CHAPTER 1
INTRODUCTION

Human beings are the most complex organisms on this planet. It is difficult to imagine how billions of microscopic parts, each one with its own identity, work together in a structured manner for the benefit of the total being. A system is an organization of various organs arranged together so that they can perform complex functions for the body. Body functions are the physiological or psychological functions of body systems. Survival is the body's most important goal and it depends on the body's maintaining homeostasis. Homeostasis is a state of relative constancy of body’s internal environment and it depends on the body's carrying out many activities in an organized manner continuously. Its major activities or functions are responding to changes in the body's environment, exchanging materials between the environment and cells, metabolizing foods, and integrating all of the body's diverse activities. In case there is any change in the homeostasis diseases set in.

A disease is an abnormal condition affecting any part of the body. Diseases are broadly classified into communicable and non-communicable disease. A communicable disease is carried by microorganisms and transmitted through people, animals, surfaces, foods, or air. Communicable diseases rely on fluid exchange, contaminated substances, or close contact to travel from an infected carrier to a healthy individuals. A non-communicable disease is a medical condition or disease which is non-infectious. Non-communicable diseases including diabetes account for 60% of all deaths worldwide.
Diabetes is known since ancient times. The first account of a polyuric state resembling Diabetes Mellitus is mentioned in Ebers papyrus the most famous document relating to the ancient practice of medicine, written about 1550 BC in Egypt. Aretaeus (81-138 AD) accurately described the symptoms of diabetes and coined the term “Diabetes” in connection with this ailment, which means “to run through” or “Siphon”. He described the disease as “Diabetes is a dreadful affliction, not very frequently among men, being a melting down of the flesh and limbs into urine” “Madhumeha” which means the urine of these patients has the taste like honey, being sticky to touch and strongly attracting ants with polyuria was first reported in Sanskrit literature dating from the 5th-6th century AD at the time of Susruta, Charaka and Vaghbata (Pickup et al 1997). In India diabetes are classified as two types: congenital and late onset. They also pointed to the relation of diabetes with heredity, obesity, sedentary life and diet (Algaonkerss et al, 1972).

Shaikh-Ul-Rais Bu Ali Ibne Sina (960-1037 AD) described the clinical features of the disease and mentioned two specific complications of the disease, namely gangrene and the collapse of sexual function. The Swiss physician Von Hohenheim (Paracelsus) reported that urine of diabetic patients contained an abnormal substance which remained as a white powder after evaporation, he concluded that this substance was salt and that diabetes was due to the deposition of salt in the kidneys causing thirst of the kidney and polyuria (Pickup et al 1997).

The modern history of Diabetes began with Thomas Willi’s observation of diabetes in 1674 AD and Matthew Dobson’s experiments in 1776 AD that conclusively established the presence of sugar in the urine and blood. Thomas Willis referred to diabetes as the “Pissing evil” and noted that
in patients with diabetes, “The urine was wonderfully sweet, as if it were imbued with honey or sugar”. He claimed that diabetes was primarily a disease of the blood and not the kidneys. Willis proposed that the sweetness first appeared in the blood and was later found in the urine. During the same era Thomas Sydenham (1624-1689 AD) speculated that diabetes was a systemic disease arising in the blood. Johann Conrada Brunner came very close to discovering pancreatic diabetes when he observed in 1682 AD that, after the incomplete removal of the pancreas from a dog, “the animal drank water very frequently and that he was very thirsty, drinking more of water in proportion to the discharge of urine” (Pickup et al 1997 and Macleod et al 1923). Matthew Dobson (1735-1784 AD) provided experimental evidence that people with diabetes pass sugar in their urine. He gently heated two quarts of urine to dryness. The residue was a whitish cake, which granulated and broke easily between the fingers and smelled sweet like brown sugar. Moreover he concluded that this substance had previously existed in the serum rather than being formed in the kidneys (Dobson 1776).

