Review Article

Diabetes Mellitus and Its Epidemiology in Uttarakhand

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ABSTRACT

Diabetes is the condition which leads to impairment of body's ability to process blood glucose. Prolonged elevated glucose level in blood may cause complication like blindness, stroke, heart and kidney diseases. Three major types of diabetes mellitus that can be developed are Type-I, Type –II and gestational diabetes. Type-I is also known as juvenile diabetes and it occurs when body fails to produce insulin. Type-II diabetes occurs when there is defect in insulin secretion and insulin resistance. Gestational diabetes occurs in women during their pregnancy, when body is prone to become less sensitive to insulin. Diagnosis of diabetes can be done by measuring blood glucose level and hemoglobin A1c (HbA1c).

Key words: *Diabetes mellitus (DM), type1 DM, type2 DM, Epidemiology, Uttarakhand .*

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INTRODUCTION

DM is a group of complex metabolic disorder associated with the elevation in blood glucose level (hyperglycemia), polyuria, weight loss, polydipsia, fatigue, etc **[1]**. It may occur due to defects in either insulin secretion, insulin action or both **[2].** Insulin is a hormone synthesized by beta-cells of pancreas results from various stimuli such as glucose, sulphonylurease and arginine. In DM, there is insufficient production of insulin by pancreas [**3**]. Levels of insulin is decreased in target tissues, mainly skeletal muscles, adipose tissue to achieve an adequate response and/or insulin resistance but if lesser extent of insulin reaches to insulin receptors in liver, then signal transduction system does not work properly leading to metabolic abnormalities [**4**]. Sometimes DM causes lifestyle disorder by creating complications in retina, kidney and nervous system [**5**]. Long term increased blood glucose level is associated with macro- and micro-vascular complications which can cause blindness, stroke, heart and kidney diseases **[6]**.

Pathophysiology of diabetes

After having meal the blood glucose levels rises, resulting in insulin secretion which is

responsible for an increase in transportation, biotransformation and storage of glucose in muscles and fat tissues. During fasting condition, liver provides blood glucose to brain, without depending on insulin level. Along with the storage of glucose, insulin is also responsible for inhibiting the secretion of glucagon and lowers the serum fatty acids' concentration leading to a decline in liver glucose production **[7]**. Insufficient insulin or insulin resistance in the body results in reduced glucose uptake in tissue that results in intracellular hypoglycemia and extracellular hyperglycemia. The intracellular hypoglycemia may cause glucogenesis and gluconeogenesis that is responsible for fats' breakdown (causing diabetic ketoacidosis) and decrease in protein synthesis and gamma globulins (causing cachexia, polyphagia, and impaired wound healing), while the extracellular hyperglycemia is responsible for hyperglycemic coma and osmotic diuresis **[8]**.

Classification of diabetes

Diabetes mellitus can be classified as **[9]:**

1. **Type I diabetes mellitus (Insulin dependent / IDDM):** Destruction of immune-mediated beta cells leads to insulin deficiency.
2. **Type II diabetes mellitus (Non-Insulin dependent / NIDDM):** Occur due to defect in insulin secretion and insulin resistance.
3. **Gestational diabetes mellitus:** is a type of DM that causes glucose intolerance with an onset of pregnancy.

Type I (Insulin dependent / IDDM) diabetes mellitus

10% of the Type 1 diabetes mellitus (T1DM) cases occur around the world. T1DM is the result of the autoimmune destruction of β cells present in endocrine pancreas.T1DM is classified as IA: autoimmune DM and IB: idiopathy DM. Type 1 diabetes is not hereditary. T1DM significantly develops around 6% in children, 5% in siblings and 50% in monozygotic twins [**10]**.

Type 1diabetes (T1D) is a chronic disease caused by immune-mediated destruction of insulin producing beta cells in the pancreas. In this type of diabetes insulin insufficiency is caused due to the destruction of beta cells and as a result patients develop hyperglycemia that is life-threatening and clinically manifests with weight loss, polyuria, and polydipsia,. Those patients who develop T1D have high-risk of Human Leukocyte Antigen (*HLA*) genes [**11**].

Diagnosis criteria for DM

Measurement of blood glucose level remains the criteria for diagnosis of DM for many years. Based on fasting plasma glucose (FPG) of 126mg/dl, glucose tolerance test of 200 mg/dl, diabetes or random plasma glucose or 2 hour plasma glucose can be diagnosed.3 Now it has been recommended by American Diabetes Association (ADA) to use the hemoglobin A1c (HbA1c) for the diagnosis of diabetes. The method that has been certified by NGSP must be used for HbA1c test and standardization must be done according to the DCCT. Hemoglobin A1c (HbA1c) is a widely used marker for chronic glycemia that involves in measuring of the non-enzymatic glycation of hemoglobin and is responsible for reflecting average blood glucose levels over a

