

Obesity, Diabetes and Cardiovascular Diseases

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Abstract

Modern day mankind is suffering from diseases which were not so wide spread few decades ago. These diseases relate to obesity, diabetes and cardiovascular events. In many countries of the world, these diseases are the main cause of morbidity and mortality. Many diseases related factors of the obesity and diabetes are interlinked to each other and both increase the risk of cardiovascular diseases (CVD) up to higher degree. The occurrence of these productivity decreasing and life- threatening diseases has increased in both developed and underdeveloped countries. In this article we have described the rising prevalence of these three diseases at national and international level, factors causing occurrence of these diseases and recommendations to manage them.

Obesity

Genetics and unhealthy lifestyle are main factors that lead to overweight and obesity. Obesity is a disease in which excess fat is accumulated in body to the extent that it may be hazardous to life and may cause many health-related issues. If the body mass index (BMI) of a person is more than 25 kg/m² then he is overweight. If BMI crosses 30 kg/m² then he is considered obese. Obesity increases the risk of a number of diseases, especially heart disease, arthritis, type 2 diabetes, cancer and also difficulty in breathing [1].

Diabetes

An individual is considered diabetic if his/ her fasting blood glucose level is 140 mg/dL or higher [2].

There are three types of diabetes:

Diabetes type I: It takes place when insufficient insulin is produced by the body. It is also known as insulin-dependent diabetes and insulin needs to be injected to the body.

Diabetes type II: In this state body become resistant to insulin, so it is also known as non-insulin- dependent diabetes.

Gestational diabetes

During pregnancy high level of glucose in blood leads to type 2 diabetes. The endothelial cells which line the blood vessels absorb more glucose than usual and ultimately results in damaged blood vessels [1].

Cardiovascular diseases (CVDs)

Diseases of blood vessels and heart may lead to CVDs. Obstructions in blood vessels are main cause for heart diseases. CVDs, particularly coronary artery disease and stroke, are the main cause of mortality throughout the world [3]. Coronary heart diseases include angina, myocardial infarction, coronary artery diseases [4]. Higher BMI act as major indication for CVDs, and high glucose level and blood pressure act as mediatory factors [3]. There are many evidences showing clear relationship

among obesity, diabetes and CVDs. Obesity leads to CVDs and diabetes, and CVDs have been observed in obese and diabetic individuals [5].

Prevalence of Obesity

Obesity is increasing gradually affecting every age group and even children. Developing countries are more prone to obesity. The occurrence of obesity is increasing day by day in developed and developing countries. Overweight people are more susceptible to diabetes, hypertension, heart diseases and dyslipidemia. The mortality rate due to obesity in United States is 300,000 per year and its prevalence is increasing day by day in all countries [6,2].

Obesity is the major stimulant of diabetes and coronary heart diseases [7]. It is estimated that world's 2.16 billion adults will cross the line for being overweight and 1.12 billion will be obese in the year 2030. In 1970s and 1980s, the level of obesity began to increase in well developed countries with good socioeconomic conditions. After that, its incidence started to increase in countries with medium income and even in countries which lie below the poverty line [8]. In past 33 years, no significant decrease is observed in the frequency of obesity in any country. Today about 32% of adult male population and 34% of female population is obese in United States. In Western Europe the frequency of obesity was 21% in both genders and in South East Asia its frequency was 5% among women and 8% among men [9].

The Asian specific cutoff value of BMI is 23Kg/m². A national survey estimated that 25% population of Pakistan to be overweight with reference to this cutoff value and 10.3% to be obese with BMI cutoff value of 27Kg/m². These estimates indicate major health issues in Pakistan [2]. Weight gain in every stage of life either in adolescence or in childhood poses serious threats and may act as risk factor for diabetes and cardiac diseases even within the range of normal BMI [10].

