

DIABETES THROUGHOUT AGES; AN OVERVIEW**Mohd Sajid*¹, Shakir M.¹, Ansari A. H.² and Zulkifle M.³**¹Lecturer, Department of Tahaffuzi Wa Samaji Tib, MTC, Mansoor, Malegaon.²Lecturer, Department of Tahaffuzi Wa Samaji Tib, NIUM, Bangalore.³Professor, Department of Kulliyat, NIUM, Bangalore.***Correspondence for Author: Mohd Sajid**

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ABSTRACT

Diabetes is not a novel ailment, its clinical manifestation and dreaded effects on almost entire body were known even to ancient physicians. The level of their understanding regarding diabetes was commensurate with the available stock of knowledge and the scientific development at that time. When we look upon the evolution of diabetes, it immediately, becomes clear that to achieve the present level of knowledge, diabetes has passed through many primitive, intermediate and advance phases of developments. The earliest evidences regarding the aetiology of diabetes were more mythological than rational as the polyurea is mentioned in the Ebers' papyrus. The detail information is discussed in the review.

KEYWORD: Unani, Diabetes, Ziyabetus, Type 2 DM.

The story of diabetes was unfolded during the age of antiquity, where the earliest description of a similar syndrome is present. Ancient physicians recorded their observations in an attempt to have a better understanding of the nature of the ailments, their origin and treatment. It is more often believed that the history of medicine began with the dawn of Greeks and that prior to the time of Buqrat (Hippocrates), there was very little stock of knowledge that could be called as an art of medicine. Nevertheless, for more than 2000 years before the birth of Hippocrates, there had been certain old civilizations wherein physician had been striving to diagnose and treat diseases.

Ancient Egypt was the first known civilization to have evidence of extensive studies on medicine and also the written records of its practices and procedures, which are present in several libraries and museums of the world in the form of papyri. The most famous of them is Ebers papyrus. This papyrus was discovered by a German Egyptologist, George Ebers in 1872. The Ebers papyrus was written about 1550 BC by a physician named Hesy Ra in the 3rd Egyptian dynasty, a lot of evidences suggest that it was copied from a series of books many centuries older; one passage of this papyrus, dates back to the first dynasty (circa 3400 BC).^[1]

The first reference to diabetes mellitus is attributed to the Eber's papyrus that mentions remedies for the treatment of excessive urination. Although the Greek physician Buqrat, "the father of medicine", did not specifically mention diabetes in his writing, but there are some accounts in the Hippocratic writings that are consistent

with the signs and symptoms of diabetes. There are certain references to excessive urinary flow with wasting of the body.

The term "diabetes" was first introduced in 1st or 2nd century BC by Demetrius of Apamia.^[2] Aretaeus of Cappadocia (930-900) used the term "diabetes" first time for a disease. It was derived from the Greek verb diabainein, itself formed from the prefix dia-across, apart and the verb bainein – walk, stand. The verb diabainein mean "to stride, walk or stand with legs asunder", hence its derivative diabetes cannot "one that stardless, or specifically a compass, siphon".^[2,3]

In addition to coining the term diabetes for a disease, Aretaeus is credited with the first accurate clinical description of diabetes which is instantly recognizable today.

This classic description begins as: Diabetes is a dreadful affection, not very frequent among men, being a melting down of the flesh and limbs into urine. The patients never stop making water and the flow is incessant like the opening of aqueducts, life is short, unpleasant and painful, thirst unquenchable, drinking and disproportionate to the large quantity of urine, for yet more urine is passed. One can not stop them either from drinking or making water. If for a while they abstain from drinking, their mouth become parched and their bodies dry, the viscera seem scorched up, the patients are affected by nausea, restlessness and a burning thirst, and within a short time, they expire.^[4]

In the same century, Jalinoos (Claudius Galen) (129-229 AD), an ancient Unani physician, who was disciple of Hippocrates and all time influential medical author / writer attached with Roman court, described diabetes in a number of his work like *Almayamir* and *Al Aaza Al Amela*. Galen described the condition as rare, as he had seen only two cases. He used the term *diarrhoea urinosa* (diarrhoea of urine) and *dipsakes* (thirsty disease).^[5,6] The first test for diabetes was the urine taste test. Jalinoos was the first physician who described the smell and taste of urine, that diabetic urine was “unchanged drinks” which may have accounted for a different aroma.