period of 2-3 months. The patient needs not too fast for HbA1c test, which makes it much easier to screen individuals for diabetes. Other than, non-fasting plasma glucose, HbA1c test have other advantages like greater pre-analytical stability and less day-to-day variance during illness and stress. HbA1c test has limitations that it is more expensive than BG measurements, has less availability in developing countries and can be misleading in patients who suffer from anemia and hemoglobinopathies that are responsible for decreasing the lives of red blood cells **[12].** Therefore, for the conditions in which there is abnormality in blood cells, glucose criteria must be employed for detection of diabetes.1-3 National Glycohemoglobin Standardization Program (NGSP) are involved in standardization of HbA1c assays. At this point of time A1C tests are not very accurate to use for diagnostic purposes. For the diagnosis of diabetes both glucose and HbA1c criteria are available but maximum time any one of these is usually sufficient to make the diagnosis by the setting of the characteristic clinical picture of polyuria, polydipsia, weight loss, and fatigue. If the clinical picture is not clear, both HbA1c test and glucose results consistent with diabetes may be required for diagnostic purposes **[13].**

EPIDEMIOLOGY

Type 1 diabetes is one of the most common chronic diseases that can occur during childhood but it can be diagnosed at any age.4 Peaks in presentation may occur during the age between 5–7 years and at or near puberty. Contradictory to most autoimmune disorders that disproportionately affect females, type 1 diabetes is more common in males. The prevalence of type 1 diabetes varies with changes in the seasons and in the month of birth. Maximum cases are evidenced in autumn and winter, and person born in the spring season has higher chances of having type1 diabetes. These concepts determine the role for an environmental agent in initiating or driving the pathogenic processes in type1 diabetes [**14**].

Type2 diabetes

Earlier it was considered as a disease of western society, but now it (T2DM) has spread to every country in the world and Asia accounts for 60% of the world's diabetic population [1]. Among immigrants and minorities obesity and T2DM have become a major medical problem. **[2, 15]** Type 2 diabetes mellitus (DM) is a chronic metabolic disorder whose prevalence has been increasing steadily around the world [**16**].

Screening and Diagnosis

Screening and diagnostic tests for DM are readily available. The test recommended for screening is the same as that for making diagnosis, with the result that a positive screen is equivalent to a diagnosis of pre-diabetes or DM.32 At the time of diagnosis about 25% of the patients with type 2 DM already have microvascular complications suggesting that they have had the disease for more than 5 years.33 According to the guidelines of American Diabetic Association (ADA) of 1997 and World Health Organization (WHO) National diabetic group criteria of 2006, it is for a single raised glucose reading with symptoms like polyuria, polydipsia, polyphagia and weight loss, otherwise

increase in the values , of either fasting plasma glucose (FPG) is 7.0 mmol/L (126 mg/dL) or with an oral glucose tolerance test (OGTT), two hours after the oral dose a plasma glucose is11.1 mmol/L (200 mg/dL) **[17]**. The recommendations of 1997 given by ADA is for diagnosis of DM that focus on the FPG, while WHO focuses on the OGTT.32 For determining blood sugar control the glycated hemoglobin (HbA1c) and fructosamine are also still useful . In many cases it has been seen that, practicing physicians frequently employ other measures too in addition to those recommended. The International Expert Committee (IEC) in July 2009 adopted the additional diagnostic criteria of an HbA1c result ≥6.5% for DM. To identify those at high risk of developing DM this committee suggested that the use of the term pre-diabetes may be phased out but identified the range of HbA1c levels ≥6.0% and <6.5%.34. As in the case of glucose-based tests, where there is no definite threshold of HbA1c at which normality ends and DM begins **[18].**

Treatment of T2DM

Table1. Represents anti-diabetic agents for the management of patients with T2DM [**19**]

Class	Drug (s)	Target	Action (s)	Disadvantages
Biguanides	Metformin	AMP-kinase	blood glucose↓ insulin sensitivity↑ cardiovascular risk↓ hypoglycemia risk↓	GI side effects lactic acidosis Vitamin B12 and folate deficiency
Sulfonylureas	Glyburide/ Glipizide/ Gliclazide/ Glimepiride	ATP-sensitive, K+ channels	insulin secretion↑	hypoglycemia weight gain
TZDs	Troglitazone/ Roziglitazone/ Pioglitazone	PPAR-γ	insulin sensitivity↑ hypoglycemia risk↓ glycemic control↑	bladder cancer risk↑ weight gain edema
AGIs	Acarbose/ Miglitol/ Voglibose	α-glucosidase	carbohydrate absorption↓	GI side effects dosing frequency
GLP-1 receptor agonists	Exenatide/ Liraglutide	GLP-1 receptors	insulin secretion↑ glucagon secretion↓ satiety↑ hypoglycemia risk↓	GI side effects acute pancreatitis renal dysfunction thyroid C-cell tumors in rodents

Gestational diabetes mellitus (GDM)

When there is intolerance in glucose at variable degrees with an onset or first recognized pregnancy. About 15–45% of babies may suffer from macrosomia as they are born to diabetic mothers and when compared to normoglycemic controls this is a 3-fold higher rate. If a baby have birth weight above the 90th percentile for gestational age or >4,000g is called Macrosomia. Unlike maternal hyperglycemia, maternal obesity has a strong and independent effect on fetal macrosomia **[20]**.