Globally in the year 2010, obesity was the major reason for 3.4 million deaths, 3.9% of years of life lost and 3.8% of disability cases. This increased prevalence demands regular monitoring of all populations. From 1980 to 2013, the occurrence of diabetes upsurge to a level of 27.5% in adults and 47.1% in children. Between the years 1980 and 2013, the number of obese people rose from 857 million to 2.1 billion throughout the world. The ratio of over-weighted men augmented from 28.8% to 36.9% and ratio of women increased from 29.8% to 38%. These ratios were monitored from 27 different

developed and developing countries. The ratios were different with different gender patterns. In developed countries the ratio of obesity and over-weight was higher in men as compared to women whereas in developing countries the prevalence ratio was higher for women as compared to men. The rate of obesity is increasing in all countries and higher prevalence was recorded in 2013 in women than in men. This rate was greatest between 1992 and 2002 [11].

Successive national health and nutrition examination surveys demonstrated an intense rise from 12.8%-22.5% between 1960 and 1994, in United States. These rising tendencies increased upto 17.8% between 1990 to 2010. The rate of obesity had been higher in adult's females as compared to children and males respectively. These higher rates indicate an estimated 86.3% population will be over-weight and 51.1% obese by year 2030 and all American adult population will either be overweight or obese by year 2048. The data from Behavioral risk factor surveillance system from years 1990 to 2008 predicted a 33% increase in obesity within next two decades [12].

Central obesity and cardiovascular diseases have strong inter-relationship and it is independent of person's BMI and stimulates insulin resistance. The common indicator and measure of central obesity is the waist circumference. Recent trends of obesity from 1999 to 2000 showed an increasing waist circumference among population. The waist circumference increased from 95.5cm, in year 1999 -2000, to 98.5cm in years 2011-2012. Similarly, central obesity increased dramatically from 46.4% to 54.2% in the years from 2000 to 2012. Both genders showed intense rise in these trends. 65.4% increase for boys and 69.4% for girls was observed in years 1998 to 2004 [13].

A survey was conducted in 2010 on rural non-pregnant females of Peshawar between the ages of 15-70 years. The results showed that 53.4% population was over-weight and 26.9% population was obese and there was a rise in prevalence of obesity with age. Obesity among women is a serious problem. Obese and over-weight women are more susceptible to blood pressure related problems and diabetes [14].

Prevalence of Diabetes

Almost 346 million diabetic patients are reported by World Health Organization (WHO), as impaired glucose tolerance and diabetes are spreading rapidly. In 2011, about 52 million people aged 20-79 years were diabetics

in Europe and by 2030 this limit will cross 64 million. People suffering from diabetes are more likely to be also affected by CVDs. 15% mortality rate is reported due to problems related to diabetes, while 50% deaths in diabetic patients are attributed to CVDs. According to National Health Interview Survey, the ratio of occurrence of people suffering from diabetes mellitus raised from 3.5% to 8.3% in 1990 and 2012, respectively [15].

WHO reported 171 million people as diabetic for year 2000 while 366 million people will be diabetic by 2030. Earlier publications of International Diabetes Federation (IDF) reported the prevalence of diabetes as 285, 246, 194, 151 million people in 2010, 2006, 2003 and 2000 respectively [16]. About 8% adults are affected from diabetes throughout the world while the ratio of people suffering from diabetes type 2 in US was 11% and 37% are prediabetics [17].

Now a days, after Africa the highest increase in the spread of the diabetes mellitus is estimated in the regions of Middle East. Within the period of 10 years, the ratio of the diabetic people increased from 2.8-3.4%. Similarly, between 1995 and 2005, the proportion of Canadian adults with DM increased by 69% [18]. In a very small period, there is a dramatic increase of diabetes in Asia as the continent has developed and urbanized very rapidly. In 1980, the number of people suffering from diabetes was 1%, while by 2008 it had reached up to 10% [19]. Being overweight may also lead to diabetes type II. According to the reports of Centers for Disease Control and Prevention the no. of people suffering from diabetes mellitus was almost doubled from 1980-2014. The data suggested that the rate of diabetes is higher among those people whose BMI is high [13]. As almost 85.2% people are facing both problems now, and by 2050 every 1 in 3 people will suffer from diabetes in America [16]. Hypertension, insulin resistance, post-delivery diabetes and dyslipidemia are all related to gestational diabetes. Person suffering from CVDs may not only have a case history of gestational diabetes but also at the risk of type 2 diabetes [20]. The no. of diabetics in 1995 was 4.3 million which may be increase up to 14.5 million by the year 2025 [21].

