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Diabetes management in healthy ageing. A mini review

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Abstract
Diabetes is a common and serious disease. However, the past 50 years have seen a growing ageing population with an increasing prevalence of type 2 diabetes mellitus (DM2). Now, nearly half of all individuals with diabetes mellitus are older adults (aged ≥65 years). Elderly people with diabetes is a heterogeneous group, in many cases the condition of diabetes is accompanied by other chronic diseases, but also by the ability of the elderly themselves to control their blood glucose. The therapeutic treatment of elderly diabetic patients must be done with special attention and a lot of thought. Special importance should be given to exercise with aerobic exercise or alternatively the application of a program of progressive increase in muscle intensity (3-5 times a week), as well as training in proper nutrition with particular emphasis on the Mediterranean diet, which seems to increase survival in adults.

KEYWORDS
DM2, insulin, ageing population

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1. INTRODUCTION

This review article recognizes the three different types of Diabetes Mellitus and focuses on type 2 Diabetes Mellitus (DM2), which occurs mainly in old age. It emphasizes the metabolic disorder that occurs, the complications of DM and the most important factors involved and constitute the risk factors. Key risk factors, including diet, physical activity, environmental pollutants, and sleep are considered guilty for the metabolic dislocations of DM and age-related complications.

Diabetes is a common and serious disease. If this disease is left unchecked, it is predicted that by 2040 approximately 642 million people will suffer from diabetes. In the European Union, the incidence of diabetes varies from 4.0 - 4.5% in Lithuania, Estonia and Ireland whereas in Cyprus, Malta and Portugal is below 10%. Diabetes increases the risk of many serious health problems, including cardiovascular disease, blindness, neuropathy, foot complications, and kidney disease. DM is a metabolic disease characterized by an increase in the concentration of glucose in the blood (hyperglycemia) and a disturbance of glucose metabolism, either as a result of decreased insulin secretion or due to a decrease in the sensitivity of the body's cells to insulin [1]. There are three types of DM.

1.1. Type 1 Diabetes Mellitus

Type 1 Diabetes Mellitus is a disease that usually occurs in adults younger than 20 years and has an autoimmune etiology, that is, the body itself, through the antibodies it produces, attacks and destroys the β-cells of the pancreas, which produce insulin, as a result of which there is little or zero insulin secretion. Approximately 5-10% of all Diabetic patients suffer from Type 1 Diabetes. 85% of cases with type 1 diabetes occur at the age of less than 20 years. The exact etiology of Type 1 Diabetes is not clearly known but the immune system plays an important role. Type 1 Diabetes is characterized by the inability of the body to produce insulin. People with Diabetes of this type must receive exogenous insulin to survive [2,3,4].

1.2. Type 2 Diabetes Mellitus

Diabetes mellitus is one of the most common chronic diseases and is a serious health problem in the world population. According to the most recent international statistics, the number of people with diabetes worldwide is more than 400 million, and it is expected to reach 640 million in 2040. It is a multifactorial disorder of carbohydrate, fat and protein metabolism whose main feature is chronic hyperglycemia [5]. Insulin is a hormone produced in the pancreas that is needed to transport glucose from the blood into the body's cells, where it is used for energy. When insulin is missing or not working properly, blood glucose levels rise [6]. Diabetes mellitus has a chronic course and in the long term can cause serious complications in all tissues and organs, eyes, kidneys, nerves, vessels, legs, heart when glucose levels remain high and are not controlled [7]. It is known that diabetes is the first cause of death from cardiovascular causes, from stroke, from myocardial infarction, so that today a diabetic is considered and treated, even if he has not shown symptoms, as a person with Coronary disease.

1.3. Gestational Diabetes Mellitus

Gestational diabetes is defined as any disorder in carbohydrate metabolism that is diagnosed or appears for the first-time during pregnancy, usually at the end of the second trimester, after the 24th week. During pregnancy the placenta produces hormones that help the fetus grow. These hormones make it more difficult for insulin to work in the body (they cause insulin resistance). In women with gestational diabetes, the pancreas cannot cope with these increased needs, resulting in increased blood glucose levels. Gestational diabetes is common and occurs in 4-8% of pregnancies [8].

