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A Systematic Review of the Prevalence and Treatment of Type 2 Diabetes in Nigeria.

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ABSTRACT

Diabetes is on the increase in Nigeria and previous systematic reviews and meta- analysis have reported estimates of the prevalence of Type 2 Diabetes Mellitus in Nigeria. However, because of differences in population characteristics, these estimates will vary across and within geopolitical zones. Despite the increase in prevalence of Type 2 Diabetes Mellitus in the country, no other systematic review has been carried out to assess diabetes treatment pattern in Nigeria. Hence, the importance of this study, as it critically reviews the disease prevalence and treatment pattern across and within geopolitical zones in Nigeria.To systematically review all prevalence and treatment studies published from January, 1998 to September, 2018. The following databases were searched for articles: PubMed Central (PMC), African Journal On Line (AJOL), Science Direct, and Connecting Repositories (CORE). Google scholar was also searched. 159 articles were identified from the databases while 12 were identified from Google Scholar. Studies that were excluded are: Studies that dealt mainly the prevalence of Type 1 Diabetes Melitus/gestational diabetes (14); studies with self reported diagnosis (12); case reports and editorials (10); studies that were not representative of the general population (7); and studies without case definitions (8) were excluded from the pool of studies to obtain 38 studies that were utilized for the review. 29 studies were used for the review of prevalence studies while 9 were used for review of treatment/drug utilization studies. For the review of prevalence of diabetes, sample size of studies used for the review of prevalence of diabetes ranged from 105 to 18,921. The South-South region recorded the highest number of studies (10 articles) while the north-east recorded the least number of studies (1 article). The highest prevalence was recorded among Oil company workers in the South-South region (23.4%) while the lowest was recorded among a group of adolescents in the South West region (0.6%). The urban settings had relatively higher prevalence than the rural settings and no particular trend was reported with regard to gender. For the review of treatment of diabetes, the highest number of studies was recorded in the South-West region (4 articles). Sample size ranged from 115 – 349. Only one study from the private facilities was used for this review. Metformin was the most prescribed monotherapy while metformin plus glibenclamide was the most prescribed combination therapy. Insulin was also used in dual or triple combination therapy with other oral hypoglycaemic drugs. Prevalence of Type 2 diabetes mellitus is on the increase in Nigeria, especially in the urban settings, among the higher socioeconomic class, and the higher age groups. Treatment of diabetes is in line with most areas of the clinical guidelines except in the area of use of glibenclamide as combination or add-on therapy and with the use of insulin as dual combination therapy.

Keywords: Systematic, prevalence, treatment, diabetes, Nigeria.

INTRODUCTION

Life of man for all times and ages has been characterized pathologically by diseased conditions of which Diabetes Mellitus constitute one of the most chronic human infirmities of all times. As a disease of prehistoric era through

antiquity, medieval, modern, and contemporary times, diabetes ravaged humanity for over millennia though perceived by different ages and peoples in diverse ways – at one time as mysterious, other times as socio-cultural omen, or human affliction. Its impact more often emanates from its debilitating pathophysiological effects which have generated over time intense characteristic and/or pathological research to unravel and treat the dreaded inferno.

Historical Background of Diabetes Mellitus

The term diabetes mellitus etymologically derives from the Greek word *diabetes* which means to pass through or simply to siphon while mellitus on the other hand, comes from the Latin word *mellitus* which translates to sweet or honey. The literal definition as such is a diseased condition in humans that cause the siphon or excess passage of sugar from the body. The coinage of the term implicates a medical condition where excess sugar is found in the blood and in the urine. Literary accounts differ as to the first scientist who coined and used the term. While some accounts refer the initial coinage of the term *diabetes* to Apollonius of Memphis around 250 BC (Diabetes History, 2018); other accounts according to [1] "recorded history attributes the first complete descriptions in the first century A.D. to Aretaeus the Cappadocian, who coined the word *diabetes* (Greek, 'siphon') and dramatically stated "... no essential part of the drink is absorbed by the body while great masses of the flesh are liquefied into urine". [2] On the other hand, the term *mellitus* was coined by the British Surgeon-General, John Rollo in 1798, in recognition of its sugar-like taste and to differentiate it from diabetes (*insipidus*) with tasteless urine [3].

Throughout Antiquity around the 1500 BC and Medieval era, diabetes mellitus was often perceived as mysterious, curse, rare disease or evil. Ancient Graeco-Roman medical practices, oriental Chinese and Indian traditional medicine, Afro-Egyptians papyrus, as well as the peoples of Ancient Near East and the Arabian Peninsula medical civilizations characterized the incidence of diabetes mellitus in one way or the other. Ancient Indian physicians referred to it as *madhumeha* ('honey urine') because it attracted ants.

Around 131-201 CE, Greek physician, Galen of Pergamum, theorized diabetes as grave affliction of the kidneys. Avicenna (980-1037), a renowned Persian polymath and physician published "*The Canon of Medicine*" in 1025 in which he provided unique characterization of diabetes mellitus as sweet urine, abnormal appetite, diabetic gangrene, sexual dysfunction and frequent urination. He also concocted a mixture of seeds (lupin, fenugreek, zedoary) as a panacea to its debilitating effects [4].

Other features of diabetes mellitus that pervaded down to medieval age include urine colour, taste, sediment and odour. This process of disease identification and examination was referred to as 'uroscopy'. This was common around the 11-12th centuries. Nevertheless, around 400–500 A.D., the quest for efficient diagnostic and pathological knowledge of the diabetes mellitus led two great indian medical scientists – Sushruta, a physician and Charaka, a surgeon after series of rigorous scientific studies identified two types of diabetes – Type 1 and Type 2. However in 1936, Harold Percival Himsworth substantially differentiated Type 1 and Type 2 diabetes as unique entities as are currently referred in medical science [5]. Further analysis of scholarly perspective on diabetes is x-rayed in the literature review.

LITERATURE REVIEW

The review of extant literature, perspectives, and scholarly horizons on the subject of Diabetes Mellitus is important. One of the practical approaches to deal with the critical issues of Diabetes is to critically and systematically review topical but relevant literature, primary reports and data that focused on the issue. Such reviews aim to broaden the horizon of knowledge on subject matter, share subjective and objective experiences on related issues,

investigate and expound the historical space for evaluating needed facts and data. As such, it creates the hypothetical modules for priming and galvanizing our systematic discourse on Diabetes.

Diabetes – what it is:

Diabetes is a chronic non communicable disease that occurs either when the pancreas does not produce enough of the hormone responsible for regulating the blood sugar in the body and/or a condition where the body cannot effectively utilize the hormone referred to as insulin. Hyperglycaemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body's systems, organs and tissues, especially the nerves and blood vessels [6]. The main symptoms of diabetes are three – polydipsia, polyphagia and polyuria – which means increased thirst, increased hunger and increased frequency of urination. There is also the feeling of tiredness or fatigue, weight loss and loss of muscle bulk. Type 1 diabetes can develop quickly, over weeks or even days whereas type 2 diabetes may develop gradually [7].

Statistically, the prevalence of diabetes over decades, despite the multimillion dollar efforts to contain and control the disease is a huge concern. It constitutes serious public health challenge not only for health stakeholders and health professionals but for international community. Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades. In 2014, 8.5% of adults aged 18 years and older had diabetes. In 2016, diabetes was the direct cause of 1.6 million deaths and in 2012 high blood glucose was the cause of another 2.2 million deaths [8].