Prevalence of CVDs

About 16.7 million deaths per year are due to CVDs throughout the world. Studies show that people who migrate from countries like Bangladesh, India and Pakistan to developed world are more prone to CVDs than the native people [22]. When Europeans are compared with population of South Asia, people suffer more from

diabetes and CVD at early age. Arterial fibrillation and elderly play an important role as risk factors for mortality caused by diabetes, stroke and hypertension [23]. In 1990, the rate of death was 100,000/ year in Pakistan as the diseases of heart, diabetes and hypertension are most common. In Pakistan, adults are highly suffering from risk of CVD, where the rate of cholesterol elevation, hypertension and smoking are 13%, 18% and 29% respectively [21].

The rate of prevalence of CVDs of the study held for the CVDs shows results for 1.5% and 3.7% in rural and urban regions of Karachi respectively, in the year of 1965 and 1973. While the evaluation of questionnaire in Metro Ville presented about 6.2% population are prone to CVD, which is almost double the rate of Karachi [24].

As the death rate increased by 25% from 1990 to 2016, so data suggests that Diabetes and CVDs are main causes of death nationally and internationally. Throughout the world, the death rate due to CVD increased up to 60% and the common risk factors responsible for CVD are high BMI, blood pressure, blood glucose and cholesterol level. The deaths due to stroke and coronary heart disease were 528 and 1497 respectively in the total of 2918 were reported per year in a study including both men and women [25]. Above age of 60 years, in women, CVD is most commonly found throughout the world except Africa. The risk of mortality in CVDs increases with diabetes by 2-4 times but this rate is higher in women than men. In 2004, a study suggested that diabetes is the main leading cause among other nine risk factors i.e. obesity, smoking, stress, hypertension, inactivity, dyslipidemia etc. for myocardial infarction. PCOS, gestational diabetes and premature menopause are the additional causes for the risk of CVDs in women. CVD risk is also less observed in lactating women as it has some protecting effect. Stress plays a role of independent risk factor, (Norhammar & Schenck- Gustafsson 2013) [26]. According to the Euro Heart Survey, people suffering from CVD have higher rate of abnormalities related to blood glucose level in both men and women. The result of OGTT predicted that the blood glucose level is normal in merely 27% men and 19% women suffering from CVD [27].

Obesity as Co-Factor in the Occurrence of Chronic Diseases

Overweight is directly associated with increasing rate of cancer, diabetes and CVDs. This problem is highly present in the middle income countries. Asians are more prone to obesity because the higher rate of abdominal fat

predisposition which further causes IGT and metabolic syndrome [28].

Obesity increases the rate of mortality and morbidity caused by CVD, along with other diseases like diabetes, cancer and sleep apnoea [29]. In 1970s, Sims and his coworkers studied the cases of young men who suffer from diabetes when they were overfed with no family background of diabetes. They invented the term "diabesity" as diabetes and obesity have close association with each other. About 90% people, with higher BMI the rate of obesity also increases, especially in people with gestational diabetes, with family background history, weight gain and abdominal obesity. Obesity was completely associated with diabetes and CVDs. Individuals of young age are more likely to be affected by over weight than elder ones [30].

Excess weight is a chronic disorder that significantly affect the cardiovascular system as it changes the physiology of system i.e. increased left ventricular mass, lower cardiac output, left ventricular wall thickness. Obesity increases the risk 2 times greater for CVDs, according to the Nurses' Health Study. In a recent study of 37, 488 were suffering from CVD in the total of 1.2 million people. As compared to normal weight people suffering with overweight have high risk of developing CVDs [13].

