INTRODUCTION

Four polypeptides with hormonal activity are secreted by the islets of Langerhans in the pancreas, namely insulin, glucagon, somatostatin and pancreatic polypeptide. The A cells secrete glucagon, B cells insulin, D cells somatostatin and F cells secrete pancreatic polypeptide.

Like other polypeptide hormones and related proteins that enter the endoplasmic reticulum, insulin is synthesized as part of a longer preprohormone. The gene for insulin is located on the short arm of chromosome 11 in humans. It is synthesized in the rough endoplasmic reticulum of the β-cells. It is then transported to the Golgi apparatus, where it is packed in membrane bound granules. These granules move to the plasma membrane by a process involving microtubules, and their contents are expelled by exocytosis. The insulin then crosses the basal laminas of the B cell and a neighboring capillary and the fenestrated endothelium of the capillary to reach the bloodstream.[1]

The physiologic effects of insulin are both far reaching and complex. Though the hormone has rapid, intermediate and delayed actions, the best known is the hypoglycemic effect. Apart from its additional effects on amino acid and electrolyte transport, action on many enzymes and growth, the net effect of the hormone is storage of carbohydrate, protein and fat. The anabolic nature of hormone which increases the storage of glucose, fatty acids and amino acids is made to call the hormone "the hormone of abundance". The constellation of abnormalities caused by insulin deficiency is called "diabetes mellitus". [1]

Diabetes is characterized by polyurea, polydypsia and weight loss in spite of polyphagia, hyperglycemia, glucosuria, ketosis, acidosis and coma. [1]

The cause of clinical diabetes is always due to deficiency of the effects of insulin at the tissue level, but the deficiency may be relative. One of the common forms type-1(Insulin Dependent Diabetes Mellitus IDDM) is due to insulin deficiency caused by auto-immune destruction of B-cells in pancreatic islets, the A, D and F cells remain intact.

Type 1 diabetes usually develops before the age of 40 and hence called juvenile diabetes. The patients with this disease usually present with various anti-B cell antibodies in plasma, but current thinking is that type-1 diabetes is primarily a T-cell mediated disease. There is a definite genetic susceptibility as well. The concordance rate is about 33%.The main genetic abnormality is in the major histo-compatibility complex on chromosome 6, making individuals with certain types of histo-compatibility antigens much more prone to develop the disease. [1]

The other variant Type 2 diabetes (Non Insulin Dependent Diabetes mellitus) occurs due to multiple disturbances in glucose homeostasis, including, impaired insulin secretion, insulin resistance in muscle, liver and adipocytes and abnormalities in splanchnic glucose uptake.

Impaired insulin secretion is found uniformly in type 2 diabetic patients in all ethnic populations. The β-cells are unable to read the severity of insulin resistance and fail to adjust their secretion of insulin to maintain normal glucose tolerance. In these patients, the fasting plasma insulin concentration is normal or increased and basal insulin secretion is elevated. Gluco-toxicity,[2] lipo-toxicity are among the acquired defects that can lead to impaired insulin secretion. Recently, deficiency of or resistance to "incretins" have been implicated in the pathogenesis of β-cell dysfunction in type -2 diabetic patients. [2]

Amylin also known as IAPP (Islet Amyloid Polypeptide) has been implicated in progressive β-cells failure in type – 2 diabetes mellitus. IAPP, which is packaged with insulin in secretary granules and co-secreted into the sinusoidal space, is the precursor for the amyloid deposits that are frequently observed in type – 2 diabetics. Following its secretion, amylin accumulates extracellularly in close proximity to the β-cells and it has been suggested that amylin deposits cause β-cell dysfunction. However this theory is not very well accepted, due to failure of inhibitory effect of amylin on insulin secretion when the peptide was infused in pharmacologic doses in rats, rabbits and humans. [2]

The number of β-cells within the pancreas is an important determinant of the amount of insulin that is secreted. Most but not all studies have demonstrated a modest reduction (20%-40%) in β-cells mass. Low birth weight is associated with the development of IGT and type -2 diabetes in a number of populations. Developmental studies in animals and humans have demonstrated that poor nutrition impair insulin secretion or reduce β-cell mass. [2]

The cross sectional studies and long term, prospective longitudinal studies have shown hyper insulinemia to precede the onset of type -2 diabetes in all ethnic populations with high incidence of type 2 diabetes. Himsworth and Kerr in 1939 were the first to demonstrate that the tissue sensitivity to insulin is diminished in type 2 diabetic patients.