Types of Diabetes

The search for the cause of diabetes engaged tens of decades of scientific enquiry among scientists, theorists and medical analysts. In 1776, Matthew Dobson empirically confirmed that the sweet taste found in urine of diabetic patients was a result of the excess sugar content. He distinguished that while diabetes was chronic in some people, it was fatal in others; thereby depicting first instance of clinical difference among diabetic patients.

However, in 1936 Sir Harold Percival (Harry) Himsworth characteristically distinguished diabetes as type 1 and type 2 as published in his scientific discourse on diabetes. He strongly argued that insulin resistance in conjunction with impaired beta-cell function proved the major causal factor of type 2 than insulin deficiency as noted in type 1 diabetes [9].

Type 1 Diabetes Type 1 diabetes known as insulin-dependent, occurs more in children and was often referred to as juvenile diabetes. Unlike type 2, there is complete insulin deficiency among patients with type 1 and as such are completely dependent on injection of hormone insulin for continued survival. Although the cause of type 1 diabetes is still scientifically unknown, symptoms include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes, and fatigue among others.

Type 2 diabetes This type of diabetes is referred to as non-insulin-dependent and occurs more frequently in adults although there is currently increasing occurrence in children in view of fast changing lifestyle. The major cause of this diabetes is the inability of the body to produce sufficient hormone insulin as needed by the patient. World diabetes statistics reveal that most people with diabetes have type 2 which occurs more among people who are obese, overweight or lack regular physical exercise. The symptoms are similar to those of type 1 diabetes.

There is increased effort to discover the exact cause of type 1 diabetes and find ultimate cure for all types of diabetes. Scientists and academic research communities across the world are intensely searching for answers to the dreaded scourge of diabetes. Researchers and medical scientists at Ottawa Hospital and The University of Ottawa are exploring the role of a bacteria-killing protein called cathelicidin antimicrobial peptide (CAMP) found in the pancreas in relation to diabetes. Also the American

Diabetes Association (ADA) funded series of research projects aimed at unraveling greater understanding of diabetes and its treatment options [10].

Gestational diabetes Gestational diabetes often times occurs among pregnant women with abnormal high blood sugar condition. This condition is referred to as hyperglycaemia. Pregnant women with hyperglycaemia have high chances of developing type 2 diabetes even after delivery. Gestational diabetes is usually diagnosed during antenatal screening and pregnant women with this disease condition are at high risk of developing health complications during pregnancy and delivery. This condition affects about 4% of pregnant women and is regarded as serious [11].

Diabetes: Pathophysiological Findings of 19 – 20th Centuries

The nineteenth through the twentieth centuries recorded hallmark of scientific breakthrough in science and technology. More than ever, scientific revolution in medical and empirical sciences though built on the precipice of preceding breakthroughs gained more insight in precision and reengineering in almost all facets of knowledge. Medical metascience witnessed improved outcomes and findings.

The scientific revolution of the 19th century was ripe in medical discoveries and scientific innovations. In 1869, Paul Langerhans, a young German anatomist, aged 22 while researching on his doctorate identified the cells that were subsequently known as 'islets of Langerhans'. [12]. In 1889, Von Mering and Minkowski, while experimenting on dogs, found that inalienable relationship between pancreas and diabetes. The experiment showed that the removal of the pancreas from dog led to diabetes and its complications and eventual death [13]. However, in 1921, Canadian researchers, Frederick Grant Banting, Charles Herbert Best and James Collip, working in Macleod's laboratory, advanced the works of Von Mering and Minkowski, ligated the pancreatic duct, causing the destruction of the exocrine pancreas while leaving the islets intact. They were able through infusion of purified hormone insulin from pancreases of cows to reverse induced diabetes in a 14-year-old boy, Leonard Thompson at the Toronto General Hospital thereby proving scientifically that insulin deficiency was the primary cause of diabetes and that insulin, as coined by de Mayer and Schaefer in 1909 and 1910 respectively has the capacity to lower significantly the level of blood glucose (Science History Institute, 2017). Banting and Best made the patent available free of charge so that millions of diabetics worldwide could get access to insulin. This led to the mass production of effective treatment for diabetes in 1922 and subsequently proved to be life-changing discovery in medical science and in the overall treatment of diabetes all over the world. It strengthened concerted action and focused research into diabetic and medical actions in policy and implementation, changing significantly the lives and longevity of ailing diabetic patients and horrendous threats posed by diabetes across the world [14]. As a mark of distinction, the World Diabetes Day is celebrated annually on November 14 which is the birthday of Frederick Grant Banting.

The ingenuity of Banting and Macleod were acclaimed in a worldwide award of the Nobel Prize in Physiology and Medicine in 1923(Science History Institute, 2017). There were other spectacular Nobel Prizes awards in Chemistry and Medicine respectively for aminoacid sequence [15] and radioimmunoassay. However, the first oral antidiabetic drugs (sulphonylureas) emerged in the 1950s and were subsequently included in the treatment armamentarium. Others, including metformin, glucosidase inhibitors and insulin sensitisers, followed in the succeeding decades with different sites of action to enable better handling and metabolic assimilation of ingested carbohydrates [16].

In 1980, the first human insulin was manufactured by Graham Bell [17]. In 1982, the first biosynthetic insulin (humulin) that is similar in chemical structure with human insulin was

developed. Syringes appeared in 1961 but, being made of glass, brought with them the attendant hazards of infections until they were replaced with disposable plastic ones. It was only 15 years later that the introduction of the first needle-free insulin delivery system by Derata in 1979 provided relatively pain-free, metered doses. Insulin pumps, inhaled insulin and oral sprays in contemporary times have significantly improved administration and therapy [18].

Diabetes epidemiology

Over the years and more conspicuously in our fast changing time and lifestyle, the scourge of diabetes has become not only the problem of the affluent, but increasingly of the middle class and the poor. The rate at which diabetes is rapidly spreading round the globe among all peoples, regions and nations is extremely worrisome despite the innovative strides in medical sciences. It is now pandemic and demand global response to contain the ravaging inferno. According to Margaret [19], the Director General of World Health Organization:

> "Diabetes is on the rise. No longer a disease of predominantly rich nations, the prevalence of diabetes is steadily increasing everywhere, most markedly in the world's middle-income countries.
>
> Unfortunately, in many settings the lack of effective policies to create supportive environments for healthy lifestyles and the lack of access to quality health care means that the prevention and treatment of diabetes, particularly for people of modest means, are not being pursued.
>
> When diabetes is uncontrolled, it has dire consequences for health and well-being.
>
> In addition, diabetes and its complications impact harshly on the finances of individuals and their families, and the economies of nations. People with diabetes who depend on life-saving insulin pay the ultimate price when access to affordable insulin is lacking [19]."

In the United Kingdom, more than two million people in the UK have the disease condition and up to 750,000 more are unaware of having the condition. In the United States 25.8 million people or 8.3% of the population have diabetes. Of these, 7.0 million have undiagnosed diabetes. In 2010 for example, about 1.9 million new cases of diabetes were diagnosed in population over 20 years. It is strongly argued that if this trend goes unchecked, it will be most probable that 1 in 3 Americans would be diabetic by 2050. This is critical and has grave consequences not only on national, regional, international, socio-cultural, economic and political affairs of nations but on the whole survival and longevity of the human race.