In a study, when normal BMI and high body fat women were compared, lower rate of consumption oxygen and resting metabolism were observed. The participants of the same group were also seen to be suffering from CVDs and metabolic syndrome [31]. With increase in BMI, the risk of diabetes, CVDs and metabolic syndrome also increases. The ratio of people who were insulin resistant is 32% and 68% when observed in normal weight and obese respectively [32].

Obesity is related with enlarged LVM, which causes morbidity and mortality in adults which in turn linked with stroke, sudden death and heart failure. Unfortunately, childhood adiposity predicts cardiac mass in adulthood. An increase in weight during childhood predicts the acquisition of excess LVM beyond what is expected with normal growth. The apparent higher LVMI in the current generation predicts higher cardiovascular risk. This study's significant finding is the higher LVMI in today's children and adolescents compared with their counterparts a generation earlier. The increase in mass of heart is rise in BMI between generations. Compared with children in 1986 to 1989, children today have a higher predicted cardiovascular risk in childhood, as well as in adulthood. Several previous large studies have shown

increasing rates of obesity not only in the US, but also in all developed countries. The comparison of children separated by approximately 2 decades found an 5 kg higher average weight (with an 11% higher average weight percentile), the average BMI was 1.8 kg/m² higher average BMI (with a 0.53 mg/kg² higher average BMI z score), and a 4-fold increase in obesity. These findings are in agreement with the increased BMI and obesity rate reported in developed countries. If the current generational changes were to continue linearly, 50% of our pediatric population would be overweight in just two generations time [33].

Obesity deteriorates the risk factors for CVDs, as it elevates the BP, blood glucose, and lipid levels and also affect the structure and function of ventricular system. Overweight is linked to most of the diseases associated to CV system like CHD, hypertension and heart failure. Obesity affects both the systolic and diastolic function of ventricles. Obesity not only alternate the LV diastolic function but also increase the circulation of blood which can cause increase in the surface area of left atrium of heart. Obesity adversely influence the health of heart system but according to some studies that CVDs are not observed in metabolically healthy obese people. Different authors revealed that mortality rate is higher in people with BMI greater than 35 kg/m². Some studies also proved that patients with normal BMI but higher percentage of body fat and circumference of weight have higher risk of CVD [34].

The risk of diabetes and CVDs is almost four times greater in obese than non-obese. The BMI in childhood approximately predicts the BMI in adulthood. Once after the onset of obesity, it's difficult to treat so management should be done to control it [35].

Diabetes Affecting the Quality of Life

In Asia, obesity and diabetes are not directly correlated. In India the frequency of obesity is low but frequency of type 2 diabetes is very high. Other Asian countries also have lower prevalence of obesity as compared to United States but higher or same frequency of diabetes. In Asian populations the risk of diabetes increased even with lower BMI than in Europeans. In middle age even a slight increase in weight is a major risk factor for diabetes in Asians. Central obesity and decreased muscle mass in Asians is now becoming the cause in insulin resistance than westerns. The increased frequency of diabetes in normal weight people is because of insulin resistance caused by metabolically obese phenotype [19].

The deposition of fat is critical factor for diabetes. The avoidance of weight gain in adolescence is the major preventive measure for diabetes. Apart from weight, quality of fat and carbohydrates is important in predicting diabetic risk. Coffee, grains, fruits and nuts decrease the risk of diabetes. Meat, refined grains, cold drinks increase the risk of diabetes. Diet rich in fruits, vegetables [36]. Beckman *et al*, in "Vascular Complications of Diabetes" pinpoint that diabetes increase risk of disease in blood vessels of all sizes and types. Macro vascular and microvascular complications are more common in diabetic patients. The main cause of illness, hospitalizations and deaths in diabetic patients is the result of vascular problems. Cardio vascular diseases aggravate the diabetic disease resulting in worse consequences. The correlation between diabetes and macro vascular diseases was made about 40 years ago which showed increased risk of myocardial infarction and death in various populations [15]. Endothelial dysfunction is the primary indicator for cardio vascular diseases in Type 1 diabetes mellitus. Several case studies demonstrate that type 1 diabetes is the cause of instability of vascular system even in children also causes impairment in dilation of vessels when blood flow increases. The thickness of innermost layers of arteries is also observed [37].

