WHO EMRO | Obesity-linked diabetes in the Arab world: a review

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Review

B. Abuyassin[1] and I. Laher[1]

مراجعة : السكري المرتبط بالسمنة في العالم العربي

بشر حسن أبو ياسين، إسماعيل لاهر

: إن العالم العربي يشهد وباء سمنة وسكري من النمط 2. إن هذا الاستعراض يلخصالخلاصة
العوامل المرضية الرئيسية التي تربط السمنة بالسكري، مع التركيز على البيانات
الوبائية الحالية المتعلقة بمرضى السكري البدينين في العالم العربي، وعلى مسببات
المرض، وعلى المحدِّدات الوراثية للسكري والسمنة . إن هناك بيانات مقلقة تتعلق
بالانتشار المتزايد للسمنة وللسكري من النمط 2 لدى الأطفال العرب . ودراسات التنسخ
تحدد عدة متغيرات جينية لدى العرب المصابين بالسكري المرتبط بالسمنة . فمتغيرات جين
بالسمنة ترتبط - المثال سبيل على - (مفرد نوكليوتيد في rs266729 أشكال تعدد) ADIPOQ
والسكري في مختلف البلدان العربية . إن هناك ثغرات في معلوماتنا عن السكري والسمنة لدى
الشعوب العربية فيما يتعلق بالمحددات العرقية الخاصة بتشخيص السكري ومعالجته . إن
إجراء المزيد من الدراسات عن روابط على نطاق المجين لدى الفئات السكانية العربية
المصابة بالسمنة والسكري يمكن أن يضيف إلى فهمنا للفيزيولوجيا المرضية لهذا المرض
وللوقاية منه ولعكس مساره الحالي .

ABSTRACT The Arab world is experiencing an epidemic of obesity and type 2 diabetes mellitus. This review summarizes the major pathological factors linking obesity to diabetes, focussing on current epidemiological data related to obese diabetic patients in the Arab world, the etiology of the disease and the genetic determinants of diabetes and obesity. There are alarming data related to the rising prevalence of obesity and type 2 diabetes mellitus in children of Arab ethnicity. Replication studies identify several genetic variants in Arabs with obesity-linked diabetes. For example, variants of the ADIPOQ gene (the rs266729 single-nucleotide polymorphism) are associated with obesity and diabetes in various Arab countries. Gaps exist in our information about diabetes and obesity in Arabpopulations in relation to ethnic-specific cut-off points for diagnosis and treatment of diabetes. Further genome-wide association studies in obese and diabetic Arab populations could add to our understanding of the pathophysiology, prevention and reversal of this disease.

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Diabète lié à l'obésité dans le monde arabe : analyse

RÉSUMÉ Le monde arabe connait une épidémie d'obésité et de diabète de type 2. La présente analyse récapitule les facteurs pathologiques majeurs liant l'obésité au diabète, en se concentrant sur les données épidémiologiques actuelles relatives aux patients diabétiques obèses dans le monde arabe, l'étiologie de la maladie et les déterminants génétiques du diabète et de l'obésité. Les données relatives à l'augmentation de la prévalence de l'obésité et du diabète de type 2 chez les enfants appartenant à un groupe ethnique arabe sont alarmantes. Des études similaires ont identifié plusieurs variantes génétiques chez les Arabes atteints de diabète lié à l'obésité. Par exemple, des variantes du gène ADIPOQ (le polymorphisme du nucléotide simple rs266729) sont associées à une obésité et un diabète dans plusieurs pays arabes. Des lacunes existent dans nos informations sur le diabète et l'obésité dans les populations arabes concernant les seuils propres aux ethnies pour le diagnostic et le traitement du diabète. Des études d'association pangénomique supplémentaires dans des populations arabes diabétiques et obèses pourraient accroître notre compréhension de la physiopathologie et de la prévention et permettraient de faire reculer la maladie.

