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Physical activity, oxidative stress and diabetes

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Abstract---Diabetes is a chronic disease in both developing and developed countries. Comfortable lifestyle, unhealthy eating habits and excess use to computer-based work may further aggravate the disease. Hyperglycemia and lack of physical activity may also contribute the formation of free radicals and advanced glycation end products (AGEs). Various physical exercises are recommended for the type 2 diabetic mellitus (T2DM) patients which may help in minimizing disease complications. Aerobic (swimming , treadmill, walking, rowing, and jumping) and endurance (biking dancing , climbing stairs & playing tennis) exercises are recommended in T2DM. Aerobic exercise carry huge impact for receiving oxygen and aggravate the cardiovascular and respiratory systems.it is one of the necessary interventions to treat T2DM. it is helpful on physiological parameters and decrease the hazard for insulin resistance DM. Numerous research has shown aerobic exercises has advantageous impact on T2DM improvement , centralize on different intensities. Endurance exercise is a exercise to increase endurance. The important for endurance in sports is frequently predicted as the essential for cardiovascular and simple muscles endurance.Many scientists around the world have focused on the impact of physical exercise in T2DM in terms of its behavior, effect on laboratory parameters, and organ injury, either as in vivo or clinical studies. In reality, in the developing nations experiencing T2DM, there is no enthusiasm for rehearsing the practice among the general public.

Concentrate deficiency is present on the Asian mainland. The cause may be due to the absence of open knowledge of exercise on the planet or even the absence of evidence to demonstrate the positive effects of T2DM practices. In this way, the main aim of the present study was to outline the discoveries of distributed writing, focusing on the degree, form of operation and clinical significance of T2DM. The survey concentrated mainly on T2DM, paying no attention to weight or metabolic disorder.

Keywords---oxidative stress, diabetes, advanced glycation, end products, physical exercise.

Introduction

Diabetes Mellitus (DM) is one of the quickest developing medical issue on the planet, which is presently coming to pestilence extent in a few nations [1]. In 2015, an expected 1.6 million people were straightforwardly caused by diabetes. Another 2.2 million people were owing to high blood glucose in 2012. Half of all people owing to high blood glucose happen before the age of 70 years. WHO extends that diabetes will be the seventh driving reason for death in 2030? [2]. It is basically because of result of way of life as absence of activity, undesirable eating regimen, weight and overweight. In the course of recent decades major financial changes have happened in Saudi Arabia. The development and thriving have acquired articulated changes the way of life of the general population. Most eminently, dietary patterns are less fortifying, and the dimension of physical exercises have declined. There is expanded utilization of quick nourishments and sugar-thick drinks (e.g., soft drinks). simultaneously innovative advances such autos, lifts, elevators, remotes are directed to a decline in dimension of different exercises. ordinary reliance on privately developed characteristic deliver, for example, organic products, vegetables and wheat has likewise moved. This has brought about the emotional increment in the diabetes pervasiveness. regarding the matter of the arrangements of diabetes mellitus, two principle classes have been expounded i.e. type 1, insulin subordinate diabetes mellitus, and type 2, non-insulin subordinate diabetes mellitus. For the obvious fact that it is more typical than type 1 diabetes mellitus, the present orderly audit focuses on type 2 diabetes mellitus (T2DM) regarding its administration. Strikingly, a total of 95% of the population has T2DM, while only 5% have type 1 diabetes mellitus[3].

Many scientists around the world have focused on the impact of physical exercise in T2DM in terms of its behavior, effect on laboratory parameters, and organ injury, either as in vivo or clinical studies. In reality, in the developing nations experiencing T2DM, there is no enthusiasm for rehearsing the practice among the general public. Concentrate deficiency is present on the Asian mainland. The cause may be due to the absence of open knowledge of exercise on the planet or even the absence of evidence to demonstrate the positive effects of T2DM practices. In this way, the main aim of the present study was to outline the discoveries of distributed writing, focusing on the degree, form of operation and clinical significance of T2DM. The survey concentrated mainly on T2DM, paying no attention to weight or metabolic disorder.