De Fronzo et al using the more physiological euglycemic insulin clamp technique, have provided the most conclusive documentation that insulin resistance is characteristic feature of lean, as well as that of obese, type 2 diabetic individuals. The combined effects of insulin and hyperglycemia to promote glucose disposal are dependent on three tightly coupled mechanisms. [2]

- Suppression of endogenous (primarily hepatic) production

- Stimulation of glucose uptake by the splanchnic tissue.(hepatic plus gastrointestinal)
- Stimulation of glucose uptake up peripheral tissues, primarily muscle.

Diabetes is sometimes complicated by acidosis and coma, and in long standing diabetes are additional complications which include micro vascular, macro vascular and neuropathic diseases. The micro vascular abnormalities are proliferative scarring of retina (diabetic retinopathy), and renal disease (diabetic nephropathy) leading to renal failure. The macro vascular abnormalities are due to accelerated atherosclerosis which results in increased incidence of stroke and myocardial infarction. The neuropathic abnormalities (diabetic neuropathy) involve the autoimmune nervous system and peripheral nerves.

Interest in monitoring the glucose concentrations of diabetic patients has increased since the publication of the diabetes control and complications trials report showing that tight control of blood glucose concentrations, by frequent testing and concomitant adjustment of insulin doses, decreases long term complications resulting from diabetes.

A computer simulation based on the Diabetes control and complication trials results estimates an additional 5 years of life, 8 years of sight, 6 years of free - from kidney disease, and 6 years free – from- amputations for a diabetic following the tight control using the standard regimen. [3]

About 1-2 billion blood glucose tests are done per year by diabetic people at work, at home, at restaurants and at a wide variety of other places. [4] The data obtained is used for testing and to determine the amount of insulin that the patients need for safety of exercise and weather extra food or a glucose tablet is needed for a blood glucose concentration that is too low. [5] Using real time data for evaluating options and making decision about the treatment of a variety of conditions is appealing to both patients and health professionals. [6]

Health professionals also use this information to determine blood glucose control and patterns of abnormal blood glucose that may require alterations in medical therapy. [7]

Despite the tremendous value of self monitoring of blood glucose for the treatment of diabetes, many patients find the testing onerous and some refuse to perform the measurement. These complaints are largely justified because self monitoring of blood glucose is painful, inconvenient, messy, embarrassing and above all expensive. [6]

Most patients consider the finger lancing necessary for obtaining blood for self monitoring of glucose to be the most painful part of diabetes therapy. The direct pain of the lancet is several folds greater than that of an insulin syringe because of the greater lancet thickness, the site of lancing (the finger tip usually used for blood glucose monitoring has many more pain fibers than does the thigh often used for insulin injections) and other factors. In addition, patients frequently complain of residual pain at the site of lancing that may last several hours and be especially distressing during important tasks, such as opening a bottle or typing.

Current techniques of blood glucose monitoring are inconvenient because they are limited by location, equipment and supplies. Patients usually start the procedure by washing their hands which requires a sink or other water supply. They must carry a lancer, lancets, blood glucose strips and a meter. Frequently they also need tissue, a water supply or a clock. The procedure takes several minutes and they must bring a logbook for their records. Many patients carry a separate bag to accommodate all these supplies. The procedure is messy. A drop of blood must be obtained from a finger and transferred onto a blood glucose strip. Unfortunately, the blood is often not limited to the strip.

Non invasive monitoring of glucose has been of particular interest because of the pain associated with invasive self monitoring. Ease of use and reduction of pain can encourage more frequent testing and hence tighter control of the glucose concentration. Patient care need and the commercial importance of NI glucose monitoring has led to a flurry of "research" by entrepreneurial and commercial concerns that have been published mainly in patent literature. However a large number of NI glucose patents lack scientific rigor and some may be based on wrong or unproved assumptions. [8]

Interest has been increasing recently in non-invasive diagnostic testing. Some of this storm from the AIDS epidemic in the west, which has provided a new rationale for hemophilia, while other factors include new development in home based diagnostic tests and a demand of samples to be collected in the home or work place. Diagnostic tests based on fluid generally use blood and urine and less frequently the esoteric fluids such as saliva, sweat and tears. [9]

Researchers are developing other methods of non invasive monitoring. Potential ways to determine blood glucose levels that include shining a beam of light onto the skin or through body tissue, measuring the energy waves (infrared, radiation) emitted by the body, applying radio waves to the fingertip, using ultrasound ,checking the thickness (also called the viscosity) of fluids in tissue underneath the skin. [10]