[1]Department of Pharmacology and Therapeutics, Faculty of Medicine, Vancouver, British Columbia, Canada (Correspondence to I. Laher: ilaher@mail.ubc.ca).
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Introduction

The population of Arab countries comprise nearly 370 million people from 22 different countries living in an area of 14 million km2 and sharing a common language. Recent statistics indicate that nearly 50% of the total Arab population are less than 25 years of age. A major health issue in the Arab world is the rising prevalence of uncontrolled weight gain. This is reflected in increases in the prevalence of several diseases, particularly type 2 diabetes mellitus (T2DM), the prevalence of which has also increased dramatically during the last 2 decades. T2DM has become a source of suffering to both patients and their caregivers. In addition, it presents a great challenge to Arab governments due to the large economic burden of diabetes in terms of cost of treatment, management of complications, disability and loss of productivity (1–5).

Obesity constitutes a large component of the pathogenesis of T2DM through various mechanisms. Obese diabetic patients have a significantly higher risk of microvascular complications and greater mortality (6,7). In addition, obesity worsens the prognosis of T2DM (8). This review summarizes the major pathological factors linking obesity to diabetes, focussing on current epidemiological data related to obese diabetic patients in the Arab world and the etiology of the disease. Finally, we will address some of the research needed to reach a better understanding of the disease that could inform efforts to control obesity-linked T2DM in Arab populations.

Search methodology

We undertook a search of the medical literature using the PubMed, Embase and Ovid databases for articles published in English language between 1980 and 2014, and included the following keywords: diabetes, obesity, Arab world, epidemiology, etiology and genetics, or their corresponding MeSH term synonyms. A total of 6055 papers were identified and screened by title and/or abstract. To ensure that we included the highest number of epidemiological studies from each country, we did not set any limitations on the study design in our exclusion criteria. However, animal or genetic studies, studies not relevant to T2DM or obesity, studies on the complications of diabetes or the effects of treatment, and non-primary data such as review articles or adherence studies were excluded (Figure 1). A total of 122 studies were considered for the article and were reviewed in full. Among these, 41 studies were excluded because the samples were not representative. Table 1 lists the Arab countries from which studies reporting the prevalence of obesity-linked type 2 diabetes mellitus were identified and analysed for this review. In addition, we included 4 studies concerning Arab immigrants in different countries not listed in Table 1 .

Pathological mechanisms

An increased body mass index (BMI) above the normal range (18.5–24.9 kg/m2) is associated with a greater risk of T2DM. In fact 90% of T2DM is attributed to excess weight (9). Several studies have found that the risk of diabetes increased by > 20-fold for females and 10-fold for males when BMI is between 30–35 kg/m2 (10,11). Several biological factors can influence insulin sensitivity; for example, pregnancy and ageing decrease sensitivity to insulin, while physical activity increases it. Obesity and insulin resistance leads to T2DM, particularly when the pancreas is unable to compensate for reduced insulin sensitivity (12). This usually occurs with obese patients, in whom certain products of adipose tissue are increased, including non-esterified fatty acids (NEFA), glycerol and pro-inflammatory cytokines.

Lipotoxicity

Lipotoxicity is central to our understanding of the role of excessive fat deposition in promoting insulin resistance, particularly in central obesity, which is mainly attributed to the accumulation of intra-abdominal (visceral) fat (13). Storage of triglycerides is promoted by persistent excessive caloric intake, leading to a state of a positive energy balance. Triglycerides increase the proportion of adipocytes that are hypertrophied, becoming more resistant to the antilipolytic effects of insulin, resulting in the release of higher amounts of fatty acids into the circulation.