Low blood glucose level is also related with cardiovascular diseases and has a positive relation with coronary heart diseases and linked with mortality in diabetic patients. This link persists over a long period of time [38]. Apart from insulin resistance and increased blood glucose many other factors contribute in increasing risk of macrovascular complications. Adipose tissue, abnormal release of adipokines and inflammation, are possible contributors of cardiovascular dysfunctionality. Central obesity and storage of fats and lipids leads towards hypoxia and long lasting inflammation. Leptin is the cytokine which is associated with vascular complications. It is adipocyte fatty acid binding protein and is epithelium derived factor [39]. It is reported from epidemiological studies that frequency of diabetes is much higher in migrants of Asia as compared to the inhabitants of host countries suggesting that environmental factors and luxurious lifestyle increase the tendency for diabetes. Moreover, these migrant populations have higher ratio of diabetes than Europeans. Higher body fat with increased ratio of waist and hip for any BMI is the common phenotype found in Asian Indians and this leads towards diabetes [40]. Diabetes and overweight are closely associated and diabetes is more prevalent in obese patients. Overweight is the main reason in 90 percent of diabetic cases. Moreover, around

197 million people have impaired glucose metabolism due to overweight and this number is more likely to increase up to 420 million by the year 2025.

Kidneys are also affected by obesity and diabetes. Approximately one third of diabetic patients have nephropathy disorders and in developing countries its frequency is increasing specifically in Asian pacific countries. In 2003, a survey was conducted according to which diabetic nephropathy is the reason for renal failure in 9 out of 10 Asian countries. This frequency of end stage renal disease increased from 1.2% of population in 1998 to 14.1% in 2000. In China, this ratio increased from 17% in 1990 to 30% in 2000 and in India 6.6 million patients with diabetes out of 30 million are at a verge of gaining diabetic nephropathy. Healthy life style is an important factor in decreasing the rate of diabetes and hypertension [28].

Nephropathic complications are long lasting and adults less than 45 years with obesity related diabetes are more affected [41]. In healthy individuals, nitric oxide production causes dilation of arterioles supplying to skeletal muscles by the action of insulin. In vitro studies demonstrated that insulin regulates nitrogen oxide synthase which synthesize nitric oxide from arginine. In insulin resistant individuals, this process is not proper. Thus insulin resistance diabetes and obesity are related with vascular health and nitric oxide plays an important role in vascular health [42]. Insulin resistance decrease the production of glycogen and increase uptake of glucose by peripheral tissues, resultantly increase hyperglycemia, hyperinsulinemia and dyslipidemia [1].

Effects of Cardiovascular Diseases

Obesity and overweight increase the frequency of cardiovascular diseases and the risk factors of CVD's are more common in adults. Data analysis showed that between years 2007 to 2010 the prevalence of diabetes was 18%, hypertension 36% and dyslipidemia 50% in adults with obesity. Other than smoking, the risk of CVDs is greatly present in obese and overweight people [43].

