

## كلية التربية الاساسية - الجامعة المستنصرية

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# The effect of metabolic syndrome in patients with type 2 diabetes mellitus: Review Israa Saleem Abdulzahra

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#### **Abstract**

A group of metabolic abnormalities known as the metabolic syndrome (MS) are typified by a number of cardiovascular risk factors that are typically linked to central fat buildup and insulin resistance. Insufficient dietary modifications and weight loss, linked to consistent physical exercise, are regarded as primary and first-choice treatments for multiple sclerosis (MS). These interventions help decrease visceral fat and belly circumference, enhance insulin sensitivity, lower plasma glucose and triglyceride concentrations, increase high-density lipoprotein levels, and ultimately lower the risk factors that lead to type 2 diabetes. The MS is a topic of study in the medical community right now since it is associated with conditions that not only have a high death rate globally but also exhibit rising occurrence.

Deregulation of the proteins, fats, and carbohydrates involved in metabolism causes type 2diabetes, which can lead to reduced insulin production, insulin resistance, or a combination of the two. With 90% of cases, type 2 diabetes is the most common of the three kinds of the disease. Being a chronic and complicated illness, diabetes necessitates close medical monitoring in order to lower risks and develop control techniques. Given its rapid epidemic expansion on a global scale in recent years, it is regarded as one of the pandemics of the twenty-first century. This review was non-systematic and advanced, examining the MS in individuals with type 2 diabetes by consulting multiple literatures and analyzing some new publications.

**Keywords:** metabolic syndrome, Diabetic Type 1 and Type 2, Insulin Resistance.



## كلية التربية الاساسية - الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

#### Introduction

The prevalence of diabetes is forecasted between 2030 and 2045 years in the 9th edition of the International Diabetes Federation (IDF) Diabetes Atlas, including estimates from 2019 to 2025. Globally, it is estimated that 463.0 million persons between the ages of 20 and 79 have diabetes, including both type 1 and type 2.1 as show (Figure 1). 463 million individuals are predicted to have diabetes in 2019, and that figure is projected to rise to 578 million by 2030 and 700 million by 2045. In 2019, diabetes-related causes of death claimed the lives of about 4 million individuals aged 20 to 79. Every year, there is an increase in the amount of children and adolescents (i.e., those under the age of 19) who have diabetes. Concurringly, over 50% of instances of diabetes go undetected, with type 2 diabetes accounting for the majority of these occurrences.

There are circumstances where a person's likelihood of developing diabetes and cardiovascular disease heart attacks and strokes is increased if they have a certain set of risk factors. The term "metabolic syndrome" (MS) refers to this discovery. Abdominal obesity, hypertension, low serum levels of HDL-c, high serum levels of TG, and elevated fasting blood glucose (FBG) are among the metabolically interrelated risk factors that make up metabolic syndrome (MS) [1]. It is a widespread health issue in the global community, with a 10% to 40% prevalence range. The development of (T2DM) and cardiovascular disease (CVD), which are the main causes of death and morbidity in older persons, has been linked to metabolic syndrome [2].





كلية التربية الاساسية – الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

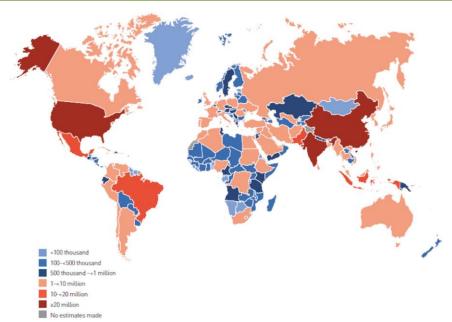


Figure (1): Total estimated number of adults (20- to 79-year-old) with diabetes in 2019. Source. IDF Diabetes Atlas, 9th Edition Metabolic syndrome (MS)

