

## REVIEW ARTICLE

# UPSURGE OF DIABETES MELLITUS AMONG SAUDIS: INTERACTION OF GENETICS, ENVIRONMENTAL RISKS AND LACK OF NATIONALIZED GUIDELINES

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## ABSTRACT

The escalating prevalence of Diabetes Mellitus (DM) in Saudi Arabia (SA) is devastating. SA is ranked the second highest country in DM prevalence in the Middle East region and the seventh worldwide. Several factors in SA are strongly correlated with increased blood glucose levels. These include the high ambient temperature, air pollution, decreased walk ability, increased urbanization, consumption of fast-food diet and low vegetables and fruit intake. In addition, the genetic factors, ethnic differences, metabolic risk factors such as obesity and hyperlipidemia have been evidenced to impact the blood glucose levels in Saudis. Consequently, Saudi population or Arabic societies in general might have different levels of Fasting Blood Glucose (FBG) and HbA1C compared to other countries due to the clustering of genetics, ethnicity, hereditary diseases, comorbidities, environmental risk factors, and the changed lifestyle. Unfortunately, lack of large community-sized studies that determine the normal blood glucose levels in the Saudi population based on their genetic, social, and environmental background is noticed. This review aimed to highlight the factors affecting the blood glucose levels in the Saudi population to help the characterization of normal and abnormal levels of blood glucose in this society. The clear understanding of the impact of the different factors on the blood glucose level in Saudis will aid the clinicians toward the proper diagnosis of DM in Saudi patients. In conclusion: the normal and abnormal levels of blood glucose in the Saudi people need to be assessed according to their ethnic, genetic, social, and environmental background. Specific normative guidelines for FBG and HbA1c values in the Saudi population needs to be implemented and utilized in generating a national guideline for DM diagnosis.

**KEY WORDS:** Diabetes mellitus; Glucose; Glycosylated hemoglobin (HbA1c); Environmental temperature; Pollution; genetics; FBG.

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## INTRODUCTION

It is not an overstatement to say that Diabetes Mellitus (DM) and its complications, are becoming the leading causes of death and disabilities internationally.<sup>1,2</sup> The World Health Organization (WHO) predicts that DM will be the seventh leading cause of mortality worldwide in 2030.<sup>1-8</sup> The International Diabetic Federation (IDF) declared that DM affects 537 million persons globally, of which 73 million are in the Middle

East and North Africa (MENA) countries and is expected to reach 135.7 million in 2045.<sup>3</sup> Unfortunately, the incidence of DM has increased tenfold in Saudi Arabia (SA) in the last three decades, reaching 17.7 % of the adult population, and is expected to rise to 24.5 % in 2035.<sup>3,4</sup> This placed SA in the seventh position of the countries with the highest diabetes prevalence worldwide and in the first position among Middle Eastern countries.<sup>5</sup> The increased prevalence of DM in SA is mostly among the young adult population,<sup>3,6</sup> whereas the prevalence of DM in elder population is reported by the IDF to be the highest in MENA at about 16.5% in comparison to 6.5% in Africa.<sup>7</sup> Multiple socioeconomic and environmental factors contribute to the high incidence of DM in MENA, including urbanization, economic expansion, decreased consumption of vegetables and fruits, and sedentary lifestyles.<sup>8</sup> In addition to DM prevalence, SA has a high prevalence of other chronic disorders

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and risk factors related to DM such as hypertension, dyslipidemia, central obesity, and increased e-cigarette smoking.<sup>5,11-13</sup>

The mounting incidence and prevalence of DM in the Saudi community imposes progressive increase in the economic burden of the health care services. The budget for the management of DM was estimated to be 25 billion Riyals in 2014.<sup>14</sup> This was expected to rise to 43 billion if the prediabetic people proceeded at the existing rate and become included in treatment programs.<sup>15</sup> The inflated financial budget of DM management programs is used up directly in the diagnosis, treatment, training programs for health-care professionals, research, and infrastructure for conducting DM-related services. The indirect cost of DM that is not calculated in the current budget results from the interference of the disease state with the productivity of the diabetic patients due to unemployment, absenteeism, disabilities and early mortality. Furthermore, the social impact of the disease on the diabetic patient and their caregiver family members includes physical and psychological suffering.<sup>16</sup>

The coming parts of this review will highlight the immense need to update the prediction measures and diagnosing criteria of DM in the Saudi people and also determining precise cut-off points for normal and abnormal blood glucose levels and HbA1c that are specifically tailored to the Saudi population taking into consideration their particular genetic, environmental, behavioral, and socio-economic background.

#### **Glycosylated hemoglobin (HbA1c) levels in the Saudi patients:**

The glycosylated hemoglobin (HbA1c) test is considered the gold standard biomarker, advocated by WHO for diagnosing DM and monitoring the response to the hypoglycemic treatment.<sup>17,18</sup> The HbA1c test has the advantage of being quantified without the necessity of prefasting. In addition, its levels give an idea about the glycemic control over the past 12 weeks. This makes it the best blood biomarker for the evaluation of the long-term glycemic control in diabetic patients.<sup>18</sup> Additionally, HbA1c is a valuable indicator of blood lipid levels in Type II diabetes mellitus (Type II DM) patients where levels of 6-9% were associated with moderate hyperlipidemia and levels of  $\geq 9\%$  were associated with severe hyperlipidemia. These levels were applicable to both male and female patients.<sup>19</sup> HbA1C levels correlate positively with vasculopathy in a recent meta-analysis study conducted on Type II DM Saudi patients.<sup>20</sup> Approximately, 10% increase in HbA1c was associated with a fourfold increased risk of diabetic ketoacidosis in Saudi patients.<sup>21,22</sup> Also, elevated HbA1c is considered as an independent risk factor for coronary heart disease and strokes in both diabetic and non-diabetic patients.<sup>23</sup> By contrast, the reduction of HbA1c by 1% in diabetic patients was

evidenced to decrease microvascular complications by 25%.<sup>24</sup> A lack of proper adjustment of HbA1c levels is associated with a several fold increase in the risk of development of diabetic cardiovascular, renal, and retinal complications.<sup>25-27</sup>