Oxidative stress

Expanding confirmations have proposed that oxidative pressure assumes a noteworthy job in the pathogenesis of DM. Oxidative pressure additionally has all the earmarks of being the pathogenic factor in fundamental diabetic confusions. Responsive oxygen species (ROS) are produced by ecological variables, for example, ionizing radiation and compound cancer-causing agents, and furthermore by endogenous procedures, incorporating vitality digestion in mitochondria. They might be portrayed by methods for a totally brisk half-presence and especially over the top level of reactivity. The influenced atom transforms into unsteady itself and goes into response with different particles it gets close to, which results in interruption of cell segments. The most astounding number of free radicals ascending *in vitro* are or start from responsive oxygen species (superoxide, hydroxyl, alkoxyl, peroxy and hydroperoxyl) or receptive nitrogen species (nitric oxide, peroxynitrite oxidized, nitrogen dioxide) (Cooper, Vollaard, Choueiri, and Wilson, 2002). [4]. As a stabilizer to the developing of detached radicals there is an arrangement of cancer prevention agent insurance which can be separated into areas: enzymatic – made out of superoxide dismutase (SOD), catalase (CAT), paraoxonase and glutathione peroxidase (GPX); and non-enzymatic – made out of the substances together with: supplements A and C, retinol, bilirubin, uric corrosive, diminished glutathione, thiols, coenzyme Q10, stretch proteins, egg whites, notwithstanding conveyance proteins and proteins responsible for Fe^{2+} I Cu^{2+} statement (transferrin – press donning proteins in plasma and ferritin – a protein that is utilized to keep intracellular iron, keeping it in dissolvable and riskless nation), which tie conceivably risky metal particles and incapacitate their cooperation in assembling of free radicals (Martinović et al., 2009) [5]. Antioxidant catalysts are endogenous and their arrangement can be changed through beyond any doubt components. The components of increased creation of enzymatic cancer prevention agents incorporate physical action and preparing (Finaud, Lac, and Filaire, 2006) [6]. In any case, the leisure activity in oxygen radicals has expanded as soon in light of the fact that the oxidative conundrum transformed into decided, which roused them to raise the issue whether the extreme oxygen supply all through exercise can result in oxidative strain and limit dangers for organic device. (Jenkins, 2000) [7]. Oxidative strain can be inspected by means of estimating the resulting.

Lipids, proteins and nucleic acids can be attacked simultaneously in living cells by ROS produced either endogenously or exogenously. There are several possible mechanisms that could facilitate the production of DM complication and cause pancreatic β cell damage by excess glucose metabolites moving along these pathways. Even so, all these pathways have ROS formation in common, which induces chronic oxidative stress in excess and over time, which in turn causes defective expression of the insulin gene and insulin secretion, as well as increased apoptosis. Different methods have been developed to evaluate biomarkers of cellular oxidative stress, and some have been suggested for the responsive assessment of antioxidant protection and oxidative harm in diabetes and its complications. Their clinical usefulness, nevertheless, is constrained by less than adequate standardization strategies and the absence of appropriate prospective large-sized, multi-marker trials.

Glycation of biomolecules in Diabetes Mellitus

It is a classical covalent reaction during which, by means of N-glycoside bonding, the sugar-protein complex is shaped through a series of chemical reactions delineated by a chemist Maillard (Singh et al., 2001) [8]. Maillard reactions are complicated and multilayer and can be analyzed in 3 steps. (i) The sugar-protein complex is shaped 1st (Amadori rearrangement), associate early product of non-enzymatic glycation lead to an negotiator merchandise that could be a precursor of all later compounds. (ii) It includes the formation of numerous negotiator merchandise, some of which area unit terribly reactive and continue with glycation reaction. (iii) Final phase consists of chemical process reaction of the complicated merchandise shaped in the second step, whereby heterogeneous structures named advanced glycation end merchandise (AGE) area unit shaped. The first position in Maillard reactions was believed to be contended solely with the high concentration of aldohexose. Nevertheless, current data show that various negotiator metabolites, even though the sugar region unites the most precursor mature compounds, i.e. -oxoaldehydes, Non-enzymatic glycation reactions are also creatively involved. Such intermediate merchandise area units are produced by metabolism (methylglyoxal) or polyolic pathways and may even be created by carbohydrate autoxidation (glyoxal).

