

Review

Predictors and Associated Risk Factors of Development of Type 2 Diabetes Mellitus

Rahmathulla Safiyul Rahman¹, Farah Almomen², Ali Artam Alajmi³, Ibrahim Asiri⁴, Sarah Basudan⁵, Munirah Alenezi³, Faisal Alabdulwahab⁶, Shihanah Al shammari⁷, Abdullah Aldakheel⁸, Abdulrahman Al Shehri⁹, Marya Alabdulmohsen¹⁰

¹ Department of Internal Medicine, Sameera Medical Center, Jeddah, Saudi Arabia

² College of Medicine, Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia

³ College of Medicine, Arabian Gulf University, Manama, Bahrain

⁴ General Physician, Ministry of Health, Khamis Mushait, Saudi Arabia

⁵ College of Medicine, King Saud bin Abdulaziz for Health Sciences, Riyadh, Saudi Arabia

⁶ College of Medicine, Vision Colleges, Riyadh, Saudi Arabia

⁷ General Physician, Ministry of Health, Riyadh, Saudi Arabia

⁸ Department of Internal Medicine, Diriyah Hospital, Riyadh, Saudi Arabia

⁹ Department of Family Medicine, Ministry of Health, Abha, Saudi Arabia

¹⁰ College of Medicine, Dar Al Uloom University, Riyadh, Saudi Arabia

Correspondence should be addressed to **Safiyul Rahman**, Department of Internal Medicine, Sameera Medical Center, Jeddah, Saudi Arabia. Email: safiyul@gmail.com

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Abstract

Diabetes is a worldwide growing metabolic disease associated with significant morbidity and mortality. Type 2 diabetes is one of the subclasses of diabetes mellitus which is more prevalent than the other classes of diabetes approximately accounting for 90% of cases and if not diagnosed and managed timely can lead to quite serious complications. The development of type 2 diabetes is associated with both modifiable and non-modifiable risk factors. The purpose of this research is to review the available information about the predictors and associated risk factors of development of type 2 diabetes mellitus. As a global epidemic and a major threat to the global economy, type 2 diabetes is high on the international health agenda. Insulin resistance and cellular dysfunction are strongly influenced by both genes and nature. Since genetic factors are uncontrollable, modifiable risk factors must be controlled to prevent type 2 diabetes. Old age, obesity, physical inactivity, smoking is among the major predictors and risk factors of type 2 diabetes also individuals having family history of diabetes are an increased risk of type 2 diabetes. Metabolic syndrome is also considered a significant predictor of type 2 diabetes. Women who suffered from gestational diabetes as well as their children, are also at greater risk of developing type 2 diabetes. Literature has revealed the potential predictors and risk factors of type 2 diabetes, which can help predict and diagnose the risk of diabetes even before symptoms develop. The risk of type 2 diabetes can be reduced by adopting a healthy lifestyle for which awareness campaigns and seminars can be beneficial in educating the public.

Keywords: *diabetes mellitus, type 2 diabetes mellitus, predictor, risk factors*

Introduction

Diabetes mellitus commonly referred as diabetes, is a metabolic disease marked by hyperglycemia, which is a physiologically abnormal condition characterized by persistently high blood glucose levels. The abnormalities in insulin production, insulin action, or both, leads to hyperglycemia and is usually presented as a metabolic dysfunction of carbohydrate, lipid, and protein in a chronic and varied manner. Diabetes has a gradual course with a complex etiology and a wide range of symptoms (1). The dysregulation of carbohydrate, lipid, and protein metabolism, which is caused by decreased insulin secretion, insulin resistance, or a combination of both results in the development of Type 2 diabetes mellitus (T2DM). T2DM is significantly more common accounting for more than 90% of all cases than other classes of diabetes mellitus including type 1 diabetes mellitus and gestational diabetes. T2DM classification can be problematic due to the unique presentation of symptoms. Many people with T2DM are asymptomatic at the time of diagnosis, whereas others present with severe hyperglycemia or diabetic ketoacidosis. T2DM can be confused with latent autoimmune diabetes in adults and maturity-onset diabetes in children (2).

T2DM is widely recognized as a critical public health issue that has a significant impact on individual life and healthcare system. In many regions of the world, rapid economic development and urbanization have resulted in an increase in the prevalence of diabetes. Diabetes has a negative impact on people's functional abilities and quality of life, resulting in severe morbidity and mortality. As per the recent reports in literature diabetes is responsible for more than one-third of deaths in adults under the age of 60. T2DM has impacted approximately 462 million people worldwide in 2017, accounting for almost 6.28% among which 4.4% aged 15–49, 15% aged 50–69, and 22% aged 70 and over, or a prevalence rate of 6059 cases per 100,000. The global burden of diabetes mellitus is increasing at a considerably quicker rate. The incidence peaks at roughly 55 years of age, and the gender distribution is similar. By 2030, the global prevalence of T2DM is expected to rise to 7079 people per 100,000, exhibiting an upward trend in all regions of the globe (3).