The American Diabetes Association (ADA) and WHO suggested a cut-off point of HbA1c  $\geq 6.5\%$  as an alternate to fasting blood glucose (FBG) of  $\geq 7.0$  mmol/L for the diagnosis of DM.<sup>28,29</sup> However, this diagnostic cut-off value of HbA1c and its pattern of association with FBG is still a point of controversy in different populations.<sup>30</sup> A cross sectional study on 1491 Korean diabetic patients showed only 31.6% who had FBG test alone ( $\geq 7.0$  mmol/l), 23.5% HbA1c  $\geq 6.5\%$  test alone, while 44.9% who had both the FBG and HbA1C met the criteria.<sup>31</sup> A systemic review evaluating seven different studies revealed HbA1c levels between 5.6% and 6.5 were associated with high risk of development of diabetes.<sup>32</sup> Nevertheless, the normal level of HbA1c in the Saudi population is not well-defined in the current literature. An early study conducted in SA found similar HbA1c level of Saudi diabetic patients to various population such as Swedish, British, and Americans.<sup>33</sup> but a recent retrospective study conducted on 12,785 diabetic male Saudi patients reported that HbA1c levels between 6.0% and 6.5% were observed in diabetic patients with borderline Fasting Blood Glucose (FBG) levels (between 7:0-8:0 mmol/l). The authors concluded that an HbA1c cut-off point of 6.5% is associated with a false negative prediction rate of 3.7% in Type II diabetic patients and recommended the use of both HbA1c and FBG for better detection of prediabetic patients in the Saudi population.<sup>34</sup> Furthermore, a comparative study performed in Zimbabwean African subjects with Saudi and Western populations had found ethnic differences in the value of HbA1c suggesting careful assessment of individual patients.<sup>35</sup> Unfortunately, there is a lack of studies that assess normal blood glucose levels in the Saudi population, and the reference data imported from other countries or suggested by international organizations sometimes does not accurately represent Saudi patients. The nonexistence of a specific cut-off point of HbA1c levels for the Saudi population may lead to an inaccurate definition of abnormal glucose plasma level in Type II diabetic patients and those with prediabetes and may also influence the follow-up of the response of the diabetic patients to the hypoglycemic treatments.

#### **Genetics factors, Consanguinity, and lifestyle impact in DM in Saudi Arabia:**

The genetic and ethnic characteristics of the Saudi population may participate in part to the intense escalation of the prevalence of DM. Glucose absorption was reported to be more rapid in Saudi Arabian subjects in comparison to native African people from Zambia.<sup>36</sup> Metabolic disorders (X-syndrome or

insulin resistance syndrome) as defined by the IFD is clustering of abdominal obesity, hyperglycemia, hypertension, and hypercholesterolemia.<sup>37</sup> Metabolic syndrome varies widely in prevalence between 10-84% globally according to the patient's age, gender, and race of the population.<sup>38</sup> Furthermore, the cut-off points of the criteria defining metabolic disorders may vary according to the ethnic distribution as reported by Saudi Abnormal Glucose Metabolism and Diabetes Impact Study (SAUDI-DM).<sup>11,39</sup> For instance, Al-rubean et al. concluded that the proposed waist circumference cut-off values are a better index than body mass index (BMI) and waist-hip ratio (WHR) for screening and predicting high-risk people for metabolic syndrome in SA.<sup>40</sup>

The rate of consanguineous marriage is as high as 57.7% in SA.<sup>41</sup> This is the highest rate in the world, where 28.4% is first cousin and 14.6% is distant relatives' marriage.<sup>41</sup> This high level of consanguinity is expected to have its influence on polygenic diseases such as DM, especially Type II DM. In addition, it might help to give more details on the genetics of Type II DM and may possibly unravel new subtypes of maturity-onset diabetes in youth.<sup>42</sup> A retrospective study on 210 diabetes relative patients in the central region of SA revealed an odds ratio of 6:2, suggesting a direct relationship with diabetes.<sup>43</sup> However, due to the small size of this study, the confirmation of this assumption will require a larger epidemiological studies.<sup>43</sup> Additionally, changes in lifestyle and eating habits in the last three decades contribute to the extensive increase in the metabolic disorders associated with glucose metabolism such as obesity and hyperlipidemia. The increased consumption of the high-caloric fast-food diet, rich in fats and carbohydrates and poor in vegetables and fruits, and tendency toward sedentary style of life have led to high obesity prevalence. Increased body mass index, obesity, and abnormal blood lipid levels are powerful risk factors for diabetes.<sup>42</sup>

#### **Air pollution and Type II diabetes mellitus:**

The impact of environmental factors on the risk of Type II DM is well-evidenced over the past decade. The Air Quality Index provided by the Saudi National Center of Meteorology reported that the major air pollutants in SA include CO, NO<sub>2</sub>, O<sub>3</sub>, SO<sub>2</sub>, PM<sub>10</sub>, and PM<sub>2.5</sub>.<sup>44-46</sup>