According to World Health Organization (WHO) Fact sheets on diabetes, globally, an estimated 422 million adults were living with diabetes in 2014, compared to 108 million in 1980. The global prevalence (age-standardized) of diabetes rose from 4.7% to 8.5% in the adult population since 1980. This reflects an increase in associated risk factors such as being overweight or obese. The consequences of diabetes in recent times have become not only chronic but increasingly fatal. Diabetes caused 1.5 million deaths in 2012. Higher-than-optimal blood glucose caused an additional 2.2 million deaths, by increasing the risks of cardiovascular and other diseases. Forty-three percent of these 3.7 million deaths occur before the age of 70 years. The percentage of deaths attributable to high blood glucose or diabetes that occurs prior to age 70 is higher in low- and middle-income countries than in high-income countries [20]. The basic facts about Global Diabetes according to WHO Report are summarized as follows:

Basic facts

- The number of people with diabetes has risen from 108 million in 1980 to 422 million in 2014.
- The global prevalence of diabetes among adults over 18 years of age has risen from 4.7% in 1980 to 8.5% in 2014.
- Diabetes prevalence has been rising more rapidly in middle- and low-income countries.
- Diabetes is a major cause of blindness, kidney failure, heart attacks, stroke and lower limb amputation.
- In 2016, an estimated 1.6 million deaths were directly caused by diabetes. Another 2.2 million deaths were attributable to high blood glucose in 2012.
- Almost half of all deaths attributable to high blood glucose occur before the age of 70 years. WHO estimates that diabetes was the seventh leading cause of death in 2016.
- Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use are ways to prevent or delay the onset of type 2 diabetes.
- Diabetes can be treated and its consequences avoided or delayed with diet, physical activity, medication and regular screening and treatment for complications [21].

WHO Intervention

World health Organization (WHO) is an international agency of the United Nations Organization. It was constitutionally created by the United Nations on April 7, 1948 to respond to growing need for global health and sustainable livelihood. WHO is working with 194 Member States, across six regions, and from more than 150 offices, and with a workforce of over 7000 people across the world who are united in a shared commitment to build a better, healthier future and secured health for everyone, everywhere. The headquarters is in Geneva, Switzerland.

The primary role is to direct and coordinate international health within the United Nations system which focuses on international public health systems; health through the life-course; noncommunicable and communicable diseases; preparedness, surveillance and response, supporting national health policies and strategies, coordinate the efforts of governments and partners – including bi- and multilaterals, funds and foundations, civil society organizations and the private sector and corporate services (WHO, 2018). As coordinating authority on international health within the United Nations, WHO works on the following programme specific areas:

International Health systems World Health Organization prioritizes public health systems and is moving towards universal health coverage. WHO works together with policy-makers, global health partners, civil society, academia and the private sector to support countries to develop, implement and monitor solid national health plans. In addition, WHO supports countries to assure the availability of equitable integrated people-centred health services at an affordable price; facilitate access to affordable, safe and effective health technologies; and to strengthen health information systems and evidence-based policy-making.

Non communicable diseases Non communicable diseases (NCDs), including heart disease, stroke, cancer, diabetes and chronic lung disease, and mental health conditions - together with violence and injuries - are collectively responsible for more than 70% of all deaths worldwide. Eight out of 10 of these deaths occur in low- and middle-income countries. The consequences of these diseases reach beyond the health sector and solutions require more than a system that prevents and treats disease.

Promoting health through the life-course Promoting good health through the life-course cuts across all work done by WHO, and takes into account the need to address environment risks and social determinants of health, as well as gender, equity and human rights. The work in this biennium has a crucial focus on finishing the agenda of the Millennium Development Goals and reducing disparities between and within countries.

Communicable diseases WHO is working with countries to increase and sustain access to prevention, treatment and care for HIV, tuberculosis, malaria and neglected tropical diseases and to reduce vaccine-preventable diseases. MDG 6 (combat HIV/AIDS, malaria and other diseases) has driven remarkable progress but much work remains.

Preparedness, surveillance and response During emergencies, WHO's operational role includes leading and coordinating the health response in support of countries, undertaking risk assessments, identifying priorities and setting strategies, providing critical technical guidance, supplies and financial resources as well as monitoring the health situation. WHO also helps countries to strengthen their national core capacities for emergency risk management to prevent, prepare for, respond to, and recover from emergencies due to any hazard that pose a threat to human health security.

Corporate services Corporate services provide the enabling functions, tools and resources that make all of this work possible. For example, corporate services encompasses governing bodies, convening Member States for policymaking, the legal team advising during the development of international treaties, communications staff helping to disseminate health information, human resources – bringing in some of the world's best public health experts and/or building and promoting valuable services. With respect to non communicable diseases, particularly diabetes, WHO aims to stimulate and support the adoption of effective measures for the surveillance, prevention and control of diabetes and its complications, particularly in low and middle-income countries. To this end, WHO:

1. provides scientific guidelines for the prevention of major non communicable diseases including diabetes;
2. develops norms and standards for diabetes diagnosis and care;
3. builds awareness on the global epidemic of diabetes, marking World Diabetes Day (14 November); and
4. conducts surveillance of diabetes and its risk factors.

The WHO "*Global report on diabetes*" provides an overview of the diabetes burden, the interventions available to prevent and manage diabetes, and recommendations for governments,

individuals, the civil society and the private sector. WHO maintains that as part of the 2030 Agenda for Sustainable Development, member countries have set an ambitious target to

(a) reduce premature mortality from NCDs – including diabetes – by one third;
(b) achieve universal health coverage and,
(c) provide access to affordable essential medicines – all by 2030.

In the same vein, WHO "*Global strategy on diet, physical activity and health*" focuses on population-wide approaches to promote healthy lifestyle including good and affordable diet and regular physical activity, thereby reducing the growing global problem of overweight and obesity among peoples [22].

Impact of Diabetes

Diabetes has serious consequences and exerts enormous impact on both the patients' health and socioeconomic relations and the entire human community. Complications arising from the overall health risk may include general morbidity, heart attack, stroke, kidney failure, leg amputation, vision loss, nerve damage and eventual painful death. In pregnancy, poorly controlled diabetes increases the risk of fetal death and other complications even to the pregnant mother.

Apart from its direct economic toll on the patients, its socioeconomic impact on aggregate economy of family and friends, community and nation, health system and providers including the ever fluctuating price of drugs and administration abound. WHO indicates that while the major cost drivers are hospital and outpatient care, a contributing factor is the rise in cost for analogue insulins which are increasingly prescribed despite little evidence that they provide significant advantages over cheaper human insulins. In most developing and poor income countries with analogue and grossly insufficient, inefficient and unregulated healthcare systems and policy frameworks, the situation is more precarious for all types of diabetic conditions than in advanced economies with comparatively advanced healthcare systems and providers [23].

Prevention of Diabetes

WHO advocates for effective mechanisms and approaches that can prevent the incidence and significantly mitigate the complications of diabetes (Type 2) and need for concerted efforts in critical research and development. These include policies and practices across whole populations and within specific settings (school, home, workplace) that contribute to good health for everyone, regardless of whether they have diabetes, such as exercising regularly, eating healthily, avoiding smoking, and controlling blood pressure and lipids.

Lifestyle changes and implementing proactive life-course perspective are paramount to preventing type 2 diabetes as well as other health conditions. It is vital to make this lifestyle changes and proactive life-course programmes early in life when eating and physical activity habits are formed and when the long-term regulation of energy balance may be programmed. This will enhance needed intervention to mitigate the risk of obesity and type 2 diabetes later in life. This is a key prevention mechanism not only for diabetes but for most critical health conditions. [24].