2. MAIN COMPLICATIONS OF DIABETES

Diabetes is a chronic, lifelong condition that requires careful control. Without proper treatment, it can lead to hyperglycemia, which is associated with long-term damage to the body and the failure of various organs and tissues. Short-term and long-term complications of diabetes include the following:

Cardiovascular disease: Diseases of the circulatory system including diseases affecting the heart and circulatory system. The most common manifestations of cardiovascular disease include angina, heart attack, heart failure, and stroke. Cardiovascular disease is the leading cause of death in diabetics and the first cause of death in industrialized countries.

Nephropathy: It is a result of the increasing amount of protein in the urine and progresses slowly, possibly resulting in kidney failure. This usually occurs many years after the initial diagnosis of diabetes and can be delayed by strict control of blood pressure and blood glucose. Diabetes has become today the most common cause of renal failure requiring dialysis or kidney transplantation in most developed countries.

Neuropathy: Damage to nerve fibers caused by diabetes. Numbness and loss of sensation in the legs are its most common indication, which is a result of nerve damage in the lower extremities. Neuropathy can sometimes cause severe pain, but is usually not noticed. Even without symptoms, diabetic neuropathy results in a higher risk of lower limb ulcers and amputation.

Retinopathy: Damage to the blood vessels that supply the retina of the eye. The small blood vessels of the retina can be damaged by high blood sugar and high blood pressure. Diabetes is the most common cause of blindness and visual impairment in the working population of the developed world [1,9,10].

However, the past 50 years have seen a growing ageing population with an increasing prevalence of type 2 diabetes mellitus (DM2). Now, nearly half of all individuals with diabetes mellitus are older adults (aged ≥65 years).

3. CAUSES OF DIABETES IN OLD AGE

The ageing process [11,12] is understood as a progressive and normal process characterized by

the reduction of physiological function. Includes changes in its anatomy, physiology and organism adaptability and leads to the degeneration of the organism's ability to regarding its functionality. Figure 1 shows the seven pillars of ageing. A natural outcome of aging is mortality which is related to chronological age. The World Health Organization 1982 defined as the starting age of the Third Age the 60th year in which and the usual commencement of retirement [13].

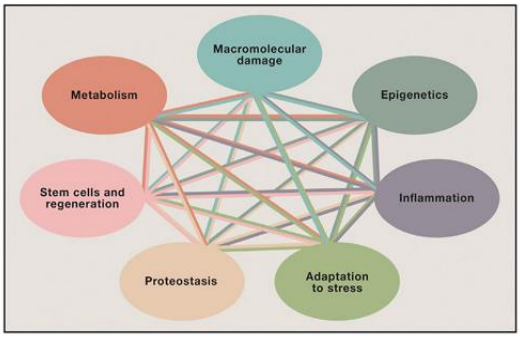

Figure 1: The seven pillars of ageing

Over the age of 65 a percentage of over 20% will develop Diabetes Mellitus, while patients who are at greater risk of complications are those over 75 years of age. The prognosis of Diabetes in elderly people is clearly more difficult compared to their non-diseased peers. In most cases, the diagnosis is made by chance during screening tests, in which high sugar values are observed. A big problem that occurs at these ages is that the doctor is not able to know how long the diabetes has existed before it manifests itself. Measurements prompt that people with diabetes die, on average, 6 years earlier than people without diabetes [14].

One of the main factors in the occurrence of Diabetes Mellitus in the Third Age is the deterioration of glucose tolerance (Figure 2). The tissues in which insulin resistance first appears, meaning the inability of cells to efficiently use normal levels of insulin, are muscle, liver and adipose tissue [15]. Normally insulin obstructs the release of glucose from the liver. However, in case of insulin resistance, the liver falsely releases glucose into the blood. Some individuals have predominantly insulin resistance but mildly impaired insulin secretion, while others have predominantly insufficient insulin secretion with less insulin resistance. Other potentially important mechanisms associated with type 2 diabetes and insulin resistance include: increased lipid breakdown within adipocytes, incretin deficiency and incretin resistance, high blood glucagon levels, increased salt and water retention by the kidneys, and metabolic dysregulation from the central nervous system [16,17]. Incretin hormones are gut peptides that are produced after nutrient consumption and stimulate insulin secretion simultaneously with hyperglycemia. GIP (glucose-dependent insulinotropic polypeptide) und GLP-1 (glucagon-like peptide-1) are the known incretin hormones from the upper (GIP, K cells) and lower (GLP-1, L cells) gut.