An association between environmental pollution and elevated glucose plasma level has been observed in several studies worldwide. Researchers noticed that living in polluted cities or working in highly polluted working environments such as oil refinery factories, welding fumes, wood factories, and incense burning shops was associated with a prevalence of prediabetes or DM.<sup>47-51</sup> They linked several pollutants such as O<sub>3</sub>, SO<sub>2</sub>, and PM<sub>2.5</sub> to the disturbance of the glucose metabolic pathways and hence to Type II DM. In addition, they found a correlation between the

disturbance of obesity indices and air pollutants.<sup>52</sup>

Recently, we noticed a negative correlation between green space environments and the prevalence of DM and its mortality rates.<sup>53</sup> One of the hypotheses that has been proposed is that green space environments motivate people to participate in physical and social activities which subsequently improve general health.<sup>54-56</sup> Even though the systems that control glucose homeostasis may not be directly affected by air pollution, one hypothesis that has been proposed which links pollution to DM is the increase in oxidative stress due to pollutant particles and hence dysfunction of macrophages and injury of the epithelial layers of the pulmonary system. Consequently, this leads to pulmonary inflammation, systemic inflammation, and insulin resistance.<sup>56-58</sup>

Some researchers linked the exposure to PM<sub>2.5</sub> and NO<sub>2</sub> to oxidative stress, necrotic disruptions, decreased insulin signaling, insulin resistance, and hence DM.<sup>57-59</sup> However, extensive studies are of great value to clarify the mechanism of the impact of air pollution on metabolic disorders.

#### **Climate change and blood glucose levels:**

Climate change is characterized by noticeable shifts in the weather patterns and the surrounding temperature leading to obvious alterations to the living environment. The human activities utilizing fossil fuels since the industrial revolution in the 1800's constitute the leading cause of these climate changes. The ecosystem in SA is specifically susceptible to the consequences of climate change due to the scarce sources of renewable water and the high dependence on fossil fuel exports. The climate in SA is semi-arid to arid desert weather that is hot in the daytime and cold at night. Temperature levels range from 35°C to 45°C throughout the country during the summer months from June to August. Unfortunately, annual rainfall levels have been decreasing severely across most of the country year after year.<sup>60,61</sup>

Global warming associated with elevated atmospheric temperature is an emerging problem that challenges living creatures worldwide and is expected to negatively influence human health.<sup>60,61</sup> SA is experiencing hot atmospheric temperatures that can reach up to 46°C outdoors in Riyadh City in the summer months. Furthermore, SA shows a yearly increase in the maximum ambient temperature by 0.8°C per decade in the period between 1978 and 2009 that is expected to rise to 1.6°C per decade by 2044.<sup>62</sup> Climate differences have been reported to affect HbA<sub>1c</sub> levels in literature.<sup>63-66</sup> In the United States of America, a positive correlation was found between DM and the increase in ambient temperature.<sup>66</sup> One of the reasons for high glucose level that has been mentioned in the literature is the lack of physical activities in the hot weather.<sup>67</sup> Also, insulin resistance was found to be negatively associated

with exposure to bright sunlight.<sup>68</sup> Alghamdi et al. reported an increase in HbA1c by 0.007% for each 1°C rise in the atmospheric temperature in a cross meta-analytic study on 168 thousand patients records in SA. The patients were at greater risk of increased HbA1C levels to  $\geq 7.0$  mmol/l in the moderate and high atmospheric months of the year in comparison to the low temperature season. Several reasons were suggested including physical inactivity, vitamin D deficiency due to avoidance of exposure to the sunlight in the hot weather, and dehydration.<sup>69</sup> In addition, changes in the thermogenic activity of the brown adipose tissue (BAT) that functions in the cold weather through glycogenolysis and increased insulin sensitivity was suggested.<sup>70</sup> However, the actual mechanism that links increased ambient temperature and elevated blood glucose level needs to be clarified by well-designed studies. Therefore, some researchers suggested combination of multiple tests in order to have a proper diagnosis of DM instead of relying on HbA1c alone in Arab countries which might give false negative results.<sup>71</sup>

#### **Vitamin D deficiency and Type II diabetes mellitus:**

Vitamin D deficiency affects about one billion subjects worldwide.<sup>72</sup> The impact of Vitamin D deficiency in various body systems gained increased interest in several diseases such as DM.<sup>73</sup> Insulin secretion by the pancreatic beta cells and the sensitivity of insulin receptors are equally considered to be calcium-dependent processes that are directly influenced by the role of vitamin D and its receptors on calcium homeostasis.<sup>74,75</sup> Furthermore, Vitamin D plays an important role as an anti-inflammatory and immunomodulatory factor which limits peripheral insulin resistance.<sup>76,77</sup> Low serum levels of 1,25-dihydroxyvitamin D [1,25(OH)2D] [ $< 50$  nmol/L] are primarily common in Type II diabetic patients.<sup>78</sup> Multiple cross-sectional studies revealed a negative correlation between vitamin D concentration in the blood and HbA1c levels in normal and diabetic adults.<sup>79-84</sup> Longitudinal studies also revealed that low vitamin D blood concentration is a predictor for Type II DM incidence.<sup>85,86</sup>

Despite the plenty of sunlight available in SA throughout the year, the hot climate and the cultural factors limit outdoor activities during the daytime. Therefore, the risk of lower vitamin D levels is considerably high in Saudi population. Recent studies reported that around 95.4 % of the young school students (6-19 years) and 89.1% of the older adults (20-62 years) were found to have low vitamin D blood concentrations.<sup>87</sup> Other studies showed that decreased vitamin D blood concentrations are correlated with the increased incidence of Type II DM among the population in the southern, eastern, and western regions of SA.<sup>88-90</sup> Further clarification to whether vitamin D deficiency and insulin resistance are associated causally, or whether they constitute two autonomous features of diabetic patients is still needed.