In 1798 AD John Rollo a surgeon, was the first who use the adjective “Mellitus” to distinguish the condition from other polyuric diseases in which glycosuria was absent and urine was tasteless. Rollo made other contributions to the study of diabetes, including descriptions of “cataract due to Diabetes” and odour of acetone on the breath of some diabetic patients (Rollo et al 1798). In 1815 AD Claude Bernard discovered that the liver releases a substance that affects blood sugar levels. In 1875 AD, he isolated a starch like substance that he called “Glycogen”, which was the precursor of glucose, “the internal secretion” of the liver. This observation established the liver’s role as a vital organ in diabetes (Mc Cradie et al 1924 and Bernard et al 1985). William Prout (1785-1859 AD) was the first, who recognized that
coma was a complication of diabetes (Prout et al 1848). Further in 1869 AD, H.D.Noyes, observed that a form of “retinitis” developed in glycosuric patients (Pickup et al 1997).

Paul Langerhans (1847-1888 AD) had noticed small clusters of ductless cells in teased preparations of pancreas; he simply described these structures without speculating as to their possible function. It was only in 1893 AD that Edouard Laguesse suggested that these clumps of cells ,which he named the “islets of langerhans” in honour of langerhans and suggested that they might constitute the endocrine tissue of the pancreas (Pickup et al 1997). In 1874 AD, Prof.A.Kussmaul described the “air hunger” of ketoacidosis (Kussmaul et al 1874).

Apollinaire Bauchardat in 1877 AD began the modern therapy of Diabetes by limiting carbohydrates in the diet, advocating fast days, and using exercise to help control glycosuria (Padfield et al 1964). In 1889 AD, Oskar Minkowski and Josef Von Mering demonstrated conclusively that removal of the pancreas from a dog results in the development of fatal diabetes. This observation firmly established the role of the pancreatic disorders in causing diabetes (Oskar Minkowski et al 1967). In 1901 AD, Eugene Undsay Opie carried out pathologic study on the pancreas, and concluded that in diabetes mellitus the islands of langerhans are destroyed or injured (Opie et al 1901).

In 1909 AD, Jean De Meyer gave the name “insulin” derived from the latin word insula (Insula means island), to the glucose lowering hormone, whose existence at that time was still hypothetical, which he postulated was produced by the islet tissue (Barron et al 1920). In 1883 AD Moses Barron concluded that the islets secrete a hormone directly into the lymph or blood
which has a controlling power over carbohydrate metabolism (Banting et al 1922). The finding of Moses Barron triggered the investigations of Frederick Grant Banting and Charles Herbert Best In December 1921 AD, they succeeded in isolating insulin and published the results of their research on “The internal secretion of the pancreas” in which they were able to demonstrate the reversal of the metabolic changes of diabetes by injection of a potent extract of the pancreatic islands (Banting 1929, Murray 1969, and Wrenshall GA et.al 1962). On 11th Jan 1922 AD, the first patient of diabetes a 14 year old boy named Leonard Thompson was treated with insulin in Toronto, Canada (Mann et al 1971).

In 1923 AD Eli Lilly begins commercial production of insulin, and called it “Isletin Insulin” (Best et al 1923). In 1925 AD Home testing for sugar in the urine through Benedict’s solution was introduced (Stanley et al 1925). In 1927 AD an oral medication called “horment” or “glukohorment” was developed as a replacement for insulin, but side effects were unacceptable (Sandmeyer et al 1927). In 1930s AD Insulin was further refined to Protamine zinc insulin, a long-acting insulin that provide more flexibility (Peter et al 1984). In late 1940 AD Helen Free developed the “dip-and-read” urine test (Clinistix) allowing instant monitoring of blood glucose levels. In 1951 AD Lawrence and Bornstein measured the amount of insulin in the blood and noted that older and obese patients with diabetes have insulin, but those who were young have none. In 1955 AD Oral drugs that help lower blood glucose levels was introduced. In 1959 AD, Two major types of diabetes are recognized: Type 1 (Insulin-Dependent) Diabetes and Type 2 (Non-Insulin-Dependent) Diabetes as per the information suggested by Defeat Diabetes Foundation.
During 1959-1960 AD Rosalyn Sussman Yalow developed the radioimmunological assay (RIA) procedure, to measure insulin with much greater precision than earlier techniques, for that she received the Nobel prize in 1977 AD (Nathanson et al 1997). In 1964 AD, the first strips for testing blood glucose were used. In 1970 AD, First blood glucose meter (Ames) and Insulin pumps were introduced. During the same year Laser therapy was used to slow down or prevent blindness due to Diabetes.

