ABSTRACT
Dermatologic issues are basic in diabetes, with around 30% of patients encountering some cutaneous association over the span of their sickness. Skin indications, by and large, show up over the span of the illness in patients known to have diabetes, however, they may likewise be the first introducing indication of diabetes or even goes before the finding by numerous years. The skin contribution can be an immune system in nature, for example, acanthosis nigricans, necrobiosis lipoidica, diabetic dermopathy, scleroderma, and granuloma annular, or irresistible as erythrasma, necrotizing fasciitis, and mucormycosis. Pharmacologic administration of diabetes, furthermore, can likewise bring about skin changes, for example, lipoatrophy and lipohypertrophy, at the site of infusion of insulin, and oral antidiabetic specialists can cause numerous skin responses as unfriendly impacts. The administration of these cutaneous signs is custom-made by the fundamental pathophysiology, however close control of blood glucose is essential in all administration systems.

KEYWORDS: Diabetes Mellitus, Insulin, Type 1, Type 2, Beta cells.

INTRODUCTION
Diabetes is a very complicated disorder that requires consistent thoughtfulness regarding diet, work out, glucose checking, and drug to accomplish great glycemic control [1]. The world's predominance of diabetes expanding each year[2]. Improving information, abilities, and certainty empowers patients to assume greater responsibility for their own condition and coordinate viable self-administration into their everyday lives [3, 4, 5]. Type 1 diabetes (T1D) is quite possibly the most well-known constant safe intervened sicknesses in kids and youths portrayed by steady obliteration of the pancreatic insulin-creating (β) cells, in the end, prompting all out insulin inadequacy in hereditarily helpless people. Obvious T1D is gone before by an asymptomatic preclinical
period, during which auto-antibodies against (β) cells structures show up into the fringe flow [6]. Seroconversion to autoantibody energy may happen right off the bat in existence with an away from during the second year of life [7, 8]. The rate of T1D has expanded in evolved nations in the course of the last 50-60 years [9]. For instance in Finland, the yearly occurrence was 12/100,000 kids <15 years old in the mid-1950s expanding to a pace of 65 of every 2006 [10, 11].

The expression "diabetes" and "Mellitus" are gotten from the Greek language. "Diabetes" indicates "a pass through, a siphon" while the "Mellitus" signifies "Sweet". It is accepted that Greeks entitled it such a way, because of the misrepresented pee extents delivered by diabetic patients which pulled in flies and honey bees [12, 13]. From the absolute previously depicted instance of DM 3000 years back by the old Egyptians and Aratus of Cappadocia(81-133AD) to 1675 when English Thomas Willis rediscover the pleasantness of pee and blood of patients [14,15] since now colossal improvement in the information for DM has been accomplished.

Diabetes Mellitus (DM) is an endocrinological problem [16-24] and not a solitary issue which is a gathering of metabolic or heterogeneous difficulty coming about because of an anomaly in insulin discharges and insulin activities or both. Nonattendance or diminished insulin thusly prompts industrious unusually high glucose and glucose narrow mindedness [25]. It is most likely the most established sickness known to man. It is additionally dark passing from the fourteenth century.

Diabetes mellitus influences 30.3 million individuals in the US [26], and an expected 25% of patients with diabetes will require a medical procedure [27]. Diabetes is a danger factor of postoperative entanglements remembering for careful site contaminations, postoperative myocardial ischemia, intense renal disappointment, ileus, and expanded length of hospitalization [28-32]. Patients with diabetes are 1.5 occasions bound to build up careful site contamination [33]. Each careful site contamination is assessed to cost $7,000 to $38,000 [34-35]. Additionally, these patients have a higher danger of mortality in the preoperative period than patients with known diabetes [36]. Hyperglycemia noted in careful or basically sick patients without a known analysis of diabetes it is regularly alluded to as stress hyperglycemia [37]. Diabetes was first portrayed 3500 years back by the antiquated Egyptians. One of the main clinical depictions was made by Aretaeus, who rehearsed medication in Cappadocia.
around 120 A.D. [38]. The term diabetes mellitus depicted a metabolic problem of different etiology portrayed by persistent hyperglycemia with aggravations in sugar, fat, and protein digestion, coming about because of failings in insulin discharge, insulin activity, or even both [39]. Diabetes mellitus can be grouped into a few kinds; anyway, there are two primary structures: type 1, likewise characterized as an insulin-subordinate type of the sickness, and type 2, a non-insulin subordinate structure. The DM2 as a rule grows more in the grown-up age, successfully fundamentally the old and additionally corpulent people. Nonetheless, as of late because of changes in the nature of the food diet and its social changes, this sickness is all the more frequently saw in youngsters [40, 41]. In this sort of illness, the discharge of insulin may appear to be typical or even over the top, however is as yet deficient to remunerate the insulin opposition [42]. They as a rule happen when the body can't create enough insulin or can't utilize insulin successfully. Insulin is a peptide hormone that controls the digestion of sugars and fats by advancing the ingestion of glucose from the blood to skeletal muscles and fat tissue [43, 44]. In 2007, 246 million instances of diabetes were assessed on the planet. A later report assessed that this number has ascended from 108 million every 1980 to 422 million out of 2014 [45-50].