## **CONCLUSION AND RECOMMENDATIONS**

Different factors affect the plasma glucose and HbA1c levels in the Saudi population, including genetic factors, ambient temperature, air pollution, social and environmental factors. The standards for normal and abnormal glucose levels in SA need to be assessed according to these facts. In addition, specific normative diagnostic criteria need to be implemented as a measure that could limit the alarming increase in the prevalence of metabolic disorders, especially Type II DM.

## **REFERENCES**

1. Al-Khlaiwi T, Alsabih AO, Khan A, Habib SH, Sultan M, Habib SS. Reduced pulmonary functions and respiratory muscle strength in Type 2 diabetes mellitus and its association with glycemic control. *Eur Rev Med Pharmacol Sci.* 2021;25(23):7363-7368. [https://doi.org/10.26355/eurev\\_202112\\_27430](https://doi.org/10.26355/eurev_202112_27430)
2. Habib SS, Al-Regaiey KA, Al-Khlaiwi T, Habib SM, Bashir S, Al-Hussain F, et al. Serum inducible and endothelial nitric oxide synthase in coronary artery disease patients with Type 2 Diabetes mellitus. *Eur Rev Med Pharmacol Sci.* 2022;26(10):3695-3702. [https://doi.org/10.26355/eurev\\_202205\\_28865](https://doi.org/10.26355/eurev_202205_28865)
3. International Diabetes Federation . Middle east & north Africa region (MENA) country report-Saudi Arabia. 2022. Available at: <https://idf.org/our-network/regions-members/middle-east-and-north-africa/members/46-saudi-arabia.html>
4. Al Dawish MA, Robert AA, Braham R, Al Hayek AA, Al Saeed A, Ahmed RA, et al. Diabetes Mellitus in Saudi Arabia: A Review of the Recent Literature. *Curr Diabetes Rev.* 2016;12(4):359-368. <https://doi.org/10.2174/1573399811666150724095130>
5. Atlas, Diabetes. "International diabetes federation." IDF Diabetes Atlas, 7th edition. Brussels, Belgium: International Diabetes Federation 33 (2015).
6. El Bcheraoui C, Basulaiman M, Tuffaha M, Daoud F, Robinson M, Jaber S et al. Status of the diabetes epidemic in the Kingdom of Saudi Arabia, 2013. *Int J Public Health.* 2014;59(6):1011-21. <https://doi.org/10.1007/s00038-014-0612-4>
7. Saeedi P, Salpea P, Karuranga S, Petersohn I, Malanda B, Gregg EW et al. Mortality attributable to diabetes in 20-79 years old adults, 2019 estimates: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2020;162:108086. <https://doi.org/10.1016/j.diabres.2020.108086>
8. Alotaibi A, Perry L, Gholizadeh L, Al-Ganmi A. Incidence and prevalence rates of diabetes mellitus in Saudi Arabia: An overview. *J Epidemiol Glob Health.* 2017;7(4):211-218. <https://doi.org/10.1016/j.jegh.2017.10.001>
9. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, et al. IDF Diabetes Atlas

