



HISTORICAL ASPECTS OF DIABETES AND DIABETIC NEUROPATHY

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ABSTRACT

Diabetes mellitus and its complications relating to nerves has not been mentioned in ancient times except by *Ibn Sina* (980-1037AD), also known as Avicenna, an Arab philosopher, who proposed possible familiarity with diabetic disorders in his famous book 'Canon of medicine' in which he mentioned two specific complications of diabetes mellitus namely gangrene and collapse of sexual function. It was not till the 18th century that Western physicians started studying and examining diabetes mellitus and its related complications. Ultimately, the works of the 19th century (de Calvi, Pavy) clearly recognized the relationship between diabetes mellitus and diabetic neuropathies. The important discovery of insulin in 1921 by Frederick G Banting, Charles Best and John Macleod crank up a wide interest and more systematic approach to research of diabetic complications, leading to S. Fagerberger's conclusion that numerous of them share the fundamental micro vascular pathology.

KEYWORDS: History; diabetes; neuropathy; complications.

INTRODUCTION

The history of diabetic complications, including neuropathies, cannot be detached from the one of diabetes itself. Ancient classical texts describing what is thought to be diabetes mellitus signify clinical records of polyuric conditions related with increased thirst, muscle wasting, and premature death. In classical texts, neuropathic fundamentals of the clinical picture of diabetes can be found very rarely. It was not until the 18th century that neuropathy became documented as a common complication of diabetes and the subject of scientific interest and systematic studies. The important discovery of insulin creates an entire new chapter in the history of diabetes and diabetic neuropathies. However, everyone will agree that the problem of diabetic complications, though broadly studied, is far from being solved.

MATERIALS AND METHODS

Exploration of published articles related with history of diabetes and diabetic neuropathy was conducted and abstracts and full articles were included for the preparation of this review from online basis. The databases utilized for obtaining information are scientific research publications from journals indexed/available through PubMed, Scopus, and Google Scholar, Science

Direct etc. Relevant facts were also obtained from general databases such as Google from a library source (Regional Research Institute of Unani Medicine, Srinagar).

OBSERVATIONS

The Ancient Period

The primitive support of diabetes seems to be the papyrus named after the Egyptologist Ebers, who established it in an ancient grave in Thebes. It is written in hieroglyphs. The precise time of its writing is unknown, but most approximate date it around 1550 BC. It contains descriptions of a number of diseases including polyuric conditions resembling diabetes, which was to be managed with a decoction of bones, wheat, grain, grit, green lead, and soil.^[1] The term "diabetes" was first used by Aretaeus of Cappadokia in the 2nd Century AD. It comes from the Greek prefix "dia" and the word "betes" meaning "To pass through a siphon" respectively.^[2] The Roman physician Galen (131-201AD) thought diabetes to be a rare disease and apparently encountered only two cases. Galen employed alternative terms for diabetes including *Diarrhoea urinosa* (diarrhoea of urine), and *Dipsakos* (thirsty disease), the later emphasizing the cardinal symptoms of excessive thirst and drinking.^[1] *Ibn Sina* (980-1037AD), also known as Avicenna, an Arab philosopher and physicist, gave more definite evidence

of possible familiarity with diabetic disorders in his 'Canon of medicine' in which he mentioned two specific complications of diabetes namely *ghangharana* (gangrene) and collapse of sexual function.^[3] *Ibn Zuhr* (1092-112 AD), writer of '*Kitab al Taiseer*', described diabetes as disease of the kidneys.^[4] Ancient Hindu physicians namely *Susruta*, *Charaka* and *Vagbhata* (5th-6th Century AD) referred diabetes as *Madhumeha* meaning honey urine.^[1]

Diagnostic Period

In European countries, diabetes mellitus was neglected until Thomas Willis (1621 – 1675) wrote *Diabetes, or the Pissing Evil*.^[5] He made references to the sweet taste of diabetic urine and thereby duplicated the observations which had first appeared in eastern medical writing over one thousand year previously.^[1] Dobson (1775) showed that the taste of diabetic urine dependent on sugar, which he demonstrated by evaporating the urine and producing the sugar in crystals. Dobson concluded that the kidneys excreted sugar and that it was not "formed in the secretory organ but previously existed in the serum of the blood".^[5] John Rollo (d, 1804) was the first to apply the adjective "*Mellitus*" (from the Latin word meaning honey) used to distinguish the condition from the other polyuric diseases in which glycosuria was absent and the urine tasteless, Latin (*insipidus*).^[1]