Advanced glycation end products

Protein modification with AGE is irreversible, as there are no enzymes within the body that may be able to hydrolyse AGE compounds. These structures then accumulate during the period of the macromolecule on that they have been fashioned. Albumin, scleroprotein, eye lens proteins, basic myelin macromolecule, nucleic acid, and lipoproteins are all examples. AGE alteration of the functioning of several proteins is now well established, thereby leading to multiple delayed diabetes complications[9]. The key biological associated with excessive glycation include: regulatory molecule binding inhibition, 7 glycated protein crosslinking, soluble protein trapping by the glycated animate stuff matrix, decreased chemical action status, enzyme inactivation, nucleic acid function abnormalities, and increased immunogenicity in relation to immune complicated.

Free radical generations are the glycation process's irreversible process. According to previous research, all glycation steps produce free radical oxygen. RAGE membrane receptors bind to the AGEs and cause pro-inflammatory status and oxidative stress. Protein glycation modifies cellular oxidative functions that cause an improper oxidative response in PMNs, such as glycated collagens. Lipid peroxidation products bind to proteins and intensify the damage caused by glycooxidation. In diabetes mellitus, aging and other pathological states of oxidative stress, glycoxydation rate rises. To minimize glycooxidation and inhibit pathological complications, physical therapies could be beneficial.

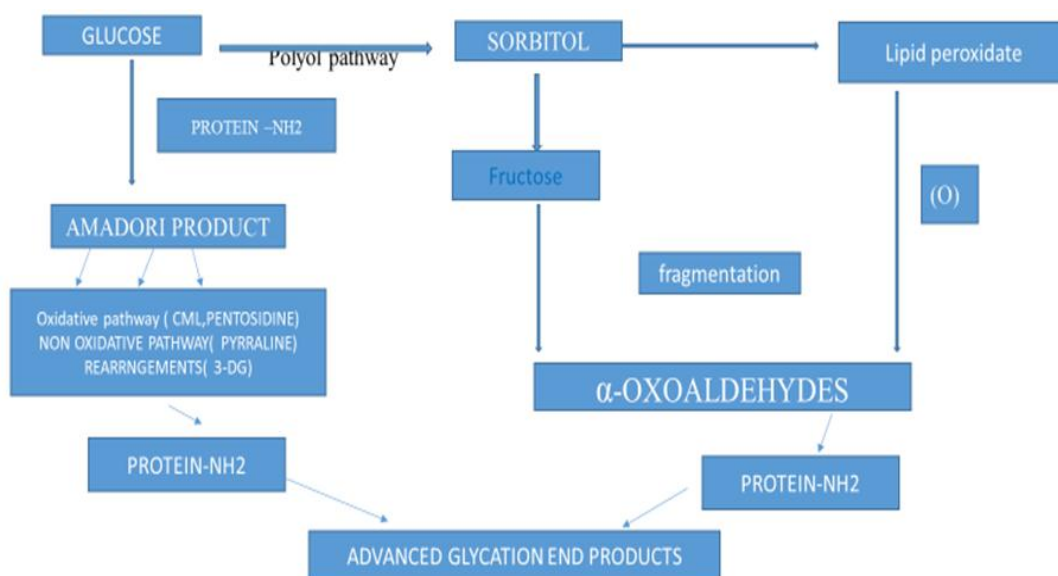


Fig. 1 Advanced glycation end products

Physical exercises and advanced glycation end products

In the modern-day population, the decrease in physical activity and functioning is widely noted and may be correlated with biomarkers such as advanced glycation end products (AGEs). AGEs prompt to age-related decrease in cell and tissue function during normal aging and have been shown to be related with declines in motor function. Apart from diet, physical exercise is increasingly seen as a vital part of the lifestyle changes that diabetic patients need to implement. As such, several studies have been performed to prove this approach's efficacy. Physical activity has many other benefits, including the reduction of inflammatory and oxidative (AGEs), besides the noticeable advantage of weight loss observed in type 2 diabetes. The Buildup of AGEs is a contributory factor in degenerative processes in several age-related diseases, especially in DM, renal failure, CV diseases, and Alzheimer's disease. As well as improving glycaemic regulation, recurrent complications in diabetic patients are subsequently delayed. The clear decrease of 1% in HbA1c in these patients decreased the overall risk of death by 21%, 14% of fatal and non-fatal myocardial infarction events, 12% of fatal and non-fatal cardiac arrests, 37% of micro-vascular complications, 19% of needed cataract operations, 43% of amputations and cardiac insufficiency in these patients.