Modifiable and non-modifiable risk factors account for risk factors related to T2DM. Modifiable risk factors include rich diets in saturated fats and simple carbohydrates, impaired glucose tolerance, metabolic

syndrome, high blood pressure, elevated plasma triglycerides, and low or limited physical activity while age more than 45 years, family history of diabetes, gestational diabetes, ethnicity are non-modifiable risk factors. Complications of T2DM can be quite serious if not managed or treated timely. The majority of these issues are a result of microvascular complications of T2DM which include nephropathy, neuropathy, and retinopathy and also macrovascular complications such as coronary artery disease, cerebrovascular diseases, and peripheral artery diseases (4). Various screening methods are designed to identify individuals at high risk of developing T2DM, with the aim of contributing to their risk factors by changing lifestyle and medical interventions as delays in diagnosis play a major role in poor glycemic control and increases the risk of associated complications. Different predictive models are available for the assessment of predictors and risk factors of T2DM as it can lead to prevention of diseases and complications (5).

T2DM is the most severe form of a progressive risk continuum with serious clinical effects. An individual's risk of developing cardiovascular disease, microvascular disease, and metabolic syndrome components such as dyslipidaemia increases when blood glucose levels are increased. Diabetes prevalence has risen considerably in recent years and is expected to continue to rise in the coming years. Patients with T2DM rarely maintain appropriate glycemic control, even with today's advanced management programs and strategies, leading to certain complications. Preventing the development of prediabetes is the most effective method to treat T2DM and its complications. The most cost-effective treatment option for the risks of cardiovascular diseases and other related complications is increasingly recognized. Many guidelines urge early identification of high-risk individuals and active management, and there is growing evidence that lifestyle modification and pharmacological therapies can reliably lower the incidence of T2DM and the associated complications (6). The purpose of this research is to review the available information about the predictors and associated risk factors of development of type 2 diabetes mellitus.

Methodology

This study is based on a comprehensive literature search conducted on May 30, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms,

according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about the predictors and associated risk factors of development of type 2 diabetes mellitus. There were no restrictions on date, language, participant age, or type of publication.

Discussion

According to the American College of Chest Physicians, as a global epidemic and a serious threat, T2DM is high on the international health agenda. In the last 20 years, the number of people with T2DM has more than doubled. According to the International Diabetes Federation, 415 million individuals worldwide had T2DM in 2015, with a projected increase to over 642 million by 2040. These figures correspond to an estimated global prevalence of 8.8% (95% confidence interval: 7.2–11.4%) in 2015 and a predicted global prevalence of 10.4% (95% confidence interval: 8.5–13.5%) in 2040. Epidemiological data

suggest an irreversible and unsustainable rise in global health spending due to T2DM, hence disease prevention should be prioritized. T2DM is caused by a combination of genetic and environmental factors. Insulin resistance and cellular dysfunction are heavily influenced by both genes and the environment. Since genetics factors cannot be controlled modifiable risk factors shall however be prevented and controlled to prevent T2DM (7). As per the statistics, over 50% of persons with diabetes remain undiagnosed, and approximately 20%-30% of patients develop complications before they are diagnosed. As a result, an alternative screening method for T2DM diagnosis is needed. In recent times, a variety of risk assessment tools based on self-assessed, biochemical measures, or genetic markers have been developed for the prediction of T2DM, and are considered more practical and valuable than the traditional blood glucose screening tests and use of such interventions can aid to delay the onset of T2DM in those with impaired glucose tolerance (8). Schematic presentation of risk factors of T2DM is illustrated in (Figure 1).