Non-esterified fatty acids

Another critical factor involved in obesity-related insulin resistance is the release of non-esterified fatty acids (NEFA) by adipocytes. Circulating levels of NEFA are elevated in the circulation, predominantly by an obesity-driven enlargement of abdominal subcutaneous adipose tissue (14). Insulin resistance develops within hours of elevation of NEFA in the plasma, while treatment with antilipolytics reduces NEFA levels and significantly improves insulin sensitivity (12,15). Circulating NEFA reduce glucose uptake by adipocytes and the liver, and further promote hepatic glucose output to cause hyperglycaemia (16). In addition, metabolites of NEFA impede insulin-stimulated glucose transport in muscle and inhibit the normal suppression of gluconeogenesis (13). Protein kinase C isoforms are also activated by fatty acid metabolites such as diacylglycerol and ceramides, resulting in a detrimental effect on insulin signalling. Moreover, the energy produced by fatty acid oxidation is utilized by the liver for gluconeogenesis which then further increases blood glucose levels (13).

Adipocyte hormones

Adipose tissue releases several protein hormones that regulate energy homeostasis and lipid and carbohydrates metabolism (17). Adiponectin, leptin, resistin and other hormones are key in developing insulin resistance and T2DM in obesity. Plasma levels of adipocyte products increase as a result of enlarged adipose tissues in obesity, with the exception of adiponectin and the newly identified visceral fat proteins omentin and vaspin (18,19). Table 2 summarizes the major roles of different protein hormones in obese subjects.

Adiponectin functions primarily by counteracting insulin resistance. Therefore, it constitutes an essential natural defensive mechanism against T2DM and other cardiovascular diseases, mainly through regulating carbohydrates and fat catabolism in liver and skeletal muscles (20). Increased adipocyte deposition leads to a marked reduction in adiponectin levels in obese diabetic patients (21). Furthermore, adiponectin levels negatively correlate with insulin resistance (22,23). Adiponectin enhances insulin sensitivity primarily by increasing fatty acid oxidation and inhibition of hepatic glucose production (24).

Plasma levels of adiponectin are reduced secondary to obesity as shown by studying people

from different countries. Measurements of serum adiponectin levels in 33 metabolically healthy and 56 metabolically unhealthy Saudi Arabians showed that the average serum adiponectin level in metabolically unhealthy subjects was 5.9 µg/mL versus 8 µg/mL in control subjects (P

Leptin is another hormone that is primarily secreted by adipose tissue and which acts through the hypothalamus to suppress food intake and to increase energy expenditure (17). Leptin increases insulin sensitivity and muscle fatty acid oxidation (17), whereas deficiencies of leptin or its receptors results in obesity and other metabolic disorders (29). Unlike adiponectin, plasma levels of leptin correlate directly with adipose tissue mass and obesity. However, failure of leptin to exert its weight-loss actions in obese subjects with hyperleptinaemia is attributed to leptin resistance, which is also a risk factor for obesity (29,30). In addition, leptin levels significantly correlate with insulin resistance (31,32). Nevertheless, it has been proposed that the leptin-to-adiponectin ratio potentially constitutes a useful measure of insulin resistance, given that obesity is largely associated with high leptin and low adiponectin levels. Interestingly, the leptin-to-adiponectin ratio negatively correlates with insulin sensitivity in non-diabetic White individuals (33).

Resistin is an adipose-tissue-derived peptide hormone discovered in 2001 and shown to be involved in the link between insulin resistance and obesity (34). This animal study revealed significant reductions in the levels of circulating resistin by the anti-diabetic drug rosiglitazone. Moreover, administration of recombinant resistin increased plasma glucose levels and, conversely, neutralizing circulating resistin reduced glucose levels and improved insulin resistance. Circulating resistin is controlled by several substances including thiazolidinediones, insulin, tumour necrosis factor alpha (TNF-α) and growth hormones (35). Data on resistin-related insulin resistance in obesity are contradictory, since several studies reported a significant association between resistin and insulin resistance in obese subjects (36,37), whereas other studies were unable to confirm this (38,39).

