



Review Article

A CRITICAL REVIEW ON CLINICAL MANIFESTATIONS OF OBESITY IN TYPE 2 DIABETES MELLITUS AND SOLUTION THROUGH PHYSICAL ACTIVITY

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ABSTRACT

Diabesity term recently coined in medical field because of the very close epidemiological and pathogenic associations between central obesity and Type 2DM. **Material and Methods:** This review is based on data collected from published research works in various journals. **Observations and Results:** cited based on research reviews to find out risk odds of obesity and physical inactivity and initiation of type 2 diabetes with solutions based on improve physical activity. **Conclusion:** Counseling would be one of the best strategies to opt physical exercise with moderate and vigorous intensity recommended as world health organization as healthy behavior to prevent and control of type 2 diabetes. Thus, Present write up is an effort to critically evaluate and assess the published research data on obesity and its association with development of type 2 diabetes and role of Physical exercises for prevention and control of type 2 DM as its solution with research evidences.

INTRODUCTION

Obesity and Type 2 Diabetes Mellitus are serious health concerns because of their increased prevalence globally. Reports of WHO cited that in 1980 nearly 108 million people worldwide had Diabetes Mellitus which increases to 422 million in 2014. This prevalence of Diabetes mellitus has been recorded to rise more rapidly in low and middle income countries than in high income countries. Premature mortality was also enhanced by 5% between 2000 and 2016 due to diabetes mellitus, while estimated 1.5 million deaths due to direct cause of diabetes mellitus was recorded. Among all diabetics most of them have diagnosed as type 2 diabetes. Number of modifiable risk factors are identified as associated risk factor of type 2 Diabetes mellitus such as excess body weight and physical inactivity.^[1]

Objective of the Review

The objective of this review is to critically evaluate and assess the published research data on obesity and its association with development of type 2 diabetes and role of Physical exercises as its solution with research evidences.

Association between Obesity and T2DM

Overweight and Obesity have been identified as major public health problem in both developed and developing countries and highly prevalent disease at all ages. More than 1.9 billion adults are overweight and 650 million are obese worldwide those are reported for nearly 2.8 million deaths. 135 million subjects have been identified as obese in India.

Obesity has been identified as one of the leading causes of death, because of the risk factor for the development of various non-communicable diseases. Approximately 44% were diagnosed with T2D, 23% with ischemic disease and 7-14% with cancers due to obesity estimated by world health organization.^[2] Result of various clinical research studies have been reported that fatter people are more prone for development of type 2 diabetes mellitus and

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vast evidences had been also proved this clinical impression.

Central Obesity and Free Fatty Acids link in the development of Type 2 DM

Presence of excess abdominal fat i.e. central or abdominal obesity or large waistline is high-risk form of obesity and is strongly responsible as risk of development of metabolic and cardiovascular complications. [3] Because, central obesity trigger changes in metabolism and releases excessive fat molecules into the blood and releases 'pro-inflammatory' chemicals, which affect insulin responsive cells and lead to reduced insulin sensitivity hence cause insulin resistance, which is identified as major trigger for development of prediabetes followed by type 2 diabetes. [4] Due to visceral fat lipolysis, 20% and 14% portal vein and total free fatty acids come into systemic circulation in obese persons nearly. [5]

This increased FFA transported to the liver and impairs insulin's ability to suppress hepatic glucose production, this raised levels of portal FFA causes hyperglycaemia, hyperinsulinaemia, and hepatic insulin resistance. Increased systemic FFA concentration also inhibits insulin-mediated glucose disposal in skeletal muscle, [6] also causes inhibition in insulin-stimulated glucose uptake in muscle and causes impaired insulin secretion by the pancreas. [7] So, non-esterified fatty acids released from adipose tissue of obese can prove the assumption the link between insulin resistance and β -cell dysfunction. [8]

Visceral Obesity and Adipocytokines link in Development of Type 2 DM

Adipose tissue abundantly secreted the adipose tissue-specific bioactive substances Adipocytokines (i.e. leptin and adiponectin). Research suggested the higher circulating plasma leptin levels is risk factor for Metabolic Syndrome especially for development of IFG. [9]