- Committee. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract.* 2019;157:107843. <https://doi.org/10.1016/j.diabres.2019.107843>
10. Grundy SM. Metabolic syndrome pandemic. *Arterioscler Thromb Vasc Biol.* 2008;28(4):629-636. <https://doi.org/10.1161/ATVBAHA.107.151092>
  11. Bahijri SM, Al Raddadi RM. The importance of local criteria in the diagnosis of metabolic syndrome in Saudi Arabia. *Ther Adv Endocrinol Metab.* 2013;4(2):51-9. <https://doi.org/10.1177/2042018813483165>
  12. Alzahrani AM, Karawagh AM, Alshahrani FM, Naser TA, Ahmed AA, Alsharaf EH. Prevalence and predictors of metabolic syndrome among healthy Saudi Adults. *The British Journal of Diabetes & Vascular Disease.* 2012;12(2):78-80. <https://doi.org/10.1177/1474651412441953>
  13. BinDhim NF, Althumiri NA, Basyouni MH. Exploring the impact of COVID-19 response on population health in Saudi Arabia: results from the "Sharik" health indicators surveillance system during 2020. *Int J Environ Res Public Health.* 2021;18(10):5291. <https://doi.org/10.3390/ijerph18105291>
  14. Dawish M, Robert A. Diabetes Mellitus in Saudi Arabia. In: Laher, I. (eds) *Handbook of Healthcare in the Arab World.* Springer, Cham.2021. [https://doi.org/10.1007/978-3-030-36811-1\\_45](https://doi.org/10.1007/978-3-030-36811-1_45)
  15. AlMazroa M. Cost of diabetes in Saudi Arabia. In proceedings. 2018 ;4(1):e10566. <https://doi.org/10.2196/10566>
  16. Alhowaish AK. Economic costs of diabetes in Saudi Arabia. *J Family Community Med.* 2013;20(1):1-7. <https://doi.org/10.4103/2230-8229.108174>
  17. Treviño G. Consensus statement on the Worldwide Standardization of the Hemoglobin A1C Measurement: The American Diabetes Association, European Association for the Study of Diabetes, International Federation of Clinical Chemistry and Laboratory Medicine, and the International Diabetes Federation: response to the Consensus Committee. *Diabetes Care.* 2007;30(12):e141. <https://doi.org/10.2337/dc07-1752>
  18. Use of Glycated Haemoglobin (HbA1c) in the Diagnosis of Diabetes Mellitus: Abbreviated Report of a WHO Consultation. Geneva: World Health Organization. 2011. PMID: 26158184.
  19. Khan HA, Sobki SH, Khan SA. Association between glycaemic control and serum lipids profile in type 2 diabetic patients: HbA1c predicts dyslipidaemia. *Clin Exp Med.* 2007;7(1):24-9. <https://doi.org/10.1007/s10238-007-0121-3>
  20. Alodhayani AA, Almansour AR, Alotaibi JJ, Alghamdi GE, Alageel M, Binabbad R, et al. Relationship Between Hba1c and Complete Blood Count Parameters In Adult Patients With Type 2 Diabetes In Saudi Arabia. *International Journal of Advanced Research* 2022;10(10):900-6. <https://doi.org/10.21474/IJAR01/15559>
  21. Al Hayek AA, Robert AA, Al-Shaikh R, Alhojele M, Aloufi S, Sabri D et all. Factors associated with the presence of diabetic ketoacidosis: A retrospective analysis of patients with type 1 diabetes in Saudi Arabia. *Diabetes Metab Syndr.* 2020;14(6):2117-2122. <https://doi.org/10.1016/j.dsx.2020.11.002>
  22. Alahmadi S, Ragaban A, Alblowi S, Aljumail E, Zarif H. Diabetic ketoacidosis; annual incidence and precipitating factors at King Abdulaziz Medical City, Jeddah. *The Egyptian Journal of Hospital Medicine.* 2018;72(7):4831-4835. <https://doi.org/10.21608/ejhm.2018.10145>
  23. Selvin E, Coresh J, Shahar E, Zhang L, Steffes M, Sharrett AR. Glycaemia (haemoglobin A1c) and incident ischaemic stroke: the Atherosclerosis Risk in Communities (ARIC) Study. *Lancet Neurol.* 2005;4(12):821-6. [https://doi.org/10.1016/S1474-4422\(05\)70227-1](https://doi.org/10.1016/S1474-4422(05)70227-1)
  24. International diabetes Federation (2017) *IDF Diabetes Atlas Seventh Edition* 2017.
  25. Kibirige D, Akabwai GP, Kampiire L, Kiggundu DS, Lumu W. Frequency and predictors of suboptimal glycemic control in an African diabetic population. *Int J Gen Med.* 2017;20;10:33-38. <https://doi.org/10.2147/IJGM.S124548>
  26. Alzaheb RA, Altemani AH. The prevalence and determinants of poor glycemic control among adults with type 2 diabetes mellitus in Saudi Arabia. *Diabetes Metab Syndr Obes.* 2018;11:15-21. <https://doi.org/10.2147/DMSO.S156214>
  27. Almutairi JS, Almigbal TH, Alruhaim HY, Mujammami MH, AlMogbel TA, Alshahrani AM et all. Self-awareness of HbA1c and its association with glycemic control among patients with type 2 diabetes: A multicenter study. *Saudi Med J.* 2022;43(3):291-300. <https://doi.org/10.15537/smj.2022.43.3.20210536>
  28. World Health Organization. *Diabetes Mellitus: Report of a WHO Study Group* [meeting held in Geneva from 11 to 16 February 1985]. World Health Organization, 1985. Available at: <https://apps.who.int/iris/handle/10665/39592>
  29. American Diabetes Association Professional Practice Committee. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2022. *Diabetes Care.* 2022;45:S17-S38. <https://doi.org/10.2337/dc22-S002>
  30. Jørgensen ME, Bjerregaard P, Borch-Johnsen K, Witte D. New diagnostic criteria for diabetes: is the change from glucose to HbA1c possible in all populations? *J Clin Endocrinol Metab.* 2010;95(11):E333-6. <https://doi.org/10.1210/jc.2010-0710>
  31. Kim CH, Kim HK, Bae SJ, Park JY, Lee KU. Discordance between fasting glucose-based and hemoglobin A1c-based diagnosis of diabetes mellitus in Koreans. *Diabetes Res Clin Pract.* 2011;91(1):e8-e10. <https://doi.org/10.1016/j.diabres.2010.09.025>
  32. Zhang X, Gregg EW, Williamson DF, Barker LE, Thomas W, Bullard KM, et all. A1C level and

