctive cases of IR and dyslipidemia, both conditions are intimately connected with each other and they tend to potentiate and worsen one against each other. The management of such (in order to combat the higher chances of CVD and other headaches that are related to these metabolic disorders) is a key step to eliminating the risk.

Dyslipidemia a major component of AIP, a powerful marker of atherogenesis, regulates the deposition of atherogenic lipoproteins into arterial wall and promotes deleterious events that activate plaque formation and arterial lumen constriction. Atherogenic lipoproteins like LDL-C invade and penetrate into the arterial wall responding to adaptive alterations which cause the inflammatory reaction. This induces the action of immune cells, namely macrophages, which basically involve engulfing oxidized lipoproteins that are modified lipoproteins and are responsible for the formation of foam cells within the arterial wall. With time, the cells absorb more and more, and this process leads to formation of fatty streaks resulting in

atherosclerotic plagues as (Tirtana, 2022) [60]. Elyamani *et al*. (2020) [16] highlighted a massive awesome correlation among the AIP, which displays dyslipidemia, and the severity of CVD in diabetic sufferers. In this have a study, higher values of AIP had been related to higher severity of CVD based at the Gensini scoring machine, indicating a sturdy affiliation between dyslipidemia and CVD improvement.

Rekhi *et al*. (2021) [51] additionally speak how a high-fats Western weight loss plan contributes to atypical fatty acid and glucose metabolism, main to weight problems, IR, and atherosclerosis. The paper highlighted the feature of endothelial disease in atherosclerosis improvement and how dyslipidemia from a high-fat diet contributes to endothelial ailment.

4.2 Inflammation
IR is often associated with chronic low-grade inflammation in the body. As cells become resistant to insulin, the release of inflammatory cytokines and other inflammatory molecules is triggered, leading to systemic inflammation. This chronic inflammation is accompanied by different metabolic abnormalities, including obesity, T2DM, and CVD (Paublini *et al*., 2023) [46].

4.3 Endothelial dysfunction
Endothelial dysfunction consequences when IR disrupts the ordinary feature of endothelial cells in blood vessels which enhances the improvement of atherosclerosis thru the buildup of lipids inside the arterial wall and accelerated AI (Ashraf *et al*., 2023, Paublini *et al*., 2023) [9, 46].

Furthermore, IR is strongly related to metabolic dyslipidemia (Figure 3). The multiplied FFA flux contributes to improved TG production and stimulates very-low-density lipoproteins (VLDL) assembly and secretion in hepatocytes. The accumulation of fats in the liver is connected to lipid peroxidation and oxidative pressure. Additionally, sufferers with NAFLD have an accelerated inflammatory marker, elevating blood sugar levels, and reducing HDL. These physiological abnormalities can result in a better risk of diabetes, atherosclerosis, and coronary artery disorder (Ormazabal, *et al*., 2018) [44].
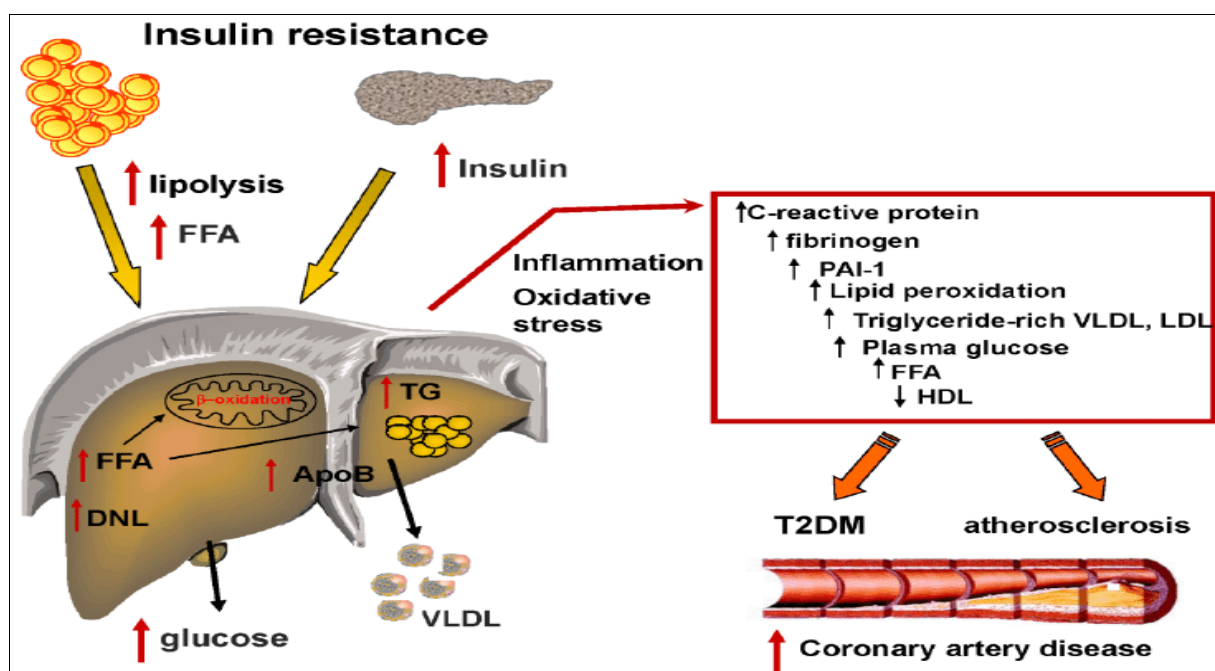