Role of Physical Exercises in DM

Physical activity is thought to contribute to an increase in the production of species of reactive chemical elements that undoubtedly cause cell damage. One of the overall defensive mechanisms that change the cells and thus the organism to beat stress is stress proteins. Still unclear is the exact relationship between stress proteins, physical activity and reactive oxygen species. Up-to-date insights from totally different analysis square measure meagre if Associate in Nursing inhibitor

food supplement is to be counseled for either athletes or physically active persons [10].

Most everyone suggests that intensive physical exercise induces oxidative stress. There is no proof that this results in short-term effects on athletic success, but it should have long-term but not significantly adverse health effects. In a 2001 study, it was emphasized that mitochondria is a key source of reactive substances (intermediates) within muscle cells, such as hydrogen peroxide, superoxide and probably the hydroxyl group. The study showed that mitochondria will also turn out to be an azotic compound that is correlated with mitochondrial oxidant assembly efficiency [11]. An in vitro study shows that mitochondria can play a minor role in the development of free radicals, while Hem proteins square measure extra} more significant in terms of the induction of aerophilic stress. A substantial supply of aerophilic tension throughout can be due to the interaction between metmyoglobin and methemoglobin with peroxides. [12].

Diabetes mellitus can be an inveterate endocrine clutter and needs to be handled unambiguously. A few complications are linked to diabetes, resulting in a life-threatening illness and the need for legitimate care. Numerous investigations have proven to play an important role in the development of T2DM. Work out not as it pushes the glycemic control forward, but it can advance the affront affectability and restore the diabetic-related complication, which is considered one of the major complications, such as cardiovascular damage. The show systematic audit summarized the degree and type of work conducted within the T2DM population based on the previous findings.

Physical work out has been recognized as one of the cornerstones of diabetes mellitus care along with diet and medication since a long time ago from the last 100 [13]. Diabetes mellitus is well known for causing vascular complications on a wide and miniaturized scale, which continue to lead to life-threatening conditions afterwards. Mortality and horrible mortality are rising, alarmingly, as well as the horrible rate of diabetes mellitus. For monitoring the infection, compelling administration with no unfavorable impact is needed. Optional helpful schemes for both form 1 and T2DM were to carry out training programs. In particular, T2DM is more impacted by the administrative program because it is an adult-onset disorder and has a promising effect on the population. In fact, the instrument is not clearly caught on by the part of the work on T2DM. In any event, it can be determined that the potential to minimize blood sugar levels in T2DM patients is to increase glucose take-up via glucose transporter 4 (GLUT4) to the skeletal muscle in the midst of the exercise. Work out, work out counting oxygen intake, work out continuity form, disconnected work out and work out resistance are critical beneficial effects on T2DM.

Role of Physical Exercise in Oxidative stress

.Physical activity is defined as any body movement made by skeletal muscles that ends in energy consumption that can be unstructured, associated with daily life activity, associated exercise scheduled, deliberate and repetitive activity, grassroots and competitive sports, and daily physical activity of moderate intensity, such as walking, exercise or games, bringing critical health activity

limits[49]. The word "physical activity" must not be confused with the term "exercise," which may be a sub-category of physical activity that is characterized by one or more elements that are prepared, coordinated, continuous and based on or maintained by the condition. health limits are brought to both mild and intense physical activity. Under the general term of "Sport", physical efforts and capabilities would be involved, an activity of a personality capable of achieving a result requiring workout and/or physical ability, which is often competitive by its nature and organisation and is mostly recognized as a sport.