Intervention/Management of Diabetes

Intervention is an integral policy framework that is targeted and implemented timely and early in life. No single policy or intervention programme can ensure total success. It calls for a whole-of-government and whole-of-society approach in which all sectors systematically consider the health impact of policies in trade, agriculture, finance, transport, education and urban planning – recognizing that health is enhanced or obstructed as a result of policies in these and other areas.

The key to successful management of diabetes and other critical NCDs is early diagnosis – the longer a person lives with undiagnosed and untreated diabetes, the worse the health outcomes and complications. As such, easy access to basic diagnostics, such as blood glucose testing, should be made available in primary health-care centres in rural and urban settings. Effective referral systems

and clinics are needed, as patients will need periodic specialist back-and-forth assessment or treatment for complications. For those who are diagnosed with diabetes, a series of cost-effective interventions can improve their outcomes, regardless of what type of diabetes they may have. These interventions include blood glucose control, through a combination of diet, physical activity and, if necessary, medication; control of blood pressure and lipids to reduce cardiovascular risk and other complications including regular screening for damage to the eyes, kidneys and feet.

Diabetes management can be strengthened through the use of standards and protocols. Efforts to improve capacity for diagnosis and treatment of diabetes should occur in the context of integrated non-communicable disease (NCD) management to yield better outcomes. At a minimum, diabetes and cardiovascular disease management can be combined. Integrated management of diabetes alongside other critical health conditions should be considered. Intervention especially in low-income countries should include national capacity and political will to provide critical health facilities in rural and urban settings, access and availability to affordable drugs, provision and access to basic technologies needed to help people with diabetes properly manage their disease, funding and effective policy implementation and overall capacity building for healthcare professionals and stakeholders.

METHODS

Study Selection

Search for articles written in English was carried out using PubMed Central (PMC), African Journal On Line (AJOL), Science Direct, Connecting Repositories (CORE) and Google Scholar. The search was limited to studies carried out from 1998 to 2018. MeSH headings were used to search for the following terms: 'diabetes mellitus', 'prevalence', 'treatment', and 'Nigeria ' including related words like 'management', 'glucose metabolic disorder', and 'hyperglycaemia'. Bibliographies of each article were also searched to in order to identify other articles could be included in the study. The last search was carried out on the 30th day of September, 2018 and a total of 43 studies were included in this review.

Inclusion Criteria

Studies that were included in this review were:

i. population studies, hospital and clinic based studies in which FPG, RPG, OGTT, or HBA1c was used as basis for diagnosing diabetes.

ii. studies that were carried out between 1998 and 2018.

iii. studies that reported prevalence rates of type 2 diabetes mellitus.

iv. studies that consisted of populations that were aged 2 years and above.

v. hospital based studies that listed the drugs that were used for the treatment of type 2 Diabetes Mellitus and their utilization rates in percentages.

Exclusion Criteria

Studies that were excluded from this review were:

i. Studies that were carried out to determine the prevalence of type 1 diabetes only or gestational diabetes.

ii. Studies in which diagnosis of diabetes was based on self reporting.

ii. Studies that were carried out before 1998 and after September 2018.

Ethical approval

This study was not carried out directly on humans but made use of cross-sectional and hospital based studies that were carried out by other researchers. Hence, there was no need to obtain ethical clearance from an Ethics Committee.

Case Definition

The diagnostic criteria used in the prevalence study were:

i. Fasting Plasma Glucose ≥ 126 mg/dl (7mmol/l). Fasting refers to no caloric intake for at least 8 hours.

ii. Random Plasma Glucose ≥ 200mg/dl (11.1mmol/l) in patients with classic symptoms of hyperglycemia or hyperglycemic crisis,

iii. Plasma glucose 2 hour post-glucose load (75g) ≥ 11.1 mmol/l. A glucose load

that contains the equivalent of 75 g anhydrous glucose dissolved in water should be used and carried out as described by the World Health Organization

iv. Glycated Haemoglobin (HbA1c) ≥ 6.5% (WHO, 1999 ; ADA, 2010). The test should be performed in a laboratory using methods that are NGSP (*National Glycohemoglobin Standardization Program*) certified and standardized to the DCCT (Diabetes Control and Complications Trial) assay.

Study Selection

Databases searched were PubMed Central (PMC), African Journal On Line (AJOL), Science Direct, and Connecting Repositories (CORE). Google scholar was also searched. As shown in the PRISMA flow chart (Figure 2.1), 159 studies were identified from all database searches which consists of PMC (71articles), AJOL (73 articles), Science Direct (13 articles) and CORE (2 articles).

In addition, 12 articles were identified from Google Scholar Searches. In all, 171 articles were identified out of which 82 were duplicates of previously identified studies and were removed from the pool of studies. The abstracts of the remaining 89 studies were screened and 36 of them did not meet the inclusion criteria and were excluded from the pool of studies. Studies that were excluded include:

a. Studies that were carried out to determine the prevalence of type 1 diabetes only or gestational diabetes (14 articles).

b. Studies in which diagnosis of diabetes was based on self reporting (12 articles).

c. Studies that were case reports, and editorials (10 articles).

This further reduced the number of articles left for review to 53. The full text articles of these 53 studies were then assessed for eligibility and 15 were excluded due to the following reasons:

a. studies that were not representative of the general population in which the study was carried out (7 articles).

b. studies without case definitions (8 articles).

Finally, the 38 studies left were then used for the systematic review. This process is described in the PRISMA Chart displayed below (Figure 2.1).

Data Collection

A modified Data extraction form was used to extract data. This extraction form was pilot tested with the first 10 studies assessed. Items that were extracted from each study include: year of study, state/geopolitical zone where the study was carried out, age of the study participants, sampling method, sample size, response rate, setting, case definition, and prevalence of diabetes.

Data was extracted by the main researcher and a co-researcher and where there were obscurities, both researchers clarified them through useful discussions.