**Epidemiology of Diabetes**

Diabetes is quickly turning into the pandemic of the 21 century. Type 2 diabetes, which is more pervasive (more than all diabetes cases) and the fundamental driver of the diabetes scourge, presently influences 5.9% of the world's grown-up populace with practically 80% of the complete in agricultural nations [51]. No place is the diabetes plague more articulated than in India as the World Wellbeing Association (WHO) reports show that 32 million individuals had diabetes in the year 2000 [52]. The Global Organization (IDF) assesses the absolute number of diabetic subjects to be around 40.9 million in India and is additionally set to ascend to 69.9 million continuously 2025 [53]. It is assessed that 366 million individuals had DM in 2011; by 2030 this world has ascended to 522 million [54]. The quantity of individuals with type 2 DM is expanding in each nation with 80% of individuals with DM living in low and center-pay nations. DM caused 4.6 million passings in 2011 [54]. It is assessed that 439 million individuals would have type 2 DM constantly in 2030 [55]. Most of the DM trouble in Africa has all the earmarks of being type 2 DM, with under 10% of DM cases being type 1 DM [56]. A Middle
for Infectious prevention and Counteraction (CDC) report assesses that DM influences about 25.8 million individuals in the US (7.8% of the populace) in 2010 with 90% to 95% of them being type 2 DM [57].

In 2007, type 2 diabetes speak to a significant general medical problem everywhere in the world, turning into a "diabetes pestilence" as expressed by Zimmet [58]. Communicated in a number of patients, the normal advancement of diabetes is additionally striking and breathtaking, as the complete number of grown-up diabetes patients (generally type 2 diabetic patients) on the planet should increment from 135 to 300 million between 1995 to 2030, primarily because of a huge increment of 171% in agricultural nations, from 84 to 228 million, while it should increment just 41% in created nations, from 51 to 72 million [59].

The assessed overall predominance of diabetes among grown-ups was 285 million (6.4%) in 2010, and this worth is anticipated to ascend to around 439 million (7.7%) by 2030 [60]. It was recorded that just in 2012 at any rate 1.5 million subtleties initiated from diabetes [61]. Internationally, starting in 2011, an expected 366 million individuals had DM, with type 2 making up about 90% of the cases [62,63]. As per the world Actuality book report in 2008, in Africa, the commonness of diabetes mellitus was 3.2% and 40,895 individuals (2.0%) were in Ethiopia [64].

In 2007, 246 million instances of diabetes were assessed on the planet. A later report assessed that this number has ascended from 108 million out in 1980 to 422 million out in 2014 [65]. Also, this examination reports that in 2015, 1.6 million passings were straightforwardly brought about by diabetes. For human wellbeing, just as in monetary terms, the weight of diabetes on the planet is tremendous, causing around 5.1 million passings every year and taking up 548 billion US dollars in wellbeing spending in 2013 (11% of the absolute spent around the world).

An assessment of the Global Diabetes Organization (IDF) demonstrated that, in 2013, 8.3% of the grown-ups populace (around 382 million individuals) experienced diabetes; and the quantity of individuals with the illness is expected to ascend to 592 million in under 25 years [66].