Visfatin is an adipocyte protein that was first reported in 2005, and derives its name from its high expression levels in visceral fat. The pathological role of visfatin in insulin resistance is yet to be examined in full. However, a recently published meta-analysis reported significant increases in circulating visfatin levels in overweight and obese subjects (40). Moreover, visfatin concentrations significantly increase in patients with T2DM where there is also a significant association between visfatin and insulin resistance. Other important factors in obesity-related T2DM are the release of pro-inflammatory cytokines by adipocytes; however their pathological role in inducing insulin resistance and diabetes is unclear. Both fasting plasma levels of TNF-α and dysregulation of interleukin-6 activity are associated with increased insulin resistance and T2DM (41).

Epidemiology

Obese diabetic patients have a worse prognosis in terms of lifetime disease outcomes when compared with non-obese diabetics and this is concerning when we consider that the prevalence of obesity and T2DM has reached alarming levels in the Arab world (42–44). While there are many similarities between the countries, they differ significantly in terms of the socioeconomic determinants of health. These differences impact the prevalence of obesity and diabetes across the Arab countries.

Adults

The global population of overweight and obese individuals in the world reached 2.1 billion in 2013 (45). The worldwide prevalence of obesity has almost doubled since 1980, with obesity rates tripling in developing countries during the past 20 years (46). Furthermore, the global number of adults with diabetes was estimated to increase from 171 million in the year 2000 to 366 million by 2030.

The Arab population are not immune from the worldwide trend in obesity. Several studies have addressed the prevalence of obesity and diabetes in different Arab countries (Table 3-1 , Table 3-2 , Table 3-3 , Table 3-4 , Table 3-5). Saudi Arabia has the 5th highest rate of diabetes worldwide, with 20% of the population being affected (47). A study of 17 232 Saudi people in a community-based national epidemiological health survey of the prevalence of obesity reported that nearly 36% of the population were obese, with the prevalence being greater in females (44%) than in males (26%) (48).

Another study in Saudi Arabia in 2000 reported the prevalence of obesity and diabetes in 14 660 individuals (49). Obesity was monitored according to the World Health Organization (WHO) classification: underweight (BMI

A later study reported on obesity levels in 14 252 diabetic patients in the Aseer region of Saudi Arabia (50). The majority (98%) of the study group were Saudi citizens. Based on the WHO classification of obesity, the study revealed that 46% of the diabetic patients were obese. Nearly 50% of obese diabetic patients had poor diabetic control (fasting blood glucose > 179 mg/dL on the last 2 readings), while only 21% of these obese diabetic patients had good diabetic control (fasting blood glucose

The prevalence of diabetes in Kuwait reached 23% in 2013 according to reports from the

International Diabetes Federation (51). The first national survey assessing levels of diabetes and other cardiovascular risk factors in Kuwaiti adults was performed by Alarouj et al. (52). They found that 48% were obese and 18% were diabetic. Nearly 48% of obese male adults were diabetic compared with 77% of female obese adults. There was a significant association between obesity and diabetes, with an odds ratio of 2.87 (P

In the UAE, the prevalence of obesity and diabetes is similar to other countries in the Arab Gulf region. The results of a national survey aimed at determining the prevalence of diabetes and its associated factors in 5758 adults in the UAE revealed that 20% had diabetes, of whom nearly 40% were obese. (53). A cross-sectional analysis of 602 individuals from different ethnic groups in the UAE studied the impact of several factors on T2DM (54). People with Middle Eastern ancestry had the highest prevalence of T2DM (42%) compared to Asian, European, African and Americans. Moreover, obesity (BMI > 30 kg/m2) was the most significant factor contributing to T2DM among all participants (P

A recent systematic review of 33 studies summarized multiple risk factors for diabetic patients in the Arab Gulf region (55). These studies reported prevalence rates of obesity between 13–37% in men and 16–49% in women. In addition, it was found that 10–20% of subjects in the region also had impaired fasting glucose.

A recent systematic review illustrates the rising prevalence of diabetes and its complications in North Africa (56). During the period January 1990 to July 2012, the prevalence of diabetes ranged from 3% in rural Sudan to 20% in urban Egypt.