However, diabetes does not develop in all individuals with insulin resistance, since a disruption of insulin secretion by the β-cells in the pancreas is also required [18].

This leads to a decrease in the total mass of muscles in the human body, an increase in fat and the use of drugs that predispose to hyperglycemia. An additional factor is the insulin secretion disorder, which occurs as a result of the normal aging of the body.

The increasing resistance of the body to insulin as the years pass, changes the distribution of adipose tissue in the body, causing an increase in visceral fat, while in older people the risk of dehydration also increases, as they have a reduced thirst mechanism, which is capable to cause fatigue but also a deficiency of cognitive functions.

Oxidative stress represents a disturbance in the balance between the production of reactive oxygen species (Reactive Oxygen Species) and the ability of a biological system to inactivate these toxic molecules and repair the damage they cause. Reactive oxygen species damage all cell components, including proteins, lipids, and DNA. Antioxidant defense mechanisms are less effective after the age of 40. This results in fatty acid oxidation and lipid peroxidation, with consequent changes in the physical properties of cell membranes and phospholipids. Free radicals react with DNA, proteins and lipids, resulting in the accumulation of products, the initiation of the degenerative process, and ultimately, the development of many serious diseases and aging.

Hyperglycemia, which accompanies Diabetes Mellitus as well as resistance to the action of insulin, are conditions in which an increased production of free radicals is found. The existing, in fact, bibliographic data advocates in favor of the opinion that these oxidizing bodies are responsible for the appearance of the complications of diabetes mellitus, but also for the phenomenon of resistance to the action of insulin itself. Studies show that in diabetes mellitus, there is on the one hand an increased production of free radicals and on the other a reduced inactivation of them, causing oxidative stress. In fact, the existence of increased

levels of oxidative stress in diabetes mellitus is particularly dangerous and participates in causing many complications. The control of the levels of oxidative stress in the diabetic patient the examination has a key importance for the prevention of damage to the vessels, but also for monitoring the course of diabetic complications and their early treatment [19,20].

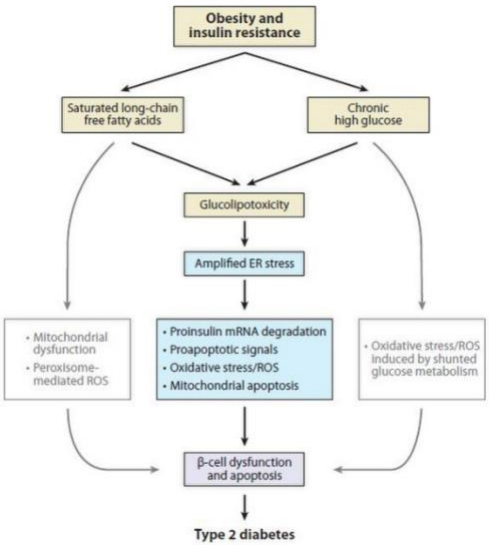

Figure 2: Causations of DM

In conclusion, causes that may worsen glucose tolerance may be, impaired glucose uptake, glycogen synthesis by skeletal muscle, decrease with age in total muscle mass, reduction of the person's physical activity and increase in fat mass and use of drugs that predispose to hyperglycemia. In old age, diabetes mellitus is associated with a growing risk of developing dementia and Alzheimer's, as well as a doubling of the risk of developing depression [21].

4. HYPOGLYCEMIC EPISODES IN OLD AGE

It is characteristic that hypoglycemia is documented in only a percentage, of the order of 5−10%, of individuals who address themselves to primary health care with a self-diagnosis of hypoglycemia. True hypoglycemia is defined as the manifestation of related symptoms with the simultaneous finding of a blood sugar (BG) value <55 mg/dL, which is usually considered the biochemical cut-off point for its diagnosis. Its investigation concerns the adoption of a differential diagnostic algorithm in order to rule out conditions, diseases and pharmaceutical factors that may be associated with the occurrence of hypoglycemic episodes, and accordingly individualized treatment is carried out [22,23,24].
Hypoglycemia is due to:

1. Improper intake, preparation-frequency of meals because a good state of the patient's mental functions is required.
2. Good condition of eyes and visual acuity.
3. Lack of patient compliance with medications.
4. Taking other medications for coexisting diseases that possibly enhance the hypoglycemic effect of diabetes treatment.

