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Review

Type 2 diabetes – An unresolved disease across centuries contributing to a public health emergency☆

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ABSTRACT

Aims: Type 2 diabetes mellitus (T2DM) is a global epidemic. However, T2DM is not a new, 21st century disease. Different populations have been struggling with this disease across a number of centuries. The question lies as to why humanity has never succeeded in keeping it in check over the course of its history.
Materials and methods: In this review, the history of T2DM and its evolution throughout the ages are revisited. The review then investigates the growing burden of T2DM across the past fourteen years within the European continent, while comparing this epidemic with the obesity burden.
Results: Various explanations for the emergence of this public health epidemic were explored ranging from lifestyle factors, high sugary food and drink, disrupted sleep pattern to obesity. Over a fourteen-year period, an evident steady incline in both T2DM and obesity prevalence rates across Europe was evident.
Conclusion: It is essential for public health officials and researchers alike to have a good grip of the past and the present diabetes epidemiology and its co-determinants. This will provide the basis for new and improved strategies to target and prevent this epidemic.

1. Introduction

Type 2 diabetes mellitus (T2DM) has been declared a public health emergency back in 2015, where 7.3 billion adults were estimated to suffer from this disease [1]. In 2017, T2DM was estimated to affect 7.5 billion adults (8.8% of adults between 20 and 79 years). This rate is expected to rise to 9.9% by the year 2045 which would then affect 9.5 billion adults [2]. However, T2DM is not a disease of this era and its existence has been documented for centuries.

2. History of diabetes mellitus

Diabetes mellitus is a disease of antiquity with the initial description attributed to the Egyptian period. An Egyptian papyrus dating back to 1550 BC described the polyuric state. Between 400 and 500 BC, Hindau physicians Charak and Sushrut, first recognized the sweetness of the diabetic urine. They also noted that this condition was prevalent in those who over indulged in sweet and fatty food, who exhibited a sedentary lifestyle and were overweight. In the second century AD, Aretaeus of Cappadocia was the first to coin the Greek word “syphon” for “diabetes”, since he noticed a man's body was not retaining fluid but rather, the body was used as a channel to release fluid [3]. Matthew Dobson from Liverpool in 1776 was the first to describe hyperglycaemia in the serum along with the presence of sweet urine in a diabetic patient [4]. The surgeon John Rollo was the pioneer in applying the adjective “mellitus”, which is a derivative of a Latin word meaning “honey” [5]. In 1815 the French Chemist Michel Chevreul discovered that the sugar in diabetic urine was glucose, leading to a change in the diagnostic methods for diabetes, from tasting the urine to measuring of glucose levels. In fact, physician Ivar Christian Bang identified a method of measuring glucose repeatedly, leading to the development of the glucose tolerance test between 1913 and 1915 [3].

In 1869, Paul Langerhans discovered “islands” of cells within the pancreas parenchyma which, later on in 1893 were named the “islets of Langerhans” by Gustave Laguesse. He suggested that these cells were responsible for pancreatic secretions, which were later on named “insulin” [6–8].

In 1921, the orthopaedic surgeon Frederick Banting and the medical student Charles Best under the supervision of Professor McLeod made the discovery of injectable insulin as a treatment for diabetes [9]. The first human experiment using injectable insulin

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was performed in January 1922 on a 14-year-old diabetic boy. It was noted that the clinical symptoms and biological abnormalities were reversed to normal [9]. However, it was observed that not everyone with diabetes had a positive outcome with insulin injections. In fact, in 1930s, both Wilhelm Falta and Harold Himsworth proposed that there were individuals who were insulin-sensitive and others who were insulin-insensitive [10,11].

The development of the "insulin clamp" technique in 1970s enabled the measurement of the hypoglycaemic action of insulin. This technique led to countless research studies to investigate insulin resistance and its relationship with T2DM [12]. As the years progressed, diabetes management became more refined. Insulin preparations proliferated with genetic engineering leading to the production of designer insulin such as fast-acting analogues *lispo* and *aspart* and the peakless basal insulin such as *glargine* and *detemir*. The revolutionary invention of the "pen" injection devices by John Ireland in 1981 made glucose management by insulin more patient friendly [13]. The oral hypoglycemic agent sulfonylureas originated in the early 1940s. These drugs proved to be insulin secretagogues [14]. The first biguanide *Phenformin* was introduced in 1959 and *Metformin* was available in the European market in 1960 [15]. More hypoglycaemic drug classes have been developed recently such as the glitazones, glucagon-like peptide 1 (GLP-1) agonists and inhibitors of the enzyme dipeptidylpeptidase-4 (DPP-4).