Some factors like, maternal pre-pregnancy body mass index (BMI), pregnancy weight gain, maternal height, hypertension and cigarette smoking shows a great impact at the time of delivery in gestational age. In a study it was found that new born babies born out of obese mothers has double the risk of macrosomia when compared to babies born out of normal weight mothers **[21].**

EPIDEMIOLOGY OF DIABETES IN UTTARAKHAND

From 30 villages a total of 1002 geriatric population was enrolled for the study which included people with age group of 60 years and above. Factors included for determining the presence and rate of diabetes mellitus in the population were socio-demographic profile such as age, gender, education qualification, physical activity, blood glucose and lipid profile. Geriatric subjects those were having fasting blood glucose ≥126 mg/dl were counted under diabetic category. Individuals whose BMI was <18.5 were considered as under- weight, 18.5-24.9 normal, 25-29.9 overweight and pre-obese ≥30 obese [22].

In this study it was found that diabetes mellitus was 14.6%, which was much lower than the studies conducted earlier in other states- Kerala (28.2%), Kashmir (27.3%), Andhra Pradesh (24%), Delhi (13%). However talking about Uttarakhand region, diabetes mellitus was prevalent in 8.7% of geriatric population. According to the documentation of National Family Health Survey-4, it has been revealed that prevalence of impaired fasting glucose was 8.8% among males and 6.1% among females adult population [22].

Out of total 1002 people, involved in the study 146 people were diabetic and 856 were non-diabetic. People in the age group of 60<70 years were 96 (65.8%), 70<80 were 39 (26.7%) and ≥80 were 11 (7.5%). In case of gender diabetic females were 94 (64.4%) and male were 52 (35.6%). In case of education qualification; illiterates found diabetic were 69 (47.3%), primary school 26(17.8%), middle school 16(11%) and high school certificate and above 35 (23.9%). Taking into account the socio economic status, diabetic case in lower class is 102 (69.9%), middle class 38 (26%) and upper class 6(41%). Measure for total triglyceride (mg/dl) was also seen and population with normal level (<150) were 349 (65.8%), borderline (150-199) were 146 (27.6%) and high level (200-499) were 35(6.6%) [22].

A second study was conducted on IPD and OPD patients at Department of Veer Chandra Singh Garhwali Government Medical College and Research Institute, Srinagar, Uttarakhand. In this study of type-II diabetes mellitus, patients of age group 35 years and above were included. The factors included in

determination of prevalence of diabetes mellitus were age, gender, occupation, BMI, blood sugar. Total subjects included in the study were 128 and out of which 76 were males and 52 were females were type- II diabetic (diabetes mellitus).In case of obesity, 28 (36.8%) were males and 30 (57.7%) were females [23].

Third study was conducted in hilly areas of Tehri Garhwal and Uttarkashi districts of Uttarakhand respectively. A total of 401 subjects were recruited for the study on prevalence on diabetes mellitus. Out of these 401 people 201 were males and 200 were females. 123 were obese having BMI ≥25 (30.7%). Subjects recruited for the study were of mean age 46.6 years. From total individuals 19 were found to be diabetic and out of these diabetic patients 6 (3%) were males and 13(6.5%) were females. The increase in diabetes mellitus in case of females could be due to increase in psychosocial stress among them. Overall prevalence of diabetes mellitus is found lower, in comparison to other parts of India, due to more physical activity in hilly areas [24].

The fourth study was conducted in Haridwar district, Uttarakhand. 500 people were selected for the study and out of this 270 were males and 230 were females. Total prevalence of type –II diabetes was 11% in males and 10.87% in females. Diabetic males were of age group 38.7±13.5 and females were 35.6±12.8 years. Males belonging to labour class having type-II diabetes were 120 (44.5%) and females were 2(0.8%). Males from government services were 20 (7.4%) and females were 15 (6.5%) and males from house hold workers were 10 (3.7%) and females were 10 (4.4%). Obese case for males was 30 (11.1%) and females were 32 (13.9%) [25].

CONCLUSION

According to literature review, we found that Uttarakhand region is least affected by diabetes as compared to the data obtained from other states like Kerala (28.2%), Kashmir (27.3%), Andhra Pradesh (24%) and Delhi (13%). In Uttarakhand, females are more prone to diabetes than males. Population under 60-70 year of age with low physical activity is likely to be affected by diabetes. The population which belongs to the lower classes is affected with diabetes because of illiteracy, ignorance and expensive medical treatments. The increased triglyceride's level, lead to increase in the insulin resistance that causes diabetes. The people of Uttarakhand of age group from 35-45 year are prone to type 2 DM. Males are found at high risk for type 2 DM when compared to females. Obesity is the main factor that increases the risk of DM.

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