Hypoglycemic episodes may not be easily recognized by the elderly, or there is still the possibility of being misdiagnosed in stroke or ischemic heart attack or an epileptic seizure. It should also be noted the reduction of the compensatory hormonal mechanisms that characterize old people and which contribute to the prolongation and non-compensation of the induced hypoglycemia, resulting in a prolongation of the hypoglycemia that can end in death.

4.1. Treatment

4.1.1. Lifestyle: the importance of exercise and nutrition in old age

Special importance should be given to exercise with aerobic exercise or alternatively the application of a program of progressive increase in muscle intensity (3-5 times a week), as well as training in proper nutrition [25] with particular emphasis on the Mediterranean diet, which seems to increase survival in adults. In conclusion, it is emphasized the importance of the combined treatment of other risk factors (arterial hypertension, hyperlipidemia), since we must not forget that we are treating the patient as a whole and not a single disease.

Mediterranean diet: Large population studies have already for years documented the very favorable effects of the Mediterranean diet. The term "Mediterranean diet" is used to describe the set of dietary habits of various countries of the Mediterranean basin in the early 1960s (Greece, Italy, Spain, France). The traditional Mediterranean Diet has the following main characteristics: high proportion of monounsaturated fat (olive oil) to saturated, moderate alcohol consumption, high consumption of legumes, high consumption of cereals, lots of fruit, plenty of vegetables, limited con-

sumption of red meat, moderate consumption of dairy products [26,27].

Physical activity: Another important factor is physical activity [28]. This helps significantly in preventing diabetes, maintaining lost body weight in obese dieters, and improving blood sugar in people with diabetes. In addition, physical exercise contributes to controlling hypertension, improving hyperlipidemia and quality of life. Studies have shown that what is important for health is systematic increased physical activity and not too intense exercise.

4.1.2. Other factors

In recent years, great emphasis has also been placed on other factors. Indicatively, in principle, the role of adequate sleep duration is mentioned. Most elderly people suffer from lack of sleep or reduced sleep duration. People who don't get enough sleep have a relatively high chance of developing diabetes in the future [29,30]. Inadequate sleep and sleep deprivation can guide to obesity, DM2 and metabolic disorderliness. Sleep disturbances influence glucose metabolism, hormone balancing, the body's circadian rhythm. DM2 development is also associated with long - term exposure to air pollution. It has been found that environmental pollution can activate inflammatory mechanisms and oxidative stress, mitochondrial inhibition and cardiac disorders [31].

4.2. Medication

The therapeutic treatment of elderly diabetic patients must be done with special attention and a lot of thought, because:

1. These patients usually have a decrease in kidney function. (determination of creatinine clearance - GFR - glomerular filtration rate)
2. Cardiorespiratory problems usually exist alongside DM.
3. These patients receive medications for the coexisting diseases and the interactions of these medications must be calculated.

There are many antidiabetic treatments [32] that are taken. Each of them targets different organs that are all involved in the pathophysiology of DM2:

1. Insulin sensitizers that control hepatic glucose production and increase its uptake by cells.
2. Tablets that enhance insulin secretion from the pancreas.
3. Tablets that inhibit the breakdown of incretins in the body (incretins are hormones that, among other things, enhance the secretion of insulin by the body).
4. Injectable treatments that promote/mimic the action of incretins, increasing the production of insulin from the pancreas and favoring the longer survival of its cells.
5. Tablets that facilitate the elimination of sugar through the urine, preventing its reabsorption by the kidney into the bloodstream.
6. Tablets that slow down the absorption of carbohydrates in the gastro-esophageal tract.
7. Insulin, an injectable drug, which is the only pharmaceutical option for DM1 but is also used in DM2 patients, when hyperglycemia is not adequately controlled with antidiabetic drugs. It is administered by subcutaneous injection using traditional needles, pens and continuous insulin infusion pumps.

5. CONCLUSION

In summary, this review article links to the types of Diabetes Mellitus, its complications and age-related DM2. Diabetes represents a prevalent problem, even in elderly patients. The development of DM in old age is attributed to the worsening of glucose tolerance and insulin secretion disorder, which is attributed to the normal aging of the human body. Key risk factors, including diet, physical activity, air pollution and sleep influence, have been recognized and linked to various metabolic disorders, including DM, and age-related complications.

CONFLICT OF INTEREST STATEMENT
The author declares no conflicts of interest.

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