Fig 3: Relationship between insulin resistance and metabolic dyslipidemia and coronary heart disease

Insulin which was a high degree, according to the studies - it was served as a speedster for the process of atherosclerosis. This takes place in numerous ways, together with.

1. Improve the patients' SREPB1-C and ACC expression leading thus to the rise of LDL production (Pino *et al*., 2019) [14].
2. Reduce the level of arterial clean muscle cells and proliferate the vascular smooth muscle cells (Zhao *et al*., 2022) [64].
3. Emphasize the release of pro-inflam.

The problem of our country with its high insulin resistance, the leading source of our expanding diabetes epidemic among other incidents and the number one cause of cardiovascular disease. Infiltration of artery's wall due to fat deposition stimulates inflammation, which promotes development of atherosclerosis, and it also leads to endothelial dysfunction that has been associated with impaired glucose mass and accelerated atherosclerosis (Henning 2021) [24].

There is a huge body of evidence indicating the existence of such relationships between IR and atherogenicity parameters as well as the development of atherosclerosis. Another step-sectional character of the research is the exploration of IR and AIP as predictors for the chance of cardiometabolic disorder in college students in their professional careers. In details, this study involves obese, overweight, prehypertensive, and hypertensive; a high degree of HOMA-IR (HOMA-IR stands for homeostatic model of IR assessment) and AIP which found in many students (Mukhopadhay *et al*., 2021 [42].

The other study laid bare the role of IR, inflammation, TG/HDL-C ratio and AIP in metabolic syndrome and how it relates to the cardiovascular diseases in Type 2 Diabetes. Organizations as HOMA-IR, IR, have already been discovered in the metabolic syndrome of diabetics patents that has the direct connection with immediate ALP and then delivered to the process of atherosclerosis study (Pourfarzam *et al*., 2016) [47].

The study done another researcher to determine the relationship that exists among CT-guided visceral adiposity, AIP, and sagittal abdominal diameter (SAD) in diabetic patients. This trial took place in the frame of the pilot investigations, in a regimen of 53 T2DM patients ranged in age between 25 and 65 years. The primary aim of the study was to assess the relationships concerning these factors in the context of AIP with cardiovascular risks in those with diabetes (Rao *et al*., 2021) [49].

Li *et al*. (2018) [33] who demonstrated hazard factors of AIP in T2DM individuals and relationship between AIP and chronic microvascular complications Parece que la Li *et al*. (2018) [33] demostraron los factores de riesgo de AIP en los pacientes T2DM y la relación entre AIP y complicaciones microvascular chronicles. They studied the included 2523 patients, and the results demonstrated that IR, as simply represented by the increased HOMA-IR, was uniquely associated with scarcity of AIP and atherosclerosis. Nevertheless, the study Miricet *et al*. (2016) [40], people with T2DM neuropathy have achieved better AIP than people with T2DM without neuropathy. To understand the effect of neuropathy on AIP, another study named Martinreport *et al*. (2016) has done more research on differentiating the AIP scores among people with and without neuropathy

Among the routine causes of diabetes that mainly is type 2, is the global increase of CVD morbidity in the presence of hyperglycemia. This complication leads to endothelial dysfunction, oxidative stress, and the ultimate elevation of LDL-c (Newsholme, *et al*., 2016) [43].