Internationally, an expected 422 million grown-ups are living with diabetes mellitus, as per the most recent 2016 information from the World Wellbeing Association (WHO) [67]. Diabetes commonness is expanding quickly; past 2013 assessments from the Worldwide Diabetes League put the number at 381 million individuals having diabetes [68]. The WHO gauges that diabetes brought about 1.5
million passings in 2012, making it the eighth driving reason for death [69].
In 2013, Bangladesh was home to in excess of 5 million diabetic patients (5.5% of the public populace). This figure is assessed to ascend to in excess of 10 million (8.2% of the populace) by 2035 [70]. Very nearly one Chinese grown-up in ten has diabetes. A recent report assessed that in excess of 92 million Chinese grown-ups have the illness, with another 150 million demonstrating early indications [71].

PATHOPHYSIOLOGY OF DIABETES

Demographics
Type 1 diabetes and type 2 diabetes differentially impact populations based on age, race, ethnicity, geography, and socioeconomic status.

Type 1 Diabetes
Somewhere in the range of 2001 and 2009, there was a 21% expansion in the quantity of youth with type 1 diabetes in the U.S. [72]. Its pervasiveness is expanding at a pace of ~3% every year all around the world [73]. Despite the fact that determination of type 1 diabetes as often as possible happens in youth, 84% of individuals living with type 1 diabetes are grown-ups [74]. Type 1 diabetes influences guys and females similarly [75] and declines the future by an expected 13 years [76]. An expected 5-15% of grown-ups determined to have type 1 diabetes really have type 1 diabetes or inactive immune system diabetes of grown-ups (LADA) [77].

Type 2 Diabetes
In the U.S. an expected 95% of the almost 30 million individuals living with diabetes have type 2 diabetes. An extra 86 million have prediabetes, putting them at high danger for creating type 2 diabetes [78]. Among the segment relationship for type 2, diabetes is more established age, race/nationality, male sex, and financial status [79]. The predominance of type 2 diabetes in the U.S. is higher for guys (6.9%) than for females (5.9) [80].

PATHOGENESIS AND PATHOPHYSIOLOGY OF DIABETES MELLITUS

Type 1 diabetes mellitus
Type 1 Diabetes is described via immune system decimation of insulin creating cells in the pancreas by CD4+ and CD8+ Lymphocytes and macrophages invading the islets [82]. A few highlights portray type 1 diabetes mellitus as an immune system illness [83]. Roughly 85% of patients have circling islet cell antibodies, and the larger parts additionally have noticeable enemy of insulin antibodies prior to accepting insulin treatment. Most islet cell antibodies are coordinated against glutamic corrosive decarboxylase (Stray) inside pancreatic B cells [84].
Type 2 diabetes mellitus

In sort 2 diabetes these components separate, with the result that the two principle obsessive imperfections in sort 2 diabetes are weakened insulin discharge through a brokenness of the pancreatic β cells, and impeded insulin activity through insulin obstruction [85].

Type 2 diabetes mellitus is a heterogeneous issue with shifting commonness among various ethnic gatherings. The pathophysiology of type 2 diabetes mellitus is described by fringe insulin obstruction, disabled guideline of hepatic glucose creation, and declining β cells work, at last prompting β cells disappointment. The essential occasions are accepted to be an underlying shortfall in insulin discharge and, in numerous patients, relative insulin insufficiency in relationship with fringe insulin opposition [86, 87].

The β cells

β cells brokenness in at first described by a debilitation in the primary period of insulin emission during glucose incitement and may precede the beginning of glucose bigotry in sort 2 diabetes [88]. In synopsis, the deferral in the principal period of insulin discharge, in spite of the fact that of some finding import, doesn't seem to act autonomously in the pathogenesis of type 2 diabetes. In some beginning stage patients with type 2 diabetes (maybe the same number of as 20%) [89, 90].

Insulin resistance

Radiating from the kaleidoscopic exhibit by Yalow and Berson of the presence of hyperinsulinism in sort 2 diabetes, insulin obstruction has been considered to assume a necessary part in the pathogenesis of the sickness [91]. Different examinations in this high danger bunch have neglected to exhibit insulin opposition, and in a similar gathering, hindered beginning stage insulin delivery and loss of ordinary oscillatory example of insulin discharge have been depicted [92, 93].