Two characteristics are necessary for the development of MS a rise in body fat accompanied by mass gain, as well as a propensity to find intraabdominal sites for fat accumulation, including ectopic fat in the pancreas, liver, and heart [3]. The lifestyle defined by easy availability to an endless supply of high-calorie, low-nutrient meals and physical inactivity is highly associated with the metabolic syndrome (MS) [4]. These habits are especially effective in the early stages of life, leading to childhood obesity, which increases the adult risk of multiple sclerosis metabolic syndromes [5]. Lipid abnormalities and cardio-metabolic risk factors are linked to metabolic syndrome [6]. Obesity and dyslipidemia are the two main causes of MS. Dyslipidemia encompasses a spectrum of quantitative disturbances in the lipid profile, such as elevated or decreased amounts of lipids and/or lipoproteins, or structural alterations, such as alterations in lipoproteins. Furthermore, a multitude of etiological factors have been associated with the onset and progression of multiple sclerosis MS, such as modified inflammatory status, accumulation of adipose tissue in the abdomen and prolonged SNS activation [7], as show in figure (2)



## كلية التربية الاساسية - الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

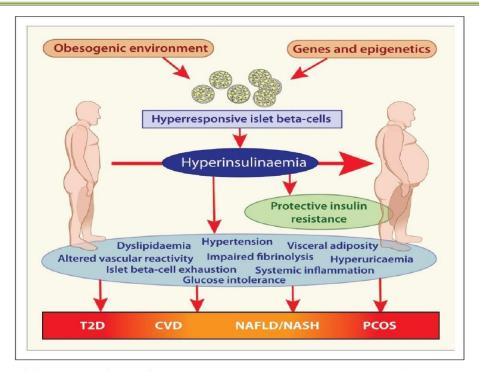


Figure (2): Represent the metabolic syndrome (Nolan & Prentki, 2019). Pathology of the metabolic syndrome

According to a study in (2011) reported a systemic low-grade inflammation appears to be a significant factor in the pathogenesis of obesity and insulin resistance [8]. Abnormal cytokine production and the start of inflammatory signaling pathways characterize the metabolic syndrome associated chronic inflammatory process [9]. Adipose tissue secretes a large number of physiologically active peptides known as adipocytokines, which share similar features with cytokines [10]. In other ways, the inflammatory event that might happen to people who are obese or who have MS is different from the classic inflammatory reaction. Low intensity reactions that are systemic and persistent are a manifestation of these inflammatory responses [11]. Obese adipose tissue inflammation may potentially result in systemic dysregulation [12]. One common risk factor cardiovascular disease and renal disorders are hypertension (HTN) [13]. A patient's likelihood of developing blood pressure can be reduced by controlling certain risk factors, such as nutrition and physical exercise, while other risk factors, including family history, are uncontrollable. Other risk factors include lifestyle, health issues, and physical conditions. Lipid abnormalities and cardio-metabolic risk factors are linked to metabolic



## كلية التربية الاساسية – الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

syndrome [6]. MS mostly consists of two factors: obesity and dyslipidemia. Dyslipidemia encompasses a spectrum of quantitative disturbances in the lipid profile, such as elevated or decreased amounts of lipids and/or lipoproteins, or structural alterations, such as alterations in lipoproteins. In patients with the typical form of T2DM, atherogenic dyslipidemia is frequently linked to obesity-related hyperglycemia, hyperinsulinemia, and the MS phenotype [14]. Adipose tissue secretes a variety of hormones known as adipokines, which have both local and systemic effects. It functions as an active endocrine organ numerous physiological processes, including the control of food intake and body weight, coagulation, insulin sensitivity, vascular function, and inflammation, are primarily mediated by adipose tissue. Numerous cells types, including macrophages, vascular cells, preadipocytes, and mature adipocytes, are found in adipose tissues. These cells secrete cytokines and adipokines, which have an impact on several organs as well as one another [15]. Overweight is a major risk factor for the development of insulin resistance (IR), which will ultimately lead to type 2 diabetes (T2DM) [16]. The process by which body fat causes IR in distant tissues is not entirely known, though. Recent data suggests that the consequences of adipose tissue activity are similar to those associated with inflammatory diseases of some kind [17]. According to [16] proposal, adipose tissue secretes inflammatory cytokines that have an endocrine effect and cause insulin resistance in the liver, skeletal muscle, and vascular endothelial tissue. This ultimately results in the development of T2DM and cardiovascular disease (CVD).