- future risk of diabetes: a systematic review. *Diabetes Care*. 2010;33(7):1665-73. <https://doi.org/10.2337/dc09-1939>
33. Alayash AI, Dafallah A, Al-Husayni H, Al-Ali AK, Al-Qourain A, Ramzan Saba M et al. Determination of glycosylated haemoglobin in normal, newborn and diabetic Saudi Arabs. *Ann Clin Biochem*. 1987;24 (3):279-82. <https://doi.org/10.1177/000456328702400307>
  34. Khan HA, Ola MS, Alhomida AS, Sobki SH, Khan SA. Evaluation of HbA1c criteria for diagnosis of diabetes mellitus: a retrospective study of 12785 type 2 Saudi male patients. *Endocr Res*. 2014;39(2):61-5. <https://doi.org/10.3109/07435800.2013.828740>
  35. Gomo ZA. The determination of glucose and glycosylated haemoglobin in a non-diabetic Zimbabwean African population. *Ann Clin Biochem*. 1985;22 (4):362-5. <https://doi.org/10.1177/000456328502200405>
  36. Cook GC. Rapid glucose absorption in Arabs in Saudi Arabia compared with that in Africans in Zambia. *Br Med J*. 1976;1(6011):688-9. <https://doi.org/10.1136/bmj.1.6011.688>
  37. Anokute CC. Suspected synergism between consanguinity and familial aggregation in type 2 diabetes mellitus in Saudi Arabia. *J R Soc Health*. 1992;112(4):167-9. <https://doi.org/10.1177/146642409211200403>
  38. Kaur J. A comprehensive review on metabolic syndrome. *Cardiol Res Pract*. 2014;943162. doi: 10.1155/2014/943162. Epub 2014 Mar 11. Retraction in: *Cardiol Res Pract*. 2019 Jan 31; 2019:4301528. PMID: 24711954; PMCID: PMC3966331.
  39. Al-Rubeaan K, Al-Manaa H, Khoja T, Ahmad N, Al-Sharqawi A, Siddiqui K et al. The Saudi Abnormal Glucose Metabolism and Diabetes Impact Study (SAUDI-DM). *Ann Saudi Med*. 2014;34(6):465-75. <https://doi.org/10.5144/0256-4947.2014.465>
  40. Al-Rubeaan K, Youssef AM, AlFarsi Y, Al-Sharqawi AH, Bawazeer N, AlOtaibi MT et al. Anthropometric cutoff values for predicting metabolic syndrome in a Saudi community: from the SAUDI-DM study. *Ann Saudi Med*. 2017;37(1):21-30. <https://doi.org/10.5144/0256-4947.2017.21>
  41. El-Hazmi MA, Al-Swailem AR, Warsy AS, Al-Swailem AM, Sulaimani R, Al-Meshari AA. Consanguinity among the Saudi Arabian population. *J Med Genet*. 1995;32(8):623-6. <https://doi.org/10.1136/jmg.32.8.623>
  42. Elhadd TA, Al-Amoudi AA, Alzahrani AS. Epidemiology, clinical and complications profile of diabetes in Saudi Arabia: a review. *Ann Saudi Med*. 2007;27(4):241-50. <https://doi.org/10.5144/0256-4947.2007.241>
  43. Anokute CC. Suspected synergism between consanguinity and familial aggregation in type 2 diabetes mellitus in Saudi Arabia. *J R Soc Health*. 1992;112(4):167-9. <https://doi.org/10.1177/146642409211200403>
  44. Kaur J. A comprehensive review on metabolic syndrome. *Cardiol Res Pract*. 2014;943162. doi: 10.1155/2014/943162. Epub 2014 Mar 11. Retraction in: *Cardiol Res Pract*. 2019 Jan 31; 2019:4301528. PMID: 24711954; PMCID: PMC3966331.
  45. Al-Rubeaan K, Al-Manaa H, Khoja T, Ahmad N, Al-Sharqawi A, Siddiqui K et al. The Saudi Abnormal Glucose Metabolism and Diabetes Impact Study (SAUDI-DM). *Ann Saudi Med*. 2014;34(6):465-75. <https://doi.org/10.5144/0256-4947.2014.465>
  46. Al-Rubeaan K, Youssef AM, AlFarsi Y, Al-Sharqawi AH, Bawazeer N, AlOtaibi MT et al. Anthropometric cutoff values for predicting metabolic syndrome in a Saudi community: from the SAUDI-DM study. *Ann Saudi Med*. 2017;37(1):21-30. <https://doi.org/10.5144/0256-4947.2017.21>
  47. Environmental Protection in KSA. Available at: <https://www.my.gov.sa>
  48. Dendup T, Feng X, Clingan S, Astell-Burt T. Environmental Risk Factors for Developing Type 2 Diabetes Mellitus: A Systematic Review. *Int J Environ Res Public Health*. 2018;15(1):78. <https://doi.org/10.3390/ijerph15010078>
  49. Climate change knowledge portal. Available at: <https://climateknowledgeportal.worldbank.org/country/saudi-arabia/vulnerability> Accessed at 10/2/2023
  50. Al-khlaiwi TM, Meo SA, Habib SS, Meo IMU, Alqhtani MS. Incense Burning Indoor Pollution: Impact on the prevalence of prediabetes and Type-2 Diabetes Mellitus. *Pak J Med Sci*. 2022;38(7):1852-1856. <https://doi.org/10.12669/pjms.38.7.6189>
  51. Meo SA, Al-Khlaiwi T, Abukhalaf AA, Alomar AA, Alessa OM, Almutairi FJ, et al. The Nexus between Workplace Exposure for Wood, Welding, Motor Mechanic, and Oil Refinery Workers and the Prevalence of Prediabetes and Type 2 Diabetes Mellitus. *Int J Environ Res Public Health*. 2020;17(11):3992. <https://doi.org/10.3390/ijerph17113992>
  52. Wang Y, Cao R, Xu Z, Jin J, Wang J, Yang T et al. Long-term exposure to ozone and diabetes incidence: A longitudinal cohort study in China. *Sci Total Environ*. 2021;151634. <https://doi.org/10.1016/j.scitotenv.2021.151634>
  53. Li YL, Chuang TW, Chang PY, Lin LY, Su CT, Chien LN, et al. Long-term exposure to ozone and sulfur dioxide increases the incidence of type 2 diabetes mellitus among the adult population aged 30 to 50. *Environ Res*. 2021;194:110624. <https://doi.org/10.1016/j.envres.2020.110624>
  54. Lee M, Ohde S. PM2.5, and Diabetes in the Japanese Population. *Int J Environ Res Public Health*. 2021;18(12):6653. <https://doi.org/10.3390/ijerph18126653>
  55. Kang N, Chen G, Tu R, Liao W, Liu X, Dong X et al. Adverse associations of different obesity measures and the interactions with long-term exposure to air pollutants with prevalent type