The liver

The capacity of insulin to stifle hepatic glucose creation both in the fasting state and postprandially is ordinary in first-degree family members of type 2 diabetes patients [94]. It is the expansion in the pace of postprandial glucose creation that proclaims the developments of IGT [95]. Ultimately, both fasting and postprandial glucose creation increment as type 2 diabetes advances. Hepatic insulin opposition is portrayed by a stamped decline in glucokinase action and a reactant expanded transformation of substrates to glucose in spite of the presence of insulin [96]. Along these lines, the liver in sort 2 diabetes is modified to both overproduce and underuse glucose. The raised free unsaturated fat levels found in sort 2 diabetes may likewise assume a job in expanded hepatic
glucose creation [97]. Likewise, late proof suggests a significant job for the kidney in glucose creation by means of gluconeogenesis, which is excessive within the sight of type 2 diabetes [98].

**DIAGNOSIS OF DIABETES**

**Diabetes Testing**

Three blood tests are available to diagnose prediabetes and diabetes

- Casual plasma (blood) glucose
- Fasting plasma glucose (FPG)
- Oral glucose tolerance test

**Postprandial Blood Glucose Test**

Measure blood glucose levels 2 hours subsequent to eating a supper. Postprandial blood glucose is generally done in individuals who have manifestations of hyperglycemia, or when the consequences of a fasting glucose test recommend conceivable diabetes, however are uncertain. Estimations of 200 mg/dL or more demonstrate diabetes. Hemoglobin A1c (HbA1c), otherwise called the glycosylated hemoglobin or glycohemoglobin test It is utilized to screen the adequacy of treatment in individuals previously determined to have diabetes. HbA1c measure the measure of glucose connected to hemoglobin (the oxygen-conveying protein in red platelets), which increment as blood glucose levels rise. Since hemoglobin courses in the blood until the red platelets bite the dust (a large portion of the red platelets are supplanted each 12 to about four months), the HbA1c test is a helpful apparatus for estimating normal blood glucose esteems over the past 2 to 3 months [102-110].

**Diagnosis of gestational diabetes mellitus**

In any event a month and a half after the pregnancy closes, the ladies ought to get an oral glucose resistance test and be renamed as having diabetes, ordinary glucose resilience, weakened glucose resistance, or impeded fasting glucose. Ladies at high danger (positive family ancestry, history of GDM, checked corpulence, and high danger ethnic gathering) should be screened as soon s achievable. In the event that the underlying screening is negative, they ought to go through retesting at 24-48 weeks. The finding of GDM is made if at least two of the plasma glucose esteems are met or surpassed [111]. It is likewise not known whether the danger of diabetes contrasts between patients distinguished as having pre-diabetes by methods for glycated hemoglobin testing and those recognized by implies fasting plasma glucose testing. Such dangers likely shift as per which test is utilized at last to make the determination. Progressing research is evaluating the estimation of danger scores that consolidate glycemic quantify as well as other
biomarkers and danger components to assess diabetes hazard [112,113].

**CLINICAL FEATURES OF TYPE 1 DIABETES**
A portion of the manifestations incorporate weight reduction, polyurea, polydipsia, polyphagia, stoppage weakness, cramps, obscured vision, and candidiasis [114]. Enduring sort 1 DM patients may vulnerable to microvascular intricacies; [115-117] and macrovascular illness (coronary supply route, heart, and fringe vascular infection) [118].

**Clinical highlights of type 2 Diabetes**
Most cases are analyzed due to intricacies or unexpectedly. Conveys a high danger of huge vessel atherosclerosis ordinarily connected with hypertension, hyperlipidemia and heftiness. Most patients with type 2 diabetes bite the dust from cardiovascular intricacies and end stage renal infection. Topographical variety can contribute in the greatness of the issues and to generally speaking grimness and mortality [119-121].

**SIGNS AND SYMPTOMS**

**Symptoms of Type 1 Diabetes**
1. Frequent urination
2. Unusual thirst
3. Extreme hunger
4. Unusual weight loss
5. Extreme fatigue and Irritability

There is a reason why diabetes is termed the silent killer. It is Important to bear in mind that these symptoms may be mistaken for an ailment in themselves or for some other disease. The best methods to diagnose this condition is to have a blood test taken. And if you have already noticed this symptoms, you should see a doctor at the earliest.