Of note is that obesity and diabetes remains a significant concern for Arab migrants to other parts of the world. The prevalence of T2DM was examined among 542 Arab-Americans in Michigan in the United States of America (USA), 95% of whom were immigrants (57). Nearly a quarter of male (22%) and nearly a fifth of female (18%) study participants were diabetic. Of these diabetic patients, 27% were obese and, importantly, there was a significant association between central obesity and diabetes, whereby 64% of male and 86% of female diabetic patients also had central obesity.

Most studies report a higher incidence of both obesity and diabetes among females in the Arab population. The relationship between obesity and several chronic diseases was evaluated in different age groups in 535 Qatari women (58). The prevalence of diabetes reached 51% in obese females aged 50 years and above, and the risk of developing diabetes was extremely high, with a relative risk of 11.21 (P

A study of Arab migrants to Australia reported similar data to those in the USA. Cardiovascular risk factors were examined in 528 Arabic-speaking patients in Sydney (59). Large numbers of

male (73%) and female (36%) patients were found to be either overweight or obese. Another study of Arab immigrants to Australia reported that those born in the Middle East and North Africa had the highest prevalence and incidence of T2DM. Their data revealed that men born in the Middle East or North Africa were 3.6 times more likely to develop diabetes than Australian-born men (P = 0.05) (60).

Adolescents and children

Genetic factors and family history play major roles in the occurrence of diabetes in Arab populations. However, obesity remains the primary risk factor for developing T2DM. The increasing number of diabetics in the younger age groups is related to the rise of obesity among children and adolescents in Arab populations. Table 4 summarizes the latest findings on obese diabetic Arab children and adolescents.

The first reported case of T2DM in children in the United Kingdom was in youths of Arab, Pakistani and Indian origins (42). This occurred in 8 children aged 9–16 years who were overweight and with family histories of obesity-linked diabetes. A study of 96 children diagnosed with diabetes between 1999–2001, 11 of whom were aged 8–18 years old and diagnosed with T2DM in Al-Ain in the UAE indicated that obesity and overweight was prevalent in this group (8 out of 11 cases), and affecting predominantly females (10 out of 11 cases) (43). Nine out of the 11 children were of Arab ethnicity (although all the children had resided in the UAE for a minimum of 3 years prior to the diagnosis of T2DM). A recently performed retrospective hospital-based cross-sectional study assess the prevalence of T2DM among children and adolescents in Khartoum, Sudan (44). Among 958 children registered at the diabetes referral centre, 38 were diagnosed with T2DM, the majority of whom were aged 11–18 years. The female to male ratio was 1.2: 1 and obesity was present in 29 out of 38 children with T2DM, with another 8 children being overweight. The majority (32/38) of children with T2DM in this report were from tribes of Arab origin.

These data about the occurrence of diabetes in children and adolescents were also confirmed in other cross-sectional studies that reported a very high prevalence of overweight and obesity among Arab male adolescents, ranging from 13% in Algeria to 60% in Kuwait (61,62). A similar prevalence of obesity and overweight occurred in females, with 16% of Palestinian and 41% of Kuwaiti adolescent girls being affected.

Etiology

A number of studies have examined some of the reasons underlying the rise in obesity in Arab populations (63–65). A cross-sectional study that examined the role of dietary habits and their relation to obesity in 661 adolescents in Dubai, UAE, reported that children (boys and girls) who

always consumed breakfast had a lower tendency to develop obesity (63). Factors leading to the risk of developing obesity included having breakfast at school rather than home, midnight snacking, watching television during meals and consuming so-called “fast-foods”.

Several factors are associated with the recent rise in obesity in the Arab world. Some factors that are thought to play major roles include rapid urbanization, the consumption of high-fat fast-foods, an inactive lifestyle and a lack of outdoor activities due to the hot and dusty climate in this region.

The prevalence of obesity and diabetes is higher in females in the Arab population. Important in this context are cultural reasons related to multiple pregnancies at short intervals and the long-held view of overweight as a desirable physique reflecting economic well-being (4).

