

# Is Reversal of Type 2 Diabetes Mellitus Possible? An Approach to Mitigate

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## Abstract

Diabetes mellitus defined as progressive and irreversible disease characterized by hyperglycaemia. It falls under top 5 cause of death and can lead to series of diseases affecting vital organs. Type 1 diabetes is hereditary disorder which leads to insufficiency of insulin in the blood. Type 2 diabetes mellitus is lifestyle dependent and occurs in later stages of life due to overweight. Excessive fat deposition in liver and pancreas leads to desensitization of receptors for insulin which leads to rise in blood glucose level. Type 2 diabetes mellitus is now known to be reversible with loss in body weight. Three methods of losing body weight are bariatric surgery, calorie restricted diet and carbohydrate restricted diet. All these methods help in reducing body fat which increases the insulin sensitivity and reduces blood glucose. Out of the three methods, carbohydrate restricted diet is proven to be most efficient.

**Keywords:** Remission, Bariatric surgery, low calorie diet, low carbohydrate diet.

## INTRODUCTION

As per American Diabetes Association, diabetes mellitus is defined as a group of metabolic diseases with clinical manifestation of prolonged hyperglycemia due to defect in insulin secretion, defect in insulin action or both. The long-term hyperglycemia is associated with damage, dysfunction and failure of different organs especially eyes, kidneys, nerves, heart and blood vessels. Diabetes is considered as the underlying cause of blindness, heart attack, stroke, kidney failure and lower limb amputation. The aetiology of diabetes mellitus can be autoimmune destruction of beta cells of pancreas with insulin insufficiency or the abnormalities that result in resistant to insulin action.[1] Majority of the diabetic cases comes under two categories. First one is type 1 diabetes mellitus which is caused by absolute insufficiency of insulin and accounts for about 5 to 10% of total diabetic cases worldwide. Second one is type 2 diabetes which accounts for about 90 to 95% and is caused by resistance to insulin and inability to produce compensatory insulin.[2] Type one diabetes is a genetic disorder which results in lack of insulin in the blood. In such case, the level of insulin will be less than the normal range in the blood. The cause of type 2 diabetes is not fully understood but it is characterised by rise in blood glucose level together with insulin level. There will be downregulation of insulin receptors which causes the loss of activity of insulin resulting in type 2 diabetes mellitus. Normal fasting blood glucose level range from 60mg/dl to 110mg/dl and post prandial of less than 140mg/dl. The renal threshold for glucose is 180 mg/dl and above this level, glucose can be detected in urine. In Both the cases, HbA1c level rises above the normal range i.e., 3 to 5% of total haemoglobin.[3]

### Facts and figures

As per international diabetes federation, 537 million people were diabetic in the year 2021 within age group 20 to 79 years, which is expected to rise to 643 million by 2030 and 783 million in 2045. This will be an increase in diabetic case by 46%. South east Asia has about 90 million diabetic cases in 2021, which will rise to 95 million in 2030 and reach 136 million by the year 2045, a rise in prevalence of diabetes mellitus by 87%. About half of the diabetic patients (about 240 million) are undiagnosed. Out of that, three fourth (3 in 4) live in low- or middle-income countries. More than 1.2 million children and adolescents are living with diabetes type 1. Total of about 6.7 million deaths had occurred due to diabetes and in the year 2019 alone, 1.5M death occurred making diabetes mellitus as the 9th leading cause of death in the world. As per WHO mortality due to diabetes has increased by 5% from the year 2000 to 2016.

As per National Diabetes Statics Report USA, it has about 37.3 million diabetic patents (11.3% of population of USA) out of which 28.7 million (72%) are diagnosed and 8.5 million (28%) of adult diabetic patents are undiagnosed).26.4 millionpeople (48.8%) above the age of 65 and are prediabetic and 96 million (36%) of population between the age group 28 to 65 are pre diabetes and can become diabetic patents in the future.[2,4-5] Every year they receive about 1.5M new cases of diabetes mellitus. [6]