Cardiac complications are more common in developing countries with higher frequency of transmissible diseases. In obese people, risk of cardiac diseases is greater and 5 times higher risk of hypertension is seen in this group. Obesity is the major contributor worldwide increase of hypertension. In 2000, one billion people had hypertension and this number is expected to increase to 1.56 billion people by the year 2025. This rise will have uneven effect in developing

countries where the frequency of hypertension is greater as compared to developed countries and cardiovascular diseases are likely to develop early in affected peoples. In Western and developing countries, the rate of effect of cardiac complications caused by diabetes is more common among minority groups and increasing ratio of waist-hip is the strong indicator of stroke and ischemia. It is estimated that in South Asians the risk of cardiovascular diseases is higher as compared to African natives or Westerners. The study demonstrates that normal weight metabolically unhealthy individuals are more prone to diabetes, cardiac diseases and mortality. These findings are in accordance with the previous researches for the association of diabetes and cardiac complications [44].

The major cause of anomalies and deaths of diabetic patients are cardiac diseases and about 68% deaths of patients are caused by CVDs. Results of National Health Interview Survey between the years 1997 to 2005, show that diabetic patients with simultaneously having cardiovascular diseases at age above 35 increased to 36%. Data from 64 studies reveals that diabetic women are at a greater risk of CHD almost 44% and for stroke the risk is 27% greater as compared to diabetic men. The risk of CVD is reported greater in women than men i.e. 2.82 and 2.16 respectively. In the association of diabetes and stroke the maximum risk in women is 2.28 and in men is 1.83. Diabetes also increases the risk of other vascular diseases. Several case studies indicate that diabetes is major risk factor for thromboembolism and sudden cardiac death and the risks are same for men and women. The combined results of 7 prospective investigations covering more than 1.6 million individuals disclose that diabetes is the reason of 24% higher risk of arrhythmia and the proportional reduction in population risk is 2.5%. About 2 fold greater risk of mortality is seen from vascular complications due to diabetes. Anyhow, in the previous decades from 1990 to 2010 rate of diabetes related complications have noticeably reduced and the rates of stroke and heart attacks almost reduced to half. However, the higher prevalence of diabetes pose serious problems [13].

The onset of atherosclerosis starts at early age of 5 to 10 years. Esters of cholesterol start depositing in the innermost layer of muscular arteries and contribute in intimal foam cell population and form fatty streak, the first visible sign of atherosclerosis. Other symptoms include malfunction of endothelial cells in pericardial vessels and inflammation of vessels [45].

The major cause of death and morbidity in diabetic patients are cardiovascular complications. Diabetic

patients are at 2-4 times higher risk of mortality caused by strokes and heart complications as compared to non-diabetic patients. The risk of coronary diseases in diabetic patients with no history of myocardial infraction is the same as in non-diabetic patients with history of cardiac complications. Therefore, National Cholesterol Education Program deliberates diabetes as key factor for cardiac diseases. Diabetic patients are also more prone towards hypertension. About 10-30% patients with Type 1 diabetes and 60% with Type 2 diabetes have hypertension. The simultaneous existence of these conditions upturns the risk of macrovascular and microvascular diseases. The development of these diseases can be decreased by proper treatment of hypertension. The onset time of hypertension in diabetic patients differs with diabetes type. Type 1 diabetic patients develop hypertension after several years of diagnosis and reflect nephropathy. Three years after development of microalbuminuria, blood pressure starts increasing. Patients with Type 2 diabetes mellitus may have problem of increased blood pressure at diagnosis or even before the elevation of blood glucose levels. Now, this combination of high blood pressure and obesity is well recognized and moving towards higher risk of cardiovascular morbidity and mortality in patients with these two conditions.

Pathophysiology

Jio, et al. in 2016 identified pathophysiological factors for non-communicable diseases in population [46]. Adipose tissue secretes adipokines which are pro-inflammatory in action. They increase oxidative stress which is due to the rise in the levels of free radicals produced by adipocytes, impaired endothelial function, decreased autophagy, activation of macrophages of adipose tissue and deposition of fat leading to lesions and plaque [13]. Following is a description of proteins responsible for increased incidence of obesity.