In order to mitigate the negative effects and toxicity of aerobic stress on wellbeing, subjects will enjoy regular, sperennial over time, physical exercise at any age, with explicit attention to aging, to reduce the adverse effects caused by free radicals. Even so, while reactive species are connected to harmful biological events, in cellular growth they are essential and function best. Often, cells have produced ways to use reactive species as biological stimuli. They act as subcellular messengers in essential molecular signal processes and modulate the activation of the catalyst and cistron. In the immunological response of cells and drug detoxification, ROS is a prerequisite for dilatation, stronger contraction, and initiation of cell death[22]. Furthermore, accumulating evidence suggests that during exercise, ROS is developed and the amount of muscle contraction is modulated. Modest supplementation with ROS enables an improvement in strength. That being said, the major rise in ROS production after strenuous exercise contributes to the occurrence of acute muscle exhaustion[50].

Physical exercise increases inhibitor defenses and decreases the levels of macromolecule peroxidation in both adults and elderly individuals[51]. Senior physically active individuals display levels of inhibitory effect and macromolecule peroxidation much like young inactive subjects, working to decelerate the method of aging-associated disability with the importance of normal physical activity. It is undeniable that moderate exercise and a balanced life style are helpful not just within bar of aerobic stress, but also jointly in the primary and secondary protection toward vas disorders, type II polygenic disorder, metabolic syndrome, and neurodegenerative diseases such as Alzheimer's disease[52]. In releasing myokines, the beneficial effects of exercise are also expressed. These molecules have auto-, para- and/or endocrine effects and include cytokines, IL-6 interleukins and alternative peptides produced, expressed and produced by muscle fibers that act to defend against diseases such as inferior inflammation-associated hardening of the arteries[53, 54].

The degree to which reactive species are beneficial or hazardous depends on the individual's exercise time, intensity, health state, and organic process status [55]. The body's inhibitor protection instruments bring inhibitor enzymes (superoxide dismutase, enzymes and antioxidants, etc.) and non-enzymatic antioxidants with them (Coenzyme Q10, glutathione, uric acid, lipoic acid, bilirubin, etc.). The formation of exercise-induced ROS ends in increased catalyst antioxidant activity, which then causes associated magnified resistance to aerobic problems, along with a good form of aerobic stress-related diseases, along with vas diseases, non-hereditary neurodegenerative disorders (Alzheimer's and Parkinson's disease), asthma, polygenic disorder and mitochondrial myopathies. CoQ10, collectively referred to as coenzyme Q, may be a fat-soluble gift molecule in most eukaryotic

cells, especially in mitochondria. It is part of the Negatron transport chain and plays a role in the production of cellular energy. The reduced form, ubiquinol, acts as a very important inhibitor within the body. CoQ10 is synthesized endogenously, and its dietary absorption is prohibited. According to it, strenuous exercise will increase the growth of muscle oxidizing agents by at least thirty minutes of vigorous and closed muscle-contracted activity, limiting efficiency. [56]. Chronic exposure to high ROS levels, exhausting the catalyst and non-enzymatic inhibitor mechanism, can become toxic, resulting in impaired cellular activity, molecular damage, apoptosis, and gangrene.

Therefore, excessive workout is damaging to untrained people, however progressive coaching permits the cells to additionally simply detoxify a bigger quantity of ROS. associate excessive physical activity may well be damaging once it induces associate altered secretion activity, changes of the sleep-wake rhythm, of the appetency, alterations of the blood pressure and of the guts rate. Nonetheless, those who are over-trained normally know an increase in their heartbeats even at rest, unable to go to bed, are anxious and/or stressed, may be hypotensive and will have a less cost-effective method.

Therefore, since it is mentioned that subjects concerned display higher levels of mitochondrial content and accumulate lower levels of ROS at the given intensity due to associated adaptive response in regular exercise than those that are untrained, the concept is that a continuing physical activity would help every younger and older population in order to favor an additional rapid recovery of the oxidization produced by strenuous exercise bouts, usually spoken by a larger aerobic take a look at, and so to protect the body from aerobic injury.