An NI body glucose monitoring device is defined by Omar S. Khalil in a review as a device that comes in contact with or remotely senses, a human body part, without protrusion through membranes or sampling a body fluid for analysis external to the part.[8]

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A urine glucose test determines whether or not glucose (sugar) is present in the urine. Glucose will overflow into the urine only when the blood glucose level is high, that is, too high for the kidneys to stop it spilling over into the urine. In most people, glucose will appear in the urine when blood glucose levels are above 10 m mol of glucose per liter. This level is called the 'renal threshold' for glucose. However, the renal threshold for glucose can be lower in some people who are otherwise healthy, during pregnancy, and in people who have a kidney disorder. In these people, glucose may be present in the urine despite the blood glucose being normal. This can sometimes make urine glucose tests difficult to interpret.

Limitations of urine glucose monitoring

- A urine glucose test does not reflect blood glucose level at the time of testing; instead, it gives an indication of blood glucose level over the past several hours. For example, some of the urine present in bladder may be 2 hours old, and may show glucose even though blood glucose may have normalised since then.
- A urine glucose test does not give any information about low blood glucose levels, as glucose is only found in the urine when the blood glucose level is above 10 mmol/L. That is, a negative urine glucose test may be the result of a normal blood glucose level or a dangerously low blood glucose level, with the urine glucose test unable to differentiate between the 2 situations.
- The results of a urine glucose test are influenced by the volume and concentration of urine that is passed, which will vary with the amount of fluid consumed and the fluid loss due to such things as heavy sweating or vomiting.
- Urine glucose tests designed for home use rely on interpreting a colour change to define the result. Subtle colour differences may be difficult to interpret.

- If a urine glucose test is not read at the specified time after applying the urine to the test strip, then the result is prone to error.
- Some medications may interfere with the results of urine glucose testing.

Advantages of urine glucose monitoring

- Urine glucose testing is easy to do: just dip the test strip in the urine and read the result at the allocated time.
- It is less painful than blood glucose monitoring — no finger pricks to collect blood!

Urine test strips are less costly than buying a blood glucose monitor and its test strips. [11]

Sweat is relatively easily obtained but the glucose concentration lags significantly behind blood glucose. Methods to increase sweating have been developed and seem to increase the timeliness of the sweat glucose measurement. [12]

The assay of saliva is an increasing area of research with implications for basic clinical purpose. Although this biological fluid is easy to manipulate and collect, careful attention must be directed to limit variation in specimen integrity. Recently the use of saliva has provided a substantial addition to the diagnostic armamentarium as an investigative tool for disease process and disorders. In addition to its oral indications, the analysis of saliva provides important information about the functioning of various organs in the body. [13]

Saliva offers distinctive advantages over serum because it can be collected non invasively by individuals with modest training. Furthermore saliva may provide a cost effective approach for the screening of large populations.

Some systemic diseases affect salivary glands directly or indirectly and may influence the quantity of saliva that is produced as well as the composition of the fluid.

These characteristic changes may contribute to the diagnosis and early detection of these diseases.

Hereditary diseases such as cystic fibrosis celiac disease, 21-hydroxylase deficiency can be detected in early age. Salivary analysis may aid in early detection of certain malignant tumors by use of tumor markers, infectious diseases like helicobacter pylori, pigeon breeders disease, Lyme disease, viral disease like measles, mumps, rubella. Saliva has been used in new born infants for detection of retrovirus infection. Saliva was also found to be a reliable alternative to serum for identification of virus HSV-1 and parvovirus B19 and HIV. Saliva has been proposed for the monitoring of systemic levels of drugs. The analysis of endocrine function is also possible with the use of saliva, salivary cortisol levels, salivary aldosterone levels, estradiol levels. [14]

Despite few limitations, the use of saliva for diagnostic purposes is increasing in popularity due to its many potential advantages. It provides an attractive alternative to more invasive, time consuming, complicated glucose monitoring tests as saliva can be collected in a non invasive manner by individuals with modest training including patients. [14]

Saliva has been used reliably for reflecting and monitoring the blood glucose concentration in the patients of diabetes mellitus. [15, 16,17,9]

Hence the present study was undertaken to quantitatively estimate the amount of salivary glucose levels in type-2 diabetic patients and explore the possibility of using saliva to reflect the glucose concentration in blood, thereby making self-measurement of glucose less invasive.