Another important factor to be considered is the association between educational level and the prevalence of obesity. The majority (82%) of diabetic female Arab immigrants to the USA had limited education (high school level or below), while the percentage of women with less than high school education in a normal glucose tolerance group was 42% (66).

Genetic implications

Despite the multiple lifestyle-based factors linking obesity to diabetes in Arab countries, there is also evidence for a strong genetically-based association between obesity and diabetes in Arab populations (Table 5).

Adiponectin is a hormone released by adipocytes (see the section on Pathological mechanisms above) that is encoded by the ADIPOQ gene (67). Several studies have reported reduced adiponectin levels secondary to novel variations in the ADIPOQ gene (68–72). There are 149 variants identified in the ADIPOQ gene (73). Although the number of variations are not directly associated with T2DM, these variations may affect insulin sensitivity in obese diabetic patients (69,74). In addition, variations in the ADIPOQ gene show a significant association with increased BMI (75,76).

Although studies on ADIPOQ genetic variations in Arab populations are still limited and there are no meta-analyses showing the frequency of Arabs carrying variants of the ADIPOQ gene, several researchers have reported that a statistically significant number of Arab obese diabetic

patients carry variants of the ADIPOQ gene (73,77).

The association between variants of the ADIPOQ gene [the single-nucleotide polymorphism (SNP) of rs266729] and the prevalence of diabetes was studied in a Jordanian population that included 420 diabetic and 230 normoglycaemic patients (78). A greater number of diabetic patients carried variants in the ADIPOQ gene, suggesting that mutations in the ADIPOQ gene strongly correlated with the risk of T2DM, at least in Jordanians. A related study of unrelated Tunisians investigated 13 different polymorphisms of the ADIPOQ gene in 917 diabetic and 748 non-diabetic control individuals. Among the 13 variants tested, a significantly higher number of diabetic patients carried 6 of the minor allelic of variants (73). Of interest is that one of the variants that showed a strong association with T2DM was the same variant (rs266729) found in the Jordanian study (73,78). A recent cross-sectional analysis examined the association of genetic variants of the ADIPOQ gene with obesity, insulin resistance, dyslipidaemia and hypertension in 328 people from one extended Omani family living in an area where first-cousin marriages represented 50% of all marriages (77). The prevalence of obesity and diabetes were 17% and 27% respectively. Two common variants of the ADIPOQ gene were identified. The frequency of SNP of rs266729 (the same SNP identified in Tunisian and Jordanian studies) significantly correlated with body weight ($P = 0.001$), waist circumference ($P = 0.037$), BMI ($P = 0.015$) and percentage of total body fat ($P = 0.003$).

As diabetes is a complex of mechanisms ultimately leading to high blood sugar levels, several studies have attempted to identify variants in different genes that may be related to the increased risk of diabetes. For example, the nuclear receptor protein peroxisome proliferator-activated receptor gamma (PPAR-γ) is of central interest in the pathogenesis of diabetes, obesity and other metabolic disorders. Activation of PPAR-γ by the thiazolidinedione type of oral hypoglycaemic drugs improves insulin sensitivity and thus control of diabetes (79). Mutations in the PPAR-γ gene, specifically the Pro12Ala polymorphism, could be a risk factor for diabetes (80). The first study examining the P allele (i.e. the risk allele) variant of the PPAR-γ gene in Arabs took place in Saudi Arabia. A case–controlled study reported that the frequency of the P allele was 0.974 and 0.968 in T2DM patients and control subjects respectively ($P = 0.633$) It is likely that the similarity in these values represented the high incidence of the risk allele in the population tested (81). In addition, the presence of the P allele in the Saudi Arabian population in neonatal samples revealed a frequency of 0.957, which is similar to the frequencies found in Japanese, Chinese and African-Americans and was among the highest (81,82). Despite the high incidence of the risk allele in the Saudi population, there are other factors at play in the increased risk of diabetes among more recent generations of the population, among whom first-cousin marriages represent about 30% of all marriages and marriages to distant relatives has a frequency of 15%. These findings increase the rate of consanguinity to nearly 60%, and increase the odds of familial aggregation of T2DM to 6.2 (83,84).