A number of Baznatinii (Bazantine) physicians during 2nd to 6th century AD, like Rofas Al Afsi (Rofas of Ephesus), Qribasius (4th century AD) Staphanus Alexandrinus (5th century AD) Aetius and Alexander of Tralles (6th century AD), used almost the same terminology while referring to the disease and considered that symptoms of excessive thirst and urination were due to the disease of kidneys and the bladder.^[7]

Chinese system of medicine also has several references to this disease. Chang Chung Ching (229AD) was a famous Chinese physician, noted that the urine was so sweet that the dog liked it.^[2]

In Indian system of medicine, there are many authors who described the diabetes in their books. *Charak Samhita* and *Sushurata Samhita* which were written by Charak and Sushurata in 400 BC and 600 BC, respectively, is described diabetes by the name of *Madhumeha*, which comprises a variety of *Prameha* – a group of twenty anomalies of urinary excretion. The ancient Hindus were the first to coin the term “honey urine” a thousand year before the first European recognized the sweet taste of urine. They also noted, the urine passed was astringent, yellow white in colour and unctuous in quality.^[8,9,10]

In addition to these, Sushurata described 2 types of diabetes in his book. First hereditary onset diabetes spawned due to genetic factor in offspring from their parents and the second type occurs due to injudicious practice of diet consumption and a sedentary life style.^[8,10]

During stint of Galen and his contemporary, Rofas Al Afsi and Descorides in 2nd and 3rd centuries, Greek medicine transcended to its apotheosis and travelled to Asia especially to Arab world, where it was preserved and substantially modified. There were few channels through which Greek medicine spread to the Arab world; the most faithful of them were the school of Alexandria (*Madarsa Askandria*) and the school of Jundishapur (*Madrassa Jundi Shah Pur*). These two schools of thought produced several eminent philosophers, authors, writers and physicians in the Arab world.^[11] In 8th century, the first Arabic book regarding diabetes, *Al Kitabul Mushajjar*, was written in tubular form by

Yohanna bin Maswaih (777-857AD) in which diabetes was described perfectly in 55th lesson.^[12]

Afterward, Abul Hasan Ali bin Sahl Raban Tabri wrote *Firdausul Hikmat* in 9th century, which is considered as the first original book in Arabic language. This book is lacking any description similar to the diabetes.

Abu Bakar Mohammad bin Zakariya Razi (865-925AD) was the most celebrated and most original Arabic physician and known as Rhazes to the west and Jalinoosul Arab among Unani world. He described diabetes mellitus in his two most popular compilations; *Kitab Al Hawi fil Tib* and *Kitab Al Fakhir fil Tib*, both are in Arabic language. According to him the cause of this disease was abnormal hot temperament of the kidneys which leads to weakness of retentive power (*Quwate Masika*) of kidney.^[13]

During 10th century, Ali Ibne Abbas Majoosi mentioned this disease in his book, “*Kamilus Sana’ah*” (*liber regius*) and described that it results due to the abnormal hot temperament of the kidneys.^[14]

The most prominent and great philosopher, Ibne Sina (980-1037AD) provided a detailed account on diabetes mellitus in “*Al Qanoon fil Tib* (*The Canon of Medicine*), describing the clinical features of the disease with abnormal appetite. He noted a sticky residue as sweet as honey remained after urine was left to stand in ambient air. A decrease in sexual function and gangrene was noted as the complications of diabetes. Ibne Sina recognized primary and secondary diabetes and also mentioned that the disease (diabetes) insidiously changes into *Zooban* and *Diq*.^[2,3,15]

During the period of Salahuddin Ayyubi, Abu Imran Moosa bin Maimoon Qartabi was a renowned physician, he claimed to have seen more than 20 cases of this disease and proposed that diabetes was caused by the sweet water of the Nile and the prevailing heat that spreads over the kidneys.^[1,16,17]

Ibne Zuhar (1091-1164AD), an eminent Arab physician born in Spain (*Undlus*) described the disease as *illat barkariah* in his book “*Kitab Al Taiseer*”, and he also proposed that disease resulted from abnormal hot temperament of kidney.^[19]

In the mid of the 12th century AD Sharfuddin Ismail Jurjani mentioned in his book “*Zakheera Khwarzm Shahi*” that the dilatation and opening of the vessels of the kidney cause *Ziyabetus*, therefore, more absorption and more excretion from the kidneys occur.^[18]

No further progress was made in the understanding of diabetes until the 16th century, when the renaissance physician Paracelsus (1443-1541AD) challenged the medical doctrine of the time and attempted to reform medical thinking. He reported that urine of diabetic

patients contains an abnormal substance which remains as a white powder after evaporation. He proposed that this substance was salt and the disease was due to the deposition of salt in the kidney. He also reported that on boiling diabetic urine 4 ounces of salt could be recovered.^[2,20]