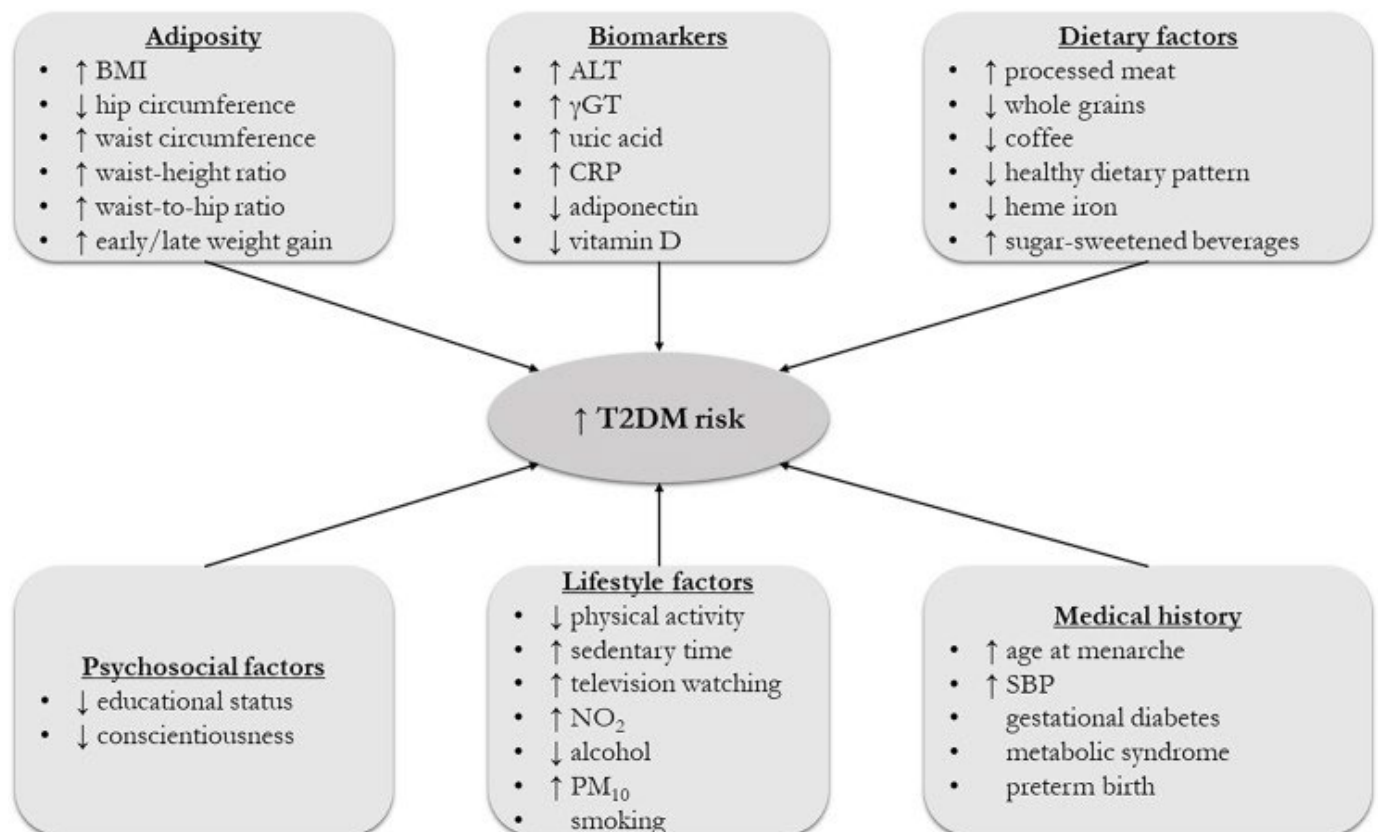


Figure 1 : Schematic presentation of risk factors of T2DM (8)

Predictors and Risk factors of T2DM

T2DM is caused by a complex interaction of genetic, environmental, and metabolic factors. People at high risk of developing T2DM include having a significant family history of diabetes mellitus, the elderly, obesity, and physically inactive. Young people are also at greater risk, not only because of their family history and genetics but also because they have become accustomed to sedentary lifestyle. Women who have had gestational diabetes before, and their children, are at greater risk of developing T2DM. Insulin resistance raises the risk of T2DM and glucose intolerance. Insulin-resistant patients also have some common T2DM risk factors such as hyperinsulinemia, atherogenic dyslipidemia, glucose intolerance, high blood pressure, prothrombic condition, hyperuricemia, and polycystic ovarian disease. Interventions aimed at altering harmful environmental factors, such as weight loss and physical activity, are currently being used to prevent and delay T2DM. For high-risk individuals, awareness of T2DM risk factors will improve diagnosis, early detection, and treatment so the chances of both microvascular and macrovascular complications can be reduced. (9).