**Symptoms of Type 2 Diabetes**
1. Exercise Urination and Thirst
2. Increased Hunger
3. Unexplained Weight Gain
4. Irritability and Fatigue
5. Blurred Vision
6. Warning Signs of Diabetes
   a) Decelerated Healing
   b) Skin and Yeast Infections plus Frequent Gum and Bladder Infections

**Other Symptoms**
1. Sexual Dysfunction in Men
2. Vaginal Infections in Women
3. Numbness/Tingling in hands and feet
   4. Itchy or Flaky Skin

**Complication of Diabetes mellitus**
Diabetes mellitus induce several complication or can co-exist with other diseases. In everyday clinical management of diabetic patients, doctors battle with diabetic complications which are very common and come in broad spectrum of manifestations.
The complications are divided in microvascular and macrovascular. The macrovascular, which are more severe, are coronary disease, stroke and peripheral neuropathy. The microvascular are sneakier and in long-term may lead on macrovascular complications are diabetic retinopathy, diabetic nephropathy and diabetic foot. In this part several case reports are present among the numerous found in literature. Neonatal diabetes is a rare form of diabetes mellitus (DM) which might occurs during the first six months of infant’s life. The two forms permanent and transient have been associated with alterations in the KCNJ11 and ABCC8 genes most frequently and the GATA6 genes less frequently. These mutations coexist with gastrointestinal and heart abnormalities. Such is a report of a Caucasian male infant with a GATA6 mutation that developed DM due to pancreatic hypoplasia, ventricular and atrial septal defect, an absent gallbladder and a right inguinal hernia [122].

DM was also correlated with Friedreich’s ataxia (FA). A 14-year-old male adolescent had insulin-dependent DM on a FA background, while being under treatment with insulin. Studies have shown that islet pancreatic cells reduction that happen in FA is the cause of DM [123]. There area cases that pancreatic neuroendocrine tumor (PNET) was connected with DM developing. Such is a case of a patient with a pancreatic somatostatin tumor [124].

ABCC8 mutation in a homozygous state was also connected with DM. The insulin-dependent DM that occurs due to this mutation can be misinterpreted with neonatal DM, although its beginning is later. In those patients sulfonylurea treatment was chosen as primary medication [125].

Despite diabetic striatopathy is a common complication on adults was only reported twice in children. In those cases along with weight loss, polyuria, and polydipsia was reported hemichorea-hemiballism that was receded after glucose control [126]. Among other taking right clinical history of a patient and not only the lean on the lab results for diabetic patients is quite important. A 37-year-old man with many diabetic complications and trouble in glucose regulation was misdiagnosed as DM type 1 while he was suffering from Neonatal DM as long as two weeks old. The proper taking of the family history revealed that his mother and his brother was also suffering from the same problem. This will help the patient now on his family making options [127]. In another report, a Caucasian woman, 55 years of age without medical history and not ever under any medication, presented with signs of
diabetic retinopathy and high blood glucose. Patient’s lab tests were found normal. The clinical history revealed recent appearance of polyuria and polydipsia. That set the diagnosis of DM type 1 which should always be in the front line of a medical doctor’s thinking. However, in this case did not conformed with the patient’s age [128].

Another category of DM complications is the infections. This category includes bone infections such as patellar osteomyelitis. Two reports of patellar osteomyelitis were revealed, both in adults diabetic women with uncontrolled blood glucose and no formerly medical history. The two patients presented with knee pain and after lab and screening tests were found that they suffered from patellar osteomyelitis. Both were treated with surgery and oral antibiotics with good prognosis. It is believed that diabetic neuropathy which causes dwindling or asence of pain is one factor of the late doctor’s consultation. It remains to be found the reasons of the increased frequency of bone and other systemic infections in patients with DM [129]. A rare complication that was recorded on a DM patient was Cryptococcosis [130]. This is a common fungal infection on patients that are under chronic immunosuppressant therapy. A 48-year-old man with a lung mass suspected to be cancer had that infection. Cryptococcosis can appear on immunocompetent patients only with a predisposing background and DM is one of them. Another uncommon fungal infection is mucormicosis which has been proven to present more often to DM patients. It remains to be investigated reasons that this occurred [131].

**THERAPY OF DM**

Diet therapy is important for the prevention as well as the treatment of all stages of type 2 diabetes. till it continues to remain high controversial and poorly understood In majority of the individuals with type 2 DM, if obesity seems along with hyperglycemia, weight reduction is the major goal of dietary therapy [132].