The Inflammation Hypothesis in the development of Type 2 DM

Excess visceral obesity, through certain inflammatory cytokines, such as IL-6, TNF-alpha, TGF b1 and monocyte chemotactic protein-1 (MCP-1) are involved independently in development of insulin resistance. These visceral inflammatory adipo(cyto)kines (IL-6, TNF-alpha, MCP-1) in liver causes non-alcoholic steatohepatitis (NASH), Pancreatic-cell dysfunction due to adipokine inflammatory injury thus decreases insulin synthesis and secretion consequently inducing insulin resistance and diabetes. [10,11]

Adiponectin which is a kind of Adipocytokine had been also shown effective on both body weight and insulin sensitivity in the liver and muscle in Animal experiments. [12] Duncan BB, et al (2004) in

prospective human study found hypo adiponectinemia can develop type 2 DM, also reduction in body weight had been shown to raise plasma adiponectin levels and improve insulin sensitivity. [13] Buttock fat working as energy reserve and remain inactive mostly. [14]

DISCUSSION

Global prevalence of Diabetes is increasing at an alarming rate which is fuelled by obesity epidemic. The obesogenic lifestyle such as lack of physical activity and ready access of highly calorific food is responsible for this. The close epidemiological and pathophysiological association between visceral adiposity and type 2 Diabetes is responsible for development of Diabetes. The complex balance between insulin secretion from beta cells of pancreas and peripheral insulin sensitivity maintain glucose homeostasis. But mostly visceral obesity due to adipokines and lipotoxicity influence this mechanism.

Research Evidences of BMI and Risk of Development of Type 2 Diabetes

Various research studies identified close association between BMI and risk of developing type 2 DM. Systematic reviews observed overweight, obese and morbidly-obese participants had strong association of developing T2DM. While weight loss was beneficial for long-term T2DM related outcomes. [15]

Hart CL, Hole DJ, et al. (2007) in prospective cohort studies found overweight and obesity as important risk factor for development of type 2 DM as they reported age-adjusted ORs 2.73 and 7.26 respectively in overweight and obese men. They also concluded that incidence of T2DM can be decrease by prevention of obesity. [16]

Nguyen NT, et al (2011), conducted study with 21,205 US adults to assess the link between type 2 diabetes and obesity and reported among them 13.6% were had T2DM. And among diagnosed type 2 DM survey adults, 80.3% were found overweight and 49.1% were obese. The result of the study was also recorded the increased incidence of type 2 DM with increase rate of severity of obesity. [17]

Studies also reported increase in BMI increases the relative risk of T2D in similar ratio, such as Resnick HE, Valsania P, et al (2000) found; annual increase of each kilogram of weight over a period of 10 years had been found associated 49% increase in the risk of developing T2D in the subsequent 10 years. While, 33% reduction in the risk of developing T2D reported if person lost even one kilogram weight annually over 10 years. [18]

Other than BMI, distribution of fat mass also influences the risk of development of T2D. For example; central (visceral) adiposity has been identified as greatest risk factor for development of type 2 DM. Waist circumference, is a valuable predictor

for later development of T2D. Studies reported association between increase in waist circumference and increased risk of developing T2D. People of Asian origin had found greater risk compare to Caucasian origin may be due to differences in fat distribution and associated levels of insulin resistance.^[19]

Future Strategies to Control Obesity and Type 2 Diabetes

The incidence of type 2 diabetes can only be reduced by adoption of healthy lifestyle measures. But as number of studies had been identified strong link between obesity and initiation of diabetes cases hence, obesity is important modifiable risk factor for prevention and control of type 2 diabetes.^[20] Even a small Reduction in body weight, can improve body's insulin sensitivity and lowers the risk of developing type 2 diabetes because in type 2 diabetic patients weight reduction significantly improves glycemic control, effectively improve insulin resistance and prevent progression from IGT to type 2 diabetes.^[21]

Solution Through Enhanced Physical Activity

Numerous studies have been proved that, both Obesity and physical inactivity are work as independent risk factors in initiation of type 2 diabetes. Rana JS, et al. 2007 in study, found positive interaction of the risk of type 2 DM in individuals who are both obese and physically inactive.^[22] Physical inactivity fast-tracks the pathogenesis of type 2 diabetes.^[23] While, physical activity by effectively reducing fat mass and by increasing fat oxidative capability can reduce the diabetogenic impact of obesity.^[24]