3. Susceptibility for type 2 diabetes

The underlying T2DM pathophysiology includes pancreatic beta cell dysfunction and development of insulin resistance [16]. An interaction between genetics (non-modifiable) and environmental (modifiable) factors increase the risk for obesity, insulin resistance and beta cell dysfunction, which ultimately lead to the development of T2DM [17–22]. Insulin resistance and cardiovascular disease risk factors (commonly associated with adiposity) appear to contribute to a substantial risk for the development of diabetes [23]. Lifestyle habits also increase the risk of T2DM. It has been reported that smoking reduces insulin sensitivity and predisposes the smoker to T2DM. Meanwhile dysfunctional sleep, with long (>8 h) and short (<6 h) stints of sleep have also been associated with increased risk of insulin resistance and T2DM, although gender differences were noted [24,25]. It is well known that dietary habits including fatty and sugary foods have an adverse effect on insulin sensitivity. Food products with added sugar, being a soda can or preserved food tin, also increase the risk of T2DM. This results from the presence of fructose, which is a component of added sugar. Fructose undergoes first pass metabolism within the liver (insulin independent), which initiates fatty acid synthesis, resulting in lipid deposition within the liver and eventual hepatic insulin resistance. In return, gluconeogenesis is promoted resulting in hyperglycaemia and the development of T2DM [26]. However, the onus of the T2DM epidemic rests on the increasing obesity rate. In fact, the T2DM epidemic is intertwined with the increasing obesity crisis and one epidemic cannot be dealt with without addressing the other.

4. The obesity epidemic

As discussed previously, the concept of excess adiposity (obesity) leading to T2DM is not something innovative to this era but it has been noted and reported as far back as the early ages. What is intriguing is the fact that only recently has this been given any real attention.

The obesity epidemic is mostly attributed to an increase in body fat deposition as a result of reduced physical activity and unhealthy dietary habits. This obesity crisis is now originating within the intra-uterine period and continuing to the end of life. In fact, the global obesity epidemic has been linked to simultaneous aging of the population, which has been occurring over the past few decades [27]. The obesity epidemic has also been unveiled amongst children worldwide, where an approximate 41 million children under the age of 5 years were estimated to be either overweight or obese in 2016 [28]. With the increasing obesity rates especially associated with high sugar and fatty food consumption, it is becoming a common occurrence to have fertile mothers providing a hyperglycaemic foetal environment to their unborn child. Such an environment predisposes the child to develop obesity, insulin resistance and T2DM later on in life [29,30]. Over the years there have been an increase in both portion size and consumption of food mostly at home and at fast-food restaurants [31]. Both of these factors promote weight gain and obesity [32]. Furthermore, the socioeconomic status of an individual has also a contributing effect on the development of obesity. Low socioeconomic status individuals are more likely to consume low cost energy-dense food rather than healthy diets based on fish, lean meat, fruit and vegetables, which tend to be higher in price [33].

5. The burden of type 2 diabetes

The pathophysiology of T2DM was established throughout the centuries along with the identification of the various diagnostic and treatment modalities. One would expect that as the years progressed the emergence of T2DM would have subsided to nothing. This is however, not the case as shown in Fig. 1, which presents a graphical illustration of the progressive prevalence of T2DM in adults (20–79 years) across eight European countries between the year 2003 and the year 2017 [34]. This brings forward the notion that T2DM prevalence is being affected by a multiplex of conditions that also need attention to, with special attention to the obesity epidemic. Table 1 illustrates clearly that as the prevalence of obesity increased across the years in Europe, a corresponding increase in T2DM prevalence occurred [35].

6. The way forward

Both the public and private global sectors, individually or in collaboration, have been working to end this epidemic. Multiple strategies and policies have been implemented across nations but unfortunately both the T2DM and obesity epidemics are on the rise.