Adiponectin

Adiponectin levels are substantially higher in healthy persons; almost double that in diabetic patients [47]. Obesity decrease the level of adiponectin a condition known as hypoadiponectinemia which results in increased rates of cardiovascular diseases. Adiponectin is an anti-inflammatory hormone with insulin sensitizing activity. In type 2 diabetes mellitus level of adiponectin in plasma is reduced. Despite of its positive effects, recent investigation propose that high level of adiponectin is interlinked with high rate of cardiovascular disease and mortality. However, individuals with high level of

adiponectin are at a lower risk of diabetes mellitus. And patients with diabetes mellitus are more prone towards cardiovascular diseases. Shortly, increased level of plasma adiponectin is directly related with lower risk of diabetes and subsequently heart diseases [48].

Leptin

Adipose tissues secrete a hormone namely leptin, it is involved in the regulation of intake of food and end energy consumption. Dietary conditions, amount of triglyceride content in adipose tissue are directly related with the release of leptin from adipocytes. Insulin sensitivity is improved by leptin as leptin obstruct lipogenesis and trigger lipolysis thus reducing the intracellular levels of lipids in pancreatic cells, liver and in skeletal muscles. In diabetic and obese patients the level of plasma leptin is increased. Leptin increase atherosclerosis by producing oxidative stress, increase the production of monocyte chemoattractant protein 1 and endothelin-1 leading towards the hypertrophy of the contractile cells of heart, the cardiomyocytes [37].

Tumor Necrosis Factor

Tumor necrosis factor alpha is associated with inflammatory action and is produced by lymphocytes, monocytes and adipose tissue. It is also involved in developing insulin resistance, obesity and diabetes. There are several pathways which demonstrate the effect of tumor necrosis factor on insulin resistance and diabetes. Increased concentration of free fatty acids in the adipocytes is triggered by Tumor necrosis factor, thus blocking the formation of adiponectin which have increased insulin sensitizing activity in adipose tissue mass. This hinders phosphorylation activity of tyrosine residue of receptor of insulin in first substrate, the key step in the intracellular signaling of the hormone.

Adipsin

Adipsin is biological molecule secreted by adipose tissue. It is serine protease and has positive relationship with insulin resistance, dyslipidemia, and adiposity. In addition to energy storage organ, adipose tissue also performs the function of endocrine gland, energy balance and in the metabolism of lipids and glucose [49].

Environmental Factors

Dietary style

To avoid non-communicable diseases, the diet must have to modify. The death rate in US due to dietary risk increases up to 26%. Diet implement direct and indirect

effect on health e.g. BP, weight gain and elevated blood glucose [13]. Now a days, trend of “Western Diet” is common, which are rich source of sugars, carbohydrates and animal sources, and most commonly in low and middle income countries. Diet consisting of plant sources is diminishing in all regions of the world [50].

It is evident from the study of Coronary Artery Disease Risk Development in Young Adults (CARDIA) that weight gain and insulin resistance risk was directly related with consumption of fast food [51]. For decades, cardiovascular effects of fish and omega-3 consumption are under study. Higher intakes also don't noticeably lessen the risk. If compared with fatal cardiac events, consumption of fish has fewer effects on nonfatal cardiac events and stroke [52]. It was noticed that Mediterranean diet if supplemented with olive oil and nuts reduces the chances of major cardiovascular events. For early control of CVDs, Mediterranean diet was proven beneficial [53].

Life Style

It is evident from epidemiologic studies that increased physical activity cut down the diabetes risk, while sedentary life style heightens the chances of risk. US National Health and Nutrition Examination Survey (NHANES) study has revealed that each two hours per day increase in time utilized for watching television (TV) has increased the chances of diabetes by 14%. On the other hand, each two hour per day increment of time spent in walking has proven to reduce 12% risk. Among sedentary behaviors, watching TV for long time was associated with peak risk. TV watching effect on type II diabetes was not linked with physical activity. Several valid reasons demonstrate the positive relationship of watching TV and diabetes. Persons spending more time before TV, exercise less resultantly reduced energy expenditure and increased food intake [49].