In diabetic patients, biochemical changes in systemic lipids would result in a quick rise in triglycerides in the liver. Additionally, insulin insufficiency will increase the production of reactive oxygen species (ROS) and chronic infection. These factors contribute to the development of atherosclerosis and CVD, which are beneficial outcomes if the IR is addressed.2016).

It is Paublini *et al*. (2023) [46], which are characteristically diabetic complications based on previous research correlating fasting serum glucose levels with the levels of extended serum lipids. They determined that atherogenicity is already done and that lipid triad is responsible and it's hard to overcome. They as well such as observe that the speed of the prescribed IR measures had equally been in favor of patients who were suffering from atherogenic dyslipidemia. Another observe become carried out to assess the connection between styles of lipid biomarkers of atherogenesis and the IR index in teenagers with an own family records of diabetes. The study, carried out on a hundred and fifty seemingly healthful young adults aged 18-25 years, along with seventy six and 74 participant with and without a circle of relatives history of diabetes, respectively showed that an effective circle of relatives history of T2DM become related to a better atherogenic lipid index and a higher IR index. Therefore, family history of diabetes in first-degree or 2d-diploma household increases the CVD danger for folks that aren't presently diabetic themselves (Sonuga *et al*. 2019) [56].

These studies demonstrate that there may be a main correlation among IR, the AIP which in the end leads to CVD hazard in diverse populations.

5. Atherogenic Index as a Predictor of Cardiovascular Risk in Diabetic Patients

In individuals with T2DM, the AIP has been invstigated as an ability predictor of cardiovascular hazard (Lumu *et al*., 2023) [36]. Numerous investigations have demonstrated a giant elevation in AIP and a correlation among it and cardiovascular chance factors in T2DM sufferers. It has been found that there may be a fine correlation between AIP and several cardiovascular danger indices, waist hip ratio, and waist circumference. AIP and HbA1C, the duration of diabetes, and fasting blood sugar do not, however, considerably correlate. Additionally, AIP has been linked to IR and a higher hazard of T2DM.According to Texis *et al*. (2023) [59], these outcomes suggest that AIP may be a useful tool for risk stratification of T2DM patients and might help prevent cardiovascular pathology in this populace.

In their report titled Atherosclerosis: A New Idea in the Treatment of Type 2 Diabetes Texis *et al*. (2023) [59] showed Atherosclerosis Imaging Procedure (AIP) as a more significant biomarker in T2DM patients. The pattern proved that serum glucose, HbA1C, and AIP had higher levels in diabetic patients than healthy people whereas HDL has lesser levels in diabetic people compared to control group. However, it concluded ip type 2 during follow up of nutritional lipid-intake routine, use of lipid reducing drugs as well as exercise regimens is associated with lowering AIP levels.

The T2DM sufferers have high chances of developing atherosclerosis and CVDSùas indicated by Yi *et al*. (2023) [63], and this link is closely associated with dyslipidemia in the process. The probe of AIP and coronary arteries lesions in different genders, were done in the population of atT2DM persons was their study.

The results indicated that coronary artery involvement volume

played a role with AIP [which was measured by the labelling of the most important coronary artery lesions] and that the relationship of these variables was also gender-related [for example, a higher degree of coronary lesion labelling was seen in female patients]. Therefore, it was concluded that the AI therapy is an effective therapeutic approach in the fight against coronary artery disease in the T2DM patients. AIP predicts lipoprotein particles and definitely correlated with hazard of atherosclerosis and CVD (Qin et al., 2020) [48].

In addition to detecting impaired glucose metabolism, AIP can investigate the degree of IR involved (Fernández-Macías et al., 2019) [19]. Recently, AIP turned into said as a new unbiased prognostic biomarker for coronary artery sickness (Wang et al., 2021) [61] and atherosclerosis past traditional hazard factors.

Further research are needed to validate those findings and explore genetic associations with AIP and other lipid ratios.