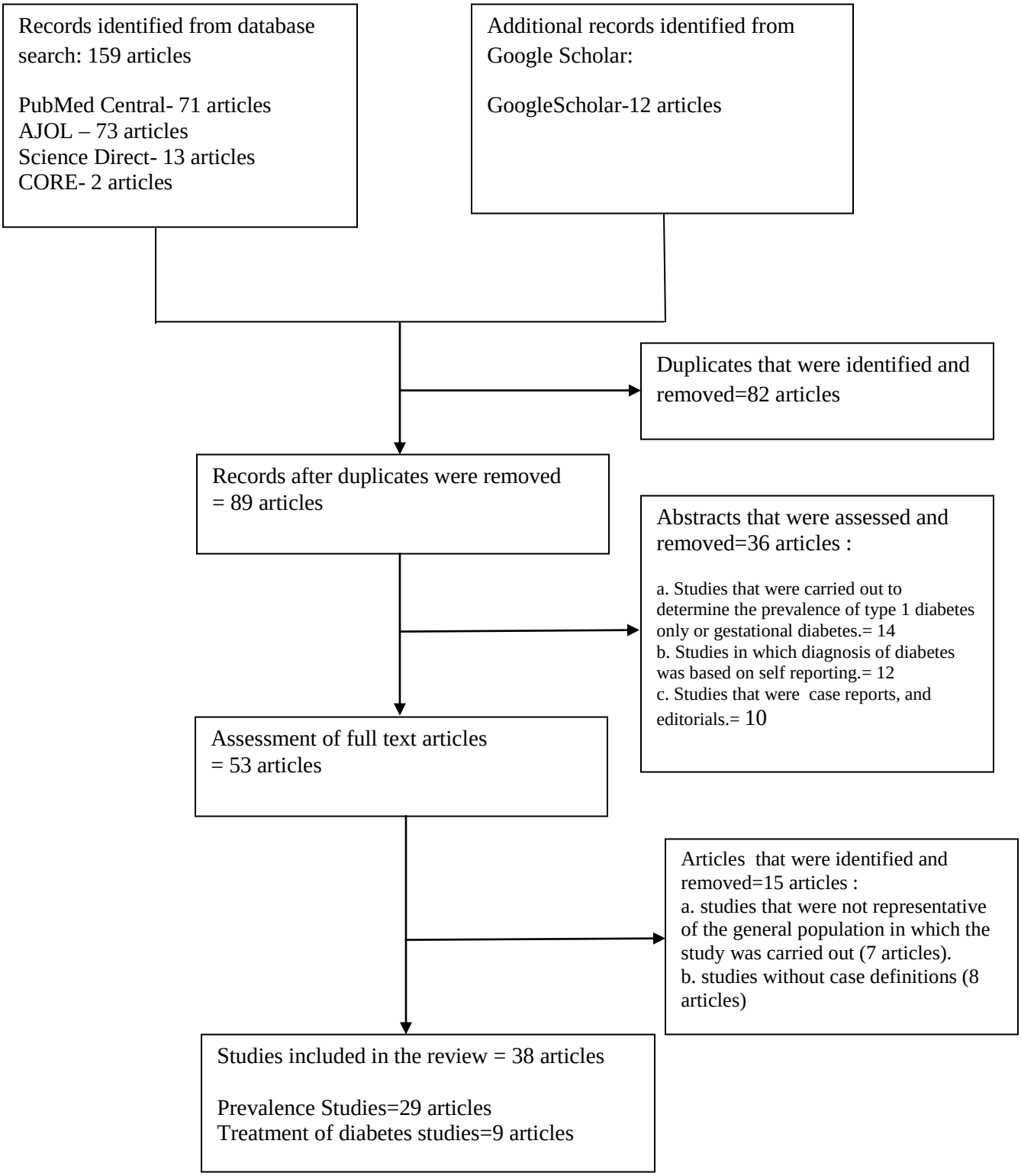

Fig 1: Flow Chart of the Studies included in the Systematic Review

Synthesis and Statistical Methods

No statistical analysis was carried out because this study is a systematic review. We were interested in describing the changes in prevalence data across different geopolitical zones of Nigeria and in critically appraising the included studies to give a wider view of the problem in Nigeria.

Analysis of the treatment data was more of a narrative synthesis which describes the types of antidiabetic drugs that are used in Nigeria and their utilization pattern. Hence, no statistical analysis was carried out.

RESULTS

Thirty eight independent studies were included in this review. Twenty nine studies were prevalence studies while nine studies were articles that dealt with the treatment of diabetes in Nigeria. These studies were published between the year 1998 and 2018.

Systematic Review of Prevalence of Type 2 Diabetes Mellitus

Table 1 shows the characteristics of all studies included for this review with the prevalence
of diabetes reported for each study.

Twenty nine studies were conducted across the 6 geopolitical zones of Nigeria. The numbers of studies carried out in each zone include: south- south (10 articles), south-west (8 articles) south-east (4 articles), north-central (3 articles); north-west (2 articles) , north-east (1 article), and 1 study which was carried out in all the states and capital of Nigeria.

The included studies were generally large; the community studies that were carried out were 22, the hospital based studies were 4 ; Secondary school was 1, Staff of University was 1 and 1 study was carried out amongst oil company staff together with some university students/staff. Sample sizes of studies ranged from 105 to 18,921. The setting where the studies were conducted included urban (14 studies), rural (8 studies), mixed (ie both rural and urban populations were used- 3studies) including semi urban (4 studies).

The age of participants ranged from 1 to 102 years old. Only 1 study was carried out solely on the adolescent age group- 10 to19 years old with a prevalence of 0.6%. The highest prevalence was 23.4% in the South-South region.

Table 1 Characteristics of all studies included in the Systematic Review for Prevalence Study

S/N	First Author	Setting	Year	Diagnostic method	Age Range/ Mean	Sample Size	Prevalence(%)		
							General	Male	Female
SOUTH-SOUTH									
1.	Nwafor A	Urban Oil company staff; university students and staff	2001	FPG, RPG	17 – 60	403	High SES- 23.4% Low SES - 16%	7.63	8.4
2.	Nyenwe E.A	Rural/ Urban Community	2003	RPG 2hr-Pg	>40	502	6.8	7.7	5.7
3.	Ojehanon P.	Urban	2006	FPG	15 – 75	1570	4.5	57.1	42.9

		Hospital							
4.	*Unachukwu C.N*	Urban Hospital	2008	FPG,RPG	≥ 10	6574	10.4	62.4	37.6
5.	Ekpenyong C.E	Urban Community	2012	RPG, FPG 2hr-pG	18-60	3500	12.7	9.7	16.0
6.	Enang O.E	Urban Community	2014	FPG/RPG	≥ 15	1134	6.5	7.1	4.7
7.	Alikor C.A	Rural Community	2015	FPG	41.32 ± 17	500	2.2	2.6	2.0
8.	Okafor U.H	Rural Community	2015	RPG	≥ 18	105	8.1		
9.	Isara A.R	Rural Community	2015	FPG	18 – 90	845	4.6	1.9	5.8
10	Oguoma V.M	Rural/ Urban Community	2017	FPG	18-89	2447	3.1	Nr	Nr
SOUTH-WEST									
11	Olatunbosun P.O	Urban Community	1998	2hr-pG	≥ 15	875	0.8	57	42.9
12	Adebayo A.M	Urban Community	2011	RPG	≥ 2	302	3.0	3.1	2.9
13	Ayodele O.E	Urban Community	2011	FPG/RPG	42.4 ± 11.2	586	3.8	59.1	40.9
14	Ogunmola O.J	Rural Community	2013	FPG	≥ 40	104	4.8	0	7
15	Oluyombo R.	Semi-Urban Community	2014	FPG	≥ 18	750	6.8	8.6	6.0
16	Oluwayemi O.I	Semi-Urban Community	2015	FPG	10 – 19	628	0.6	Nr	Nr
17	Adeoti A.O	Urban Hospital	2015	FPG, RPG, 2hr-pG	16 – 102	3,750	18	Nr	Nr
18	Rasaki O.S	Rural Community	2017	FPG	≥ 18	10,000	4.6	6.3	93.7
SOUTH-EAST									
19	Okafor C.N	Rural community	2014	FPG	≥ 18	137	8.8	*	8.8

20	Ejike C.C	Semi-Urban Community	2015	FPG	30 – 74	365	3.0	2.3	3.6
21	Adogu P	Urban Hospital	2015	FPG/RPG	≥ 1	18912	10.7	52.1	47.9
22	Okwuonu C.G	Semi-Urban community	2017	FPG/RPG	<20-≥60	328	7.9	7.2	8.5
*only women were used in this study									
NORTH-CENTRAL									
23	Puepet	Urban Community	2008	2hr-pG	≥ 15	902	4%		
24	Etukumana E	Rural Community	2013	FPG,RPG	≥15	750	4.1	5.2	3.0
25	Agaba E.I	Urban University staff	2017	FPG	≥ 18	883	8%	6.9	9.7
NORTH-WEST									
26	Bello-Ovosi B.O	Urban Community	2018	RPG	23 – 87	181	23.3	9	33
27	Sabir A.	Rural community	2013	FPG,RPG,2 hr-Pg	18-95	393	0.8	0.3	0.5
NORTH-EAST									
28	Gezawa I.D	Urban Community	2015	FPG	15-70	242	7.0	10.4	4.8
ACROSS ALL STATES AND THE CAPITAL									
29	Kyari F.	Rural/Urban Community	2014	RPG	≥ 40	13,591	3.3	3.9	2.7