- 2 diabetes mellitus: The Henan Rural Cohort study. *Environ Res.* 2022;207:112640. <https://doi.org/10.1016/j.envres.2021.112640>
56. Meo SA, Al-Khlaiwi T, Aqil M. Impact of the residential green space environment on the prevalence and mortality of Type 2 diabetes mellitus. *Eur Rev Med Pharmacol Sci.* 2022;26(10):3599-3606. doi: 10.26355/eurrev\_202205\_28856. PMID: 35647842.
  57. Reynolds W, C.F. Drury C, Yang X, Tan C. Optimal soil physical quality inferred through structural regression and parameter interactions. *Geoderma*, Volume 146, Issues 3-4, 2008, Pages 466-474. <https://doi.org/10.1016/j.geoderma.2008.06.017>
  58. Lee AC, Jordan HC, Horsley J. Value of urban green spaces in promoting healthy living and wellbeing: prospects for planning. *Risk Manag Healthc Policy.* 2015;8:131-7. <https://doi.org/10.2147/RMHP.S61654>
  59. Squillacioti G, Carsin AE, Bellisario V, Bono R, Garcia-Aymerich J. Multisite greenness exposure and oxidative stress in children. The potential mediating role of physical activity. *Environ Res.* 2022;209:112857. <https://doi.org/10.1016/j.envres.2022.112857>
  60. Liu F, Chen G, Huo W, Wang C, Liu S, Li N et al. Associations between long-term exposure to ambient air pollution and risk of type 2 diabetes mellitus: A systematic review and meta-analysis. *Environ Pollut.* 2019;252(Pt B):1235-1245. <https://doi.org/10.1016/j.envpol.2019.06.033>
  61. Fabricio G, Malta A, Chango A, De Freitas Mathias PC. Environmental Contaminants and Pancreatic Beta-Cells. *J Clin Res Pediatr Endocrinol.* 2016;8(3):257-63. <https://doi.org/10.4274/jcrpe.2812>
  62. Yitshak Sade M, Shi L, Colicino E, Amini H, Schwartz JD, Di Q et al. Long-term air pollution exposure and diabetes risk in American older adults: A national secondary data-based cohort study. *Environ Pollut.* 2023;320:121056. <https://doi.org/10.1016/j.envpol.2023.121056>
  63. Guo Y, Gasparrini A, Armstrong BG, Tawatsupa B, Tobias A, Lavigne E et al. Heat Wave and Mortality: A Multicountry, Multicommunity Study. *Environ Health Perspect.* 2017;125(8):087006. <https://doi.org/10.1289/EHP1026>
  64. Gasparrini A, Guo Y, Hashizume M, Lavigne E, Zanobetti A, Schwartz J et al. Mortality risk attributable to high and low ambient temperature: a multicountry observational study. *Lancet.* 2015;386(9991):369-75. [https://doi.org/10.1016/S0140-6736\(14\)62114-0](https://doi.org/10.1016/S0140-6736(14)62114-0)
  65. Tarawneh, Q.Y.; Chowdhury, S. Trends of Climate Change in Saudi Arabia: Implications on Water Resources. *Climate* 2018; 6,8. <https://doi.org/10.3390/cli6010008>
  66. Raphael A, Friger M, Biderman A. Seasonal variations in HbA1c among type 2 diabetes patients on a semi-arid climate between the years 2005-2015. *Prim Care Diabetes.* 2021;15(3):502-506. <https://doi.org/10.1016/j.pcd.2020.11.013>
  67. Moses RG, Wong VC, Lambert K, Morris GJ, San Gil F. Seasonal Changes in the Prevalence of Gestational Diabetes Mellitus. *Diabetes Care.* 2016;39(7):1218-21. <https://doi.org/10.2337/dc16-0451>
  68. Takebayashi K, Yamauchi M, Hara K, Tsuchiya T, Hashimoto K. Seasonal variations and the influence of COVID-19 pandemic on hemoglobin A1c, glycoalbumin, and low-density lipoprotein cholesterol. *Diabetol Int.* 2022;13(4):599-605. <https://doi.org/10.1007/s13340-022-00574-1>
  69. Speakman JR, Heidari-Bakavoli S. Type 2 diabetes, but not obesity, prevalence is positively associated with ambient temperature. *Sci Rep.* 2016;6:30409. <https://doi.org/10.1038/srep30409>
  70. Chaabane S, Chaabna K, Doraiswamy S, Mamtani R, Cheema S. Barriers and Facilitators Associated with Physical Activity in the Middle East and North Africa Region: A Systematic Overview. *Int J Environ Res Public Health.* 2021;18(4):1647. <https://doi.org/10.3390/ijerph18041647>
  71. Noordam R, Ramkisoensing A, Loh NY, Neville MJ, Rosendaal FR, Willems van Dijk Km et al. Associations of Outdoor Temperature, Bright Sunlight, and Cardiometabolic Traits in Two European Population-Based Cohorts. *J Clin Endocrinol Metab.* 2019;104(7):2903-2910. <https://doi.org/10.1210/jc.2018-02532>
  72. Alghamdi AS, Alqadi A, Alghamdi F, Jenkins RO, Haris PI. Higher ambient temperature is associated with worsening of HbA1c levels in a Saudi population. *Int J Clin Exp Pathol.* 2021;14(8):881-891. PMID: 34527131; PMCID: PMC8414425.
  73. Carpentier AC, Blondin DP, Virtanen KA, Richard D, Haman F, Turcotte ÉE. Brown Adipose Tissue Energy Metabolism in Humans. *Front Endocrinol (Lausanne).* 2018;9:447. <https://doi.org/10.3389/fendo.2018.00447>
  74. Pinelli NR, Jantz AS, Martin ET, Jaber LA. Sensitivity and specificity of glycated hemoglobin as a diagnostic test for diabetes and prediabetes in Arabs. *J Clin Endocrinol Metab.* 2011;96(10):E1680-3. <https://doi.org/10.1210/jc.2011-1148>
  75. Chowdhury R, Kunutsor S, Vitezova A, Oliver-Williams C, Chowdhury S, Kieffe-de-Jong JC, et al. Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies. *BMJ.* 2014;348:g1903. <https://doi.org/10.1136/bmj.g1903>
  76. Bikle D. Nonclassic actions of vitamin D. *J Clin Endocrinol Metab.* 2009;94(1):26-34. <https://doi.org/10.1210/jc.2008-1454>
  77. Al-Shoumer KA, Al-Essa TM. Is there a relationship between vitamin D with insulin resistance and diabetes mellitus? *World J Diabetes.* 2015;6(8):1057-64. <https://doi.org/10.4239/wjd.v6.i8.1057>
  78. Bland R, Markovic D, Hills CE, Hughes SV, Chan SL, Squires PE et al. Expression of 25-hydroxyvitamin D3-1alpha-hydroxylase in pancreatic islets. *J Steroid Biochem Mol Biol.* 2004;89-90(1-5):121-5. <https://doi.org/10.1016/j.jsbmb.2004.03.115>