6. Assessment of atherogenic risk in T2DM Population

Besides the increased risk of cardiovascular diseases, type II diabetics are prone to a rise in their atherogenic chances, so preventive measures could be taken as long as the aforementioned consequences are assessed. The work of AIP have been found in male T2DM increased risks containing coronary artery lesions and also linked with or taking risk of MACEs and cardiovascular in T2DM sufferers (Chtioui et al., 2023) [12].

In Ethiopia, it was structured that diabetes type 2 sufferers had the highest AIP stages, impaired glucose regulate, and higher chance of cardiovascular sickness. These results emphasize a main mechanism of AIP relying on atherogenic risk evaluation which is applicable within the diabetes type 2 population especially among males patients. Cardiologists may possibly also utilize the echocardiogram as an effective screening tool for high-risk patients to prevent cardiovascular events (Amare et al., 2022) [3].

Phrased differently that the T2DM patients have higher levels of cardiovascular involvement (AIP), which is significantly associated modelling risk profile for cardiovascular disease (CRA) (Kim et al., 2022) [30].

And like that, Hu et al. (2023) [25] scrutinized the relation between AIP and coronary artery lesion in T2DM patients and discovered AIP as a sensitive marker of coronary artery disease only in male disease affecters, but not extremely sensitive in female T2DM involving individuals. Moreover, devised by Lyu et al. (2021) [38], the coronary cardiovascular risk profile of participants with T2DM was found to be 67.3% who are at intensive cardiovascular risk (>10%) through the Systematic Coronary Risk Evaluation (SCORE) system.

7. The Impact of Insulin Sensitivity on Vascular Health in Diabetes

Insulin sensitivity has a prime effect on vascular fitness in T2DM (Manrique-Acevedo et al., 2023) [39]. In patients withT2DM, intensive antidiabetic therapy and maximum suitable glycemic control improves microvascular feature however worsens carotid atherosclerosis. Furthermore, healthy eating plan-prompted weight loss has been proven to growth vascular insulin sensitivity in sufferers with T2DM, particularly in girls (Antoniou et al., 2021) [7]. Furthermore, it's been found that peripheral vascular dynamics are impaired in T2DM sufferers, leading to vascular harm. Cold stress testing using image plethysmographic pulse wave parameters has been used to quantify these vascular dysfunctions, however the recovery trend is slower in sufferers with T2DM

as compared to wholesome topics. Overall, the ones findings underscore the significance of insulin sensitivity in keeping vascular fitness in T2DM and propose that interventions targeted on IR and glycemic manipulate could have beneficial effects on vascular feature (Khandelwal et al., 2023) [29].

A have a look at of vascular outcomes after tightened glycemic control in poorly controlled lengthy-time period T2DM sufferers found that short-time period aggressive glycemic manage become related to advanced microvascular feature however additionally with worsening carotid atherosclerosis (Antoniou et al., 2021) [8].

Another take a look at the improvement of vascular insulin sensitivity through eating regimen-delivered about weight loss in T2DM patients discovered that diet plan-prompted weight reduction extended vascular insulin sensitivity in patients with T2D, particularly in ladies patients (Smith et al., 2023) [55].

Researchers investigated how sex and weight reduction through weight-reduction plan have an effect on blood vessel reaction to insulin in T2DM. They observed that ladies have been simply less possibly to have impaired blood vessel reaction due to obesity. Additionally, weight-reduction plan-triggered weight loss superior blood float to the legs inspired through insulin, with this effect being more pronounced in girls (Manrique-Acevedo et al. 2023) [39].

7.1 Clinical Implications and Future Directions

Understanding the relationship between IR, atherogenic index, and CVD threat in the management of type2 diabetes mellitus has crucial scientific implications. IR is a critical component in T2DM pathogenesis and is related to expanded danger of CVD. Atherogenic indices such as the AIP and triglyceride-glucose (TyG) index are useful markers to perceive individuals at chance for CVD even when anthropometric and biochemical parameters are ordinary. Studies have proven that IR is intently related to dyslipidemia, a regarded risk aspect for CVD. High triglyceride ranges and low HDL-C are not unusual in individuals with IR and T2DM (Subramaniam et al., 2023) [58].