#### Mechanism of onset of diabetes

Type 1 diabetes characterized by insufficiency of insulin in the blood is a hereditary disease due to mutation of the gene. Its manifestation starts in childhood and persist throughout the life. Type 2 diabetes is can also be called as lifestyle related diabetes and is most common in overweighted people. Accumulation of body fat is considered as major cause of type 2 diabetes. When excess amount of carbohydrates is consumed, some amount is used for energy and remaining is stored as glycogen for short term and as triacylglycerol for long term. When more amount of triacylglycerol gets accumulated in liver, it leads to nonalcoholic liver cirrhosis. This reduces the ability of liver for glycogenesis, elevating the level of blood glucose. Gain in body weight also Increases the fat content of pancreas which hampers insulin synthesis and the sensitivity of cells for insulin. This further hinders the insulin activity leading to severe rise in blood glucose. People blame cholesterol and reduces fat intake to reduce body weight but as per Satyanarayan, only less than 40% of dietary fat is absorbed as fat absorption depends on availability of bile salt and is a complex process. Those amounts of fat are used for hormone synthesis, formation of biomembrane and other structural proteins. It also states that among the different monosaccharides, fructose is very easily converted to triacylglycerol as stored form of energy.[7]The main culprit for gain in body weight is carbohydrate especially sweets edibles and not fat products. Therefore, controlling the carbohydrate intake is found to be more effective in reducing body weight than controlling the fat intake.

In earlier years, wheat products (Atta and Maida) were recommended for diabetic patents due to high content of roughage and indigestible carbohydrate as supplement to rice but recently wheat is found to contain gluten which can directly destroy the beta cells of pancreas leading to progression in diabetes. This is also thought to be the major cause of diabetes epidemic in South East Asian countries, especially India.

#### Methods of remission of type 2 diabetes

Until recent years Diabetes mellitus was thought to be progressive and irreversible disease. It is just about a decade ago when scientist knew that type 2 diabetes could be reversed back and normal blood glucose level could be achieved. It is only in 2016 that WHO global health report on diabetes added a section on reversal or remission of type 2 diabetes and stated that it can be achieved through weight loss and calorie restriction or bariatric surgery. [8] Since then, many methods and techniques were tested and clinical trials were conducted for the remission of type 2 diabetes. The term “reversal” or “remission” are generally used for improving the health of a diabetic patents and the term “cure” has not yet been used since there exists the chance of reoccurrence after the remission.

As per WHO, type 2 diabetes can be prevented or onset can be delayed with a healthy diet, regular exercise, maintaining a healthy body weight and avoiding any sort of tobacco products. [9] The centric idea of reversal of type 2 diabetes is weight loss. Three major ways are recommended for weight loss or reversal of type 2 diabetes and they are bariatric surgery, calorie restricted diet and carbohydrate restricted diet. [10]

##### a) Bariatric surgery

It is a term for collective surgeries meant for weight loss or to create a gastric bypass which reduces the rate of absorption of digested food and help in weight loss. It is generally done when diet and exercise have failed to reduce weight or due to possibility of severe disease due to existing weight. Second Diabetes surgery summit held in 2016 declared that bariatric surgery can be done to treat type 2 diabetes. [11] Bariatric surgery is not much common in South East Asian countries due to its cost and fear of patients to undergo surgery. In US the average cost of bariatric surgery is about \$14,389. [12] Bariatric surgery has proved to be effective and have shown positive result within hours to days. [13] It has achieved 80% remission rate but rate of long-term remission and side effects are not known. [14] Though it is effective in reducing body weight and remission of type 2 diabetes, it is not without any risk. The post-surgical complication accounts for 13% to 21% which includes medication intolerance, need for reoperation, post-surgical infection, etc. [15] During clinical trial, for about 10% to 15% of patents, remission of diabetes couldn't be successful after bariatric surgery. [16] Addition to that about 25% to 35% patents regained weight and again became diabetic patents within 1 to 4 years, needing further treatment from the beginning. [17] In an

observation made by Swedish doctor, 72% of remission was achieved at 2 years from selected number of people but only 36% of the sample could maintain the reversed state of type 2 diabetes at 10 years. [18] In contrast to bariatric surgery as a means for reversal of type 2 diabetes mellitus, some researchers have given their statement that, it is not actually the bariatric surgery that is causing the reversal of diabetes but the inhibition of oral intake of food after the surgery makes the body to use the stored fat as energy source during the period that helps in reducing the body weight and cause the remission. Therefore, the mechanism of bariatric surgery causing the remission of diabetes is not clearly known.

#### b) Calorie restricted diet or low calorie diet

Calorie intake is one of the factors that contributes to weight gain. When calorie intake is more than the required amount, body stores the surplus energy as triacylglycerol which leads to increase in body weight and internally leads to formation of fatty liver. The phenomenon behind low calorie diet helping in remission of type 2 diabetes is that, when oral energy consumption (fat or carbohydrate) is below the daily requirement of the body, body starts using stored fat for energy as a result, body weight (stored body fat) is reduced. This leads to increase in production and sensitivity of the insulin.