Types of Exercise

Two primary exercises are referred to as aerobic and endurance. Compared to aerobic exercise, resistance exercise was shown to create less impression on diabetics, though some research were shown to use resistance exercise as an alternative therapeutic agent in T2DM. In addition, it may also be because the use of equipment relies on resistance exercises. It can be costly, effective and expensive and needs close supervision. Owing to its disruptive nature, the preparation curriculum for sedentary citizens to undergo resistance training is extremely likely to be discontinued [35]. And from the other hand, aerobic exercise consists of simple training plans that are devoid of equipment use and have had several beneficial effects on T2DM [36-39].

Aerobic exercise

Aerobic exercise is an exercise that enhances oxygen intake and increases the functioning of the cardiovascular and respiratory systems. Aerobic exercise is a valuable therapeutic method for T2DM, since it has beneficial effects on physiological parameters and reduces the metabolic risk factors in insulin resistance diabetes mellitus. Many other research have shown the beneficial effects of aerobic exercise on T2DM improvement, focusing on different intensities. Swimming, swimming, treadmill, walking, rowing, running, and jumping rope are all aerobic exercises [14,15]. In patients with diabetic

neuropathy, mild aerobic activity contributes to blood pressure maintenance[16]. Even then, several randomized trial trials have shown that high-volume aerobic exercise results in weight loss with a large increase in insulin sensitivity[17]. Physical markers, including glycemic regulation, fasting blood-glucose level and lipid profile, are improved by aerobic exercise. In addition, endothelial function can be rebuilt and arterial stiffness decreased, which would be the beneficial parameter for T2DM cardiovascular event generation [18-21]. Both insulin and exercise promote glucose uptake through the glucose transporter (GLUT4) into the skeletal muscle from the intracellular to the cell surface[22-23]. Insulin receptor defects exist in T2DM, resulting in impaired glucose uptake and GLUT4 translocation [24]. Even so, by providing GLUT4 translocation, exercise therapy could restore the defects of insulin. A diabetes fitness schedule should include a mix of physical exercise such as cycling, trading facilities and training in strength. The advantages of walking and exercise in general entail dropping the level of blood glucose. Gaining the ability to use insulin in the body.

Endurance type exercise

Endurance exercise is, along with strength, balance and endurance, one of the four forms of exercise. Preferably, a balanced fitness routine will include all four forms of exercise, and in its Suggestions for Physical Activity in Adolescents, AHA offers easy-to-follow instructions for endurance and strength training. Not all of them need to be performed every day, but variety helps keep the body fit and safe, and makes it fun to exercise. To keep your body fit and safe and to keep your physical activity routine enjoyable, you should do a variety of exercises. Endurance exercises involve activities like walking, jogging, swimming, and biking that boost the breathing and heart rate. The operation of endurance keeps the heart, lungs and circulatory system safe and increases your overall fitness. As a result, the risk of certain diseases such as diabetes, heart disease and stroke can be minimized by individuals who get the recommended daily physical activity. Resistance exercise, often known as the resistance training, (8,9,32,168) is an important element of recovery services for individuals with functional impairment and an integral component of conditioning programs for those who wish to encourage or preserve health and physical well-being, possibly improve performance of motor skills, and avoid or minimize the risk of injury and illness. (8,105,118) Based on previous research, the defending system of erythrocytes toward free-radical harm is strengthened after an 8-week PRT program and therefore can be used as a useful approach to relieving oxidative stress [ref.]

Oxidative stress and diabetes mellitus

Growing research has indicated that oxidative stress plays a significant role in diabetes mellitus pathogenesis (DM). The pathogenic factor for underlying diabetic complications also appears to be oxidative stress. Environmental factors, such as ionizing radiation and chemical carcinogens, as well as endogenous processes, including energy metabolism in mitochondria, generate reactive oxygen species (ROS). Lipids, proteins and nucleic acids can be attacked simultaneously in living cells by ROS produced either endogenously or exogenously. There are several possible mechanisms that could facilitate the production of DM complexity and cause pancreatic β cell harm by excessive glucose metabolites moving along these

routes. Even so, all these routes have ROS formation in common, which induces chronic oxidative stress in overload and over time, which in turn causes deficient expression of the insulin gene and insulin secretion, and also increased apoptosis.