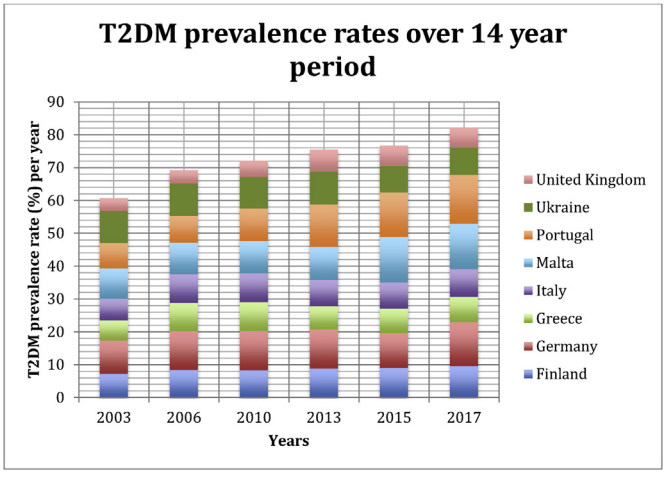

Fig. 1. T2DM prevalence rates over a 14- year period in 8 European countries [34].

Table 1
Prevalence rates of obesity and T2DM across 14 years in Europe. Adopted from WHO Global Observatory data and International Diabetes Federation Atlases [34,35].