Physical activity is one of the best techniques of type 2 Diabetes management due to enhanced energy expenditure, significant weight loss, improve insulin sensitivity, and quality of life. For disease prevention in adults, in 2020 world health organization had been provided the guideline on physical activity and sedentary behaviour. According to this guideline at least 150- 300 minutes of moderate-intensity aerobic exercises or 75 to 150 minutes vigorous exercises is needed. Even similar combination of vigorous and moderate exercise or activity can also be performed in a week. Along with these physical activity 2 or more than 2 days per week muscle strengthening activity in which maximum major muscle groups should involve is recommended. WHO again emphasized that for additional health benefits it is better to engage in moderate physical activity for more than 300 minutes per week or vigorous activity more than 150 minutes per week.^[25]

Research Evidences of Weight Reduction by Physical Activity and Control of type 2DM

Donnelly JE, et al. (2009) in study identified that 150 minutes/week of moderate-intensity physical activity (equivalent to a brisk walk) alone may cause

weight loss (~2-3kg).^[26] Indeed, 200-300 min/week physical exercise for a longer time can do significant weight reduction and minimize weight regain long-term.^[27] Even modest weight loss has a favourable effect in prevention of diabetes. And among all kinds of solutions physical exercise with or without diet found to be more effective.^[28]

Brettfeld C, Maver A, et. al (2016) reported, a 5% reduction in body weight followed up by regular moderate intensity exercise could reduce type 2 diabetes risk by more than 50%.^[29]

Eriksson, KF, Lindgarde, F. in Sweden conducted 6-year Prospective Study to find out the effect of healthy diet and physical exercise in Prevention of type 2 diabetes mellitus. Result of the study identified healthy diet and regular exercise improved glucose tolerance in the active group, who had a lower rate of progression to type 2 diabetes (11 versus 29%).^[30]

Tuomilehto J, Lindstrom J, et al. (2001) had been conducted Diabetes Prevention Study by changes in lifestyle among patients with impaired glucose tolerance (mean age 55 years, mean BMI 33.2). Result of the study indicated 23% incidence of diabetes was significantly lower in subjects those were lost 3.5 kg weight (vs 0.8 kg in the control group) through exercise.^[31] Similar results were obtained by Knowler WC, Barrett-Connor E, et al. (2002) in the Diabetes Prevention Program (DPP).^[32]

Research Evidences of Reduction in Insulin Resistance by Physical Activity and Control of type 2 DM

Physical exercise can effectively reduce insulin resistance. Even more than 30 min daily walk or cycling to and from work was also significantly and inversely associated with risk of type 2 DM.^[33] In the US Diabetes Prevention Program (DPP), the 3234 nondiabetic persons (mean age 51 years, mean BMI was 34 kg/m²) those were having elevated fasting and post-load plasma glucose levels were randomized into three group i.e. placebo, metformin, and a lifestyle modification program (low-calorie, low-fat diet plus physical activity of moderate intensity for at least 150 minutes per week). The incidence of DM was reported 11.0, 7.8, and 4.8 cases per 100 person per year in the placebo, metformin, and lifestyle intervention groups after 2.8 years average follow-up, respectively. The lifestyle intervention was significantly reported more effective than metformin by reducing the incidence by 58% and metformin by 31% compared to placebo.^[34,35]

Mayer Davis EJ, et al. (1998) among 1467 participants age between 40 to 69 years and found that both vigorous and non-vigorous activities were associated with higher insulin sensitivity.^[36]

The British Regional Heart Study (Wannamethee SG *et al.* 2000) among 5159 men aged between 40–59 years examined the role of serum insulin concentration and their components in the relationship between physical activity and the incidence of type 2 DM and reported that physical activity was significantly and inversely associated with serum insulin concentrations and the incidence of type 2 DM.^[37]