Systematic Review of the Treatment of type 2 Diabetes Mellitus

Table 2 displays relevant information about the studies included for the review. 9 studies were used in carrying out the systematic review. All studies were carried out across 4 regions of the country. 4 of the studies were carried out in the South-West while only 1 study was carried out in the South-East region, North-Central and North-East regions respectively. 6 of these studies were carried out in Teaching Hospitals, while 1 study was carried out in a private health facility. The sample size of the studies used in this review ranges from 115 to 349. The studies were carried out between 2006 and 2017. Oral antidiabetes medications were generally more used than insulin with rates of 71% in UCH, 85.7% in OAUTH and 76.5% [25]; [26]. The utilization rates of insulin were 26.4%, 2.5%, 8.2%, 0.6% and 7.7% [27]. Out of all 5 studies in which utilization rates of biguanide/metformin was reported, 4 studies reported that the Biguanides/metformin were the most utilized of all the antidiabetic

medications, with utilization rates of 65.9%, 55.8%, 58.7%, and 76.9% [12]; [13]; [14]; [15]. Only 1 study reported low utilization rate of biguanide/metformin (4.2%) [22]. 2 studies reported the percentage of patients that were prescribed more than 4 medicines as 55.2%, 53.3% and 73.0% [1]; [3].

Table 2 Studies included in the Systematic Review for treatment of Type 2 Diabetes Study

	First Author	Setting	Year	Study Design	Sample Size	Drugs Prescribed	Drug utilization (%)
1	Enwere O.O	UCH	2006	Cross-Sectional	349	Biguanides	65.9
						Sulphonylureas	54.2
						Insulin	26.4
2	Uwakwe J.N	Private Health Facility in Jos	2009	Retrospective	120	Biguanide only	4.2
						Sulphonylurea alone	18.3
						Biguanide + sulphonylurea	60.8
						Biguanide + sulphonylurea + thiazolidinedione	3.3
						Insulin + biguanide	10.8
						Insulin alone	2.5
3	Adisa R.	UCH & OAUTH	2013	Cross sectional	170	OAM	76.5%
						OAM + Insulin	15.3%
						Insulin alone	8.2%
						Single OAM	
						Metformin	9%
						Glimepiride	1.3%
						Others: Glibenclamide, gliclazide, Rosiglitazone, Pioglitazone, voglibose, acarbose	0%
						Glyburide/Metformin (Fixed)	1.3
						Glimepiride/Metformin (Fixed)	1.3
						Pioglitazone/Metformin (Fixed)	8.4

						Glibenclamide + Metformin (Nonfixed/co-administered)	33.4	
						Glimepiride + Metformin (Nonfixed/co-administered)	23.9	
						Glimepiride + Pioglitazone (Nonfixed/co-administered)	1.2	
						Gliclazide + Metformin (Nonfixed/co-administered)	0.6	
						3- OAM combination		
						Glimepiride + Metformin + Pioglitazone	12.9	
						Glibenclamide + Metformin +Pioglitazone	7.1	
4	Ogbonna B	NAUTH	2014	Retrospective	286	Metformin	55.8	
						Glibenclamide	35.1	
						Pioglitazone	6.8	
						Glimepiride	1.0	
						Gliclazide	0.8	
						Insulin	0.6	
5	Fadare J	LAUTH	2015	Cross-Sectional	129	Metformin	58.7	
						Glibenclamide	25.9	
						Glimepriride	13.8	
						Vidagliptin	1.1	
						Pioglitazone	0.5	
						Combination Oral Hypoglycaemic Agent(OHA) therapy	57.4	
						OHA and insulin	14	
						Metformin only	11.6	
							UCH	**OAUTH**
6	Adisa R.	UCH & OAUTH	2016	Prospective	185	OAM	71	85.7
						OAM + Insulin	15.9	14.3
						Insulin alone	13.1	0%
						≤ 4 meds	46.7	27.0

						>4 meds	53.3	73.0
						Generic versus proprietary prescription		
						Exclusively generic medications	71.7	39.7
						Exclusively proprietary medications	12.3	15.9
						Generic plus proprietary medicine	16	44.4
7.	Okoro R.N	UMTH Maiduguri	2017	Retrospective	115	Monotherapy n=26		22.6%
						Metformin		76.9
						Glimepiride		7.7
						Vildagliptin		7.7
						Insulin		7.7
						Dual Therapy n =74		64.35%
						Metformin,Glibenclamide		63.5
						Metformin,Glimepiride		21.6
						Metformin,Vildagliptin		9.5
						Glibenclamide,Vildagliptin		2.7
						Metformin,Insulin		2.7
						Triple therapy n =3		2.61%
						Metformin, Glibenclamide, Insulin		33.3
						Metformin,Glibenclamide,Piog litazone		33.3
						Metformin,Glibenclamide,Vild agliptin		33.3

						Fixed Dose Combination n = 12	10.43%
						Metformin + Glibenclamide	66.7
						Metformin + Vildagliptin	33.3
8	Olurishe C	ABUTH	2012	Retrospective	110	Sulphonylureas	1.81
						Biguanides	10
						Sulphonylureas/ Biguanides	49.09
						Sulphonylureas/ biguanides/glitazones	17.27
						Fixed dose(Sulphonyl Ureas/Biguanides)	8.18
						Insulin/oral hypogly caemic agents	10.90
						Insulin	2.72
9	Jimoh A	UDUTH	2012	Cross-Sectional	348	Metformin+Glibenclamide	76.7
						Metformin+Glibenclamide+pio glitazone	10.6
						Metformin+Glibenclamide+ins ulin	5.2
						Metformin+pioglitazone	3.7
						Metformin+insulin	0.9
						Metformin + Gliclazide	2.0
						Pioglitazone + Glibenclamide	0.9

Nr-not reported

DISCUSSION

Studies were carried out in the south than the north. Similar findings have been reported in a review carried out by [7]. In addition, the urban areas/areas of higher socioeconomic status recorded higher prevalence of diabetes mellitus than the rural areas/ areas of lower socioeconomic class. This is as a result of urbanization which results in sedentary lifestyle and poor diet in the urban areas. Similarly, this same finding was reported in a review carried out by [4].

The highest prevalence recorded in this review was from the south-south zone with a prevalence of 23.4% among the workers of the Agip Oil Company, Port Harcourt [2]. On the other hand, the lowest prevalence occurred among Secondary School adolescent students in the South West Zone with a prevalence of 0.6% [8].

Only 3 of the 29 studies included in this systematic review had prevalence rates (0.8%, 0.6%, 0.8%) that were lesser than the prevalence rate of 2% that was reported by the IDF [4]; [5]; [6]. This shows that reports from the IDF which are usually gotten from projections of prevalence rates in countries may actually underestimate the true prevalence of the disease in Nigeria.

It was also observed that there was a dearth of studies carried out in the Northern part of the country especially in the North-East region. Hence, researchers should be motivated by policy makers to carry out studies that focus on determining the prevalence of diabetes in this geopolitical zone.