79. Hewison M. An update on vitamin D and human immunity. *Clin Endocrinol (Oxf)*. 2012;76(3):315-25. <https://doi.org/10.1111/j.1365-2265.2011.04261.x>
80. Chagas CE, Borges MC, Martini LA, Rogero MM. Focus on vitamin D, inflammation and type 2 diabetes. *Nutrients*. 2012;4(1):52-67. <https://doi.org/10.3390/nu4010052>
81. Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc*. 2006;81(3):353-73. <https://doi.org/10.4065/81.3.353>
82. Manickam B, Neagu V, Kukreja SC, Barengolts E. Relationship between glycated hemoglobin and circulating 25-hydroxyvitamin D concentration in African American and Caucasian American men. *Endocr Pract*. 2013;19(1):73-80. <https://doi.org/10.4158/EP12168.OR>
83. Dalgård C, Petersen MS, Weihe P, Grandjean P. Vitamin D status in relation to glucose metabolism and type 2 diabetes in septuagenarians. *Diabetes Care*. 2011;34(6):1284-8. <https://doi.org/10.2337/dc10-2084>
84. Carrillo-Vega MF, García-Peña C, Gutiérrez-Robledo LM, Pérez-Zepeda MU. Vitamin D deficiency in older adults and its associated factors: a cross-sectional analysis of the Mexican Health and Aging Study. *Arch Osteoporos*. 2017;12(1):8. <https://doi.org/10.1007/s11657-016-0297-9>
85. Kositsawat J, Freeman VL, Gerber BS, Geraci S. Association of A1C levels with vitamin D status in U.S. adults: data from the National Health and Nutrition Examination Survey. *Diabetes Care*. 2010;33(6):1236-8. <https://doi.org/10.2337/dc09-2150>
86. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. *J Clin Endocrinol Metab*. 2007;92(6):2017-29. <https://doi.org/10.1210/jc.2007-0298>
87. Mitri J, Muraru MD, Pittas AG. Vitamin D and type 2 diabetes: a systematic review. *Eur J Clin Nutr*. 2011;65(9):1005-15. <https://doi.org/10.1038/ejcn.2011.118>
88. Deleskog A, Hilding A, Brismar K, Hamsten A, Efendic S, Östenson CG. Low serum 25-hydroxyvitamin D level predicts progression to type 2 diabetes in individuals with prediabetes but not with normal glucose tolerance. *Diabetologia*. 2012;55(6):1668-78. <https://doi.org/10.1007/s00125-012-2529-x>
89. Grimnes G, Emaus N, Joakimsen RM, Figenschau Y, Jenssen T, Njølstad I et al. Baseline serum 25-hydroxyvitamin D concentrations in the Tromsø Study 1994-95 and risk of developing type 2 diabetes mellitus during 11 years of follow-up. *Diabet Med*. 2010;27(10):1107-15. <https://doi.org/10.1111/j.1464-5491.2010.03092.x>
90. Zoppini G, Galletti A, Targher G, Brangani C, Pichiri I, Negri C et al. Glycated haemoglobin is inversely related to serum vitamin D levels in type 2 diabetic patients. *PLoS One*. 2013;8(12):e82733. <https://doi.org/10.1371/journal.pone.0082733>

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**AUTHORS' CONTRIBUTION**

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	TA, AK
Acquisition, Analysis or Interpretation of Data:	TA, AK
Manuscript Writing & Approval:	TA, AK

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.



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