Experimental Period

The Nineteenth century was very important for most streams of medicine. In 1815, the French chemist Michel Chevreul (1786-1889) proved that the sugar present in diabetic patient's urine was glucose. Sugar metabolism was clarified by the work of Claude Bernard (1813 – 1878). He concluded that the glucose was normally present in blood and showed that it was stored in the liver as (glycogen) for secretion into blood stream during fasting. In 1889, Minkowski and Von Mering reported that pancreatectomy caused severe diabetes in canines. In 1893 Laguesse suggested that the pancreatic islets discovered by Paul Langerhan in 1869, produced an internal secretion that regulates glucose metabolism. The first truly successful treatment for diabetes was finally made available in 1920 when Frederick Banting, Charles Best, and John James Macleod discovered insulin.^[5]

Peripheral neuropathy caused by diabetes mellitus was documented only in 1864 by Marchel de Calvi. The loss of deep tendon reflexes in the lower limbs was described by Bouchard (1887), spontaneous pain and hyperesthesia or dysesthesia by Pavy (1885), motor manifestations by Bruns and Martin Charcot (1890) and cranial nerve involvement by Ogle (1896). While Leyden, (1893) and Pryce, (1893) put a classification of the different manifestations of the disease as follows:

1. Hyperaesthetic or neuralgic form
2. Motor or paralytic form
3. Ataxic or pseudotabetic form

It was Rundles who in 1945 first drew interest to the autonomic nerve involvement in diabetes. Later on, researchers turned their attention to the pathogenetic mechanisms resulting in peripheral neuropath.^[6]

The Modern Era

Frederick G Banting, Charles Best and John Macleod's important discovery of insulin in 1921 transformed not only the world of diabetes mellitus, but also the entire history of medicine.^[7] The post-insulin period brought an increase in research performance associated with diabetic neuropathies. Various authors, including Jordan and Broch (1936) experienced a familiar dissociation between neuropathic symptoms and objective signs of disease.^[8,9]

Wayne Rundles from the University of Michigan published a research paper of one twenty five case reports of diabetic neuropathy. His clarification created a basis for the proposal that development of neuropathy is dependent on the extent of glycemic control.^[9] The research work of Rundles, and Root, contributed to the understanding of diabetic autonomic neuropathy.^[11] Garland gave a description of the mainly proximal neuropathy not associated with sensory disturbances. He named the state as diabetic amyotrophy.^[12,13] Stainess and Downie, in the early sixties, started using quantitative sensory testing and nerve conduction velocity studies in neuropathy research.^[14,15]

In 1959, Sven-Erik Fagerberg from Goteborg, comprehensively studying 356 cases of diabetes mellitus, gave an affiliation among diabetic neuropathy, retinopathy and nephropathy. In approximately 50% of the cases, he performed microscopic investigation of peripheral nerves and discovered significant abnormalities in the nerve microvasculature, especially prominent in those with clinical signs of neuropathy. By combining epidemiological and pathological evidence, Fagerberg gave a theory that diabetic neuropathy, retinopathy, and nephropathy have fundamental microvascular pathology.^[16] In the field of diabetic neuropathies, the end of the 20th Century will be remembered as the period of huge clinical trials testing potential therapeutic agents. So far none of the agents tested, with the exception of insulin; have both safe and effective in altering the course of diabetic neuropath.^[17] Therefore, the battle continues.

CONCLUSION

Diabetes mellitus has been observed and reported all over written history since 1500 BC. Rigorous scientific research worldwide has brought new insight into the disease. Yet, much remains to be done and the cure has remained indefinable. With improving quality of life and increasing affluence, the world is now experiencing the rising epidemic of obesity predisposing to type-2 diabetes mellitus. As the disease itself and its complications inflict great social and economic burdens, attention of medical professionals should increasingly be

directed towards rising awareness of diabetes and promoting healthy life style to prevent the development of the disease.

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