Different methods have been developed to evaluate biomarkers of cellular oxidative stress, and some have been suggested for the responsive evaluation of antioxidant protection and oxidative harm in diabetes and its complications. Their clinical usefulness, nevertheless, is constrained by less than adequate centralization strategies and the absence of appropriate prospective large-sized, multi-marker trials. By modifying the intensity of exercise-induced oxidative stress, exercise intensity has been shown to play a significant role in ROS formation [25-26]. The generation of ROS increases throughout aerobic exercise due to a higher intake of O₂ and, subsequently, a higher leaking of electrons from the electron transport chain [27]. Oxidative damage is observed when ROS generation exceeds antioxidant defenses (i.e. when exercise intensity is greater than 60-70 percent of maximum oxygen uptake) [28]. Chronic exercise repetition, e.g exercise preparation, may be able to establish compensation for oxidative stress in skeletal muscle fibers[29] by means of antioxidant and repair system adaptation. This could contribute to a decreased degree of oxidative damage at rest and improved oxidative stress resistance[30-33]. Emphasis has recently moved to training modalities other than conventional constant aerobic training, like high-intensity discontinuous training (HIDT). This training stage is defined by short, sporadic periods of vigorous activity interspersed with periods of rest or exercise at low intensity[34].

In order to avoid acute complications and to minimize the risk of long-term consequences, diabetes is a chronic condition that needs ongoing medical attention and patient self-management awareness. The treatment of diabetes is complicated and needs several challenges to be solved, beyond glycemic control. There is a wide body of evidence that suggests a number of approaches to enhance the outcome of diabetes. The main cause of mortality for people with diabetes is CVD(Cardio vascular disease). It really is an important contributor to diabetes mortality rates and directly and indirectly diabetes expenses. Clinical studies on exercising in people with dm by the ADA (American Diabetes Association) has outlined the importance of exercise in the diabetes treatment plan[40-41]. DM is a multi-aetiology metabolic disorder characterized by hyperglycaemia arising from insulin secretion deficiencies, insulin action, or both, and associated with carbohydrate, fat, and protein metabolism disturbances [42]. A increasing global health issue is Diabetes Mellitus (DM). In 2000, an estimated 171 million people worldwide were harmed by diabetes; this had risen to over 366 million by 2011 and figures are projected to reach 552 million by 2030[43].

Conclusion

Due to rapid economic growth, urbanization and shifts in lifestyle habits in the region, the highest prevalence of diabetes overall is projected to occur in the Middle East and North Africa [43]. The Kingdom of Saudi Arabia (KSA) is not exempt from this worldwide epidemic [44] and diabetes is the country's most difficult health problem [45]. Approximately 0.9 million people were diagnosed

with diabetes in 1992, as per a study by the Saudi Arabian Ministry of Health, but this number grew to 2.5 million people in 2010, reflecting a 2.7-fold rise in prevalence rate in much less than couple of decades. 4660 diabetes patients visited family and medical clinics across Saudi Arabia in 2015[46]. This growing burden of diabetes is due to multiple factors, including an increasing rate of obesity and an aging population[47]. Other related chronic problems are usually encountered in patients with diabetes, resulting in severe complications [48].

For instance, among patients with diabetes, the incidence of end-stage renal disease is higher[49] and accounts for between 24% and 51% of those undergoing renal replacement therapy [50]. Patients with diabetes are two to four times more likely to develop cardiovascular disease compared with the general population and two to five times more likely to die from this disease[51]. Diabetes puts a huge burden on healthcare facilities and the society as whole and, in relation to its effect on individuals[52]. Diabetes contributed for 11% of overall healthcare spending globally in 2011; the yearly cost of diabetes in Saudi Arabia has also been evaluated at even more than \$0.87 billion[49]. The mixture of diet and exercise is the best way to manage symptoms of diabetes in patients who are not insulin-dependent. Using a daily exercise treadmill also helps patients to reduce their blood glucose levels sufficiently to be able to change or remove their medication rates. T1DM, T2DM and GDM are the three most popular diabetes forms [48].

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