Genome-wide association studies (GWAS) identified several gene variants associated with T2DM. These included the CDKAL1 SNP, which is thought to be a major genetic risk factor for T2DM in several ethnic groups. Mutations in the CDKAL1 gene impair beta-cell function without affecting insulin sensitivity (85-87). Notably, variants of the CDKAL1 gene were shown to have no association with T2DM in Moroccan patients (88). However, in a Lebanese study there appeared to be an association between T2DM and 2 common variants of the CDKAL1 gene (89).

Variants in the insulin-like binding protein 2 (IGF2BP2) gene are associated with T2DM in several ethnic groups (90,91). A replicate study in a Lebanese Arabs population identified 2 SNPs of IGF2BP2 (rs4402960 and rs1470579) that were strongly associated with T2DM (92). Moreover, an additional cross-sectional replication study in Arab-Lebanese was able to genotype 19 representative SNPs in 15 potential T2DM loci, derived earlier from the European GWAS (93). After correcting for multiple comparisons, their findings revealed that 5 SNPs (rs792837 in the COL8A1 gene, rs2237892 and rs2237895 in KCNQ1, rs729287 in ALX4 and rs4430796 in HNF1) were significantly associated with T2DM.

Finally, the search for genetic determinants of diabetes and obesity within Arab populations has recently become a focus of attention. However, comprehensive coverage of this topic is beyond the scope of this review.

Ongoing efforts to combat obesity-linked diabetes

The prevalence of obesity in Arab populations is a major concern. In addition to the risk of developing diabetes, obesity increases the risk of hypertension, cardiovascular diseases and some types of cancers. In fact, these complications represent about 50% of all deaths in the Arab region (94).

Obesity-linked diabetes is a preventable disease, and decreasing body weight reduces the risk of T2DM and its complications (95–97). Such findings encouraged decision-makers in different Arab nations to collaborate in trying to limit the rise in obesity-related diabetes.

The Arab Taskforce for Obesity and Physical Activity developed a 5-year strategy to combat obesity (98), and first presented this at the Third Arab Conference on Obesity held in Bahrain in 2010 where there were contributions from 14 Arab countries. The proposed strategy aimed to suit all Arab nations in a manner that was consistent with the diversity of socioeconomic status and cultures across the region. The primary goals of the strategy are to:

promote healthy dietary habits and increase physical activities to reduce the incidence of overweight and obesity;

reduce risk factors for noncommunicable diseases resulting from obesity, poor dietary habits and lack of physical activity;

raise awareness about the complications of obesity and the overall benefits of increasing physical activity in preventing complications;

enhance collaborations between governments, the private sector and community institutions to provide healthy environments through healthy lifestyles;

conduct research related to nutrition and the risk factors for obesity; and

develop national guidelines for controlling the rise in obesity, particularly in children (98–100).

Future directions

Although the prevalence of obesity-related T2DM is increasing rapidly in all age groups of the population in the Arab world, the extent of investigation into this phenomenon and the measures aimed at curbing the epidemic are insufficient. Crucial information on obesity and diabetes in various Arab populations is not available. Studies concerning the ethnic-specific obesity cut-off points for the risk of diabetes exist for other ethnic groups. For example, it has been shown that BMI values of 25 kg/m2 (South Asian) and 27 kg/m2 (African-Caribbean) carry a risk of developing T2DM equivalent to a BMI of 30 kg/m2 for Europeans (101). Another prospective cohort study investigated the protective effect of physical activity, using 65 identified SNPs as genetic risk markers for T2DM in a population of White participants who were tracked for a mean of 7.8 years (102). Predictably, the incidence of T2DM was lower in physically active subjects, but the strongest association between physical activity and the incidence of T2DM was observed in a group with a low genetic risk score and, conversely, the weakest association occurred in the high genetic risk group. These results suggest that the protective effect of physical activity against T2DM is highly dependent on the genetic risk an individual is carrying, and these data may be of importance in Arab populations that have traditions of

consanguineous marriages.