A panel of blood tests called dyslipidemia is used to monitor lipid abnormalities that raise the risk of pancreatitis, cancer, cardiovascular disease, and other conditions [18]. MS mostly consists of two factors: obesity and dyslipidemia. A spectrum of quantitative disturbances in the lipid profile, such as higher or lower levels of lipids and/or lipoproteins, or structural modifications, such as changes in lipoproteins, are referred to as dyslipidemia [19]. This state has been linked to the growth of obesity-related comorbidities and the primary major risk factor for CVD [20]. Also found a correlation between the obesity pandemic and the rising prevalence of MS.

#### **Diabetes Mellitus (DM)**

A collection of metabolic or diverse illnesses brought on by abnormalities in insulin secretion, action, or both, constitute diabetes mellitus (DM), an endocrine disorder rather than a single disorder. Characterized by chronic



## كلية التربية الاساسية - الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative insulin deficiency [21]. Consequently, glucose intolerance and excessively elevated blood sugar are caused by decreased or absent insulin. Perhaps the oldest known sickness to humans is this one. Since the 14th century, it has also been known as "black death." [22]. Type 1 diabetes mellitus (T1DM) and type 2 diabetes mellitus (T2DM) are the two main kinds of diabetes [23]. According to [24], diabetes is a collection of diverse conditions linked to either an excess or insufficient secretion of insulin. Disturbances in the systems that control the mobilization and storage of metabolic fuels, such as anabolism and catabolism, give rise to these difficulties from faulty insulin action, secretion, or both, of proteins, lipids, and carbs [25]. Combining hereditary variables (lower insulin production and tolerance) with environmental factors (overeating, obesity, lack of exercise, stress, and aging) results in type 2 diabetes. Usually, there are several genes involved as well as environmental influences to varied degrees in this complex disease. A noteworthy discovery in the field of pathogenesis indicates that Japanese people exhibit a reduced ability to secrete insulin following sugar loading, indicating a reduced potential for pancreatic β cells [26]. One of the frequent effects of T2DM is peripheral neuropathy. You must keep this consideration because, if left untreated, it is the main contributor of diabetic foot troubles and subsequent physical disadvantage [27].

## **Epidemiology of Diabetes Mellitus**

Based on estimates from the World Health Organization (WHO) in 1997, there are over 135 million people worldwide who have diabetes. By 2025, that number is expected to rise by 120%. According to estimates, 50% of Americans with diabetes go undiagnosed [28]. The sixth leading cause of death is diabetes mellitus. Individuals with diabetes mellitus are twice as likely to die at the same age as healthy people. Diabetes by itself does not cause death; rather, the consequences of the disease's complications. Additionally, the population of Europe is seeing a rise in the incidence of DM as a result of routine changes that result in a drop in the normal activity and advance obesity [29]. It is anticipated that there would be 60 million cases of T2DM in the Middle East by 2030 [30]. On the other hand, according to data from the Iraq Ministry of Health, 10.2% of Iraqi persons are injured, placing the country 30th globally and ninth in the Arab World [31].



## كلية التربية الاساسية - الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

#### **Insulin Resistance (IR)**

Insulin resistance (IR) is a pathogenic condition where cells do not react to the insulin hormone as they should. All humans normally experience several years of insulin resistance before developing Type 2 diabetes, which is frequently complex and includes hereditary components [32]. Insulin resistance and a decline in insulin production are the two main characteristics of T2DM pathophysiology, therefore, insulin resistance can be brought on by a sedentary, contemporary lifestyle, abdominal obesity, and an excess of adipokines; compensatory hyperinsulinemia preserves normal resistance to glucose at an early level. Around 25% of individuals without diabetes produce insulin resistance within the same limits as T2DM patients [33]. As a result of ongoing increases in insulin resistance and/or reductions in insulin secretory compensating responses, poor glucose tolerance developed. Elevations in glucose, insulin, and free fatty acid (FFA) trigger the overproduction of reactive oxygen species (ROS), oxidative stress, and the activation of stress transduction factor pathways. This may result in decreased insulin secretion and activity, hastening the onset of type 2 diabetes as shown Figure (1-2) [34].