Exercise helps to prevent type 2 DM and control all types of diabetes cases. Muscular sensitivity to insulin can be improved by physical activity. The mechanism involved are increased blood flow to the tissues and reduced free fatty acid and intra abdominal fat level [133].

**Oral hypoglycemic drugs**

**Sulfonylureas and the newer glitinides**

Sulfonylureas have been utilized to treat type 2 diabetes since 1942 and require useful pancreatic beta cells for their hypoglycemic impacts [134]. They have an islet beta cytotoxic activity.[135]. The meglitinides are
generally new class of insulin secretagogues [136]. The two of them act by prompting insulin emission. The glitinides have a more quick activity of beginning and more limited span of impact than sulfonylureas and are given before a dinner to animate prandial arrival of insulin. The normal reduction in HgA1c is 1-2 mg/dL. Both these meds can prompt hypoglycemia and weight pick up [137].

**Biguanides – metformin**

They invigorate fringe use of glucose, increment the affectability of muscle to insulin activity and diminish the intestinal assimilation of glucose and prompts a normal reduction in HgA1c of 1-2 mg/dL by decreasing hepatic gluconeogenesis [138]. Patients of renal or hepatic illness, hypoxic pneumonic infection, or cardiovascular breakdown are inclined to lactic acidosis due to decreased medication disposal or diminished tissue oxygenation. Liquor ingestion may likewise hasten lactic acidosis [139]. Metformin is an insulin saving specialist and doesn't expand weight or incite hyperglycemia. It should be given first-line in stout kind 2 diabetics [140].

**Plant remedies in the management of DM**

Spices are utilized by humankind since its root on the earth for mitigating infirmities and for the support of general wellbeing. Since antiquated occasions, plants stayed a significant normal asset on the planet [141]. Principally clans gave the information base with respect to therapeutic properties of the spices and these plants have an incredible interest in both created and agricultural nations [142]. World Wellbeing Association assessed that 80% of the total populace depends on customary drugs to meet their essential medical care needs, most sorts of which use cures from plants. Indeed, even the cutting edge pharmacopeia actually contains in any event 25% of medications got from plants and numerous others which are semisynthetic, based on model mixes segregated from plants [143]. Late examinations recommend that more than 9000 spices are known as therapeutic applications among different societies and nations. Distinctive native therapeutic frameworks, for example, Allopathy, Siddha, Ayurveda, and Unani utilize a few plant-animal varieties for the treatment of illness [144]. As of late, it is imperative that all frameworks of customary plant drugs winning on the planet should be urged in the event that we proposed to discover remedy for that infection where the cutting edge manufactured prescriptions have fizzled or where the advanced is past the range of the helpless countries [145]. In India, customary plant cures have utilized in the
treatment of different illnesses since the hour of Charaka and Shusrutha [146]. India has an exceptional situation in the territory of natural prescriptions since it is one of only a handful few nations which are fit for developing the vast majority of the significant plants utilized both in the current and conventional arrangement of meds [147]. Interest in the natural medication area is developing quickly expanding by 12%-15% worth every year [148].

CONCLUSION
The term diabetes mellitus incorporates a few diverse metabolic issues that all, whenever left untreated, bring about unusually high grouping of a Sugar called glucose in the blood. Diabetes mellitus type 1 outcomes when the pancreas no longer delivers critical measures the hormone insulin, generally attributable to the immune system pulverization of the insulin-creating beta cells of the pancreas. Diabetes mellitus type 2, conversely, is currently thought to result from immune system assaults on the pancreas or potentially insulin opposition. The pancreas of an individual with type 2 diabetes might be delivering ordinary or even anomalous a lot of insulin. The principle objective of diabetes the executives is, beyond what many would consider possible, to reestablish starch digestion to an ordinary state. To accomplish this objective, people with an outright inadequacy of insulin require insulin substitution treatment, which is given through infusions or tablets. Insulin opposition, conversely, can be remedied by dietary changes and exercise. Different objectives of diabetes the board is to forestall or treat the numerous difficulties that can result from the illness itself and from its treatment. By monitoring the glucose level, diabetes can turn into a patient's body and he/she can appreciate life happily.

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