Atherogenic signs consisting of AIP and TyG can offer extra insight into cardiovascular threat past traditional lipid profiles; early popularity and addressing of IR within the management of T2DMcan assist improve glycemic control and reduce CVD hazard. Monitoring atherogenic indices alongside traditional biomarkers can decorate CVD evaluation in diabetic patients. In addition, intervention focused on each IR and dyslipidemia can also have a superb impact on cardiovascular risk discount in sufferers with T2DM. Therefore, clinicians handling sufferers with T2DM need to take into account assessing IR, tracking atherogenic indices, and addressing these factors as part of a complete technique to lowering cardiovascular threat in this population (Azeez. 2021) [10].

Current remedy options for patients with type2diabetes mellitus with high atherogenic index and IR can also include a complete method that addresses each glycemic manipulate and cardiovascular threat elements (Padhi et al., 2020) [45]. The subsequent remedy strategies can be considered:

8. Lifestyle Modifications

8.1 Dietary Modification: Making a balanced diet a habit, rich in fruits, vegetables, whole grains, and lean protein, can significantly enhance body's capability for the effective usage of insulin. This is called insulin sensitivity. By incorporating these healthy options, you'll also be positively influencing lipid profile, which refers to the levels and types of fats

circulating in your bloodstream (Diab *et al*., 2023) [15].

8.1.1 Physical Activity

Regular physical activity strengthens the heart, improving its ability to pump blood efficiently. It also lowers blood pressure, reduces LDL, and increases HDL, all of which contribute to a healthier cardiovascular system and a lower risk of CVD and stroke (Diab *et al*., 2023) [15].

8.2. Pharmacological Interventions

8.2.1 Antidiabetic Medications: While diet and exercise are crucial for managing T2DM, medications often play a vital role in keeping blood sugar levels under control, such as sulfonylureas, metformin, DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT-2 inhibitors are commonly used to manage blood glucose levels in T2DM patients.

8.2.2 Lipid-Lowering Agents

Statins and other lipid-lowering medications play a crucial role in managing dyslipidemia and preventing CVD events (Wilcox *et al*., 2020) [62].

8.2.3 Vitamin B12 Supplementation

Emerging evidence suggests a potential link between vitamin B12 deficiency and IR. In cases of low vitamin B12 levels associated with IR, supplementation may be considered to improve metabolic parameters and reduce cardiovascular risk (Padhi *et al*., 2020) [45].

8.3 Monitoring and Follow-Up

Effective management of patients often necessitates serial evaluation of metabolic parameters. Regularly monitoring blood glucose levels, lipid profiles (including LDL-C, HDL-C, and triglycerides), atherogenic indices (e.g., LDL-C/HDL-C ratio), and IR markers (e.g., HOMA-IR) provides valuable data for treatment guidance. This continuous assessment allows healthcare providers to dynamically adjust interventions (medications, lifestyle modifications) to optimize patient outcomes (Berberich & Hegele 2022) [11].

Collaboration with a multidisciplinary healthcare team, including endocrinologists, dietitians, and cardiologists, can help optimize patient care and outcomes (Evert *et al*., 2019) [17].

8.4 Individualized Treatment Plans

Effective management of T2DM with hyper atheroma and IR requires a treatment plan that addresses the specific needs of each patient, taking into account factors such as comorbidities, tolerability of pharmacotherapy, and lifestyle preferences (Richardson *et al*., 2022) [52]. In general, a holistic approach combining life style modification, pharmacologic.

9. Conclusion

This review underscores a potentially significant link between IR and AIP in T2DM patients. The observed positive correlation suggests that AIP could serve as a valuable clinical marker to identify individuals at higher risk for CVD. This review also highlights the atherogenic lipid profile commonly observed in patients with insulin-resistant T2DM. Investigating the efficacy of lifestyle modifications, particularly diet and exercise interventions, presents a promising non-pharmacological approach for managing this condition. By improving insulin sensitivity alongside reducing IR, these lifestyle changes could offer significant benefits.

The established association between IR and AIP in T2DM offers valuable insights for assessing cardiovascular disease risk in this patient population. Exploring the underlying mechanisms and investigating the potential applications of AIP as a clinical tool hold promise for improving cardiovascular outcomes in patients with T2DM.

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