Smith DA, *et al.* (2016), search 28 prospective studies on total Physical activity or leisure-time Physical activity and risk of type 2 diabetes. Results of study suggested, an overall risk reduction of 26% (95% CI 20%, 31%) for type 2 diabetes among those were achieved 150 min/week of moderate activity compare to inactive individuals. And 36% (95% CI 27%, 46%) risk reduction those were doing 300 min/week moderate activity.^[38]

Table 1: Research Evidences of Regular exercisers benefits in control of type 2 DM

Action on Insulin Resistance and lower Risk Reduction of DM	Reference
Mild to moderate intensity exercise (walking and jogging for 10-30 min per day, 3-5 days a week) improved Insulin sensitivity by increases in GLUT4 protein, IRS1 and PI3-kinase protein in skeletal muscle.	Sato Y, Nagasaki M, Kubota M, <i>et al.</i> (2007). ^[39]
Regular exercise influences IFG/IGT and obesity, by improved glucose metabolism, muscle respiratory capacity, mitochondrial respiratory chain activity and beta-oxidation.	Earnest CP (2008). ^[40]
Three year follow up study reported 58% lower risk of development of DM in participants followed a low-fat diet and averaged 150 min of weekly moderate-intensity activity (e.g., brisk walking) than control subjects.	Knowler WC, Barrett-Connor E, Fowler SE, <i>et al.</i> (2002). ^[41]
The physical activity participants were reported a 44% lower DM incidence compare to only weight reduction.	Hamman RF, Wing RR, Edelstein SL, <i>et al.</i> (2006). ^[42]
Finnish lifestyle study, reported 58% reduction in DM risk in its participants those were doing 30 minutes of daily walking and occasional resistance training, lost body weight, reduce their fat intake, ate more fiber.	Tuomilehto J, Lindstrom J, Eriksson JG, <i>et al</i> (2001). ^[43]
64% less risk of development of DM reported in participants those were doing moderate to vigorous physical activities.	Laaksonen DE, Lindstrom J, Lakka TA, <i>et al</i> (2005). ^[44]
30 min of moderate walking, 3-7 day per week for 6 months reversed prediabetic state of participants by enhancing Insulin sensitivity.	Duncan GE, Perri MG, Theriaque DW, <i>et al</i> (2003). ^[45]
Enhance insulin sensitivity due to prolonged exercise	Sigal RJ, Kenny GP, Wasserman DH, <i>et al</i> (2004). ^[46]
Improvements in insulin sensitivity in women with T2 DM have been reported for equivalent total energy expenditures by low or high-intensity walking.	Braun B, Zimmermann MB, Kretchmer N(1995). ^[47]
Physical exercises reported to improved insulin sensitivity by responsiveness of skeletal muscles to insulin and basal blood glucose uptake by increased activity of proteins involved in glucose uptake and metabolism and insulin signal transduction, such as adenosine monophosphate-activated protein kinase.	Hawley JA, Lessard SJ (2008). ^[48]

Establishment of Counseling Clinics

Counseling would be one of the best strategy to create awareness about the obesity as important risk factor among all risk factors for development of type 2 diabetes mellitus and need to maintain proper weight by adopting physically active lifestyle by involving them self in moderate to vigorous intensity exercises to prevent the development of type 2 DM or to control hyperglycemia for obese type 2 DM patients. It could also be used as a first-line treatment strategy for management of type 2 DM.

CONCLUSION

This article reveals that to control diabetic epidemic, it is need of the hour to screen the obesity and physical inactivity as risk factor for type 2 DM and use the strategies which can maintain normal body weight before the development of type 2 DM. Reviews of various studies observed the strong link between central obesity and initiation of type 2 diabetes and some of the research results had been also established that physical inactivity is main factor for obesity, actually these factors are interacting with each other. Additionally, it is also established that even a small

reduction in body weight can improve body's insulin sensitivity.

Hence, though various interventions are in use to control hyperglycemia. But among all, physical exercise had been found to be more effective in the prevention of development of type 2 Diabetes and its further management due to its significant weight loss action, by increasing fat oxidative capability and by enhancing insulin sensitivity level, which could be effectively work to reduce the diabetogenic impact of obesity. So, effectively prescribe exercise for the obese patient with or without prediabetes or diabetes can effectively control diabetes and prevent community from development of type 2 diabetes mellitus.

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