Smoking

For diabetes, smoking is a self-sufficient risk factor. A survey has summarized that in smokers there are 45% more chances of developing diabetes as compared to nonsmokers. Risk of diabetes also linked with frequency of cigarette smoked. Moreover, smoking is directly associated with obesity and abdominal fat, reputable risk factor for diabetes and insulin resistance. In smokers, amassing of adipose tissue is because of elevated cortisol levels in plasma. While in women, smoking has anti-estrogenic effects and tends to reduce plasma testosterone in men. From several trials it has proven that diabetes can be prevented. In China, first diabetes prevention trial was accomplished [19].

Smoking in diabetic patients is associated with weakening of metabolic control which in turn linked with a high risk of macro and micro-vascular complications. Smoking enhances fatty acid levels. It is noteworthy that patients of T2DM have low capacity for exercise because of age. In diabetic patients, exercise enhances the insulin sensitivity just as it does in non-diabetic patients. IR is present in greater amount in diabetic patients that can be mediate by variety of abnormalities in glucose metabolism. These abnormalities has decreased glucose transporters, insulin receptors, and decline in intracellular enzymatic activity and reduced level of oxygen during exercise. Increase in physical activity increases the activity of mitochondrial enzyme and augments insulin sensitivity, conversely in diabetic patients' number of muscle capillaries affected by micro-vascular complexes, not increase in number [54].

Aging

Between 1998 and 2010 to 2012, incidence of diabetes increased from 3.55% to 10.00% in men and from 3.51% to 5.62% in women. After modification in age, central obesity, physical activity and 90BMI, diabetes frequency increased in both genders [55]. In the 2011 survey, DM and IFG prevalence increased linearly with advancing age; subjects in the 65–70 years category were nine times more likely to have DM than the youngest age group. Indeed, this is the first national survey to include elderly individuals aged 65–70 years, shedding light on the magnitude of the burden associated with caring for the aging population with DM. In the face of increased life expectancy and the graying of the population seen in the past two decades in Iran, a large proportion of elderly individuals with DM will continue to live with the disease. In 2001, 19.7% of US Medicare beneficiaries aged ≥ 67 years had DM with newly diagnosed cases increasing by 36.9% from 1994 [18].

Depression

Mechanism of hypercortisolemia was observed in patients with central obesity caused by depression as changes in both secretion and sensitivity of insulin causes interruption in glucose regulation. Depression is coupled with changed rhythm of diurnal cortisol and HPA axis dysregulation that increases the cortisol secretion. In fact, metabolic effects discharged by adipose tissue and elevated cortisol level results in insulin resistance in depressed individuals and can intensify obesity-linked glucose dysregulation [56].

Management

Generally, even the regular treatment of these diseases does not provide any surety for betterment. This lifetime illness gets worse and more complicated with time. Current method of treatment is not sufficient [57]. Independently, any initiative is not as effective as much as multidimensional intervention which include every possible level i.e. from low to high [58]. The WHO established Global Strategy in 2003, which mainly focuses on the health, life style and dietary modifications which increase the resistance against the current discussed diseases. Nutrition and health related programs are introduced in many countries like China, Brazil, Pakistan and India. These programs are facing large opposition from consumers and many food companies. But our main mission is to overcome these hindrances and apply possible approaches to control the increasing trend of hypertension, obesity and diabetes [28]. The Pakistan diabetes prevention program (PDPP) was introduced in Pakistan in 2011, to control and avoid non- communicable diseases, by Aga Khan University in association with IDF [59,60].

Conclusion

Above mentioned literature depicts an alarming scenario about the rising prevalence of obesity, diabetes and cardiovascular diseases throughout the world. These diseases render not only the individual human lives less productive and miserable but cost national economies unwanted financial healthcare loss. Besides genetics, physical inactivity and unhealthy eating habits are major causes of these diseases. Policies need to be formulated at national and international levels to create awareness about possible causes of these burgeoning diseases and the ways to treat (or manage) them.

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