# Type2 diabetes and metabolic syndrome

Diabetes, a chronic, advanced illness indicated by high blood sugar, is caused by the body's ineffective use of insulin. Millions of people worldwide suffer from type 2 diabetes (T2DM), which can have life-threatening complications of diabetes is not well controlled [35]. A collection of metabolic abnormalities that talk about an increased risk of T2DM and CVD make up metabolic syndrome [36]. Atherogenic dyslipidemia is frequently linked to hyperglycemia in individuals with the common form of T2DM, namely with hyperglycemia associated obesity, Insulin resistance hyperinsulinemia, and the MS phenotype [14] .Activation of the innate immune system occurs prior to the development of T2DM, this suggests that T2DM is an innate immune system illness responsible for the persistent cytokine-mediated acute phase response and chronic low-grade inflammation; increased inflammatory markers such as C-reactive protein (CRP), TNF-α, and IL-6 indicate the development of glucose problems and type 2diabetes [37]. Obesity-related MS is significantly influenced by insulin resistance. Early onset and correlation with mild glucose intolerance offset by elevated insulin secretion. Insulin resistance is a major factor in type 2 diabetes when associated with decreased insulin production. Insulin



## كلية التربية الاساسية - الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

resistance is the greatest predictor of type 2 diabetes and is crucial to the elevated risk of cardiovascular disease associated with multiple sclerosis [38]. Inversely correlated with high-density lipoproteins (HDL) cholesterol and insulin sensitivity index, high-sensitive CRP is positively correlated with body mass index (BMI), waist circumference, cholesterol, triglyceride (TG), low-density lipoproteins (LDL) cholesterol, fasting insulin, and plasma glucose [39]. Insulin resistance (IR) has been extensively researched in MS patients with T2DM and is considered the pathophysiological predisposing factor for T2DM so, the hallmark of inadequate insulin activity in the adipose, skeletal, and hepatic tissues is insulin resistance [40]. Increased adipose tissue FFA release, endothelial dysfunction in the arteries, increased gluconeogenesis in the liver, and impaired muscle glucose clearance are all caused by IR. An increased production of insulin (compensatory to maintain euglycemia) as a result of defective insulin function results hyperinsulinemia. Glucose elevated if this compensatory malfunctions moreover, elevated levels of free fatty acids in the bloodstream suppress insulin signaling, which in turn causes IR [41]. Adipose tissue serves as a highly metabolically active organ that produces a wide range of bioactive particles, including FFAs. FFA release is increased in cases of abdominal obesity. Furthermore, certain inflammatory cytokines produced in greater amounts while anti-inflammatory adipokines produced less frequently [42]. It has been proposed that hypertension (HTN) and insulin resistance (IR) are related through a number of mechanisms. Hyperglycemia causes modifications in the composition of lipoproteins and a decrease in HDL-C, When IR occur, the endothelium's ability to respond to IR's vasodilator action may be inhibited, leading to vasoconstriction [43]. One important aspect of MS linked to obesity is insulin resistance; Elevated insulin production may compensate for early stage insulin resistance and associated mild glucose intolerance IR is important in T2DM when associated with reduced insulin secretion, therefore Insulin resistance is the best indicator of type 2 diabetes and a significant contributing factor to the increased risk of cardiovascular disease (CVD) linked to multiple sclerosis [37]. The induction of metabolic changes due to IR may have an impact on the development of accelerated atherosclerosis and CVD disease. Raising blood glucose and insulin concentrations may also contribute to it, in addition to processes such as dyslipidemia, hypertension, and systemic inflammation [44]. Show figure (3).