In general, the age groups with the highest prevalence rates were reported to be: ≥ 35 years ,41-50 years, 45 – 64 years, 51 – 60 years, 55 – 64 years and 61- 70 years [1]; [2]; [3]; [4]; [5]; [7]. On the other hand, the lowest prevalence rates were recorded in the following age groups: 1-10 years & 11 – 20 years, < 20 years, 25 – 34, < 30 years, < 35 years and < 45 years [9].

With regards to prevalence in females and males, no specific trend was noticed, that is, no remarkable difference between the prevalence pattern in males and females was observed between these 2 groups.

Discussion for the treatment of diabetes mellitus

Biguanide (Metformin) was the most prescribed of all medications used in treating Type 2 Diabetes Mellitus (either singly or as a combination) in all the studies carried out in teaching hospitals except for the private health facility where the sulphonylureas (when used singly) were the most prescribed oral antidiabetic medication. This is in tandem with what is obtainable in other parts of the world where metformin is also the most utilized antidiabetic [9]. However, in some other studies, sulphonylureas where the most prescribed class of antidiabetics [18]

In this review, studies that reported use of combination therapy, recorded that the combination of biguanide (metformin) and sulphonylurea (glibenclamide) were the most prescribed. In the same vein, it has been reported that metformin and glibenclamide were the most prescribed antidiabetics in other studies carried out in Brazil and India [15]; [16]. On the contrary, in some other countries, metformin plus glimepiride is more used than metformin plus glibenclamide [12]; [13]. Also, majority of patients were prescribed more than 4 medications.

Combination of oral antidiabetic medications were used more than the combination of Oral Antidiabetic Medications and Insulin. This result was similar to results gotten from an antidiabetic drug utilization study carried out in India by [15]. In Mandal's study it was reported that Oral hypoglycemic agents were preferred to Insulin as monotherapy as well as in combination with other oral hypoglycemics. Similarly, another study reported that dual combination therapy was prescribed more than combination of oral hypoglycaemics and insulin [17].

As observed in our review, proprietary or brand prescribing was also practiced at UCH and OAUTH but the frequency of its practice was recorded in less than one quarter of all the prescriptions studied in each of these hospitals [24]. Similar result was recorded by Sarumathy et al in another study carried out in India [27]. Results that are not similar to that reported in our study has also been recorded in India in which majority of drugs prescribed were in their brand names [25]. In fact, in 2 other studies carried out in India and Bangladesh, all the drugs prescribed were written in their brand names [3]; [4].

In addition, this review revealed that about 10% of all drugs prescribed in the University of Maiduguri Teaching Hospital were fixed dose combination drugs.

However, in some studies carried out in other climes, the fixed dose combination preparations were the most prescribed [7]; [8]; [9]. Fixed dose combination preparations will reduce pill burden and improve adherence but cost and affordability should be considered when prescribing FDC preparations.

In conclusion, the result from our study reveals that the drugs prescribed for Type 2 Diabetes Mellitus in Nigeria is in line with current International Diabetes Federation (IDF) Clinical Practice Recommendations for managing Type 2 Diabetes in Primary Care. However, this IDF document also states that sulphonylureas are appropriate as combination or add-on therapy, except for glyburide or glibenclamide (IDF, 2017). Studies have also been carried out in support of this recommendation. A study carried out by Riddle revealed that early mortality with the use of glyburide/glibenclamide was almost 3-fold higher than when glimepiride or gliclazide were used [21]. In other studies, glyburide/glibenclamide was also associated with a higher risk of hypoglycaemia than other sulphonylureas like glipizide or glimepiride [10]; [11]. Hence, caution should be exercised by Nigerian practitioners when considering the use of glyburide/glibenclamide in treatment of their patients, especially the elderly who are at high risk of hypoglycaemia.

Some of the studies reviewed, used insulin as one of the drugs in their dual antidiabetic combination therapy [7]This practice is not in line with that projected by the IDF. The IDF recommends the use of 2 oral hypoglycaemic agents and it also states that insulin should only be added to make up a triple therapy. The IDF also recommends the use of 3 oral hypoglycemic agents.

In addition, the IDF supports the use of fixed combination therapy whenever possible since it promotes patient's adherence to therapy (IDF, 2017). However, majority of Nigerians may not be able to afford fixed combination therapy. The low use of fixed combination therapy observed in this review may be because of its high cost. Since diabetics are meant to be on their medication for a lifetime, the cost of their medication is a very crucial factor in their management and hence health practitioners should take cost into consideration when prescribing antidiabetic drugs. This is very important in a country like Nigeria where the minimum wage of her citizens is $49 and where there is minimal health coverage for her masses- less than 5% of Nigerians have health insurance coverage [20].

CONCLUSION

Generally, the prevalence of Type 2 Diabetes Mellitus is on the increase in Nigeria, most especially in regions of higher socioeconomic status and in the urban areas. Type 2 Diabetes Mellitus is also more prevalent in older age groups than in the younger age groups. Notwithstanding, Diabetes Mellitus was also observed among some adolescents in the South-West zone. In addition, no particular trend was observed when prevalence in males and females were compared.

The treatment of Type 2 Diabetes is in tandem with current treatment guidelines in most areas, but care and caution should be taken in these specific areas that are not recommended by the guidelines, though are practiced by majority of the health practitioners in Nigeria:

i. use of glibenclamide/glyburide either as combination or add-on therapy with metformin.

ii. use of insulin in dual combination therapy.

RECOMMENDATION

1. The Research Institutes should carry out more researches in the area of prevalence and treatment of Type 2 Diabetes Mellitus regularly as this will help in reducing the prevalence of Type 2 Diabetes Mellitus. More prevalence studies carried out in different regions of Nigeria will provide evidence that will enable the policy makers to better plan budgets that are specific to the medical

needs of a particular region. In the same vein, more treatment/drug utilisation studies should be carried out so that lapses in our treatment protocols are easily noticed and corrected so as to ensure proper management of diabetic patients in Nigeria.

2. Therapeutic Committees should be reinvigorated and mobilized to carry out routine critical assessment of Type 2 diabetic patients prescriptions. This will enhance and enable the prompt detection and correction of prescription errors. In the long run, it will reduce significantly the patient's risks of developing complications (and burden to the society) that arise from Type 2 Diabetes Mellitus.

3. The policy makers should encourage intercollaboration between the Ministry of Education, Ministry of Health, and Ministry of Agriculture towards combating the incidence of Type 2 Diabetes Mellitus. Campaigns and Seminars should be organized aimed at promoting healthy lifestyle and preventing the disease among Nigerians. Topical issues such as proper diet, importance of exercise/dangers of living a sedentary lifestyle, early detection and screening, recognition of signs and symptoms of the disease and complications of the disease should be highlighted. The target population should also include children and not only adults because in recent times, Type 2 Diabetes have also been detected in children.

4. The Government should create an enabling environment that will help in fostering a healthy lifestyle. E.g. in the workplace and schools, specific periods should be set aside for exercise; time for games should be set aside in the schools; fields and pedestrian tracks where individuals can exercise themselves should be set up by the Government. All these will help to curb the increasing prevalence of obesity which is a risk factor to Type 2 Diabetes Mellitus. The Government can also increase the tax paid by alcohol breweries and industries that produce food items that predispose individuals to Type 2 Diabetes Mellitus. This will prevent people from purchasing these products since the cost of purchasing these items will also be high

5. Since diabetic patients have to be on their drugs for as long as they live, the Government should organize a special type of insurance program for them. This will enable them take their drugs as required and thus reduce their risk of developing complications and thus will help reduce the burden of the disease in Nigeria..