The lack of sufficient GWAS in T2DM is troublesome, particularly in the context of the epidemic of obesity and diabetes in Arab populations. A recent systematic overview of genetic studies of T2DM in South Asians reported that the only 2 GWAS performed in South Asian diabetics were able to identify susceptibility genes that were not detected in European GWAS (103). Other studies in Caucasian Europeans reported significant variations in serum adiponectin levels after 4 weeks of high monounsaturated fatty acids diets; variations were attributed to genetic polymorphisms at the ADIPOQ gene locus (104). On the other hand, a study of Saudi Arabians with T2DM found no significant association between 2 SNPs (T45G and G276T) and circulating adiponectin or insulin resistance (105).

The very limited GWAS performed in diabetic and obese Arab populations have yielded valuable information, indicating that more studies might add crucial insight into T2DM in terms of prevention or even treatment. Therefore, the search for genetic determinants of diabetes and obesity in Arab populations should be prioritized.

Summary

Diabetes has a complex pathophysiology and management strategy. Obesity is the main risk factor attributed to diabetes in the Arab world. The sedentary lifestyle in most of Arab countries, coupled with a hot climate and unique cultural barriers to physical activities, are important factors to be considered in the rapid increase in the prevalence of obesity among Arab countries. However, studies among Arab migrants to countries where the lifestyle is known to be more active, showed that the risks of obesity and diabetes remain elevated. For example, the Australian Institute of Health and Welfare reports that immigrants from the Middle East and North Africa have the highest prevalence of diabetes and the second highest prevalences of overweight, hospitalization and mortality related to diabetes among all immigrants to Australia (60).

Most of the available epidemiological data show that Arab females are more prone to obesity and diabetes. Several factors could account for these findings, but especially important are the persistent social and cultural barriers to physical activities. Recently published data on T2DM in children and adolescents are concerning. This unusual age-related disease has been highlighted in several epidemiological studies of the prevalence of obesity in Arab schoolchildren.

The widespread epidemic of obesity-related diabetes in Arab populations has been analysed in a limited number of genetic studies. For example, the variant rs266729 in the ADIPOQ gene was significantly associated with diabetes in Tunisian and Jordanian populations, and with obesity in an extended Omani family. Another factor aggravating the genetic basis for T2DM in Arab countries is the common practice of marriage with first- or second-degree relatives. In a study of Saudi Arabian males nearly 63% of diabetics had a positive family history of diabetes compared with around 22% in the control non-diabetic group (P

Strategies for combatting obesity in the Arab world by the Arab Taskforce for Obesity and Physical Activity appear promising, although this requires sustained collaboration among many decision-makers across the region.

Finally, there is a lack of quality data regarding obesity-related diabetes in Arab populations. Gaps exist in our information about diabetes and obesity, in particular in relation to ethnic-specific cut-off points for diagnosis and treatment of diabetes. In addition, further GWAS in obese and diabetic Arab populations could add to our understanding of the pathophysiology, prevention and reversal of this disease.

Limitations

There were both limitations and strengths of this literature review. First, we critically appraised only those studies that met our inclusion criteria. Secondly, despite sociocultural similarities among Arab countries, ethnic differences between populations may well play a significant role in the epidemiological variations related to obesity and diabetes, since the Arab population is widely distributed across both Asia and Africa. Nevertheless, we aimed to comprehensively review the burden of obesity-related T2DM in the Arab world by carefully evaluating the available epidemiological data from each country. To our knowledge, this is the first paper to explore the great health burden of T2DM in children and adolescents in the Arab world.

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