Many clinical trials and observations were made using low calorie diet. All those trials were collaborately called as DiRECT (Diabetes Remission Clinical Trials). In one of this trials, 306 diabetic patents were taken. They were neither on insulin nor detected as diabetes patents more than 6 years ago. [19] They were on low calorie diet of 825 to 853Kcal/day for 3 to 5 months and other foods were reintroduced step wise together with maintaining the body weight within normal range. At 1 year, 46% reversal was achieved with HbA1c<6.5g/dL without hypoglycemic medication and at 2 years reversal rate dropped to 37%. [20] Based on drop in the remission rate at 2 years, it was understood that huge level of calorie restriction was needed to induce enough level of weight loss for remission of diabetes mellitus. It was also found out that remission was effective for those with short duration of diabetes (generally less than 4 years of onset), HbA1c closer to the threshold level and those taking few hypoglycemic drugs. [21-22]

Another study was done among 11 type 2 diabetes patients who were detected as type 2 diabetes within 4 years. They were given very low calorie diet, i.e. 600Kcal/day and at 2 months, positive response was observed. Fasting plasma glucose was found to decrease from about 165mg/dl to about 106mg/dl. HbA1c was found to decrease from 7.4g/dl to 6g/dl. Likewise, fasting insulin level was found to drop from about 151pmol/l to 65pmol/l and hepatic glucose production rate from about 2.4 to 1.71mgKgffm-1Min-1. Insulin sensitivity rate was found to increase from 43% to 74%. Hepatic and pancreatic triacylglycerol was found to decrease by 70% and 77.5% respectively. Plasma lipid was found to drop from about 43.2g/dl to about 21.6g/dl. Like in all other methods weight loss was considered the main pillar which was found to happen by about 15% of initial body weight. [23] Though this study proved that very low calorie diet can reverse type 2 diabetes but very low calorie diet over long period can cause other complications and maintaining the weight upon increasing the calorie was most difficult thing found to be achieved.

Another trial was carried out in Bengaluru, India. 32 type 2 diabetes patients were treated with intensive lifestyle therapy. They were given low calorie diet of 1500Kcal/day with brisk walk for 1 hrs/day. 75% out of 32 got diabetes reversed in 1st year and same reversal rate could be maintained in 2nd year. They had found out that 2 patents who gained 3 to 4 kg of weight in between 1st and 2nd years had recurrence of diabetes [24]

#### c) Carbohydrate Restricted Diet

Consumption of carbohydrate less than RDA is called carbohydrate restricted diet. It is of two types, low carbohydrate diet where the total daily consumption of carbohydrate is less than 130 g/day and very low carbohydrate diet where per day consumption of carbohydrate is between 20 to 50 grams. It is also called as ketogenic diet. Protein and fat intake is not changed in this diet. The mechanism behind reversal of type 2 diabetes by carbohydrate restricted diet is, when carbohydrate is less than required, body will mobilize the stored triacylglycerol as energy source which will be converted to ketone bodies and later used as energy source. [25] During clinical trials for carbohydrate restricted diet for one year, 60% of the patents could reverse type 2 diabetes with plasma glucose below threshold level and HbA1c below 6.5% without hypoglycemic drugs. [26] Maintaining hypoglycemic level at 2 years was possible with 73% from the 60% at year 1. For this study diabetic patents for more than 8 years and those already on insulin treatment for one year were also included. This proves that carbohydrate restricted diet can sustain the reversed state of hypoglycemic level and also can reverse the patents who are already on insulin treatment within one year.[27]

Type 2 diabetes can be reversed by restricted diets and regular exercise which helps in reducing body weight and fat deposition in liver and pancreas. Excess body weight is proved as the root cause for type 2 diabetes and reduction in it by any means will improve the condition. Avoiding ultra-processed food and red meat and going for low carbohydrate diet, if possible fermented food like yoghurt and daily exercise should be encouraged for pre and early detected type 2 diabetes patents. Remission is much less likely once the person is on insulin or those with more than ten years on diabetes. Therefore, early counselling and diet guidelines are more important than prescribing medicines by the physician.

## Conclusion

Among all the methods, carbohydrate restricted diet proved to be most efficient in reversing type 2 diabetes followed by calorie restricted diet and then bariatric surgery. Achieving more than 60% remission rate by simple diet control is a great discovery in the history of diabetes therefore every pre diabetic and early detected diabetic patients should be properly counselled and made to control their dietary habit to reduce the chance of progressing to diabetic patents. People should be informed about the possibility of remission and encourage early screening and diagnosis as being late reduces the chance of remission.

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