Findings of a prospective cohort Danish population study in 2018 depicted that high body mass index, antihypertensive treatment, age, cardiovascular disease, waist-circumference, fitness compared to peers, and family disposition for T2DM were the top seven self-rated predictors in order for T2DM. The area under the curve for Leicester risk assessment score was 77.1, 75.4 for Danish diabetes risk score, and 67.9 for Finnish diabetes risk score and 20% of the study population was undiagnosed for T2DM also undiagnosed T2DM is linked to a high BMI and self-reported cardiovascular illness (10). Ismail stated in his study findings that the risk of T2DM is highly linked to quantity and quality of sleep, smoking, dyslipidaemia, hypertension, ethnicity, family history of diabetes, obesity, and physical inactivity. Both the quantity and quality of sleep have been linked to the development of T2DM. The link is higher in women who sleep for longer periods of time and in males who sleep for shorter periods of time. It has also been discovered that smoking is a substantial risk factor T2DM and both active and passive smokers are prone to the risk of T2DM. Furthermore, for the first 5–10 years after quitting smoking, the risk of acquiring T2DM remains significant in ex-smokers. The development of T2DM is closely linked to a family

history of diabetes among first-degree relatives. Furthermore, a family history of diabetes indicates a link between obesity and T2DM. Obesity has been discovered to be a strong risk factor for the development of T2DM, with the link being higher in women than in males (11). Shin concluded in his study that metabolic syndrome is a strong predictor for T2DM and can aid in diagnosis and evaluation of diabetes in clinical practice (12).

Findings of a prospective cohort study showed that following a median follow-up period of 45 months, 116 (29.4%) of the 395 women with gestational diabetes developed diabetes. Women with gestational diabetes, who later developed diabetes had a significantly higher weighted genetic risk score (9.36 ± 0.92 vs 8.78 ± 1.07 ; $p < 1.56 \times 10^{-7}$) than those who did not. The C statistic improved marginally from 0.741 without the weighted genetic risk score to 0.775 and with the weighted genetic risk score ($p = 0.015$) in a sophisticated clinical model adjusted for age, pre pregnancy body mass index, family history of diabetes, blood pressure, fasting glucose, and fasting insulin concentration. When the weighted genetic risk score was added to the clinical model, reclassification improved slightly (continuous net reclassification improvement 0.430 [95% confidence interval 0.218, 0.642]; $p = 7.0 \times 10^{-5}$). The weighted genetic risk score was found to be strongly linked to the development of diabetes in the future among women with gestational diabetes (13). Findings of meta-analysis in 2018 showed that low physical activity, sedentary lifestyle, and increased duration of television watching, alcohol consumption, smoking, air pollution, and some medical conditions such as elevated systolic blood pressure, late menarche age, gestational diabetes, metabolic syndrome, preterm birth all present strong evidence for an increased risk of T2DM (7).

According to data collected in the Arabic world, the prevalence of T2DM has increased uncontrollably during the previous two decades, particularly in Gulf Cooperation Countries. Obesity is linked to strong risk factor for T2DM in Arab nation. Other important predictors of T2DM in the area are fast urbanization, unhealthy diet, and a lack of physical activity. T2DM has now surpassed cancer as the fifth biggest cause of mortality in the Arab world, owing to an unchecked upsurge of T2DM in the Arab world (14). El-Kebbi stated in his study that The Middle East and North Africa

region had the highest prevalence of diabetes in the world in 2019, at 12.2%, accompanied by significant morbidity and mortality. Obesity, physical inactivity, urbanization, and poor eating habits, in addition to the genetic predisposition of the local population, have all been linked to the high prevalence of diabetes and prediabetes in the area. These risk factors also result in the onset of type 2 diabetes in children and adolescents and affect the quality of life of these young people. (15).

Results of Saudi review study in 2016 revealed that obesity, physical inactivity, poor dietary habits, smoking, and aging are the leading risk factors for T2DM (16). Results of another Saudi cross-sectional study in 2020 showed that the frequency of T2DM was 34.6% being more prevalent among older age respondents and females and is significantly associated with obesity, high cholesterol and triglyceride levels (17). Findings of another Saudi cross-sectional study in 2018 revealed that high waist-hip ratio, long history of diabetes, living in a remote location, a low household income, a low intake of fruits and vegetables, a low level of physical activity, a lack of knowledge about haemoglobin A1c, and the use of injectable medications were all independent risk factors for inadequate glycemic control among the T2DM patients (18). Well-established literature is present regarding the risk factors and predictors of T2DM however, for the prevention and control of T2DM better implementation of preventive strategies is need of hour and conduction of randomized control trial and their effective outcome can aid in this aspect also will have significant contribution to literature

Conclusion

T2DM is a disease of global concern due to its rapid increase over recent years however the disease can be prevented by intervening on modifiable risk factors early in the disease's development. Studies in literature have revealed modifiable risk factors for T2DM, which could help predict and diagnose diabetes risk before symptoms appear. T2DM risk may be reduced by adopting a healthy lifestyle more awareness campaigns and seminars are needed to educate public regarding prevention. Also, future randomized clinical trials should focus on identifying effective techniques for changing harmful daily habits and dietary patterns that predispose to disease.

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Data that support the findings of this study are embedded within the manuscript.

Authors' contribution:

All authors contributed equally to the drafting, writing, sourcing, article screening and final proofreading of the manuscript.

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