## كلية التربية الاساسية - الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

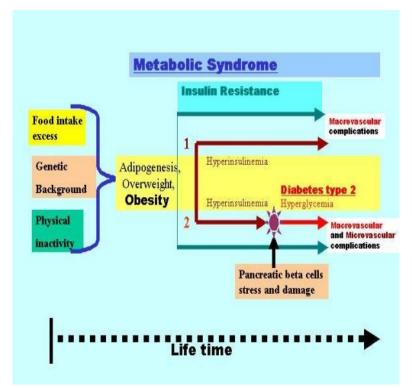


Figure (3): The relationship between metabolic syndrome, insulin resistance, hyperinsulinemia and hyperglycemia (overt type 2 diabetes) [46]

#### Conclusion

Most of the research in this review shows that multiple sclerosis (MS) is a cluster of problems that, when linked to other illnesses, result in serious changes in the human body that especially impacts individuals with type 2diabetes. The length of diabetes, a factor that may slow or speed up the onset of MS because of the numerous comorbidities connected to, such as circulatory and cardiac issues. It is possible to consider that the environment in which the person lives (e.g., the place of residence or the geographic area) may be conducive to this type of disease. Other aspects, such as labor and working circumstances, hygienic practices, and social factors, can be considered in addition to the environment.

#### **Recommendations**

The necessity of a comprehensive and unbroken perspective is recognized on a global scale, not just with regard to diabetes but also with regard to the myriad other comorbidities with which it may be linked, including multiple sclerosis.



#### كلية التربية الاساسية - الجامعة المستنصرية

**Journal of the College of Basic Education** 

Vol.30 (NO. 126) 2024, pp. 81-94

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**Journal of the College of Basic Education** 

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**Journal of the College of Basic Education** 

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# تأثير متلازمة التمثيل الغذائي في المرضى الذين يعانون من مرض السكرى من النوع2

#### مستخلص البحث:

يتم تحديد مجموعة من التشوهات الأيضية المعروفة باسم متلازمة التمثيل الغذائي (MS) من خلال عدد من عوامل الخطر القلبية الوعائية التي ترتبط عادةً بتراكم الدهون المركزية ومقاومة الأنسولين. تعتبر التعديلات الغذائية غير الكافية وفقدان الوزن، المرتبطة بالتمارين البدنية المستمرة، من العلاجات الأولية والاختيار الأول لمرض التصلب المتعدد .(MS) تساعد هذه التدخلات على متقليل الدهون الحشوية ومحيط البطن، وتعزيز حساسية الأنسولين، وخفض تركيزات الجلوكوز في البلازما والدهون الثلاثية، وزيادة مستويات البروتين الدهني عالي الكثافة، وفي النهاية تقليل عوامل الخطر التي تؤدي إلى مرض السكري من النوع الثاني. يعد مرض التصلب العصبي المتعدد موضوعًا للدراسة في المجتمع الطبي في الوقت الحالي نظرًا لأنه يرتبط بحالات ليس لديها معدل وفيات مرتفع على مستوى العالم فحسب، بل تظهر أيضًا حدوثًا متزايدًا .يؤدي تحرير البروتينات والدهون والكربوهيدرات المشاركة في عملية التمثيل الغذائي إلى الإصابة بمرض السكري من النوع والدهون والكربوهيدرات المشاركة في عملية التمثيل الغذائي إلى الإصابة بمرض السكري من النوع الثاني، مما قد يؤدي إلى انخفاض إنتاج الأنسولين، أو مقاومة الأنسولين، أو مزيج من الاثنين في المرض. نظرًا لكونه مرضًا مزمنًا ومعقدًا، فإن مرض السكري يتطلب مراقبة طبية دقيقة لتقليل المخاطر وتطوير تقنيات السيطرة عليه ونظراً للتوسع الوبائي السريع على نطاق عالمي في السنوات المخاطر وتطوير أحد أوبئة القرن الحادي والعشرين.

الكلمات المفتاحية: متلازمة التمثيل الغذائي، مرض السكري من النوع1 والنوع 2، مقاومة الانسولين

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