With Galen, the period of speculation, Aetius, Alexander Trallianus and Ibne Sina centered the disease in the kidney, while Paracelsus and Fransiscus Sylvius regarded it as a chemical disorder of the blood.^[21] But in the 17th century diabetes got a relatively clear explanation when in 1677AD Thomas Willis (1621-1675AD) referred it as the “pissing evil” and noted that in patients with diabetes, the urine is wonderfully sweet, as it were imbued with honey or sugar. He pointed that sweetness first appears in the blood and latter in urine and also claimed diabetes was primarily a disease of the blood not the kidney. It is claimed that Willis was the first who described the saccharine nature of urine.^[1,2,22,23,24]

Another celebrated physician of the 17th century, Thomas Sydenham (1624-1689AD) speculated that diabetes was a systemic disease arising in the blood where “chyle” was incompletely digested and its non absorbed residue had to be excreted.^[4,20]

In 1682AD, John Conrada Bruner (1653-1727AD) came very close to discovery of pancreatic diabetes. When he practically removed the pancreas of a dog and observed that the dog passed urine frequently and got very thirsty, intake of water was in equal proportion to that of urine output.^[20,22,23,24]

After Brunner, it was Cullen who was first to distinguish between 2 types of diabetes. He classified the diabetes on the basis of properties of urine such as smell, colour and flavour of honey, and diabetes insipidus with limpid but not sweet urine. He also added the descriptive adjective mellitus, the Latin word for honey.^[1,20]

In 1776AD, Mathew Dobson (1735-1784AD) performed a diagnostic experiment that lead to the belief that diabetes was not just a disease of kidneys, but rather a systemic disorder. Dobson evaporated the urine of a diabetic patient to discover the presence of a substance like brown sugar in taste and appearance which could not be distinguished from sugar, except its sweetness, which left a slight sense of coolness on the palate. He also observed that diabetic patients had the sweetish taste of sugar in their blood. This confirmed the relationship between the sugar present in the blood and that excreted in the urine.^[2,25]

In 1788AD, Thomas Cowley described that diabetes may follow the damage to the pancreas, such as following calculus formation.^[20]

In 1798AD, John Rollo, a surgeon general of royal artillery, thought the stomach as the seat of the trouble

and its immediate cause was a morbid condition of stomach evolved from vegetable substances containing saccharine maltose, which is quickly separated as a foreign body by the kidneys.^[20,21] He also established the link between the food consumed by diabetics and the amount of sugar in the urine. Rollo recorded the amount and kind of food eaten by his diabetic patients and then weighed the “sugar cake” which remained after evaporating the urine. He observed that carbohydrates increase sugar level, and animal product consumption resulted in less sugar yield in urine. He promoted the idea that the treatment for diabetes should be a diet low in carbohydrates and high in fat and protein. This modification of diet became the recommended treatment for diabetes until the discovery of insulin.^[2]

Several historians claimed, it was John Rollo who first used the term “mellitus” to distinguish it from other polyuric conditions in which glycosuria was absent. Cataract and odour of acetone in diabetics’ breath was also described as complications of diabetes by Rollo.^[26]

John Peter Frank (1745-1821AD) defined and named the two forms of diabetes as diabetes incipidus (spurious) and diabetes mellitus (versus).^[21]

In 1815AD, Michel Eugene (1786-1889AD), a chemist published his experimental findings on urine and stated that the sugar eliminated in diabetes mellitus was grape sugar (glucose, dextrose), which, Tiedman and Gemelin found normally secreted in the intestine in 1821AD.^[27]

In 1839, John Elhotson spoke about “grief, chill” and excess of venery as possible etiological factors for diabetes in his book “Principles and practice of medicine”.^[28]

The first clinical test for glycosuria was developed in 19th century. Karl Trommer developed a qualitative test for sugar and Hermann Von Fehling developed a quantitative test in 1841AD.^[2]

William Prout (1785-1859AD) during mid 19th century revealed, exposure to cold, attacks of rheumatism and gout, the drinking of cold fluids while heated, and mental anxiety and distress as the most frequent exciting causes of diabetes. He was first who recognized the coma as a complication of diabetes.^[20,29]

The experimental or metabolic studies of the disease begins with the great name of Claude Bernard (1813-1878AD), it was established by his experiment that the doctrine of the liver as the sugar making plant in diabetes (glycogenic function), and isolated glycogen, which was a product of glucose metabolism in the liver and propounded the concept that the altered glucose metabolism in liver, was the cause of diabetes.^[21,30]

In 1869AD it was observed that a form of retinitis develops in glycosuria patients.^[31] During the same year

Paul Langerhans, a German medical student, described in his doctoral dissertation, an unknown isolated group of special cell in pancreas but he could not reveal its function.^[32] Many instances of pancreatic atrophy were reported in diabetic peoples thereafter and by 1878AD the clinician Lancereaux put forward the doctrine of the identity of pancreatic diabetes with the classical emaciated form.^[21]