Country	2003		2006		2010		2013		2015		2017
	Obesity (%)	T2DM (%)	Obesity (%)	T2DM (%)	Obesity (%)	T2DM (%)	Obesity (%)	T2DM (%)	Obesity (%)	T2DM (%)	T2DM (%)
Albania	14.4	3.8	16.2	4.8	18.7	4.8	20.5	2.8	21.7	12.0	11.93
Andorra	23.9	7.7	24.8	7.8	26.0	8.8	27.0	7.6	27.7	11.9	12.7
Armenia	15.1	–	16.0	–	17.5	8.7	19.0	2.64	20.2	7.2	7.56
Austria	16.2	9.6	17.5	11.1	19.2	11.2	20.5	9.27	21.5	9.5	9.93
Azerbaijan	12.8	6.9	14.0	6.9	15.9	7.1	17.8	2.28	19.2	6.3	6.92
Belarus	20.9	6.9	22.1	9.2	23.7	9.1	25.1	6.26	26.1	6.5	7.14
Belgium	19.7	4.2	20.8	7.9	22.2	8.0	23.3	6.45	24.1	6.7	6.81
Bosnia and Herzegovina	14.5	9.6	15.5	9.0	17.0	9.1	18.1	12.4	19.0	12.3	12.63
Bulgaria	21.1	10	22.4	10.1	24.3	9.0	25.8	7.63	26.9	8.4	8.16
Croatia	20.4	5.8	21.8	9.5	23.8	9.2	25.4	6.97	26.5	6.8	6.9
Cyprus	17.6	5.1	18.7	10.3	20.1	10.4	21.3	10.24	22.2	10.4	10.43
Czech Republic	23.2	9.5	24.3	9.7	25.8	8.7	27.1	9.23	28.0	9.9	9.63
Denmark	16.3	6.9	17.5	7.5	19.0	7.7	20.1	8.58	20.9	9.9	9.86
Estonia	19.7	9.7	20.4	9.9	21.6	9.9	22.7	7.71	23.4	6.0	6.11
Finland	19.5	7.2	20.8	8.4	22.4	8.3	23.6	8.85	24.5	9.0	9.56
France	18.1	6.2	19.3	8.4	20.8	9.4	22.0	7.5	22.8	7.4	7.26
Georgia	15.5	9.0	16.9	9.1	19.0	9.2	21.0	2.96	22.5	7.5	7.98
Germany	19.7	10.2	21.0	11.8	22.8	12.0	24.2	11.95	25.2	10.6	13.4
Greece	20.9	6.1	22.4	8.6	24.4	8.8	25.9	7.01	26.9	7.5	7.71
Hungary	21.9	9.7	23.3	9.8	25.3	8.8	26.9	7.61	28.1	9.3	9.64
Iceland	17.7	2.0	19.0	2.0	20.5	2.1	21.8	3.96	22.7	7.6	8.05
Ireland	17.9	3.4	19.7	5.6	22.4	5.7	24.7	6.47	26.2	5.3	4.65
Israel	21.9	7.1	23.0	7.8	24.5	7.1	25.6	6.65	26.3	8.5	8.63
Italy	17.9	6.6	19.1	8.7	20.6	8.8	21.7	7.95	22.5	7.9	8.45
Kazakhstan	14.6	5.5	15.8	5.6	17.6	5.6	19.3	4.87	20.6	6.2	6.9
Kyrgyzstan	9.5	4.3	10.4	4.3	11.9	4.3	13.5	5.02	14.7	5.2	6.05
Latvia	21.5	9.9	22.3	10.0	23.5	9.9	24.5	6.17	25.3	7.3	7.63
Lithuania	23.8	9.4	24.6	9.7	25.9	9.7	27.1	4.9	27.9	5.5	5.56
Luxembourg	18.4	3.8	19.8	6.9	21.5	7.0	22.8	5.78	23.7	5.7	5.89
Malta	25.6	9.2	27.0	9.7	28.7	9.8	29.9	10.14	30.6	13.9	13.81
Montenegro	18.5	–	20.1	–	22.1	8.4	23.5	12.51	24.4	12.8	12.85
Netherlands	15.9	3.7	17.6	7.3	19.9	7.7	21.5	7.5	22.6	7.9	8.16
Norway	18.7	6.7	20.2	4.7	22.0	4.7	23.5	5.9	24.5	7.8	8.11
Poland	19.6	9.0	20.7	9.1	22.5	9.3	24.0	6.5	25.0	7.6	7.82
Portugal	16.1	7.8	17.7	8.2	19.9	9.9	21.5	12.96	22.7	13.6	14.9
Romania	18.0	9.3	19.1	9.4	21.0	8.4	22.7	5.14	23.9	10.6	12.48
Russian Federation	21.1	9.2	21.9	9.0	23.2	9.0	24.4	10.03	25.2	11.1	8.12
Serbia	17.5	–	18.8	–	20.6	8.6	22.0	12.35	23.0	13.2	13.35
Slovakia	16.9	8.7	17.9	8.8	19.5	7.7	20.9	10.16	21.9	9.9	10.69
Slovenia	17.1	9.6	18.2	9.8	19.8	9.9	21.1	10.33	22.0	10.7	10.81
Spain	20.8	9.9	22.1	7.5	24.0	8.7	25.5	10.83	26.6	10.4	11.23
Sweden	16.9	7.3	18.1	7.2	19.6	7.3	20.8	6.36	21.6	6.3	7.2
Switzerland	16.1	9.5	17.2	11.2	18.8	11.3	19.9	7.45	20.8	7.7	7.89
Tajikistan	7.3	3.7	8.1	3.5	9.5	3.6	10.9	4.48	12.0	4.5	5.39
Turkey	22.4	7.0	24.5	7.1	27.4	7.4	29.8	14.58	31.4	12.5	12.54
Turkmenistan	10.7	4.0	11.9	4.0	13.8	4.1	15.5	4.05	16.8	5.2	5.96
Ukraine	21.1	9.7	22.0	9.8	23.3	9.6	24.6	2.99	25.6	8.0	8.23
United Kingdom	21.5	3.9	23.2	4.0	25.7	4.9	27.5	6.57	28.9	6.2	5.95
Uzbekistan	9.3	4.0	10.3	4.0	11.9	4.0	13.5	5.05	14.7	5.2	6.48

Having a good understanding of the available knowledge along with keeping up to date with the continuous advancement in research and technology should empower a multidisciplinary approach towards this epidemic. Collaborations between different stakeholders, both at a local and international setting are required. In fact, the control of T2DM needs to consider the biological (genetics) factors, the behavioural factors, the socioeconomic conditions as well as the health care services available. Every sector provides a challenge, but it is the combination of all aspects that will provide the basis towards success.

Conflicts of interest

None.

Data availability

http://www.diabetesatlas.org and http://apps.who.int/gho/data/node.main.A896?lang=en.

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Contribution statement

The author performed the literature review and constructed the manuscript.

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