6. The capacity of the ministries of health should be strengthened to exercise a strategic leadership role and engage stakeholders across various sectors and society. Set national targets and indicators to foster accountability. Ensure that national policies and plans addressing diabetes are fully costed and then funded and implemented.

7. Strengthen the health system response to NCDs (Non Communicable Diseases), including diabetes, particularly at primary-care level. Implement guidelines and protocols to improve diagnosis and management of diabetes in primary health care. Establish policies and programmes to ensure equitable access to essential technologies for diagnosis and management. Make essential medicines such as human insulin available and affordable to all who need them.

REFERENCES

1. Adeloye, D., Ige, J., Aderemi, A., Adeleye, N., Amoo, E., Auta, A., and Oni, G. (2017). Estimating the prevalence, hospitalisation and mortality from type 2 diabetes mellitus in Nigeria: a systematic review and meta-analysis. *British Medical Journal Open* ;7:e015424. doi:10.1136/bmjopen-2016-015424.
2. Allan, F. Diabetes before and after insulin. *Med Hist*. Jul; 16 (3): 266 – 273. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1034981/. Accessed on 3rd September, 2018
3. American Diabetes Association. (2010). Diagnosis and classification of diabetes: diabetes care. *Diabetes Care.*;33(Suppl

1):S62–9. Retreived from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2797383/. Accessed on 18th August, 2018.

4. Bell, G., Pictet, R., Rutter, W., Cordell, B., Tischer, E., and Goodman, H. (1980). Sequence of the human insulin gene. *Nature;* 284, : 26–32. Retrieved from: https://www.nature.com/articles/284026a0. Accessed on 6th october, 2018.
5. Chinenye, S., and Young, E. (2011).State of Diabetes Care in Nigeria. *The Nigerian Health Journal.*, 11, pg 101.No 4, October – December. Retrieved from https://www.ajol.info/index.php/nhj/article/viewFile/90531/79950.
6. Gezawa, ID., Puepet, FH., Mubi, BM., Uloko, AE., Bakki, B., Talle, MA., and Haliru. (2015). Socio-demographic and Anthropometric risk factors for Type 2 diabetes in Maiduguri, North-Eastern Nigeria.
7. IDF Africa Region. Retrieved from https://www.idf.org/our-network/regions-members/africa/members/20-nigeria.html. Accessed on 16th August, 2018.
8. IDF. (2017). Diabetes Atlas. 8th Edition. Retreived from https://www.idf.org/e-library/epidemiology-research/diabetes-atlas/20-atlas-5th-edition.html. Accessed on 15th August, 2018.
9. Lakhtakia, R. (2013), "The History of Diabetes Mellitus", Sultan Qaboos University Medical Journal, August, 13(3): 368 – 370; retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3749019/#b4-squmj1303-368-370 Accessed on 25th October 2018.
10. MacCracken, J and Hoel, D. From ants to analogues: Puzzles and promises in diabetes management. *Postgrad Med.* Apr;101(4). 138 – 40. Retrieved from: https://www.ncbi.nlm.nih.gov/pubmed/9126208. Accessed on 1st October, 2018.
11. Mandal, A. (2018). History of Diabetes. News Medical Life Sciences, Retrieved from: https://www.news-medical.net/health/History-of-Diabetes.aspx. Accessed October 20, 2018.
12. Nyenwe, A., Odia, O., Ihekwaba, A., Ojule, A., and Babatunde, S. (2015). Type 2 diabetes in adult Nigerians: a study of its prevalence and risk factors in Port Harcourt, Nigeria. *Diabetes Research and Clinical Practice.* 14 (3): 137 – 142. DOI: https://doi.org/10.1016/j.diabres.2003.07.002
13. Okafor, UH., Ahmed, S, Unuigbe, E. (2015). Screening for risk factors of chronic kidney disease in a community in Niger Delta Nigeria. *Annals of African Medicine.* DOI: 10.4103/1596-3519.149916
14. Sabir, A., Ohwovoriiole, A., Isezuo, S., Fasanmade, O., Abubakar, S., and Sandra Iwuala. (2013). Type 2 Diabetes Mellitus and its Risk Factors among the rural Fulanis of Northern Nigeria *Annals of African Medicine. 12(4)217 – 222. Retrieved from* **DOI:** 14.4103/1596-3519.122689.
15. Saenz A, Fernandez- Esteban I, Mataix A, Ausejo Segura M, Roqué i Figuls M, Moher D. (2005). Metformin monotherapy for type 2 diabetes mellitus. Cochrane Database of Systematic Reviews. Issue 3. Art. No.: CD002966. DOI: 10.1002/14651858.CD002966.pub3.
16. Sahel Medical Journal. 18 (5):1-7. Retrieved from Diabetes.co.uk. Diabetes and Hypoglyceamia. (2018). Retrieved from: https://www.diabetes.co.uk/diabetes-history.html. accessed 10/25/2018
17. Sakula, A. (1988). Paul Langerhans (1847-1888): a centenary tribute. J R SocMed. Retrieved from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3749019/#b4-

squmj1303-368-370 Accessed 5th October 2018.
18. Sattley, M. (2015). The History of Diabetes Mellitus. Retrieved from: https://www.diabeteshealth.com/the-history-of-diabetes. Accessed: 4th September, 2018.
19. Science History Institute. (2017). Frederick Banting, Charles Best, James Collip, and John Macleod. Retrieved from https://www.sciencehistory.org/historical-profile/frederick-banting-charles-best-james-collip-and-john-macleod. Accessed on 6th September, 2018.
20. Uloko, A.E., Musa, B.M., Ramalan, M.A., Gezawa, D.I., Puepet, F.H . Uloko , A.T.... ... Sada, K.B. (2018). Prevalence and Risk Factors for Diabetes Mellitus in Nigeria: A Systematic Review and Meta-Analysis. *Diabetes Ther apy*. 9:1307–1316. Retrieved from: https://doi.org/10.1007/s13300-018-0441-1. Accessed on 2nd September, 2018.
21. Vengurlekar, S., Shukla, P., Patidar, P, Bafna, R., and Jain, S. (2008). Prescribing Pattern of Antidiabetic Drugs in Indore City Hospital**.** *Indian Journal of Pharmaceutical Science.* 70 (5): 637 -640. doi: [10.4103/0250-474X.45404]
22. WHO. (1999). Definition, diagnosis and classification of diabetes mellitus and its complications report of a WHO consultation. Part 1, Diagnosis and classification of diabetes mellitus. Geneva : World Health Organization. http://www.who.int/iris/handle/10665/66040 . Accessed on 18th August, 2018.
23. WHO. (2016). Global Report on Diabetes. Retrieved from: http://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf;jsessionid=A6F5FCE2DCF17FE08C1FA99492C8A54B?sequence=1 Accessed: November 02, 2018.
24. WHO. (2017). Diabetes Fact Sheet. Retreived from http://www.who.int/news-room/fact-sheets/detail/diabetes. Accessed on 15th August, 2018.
25. WHO. (2017). Diabetes Fact Sheet. Retreived from http://www.who.int/news-room/fact-sheets/detail/diabetes. Accessed on 15th August, 2018.
26. WHO. (2018). Diabetes Programme. Retreived from http://www.who.int/diabetes/action_online/basics/en/index3.html. Accessed on 17th August, 2018.
27. Wu, B. (2017). History of Disease: Past treatments and new discoveries. Medical News Today. Retrieve from: https://www.medicalnewstoday.com/articles/317484.php.