By 1889AD Josef Von Mering and Oskerminkewski reproduced the classical type of diabetes in a dog by complete excision of pancreas, after this experiment it was thought that the internal secretions of pancreas were involved in the etiology of diabetes mellitus. This was the turning point in determining the endocrine function of pancreas.^[33]

In 1901AD Eugene Undsay Apie's study on diabetes mellitus established the fact that any injury or lesion of the pancreas which caused hyaline degeneration of 'Islets of Langerhans' causes diabetes mellitus, and it was confirmed by S. Sobdeff in 1902AD and McCollum in 1909AD.^[21,34]

In 1908AD, two German scientists George Zveler and Niculus Paulesco had prepared potent pancreatic extract to suppress the glycosuria, but it had serious side effects.^[35]

Ernest Scotts published an article on influence of intravenous injection of an extract of pancreas on experimental pancreatic diabetes in 1912AD. He observed remarkable reduction in the sugar level as well as total urine output after the injection of extract in depancreatised dog.^[36] The technique of making alcoholic extracts was also improved by Scotts.^[21]

In 1916 Schaefer bestowed the name "insulin" for the hypothetical hormone or active principle of the internal secretion from the Islets of Langerhans but some historians are of the opinion that it was Jean De Meyer who suggested the term "insulin" to the secretion of the Islets of Langerhans. The term "insulin" derived from the Latin word "insula" means islands.^[21,37]

In 1917AD, DM Davis published a report and described the relationship between experimental elevation in glucose level and appearance of glucose in urine. The study supported the understanding of mechanism of glycosuria in diabetes.^[38] Further, Moses Barron (1883AD) gave the conclusion regarding the relationship of Islets of Langerhans to diabetes.^[39]

In 1921AD, Fredrick Madison Allen of The Rock Feller Institute, New York, a leading diabetes specialist, published an article "Total dietary regulation in treatment of diabetes", in which he introduced a therapy of strict dieting dubbed "the starvation treatment" as a way to manage diabetes.^[40]

The endocrine role of pancreas in metabolism and indeed the existence of insulin were not further clarified until 1921AD, when Sir Fredrick Grant Banting and Charls Herbert Best repeated the work of Von Mering and Minkeski after inspiration from Dr Moss Barren's experiment. They improved Scotts's method of extraction and obtained a concentrated extract which was found successful in seven cases.^[21] They also demonstrated the reversal of induced diabetes in dogs by giving them an extract of the pancreatic Islets of Langerhans of a healthy dog. Banting and Best first injected themselves with the extract to test the safety before giving it to the diabetic patients. Leonard Thompson was the first diabetic patient who was administered insulin, made from beef pancreas by his physician, Dr Camp Bell, lived several years with the help of insulin. In 1923AD, the Nobel Prize in medicine and physiology was jointly awarded to Banting and Macleod; both shared the prize money with Best and Collip, respectively.^[41]

The discovery and isolation of insulin in 1921-1922AD was one of the greatest event in the history of medicine. After the incredible invention of insulin, studies were continued and researches were focused on isolation of insulin which could be used therapeutically. In this relation, Danes produced a puper type of insulin "mono component of insulin" and consequently highly purified insulin was made.

In 1926AD John Abel purified insulin and isolated its crystalline structure. His studies on insulin helped to develop modern concept of protein chemistry. In 1958 Fradrick Sanger was awarded the Nobel Prize in chemistry for his work on the structure of protein, especially that of insulin and exact amino acid sequence of the protein insulin was discovered.^[1,42]

The distinction between Type 1 DM and Type 2 DM was first made by Dr. Herald Percival (Harry) Himsworth and the report was published in 1936AD in January addition of Lancet.^[43]

The development of radioimmune assays of peptide hormone technique by Rosalyn Yellow and Soloman Berson in 1957AD made it easy to understand the cause of diabetes and its scientific investigation. Their research brought a revolution in biological and medical field. In 1977AD they were rewarded with Nobel Prize for their exemplary invention in medical arena.^[44]

Human insulin became available in the early 1980AD and was the first commercial product developed by recombinant DNA technology.

Type 1 DM and Type 2 DM are recognized by the American Diabetes Association. These types were also known as insulin dependent diabetes mellitus (IDDM) and non insulin dependent diabetes mellitus (NIDDM). The name insulin dependent diabetes mellitus for Type 1

and non insulin dependent diabetes mellitus for Type 2 were formally dropped in 2003AD.^[20]

Nowadays researchers are looking for, to explore new aspects of diabetes and to its management easy, safe and cost effective in order to manipulate cells so they can secrete insulin. They are trying to develop insulin patches and inhalation evolving genetic engineering and thus make the drug delivery convenient.

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