In 1973 AD, U-100 insulin was introduced. In 1976 AD, the glycosylated hemoglobin test was introduced as a monitor of glycaemic control. The manufacturing of insulin changed dramatically with the advent of DNA technology that allows synthesis of a genetically engineered human” type of insulin, and in 1978 AD, production of the first recombinant DNA insulin was announced. In 1983 AD, the first biosynthetic human insulin known as “Accu-Chek” (allows blood glucose self-monitoring) was introduced. In 1996 AD, the FDA approved the first recombinant DNA human insulin analogue, lispro (Humalog).

In 2001 AD, FDA approved Cygnus first-generation model of the GlucoWatch Biographer, measures glucose levels frequently, automatically and non-invasively to identify trends in fluctuating glucose levels. In 2003 AD, the names Insulin Dependent Diabetes Mellitus (IDDM) for Type 1 and Non Insulin Dependent Diabetes Mellitus (NIDDM) for Type 2 diabetes are formally dropped.

Health and Commonwealth Government have identified diabetes to be a significant and growing global public health problem with the expected incidence in Australia to increase from 4% to 10% by 2010
(Cornforth et al 2004). By 2020, the number is expected to double and reach
epidemic proportions, even as half the numbers of diabetics in India remain
undiagnosed. Diabetes has debilitating consequences on many of the body’s
vital organs if remained unchecked and controlled, the biggest problem being
that of eyesight. It affects eyes, kidney, heart and every single vital organ of
the body (Dr.K.Bhujang Shetty 2007). According to the survey of Novo
Nordisk (2007), India has the dubious distinction of being the diabetic capital
of the world. Home to around 33 million people are affected with diabetes,
19% of the world’s diabetic population is from India. Nearly 12.5% of
Indian’s urban populations have diabetes. The number is expected to escalate
to an alarming 80 million by the year 2030. Amputation is very common in
diabetic patients in India and it is reported that 40,000 legs are amputated
every year and 90% are due to infections (International Diabetes Federation).
Diabetes patients can often experience loss of sensation in their feet. Even the
smallest injury can cause infection that can be very serious. 15% of patients
with diabetes will develop foot ulcers due to nerve damage and reduced blood
flow. Diabetes slowly steals the person’s vision. It is the cause for common
blindness and cataracts (Dr.Vinod Patel 2008). Cardiovascular diseases are
rising, nearly 3.8 crore cases were detected in 2005 and experts believe the
number will go upto 6.4 crore by 2015. Various studies have shown that the
high incidence of diabetes in India is mainly because of sedentary lifestyle,
lack of physical activity, obesity, stress and consumption of diets rich in fat,
sugar and calories (Aarogyam Preventive Health Care Magazine: Thyrocare’s
2006). The sad part of this silent killer is people are either ignorant of the
facts or mismanage the disease, it is said that “Ignorance is bliss; but not so
for diabetes”.
1.1 PROBLEM STATEMENT

The major task of medical science is to prevent and diagnose the diseases. The quality of diagnosis totally depends on the clinical data and on the expert’s talent. Clinical databases are widely used today within many clinical specialties and new databases are rapidly emerging. Clinical databases are a wide concept extending over many different clinical tasks. Due to uncertainty and huge amount in clinical data, information is imperfect, fragmentary, not fully reliable, unclear, ambiguous, or deficient in some way. The existence of uncertain factors with errors is numerous in medical domain and it is to be solved in an efficient way. Medical inaccuracy can be solved with the help of expert’s knowledge. As the expert’s knowledge is so valuable and unstated in nature which cannot be used as it is, therefore inferring them in terms of rules is the best way to resolve the uncertainty.

Physician often decide on what is good for the patient based on their better knowledge of the disease and their assumptions are at best empirical. Physicians use learning method to diagnosis. They have to solve the problem of deducing certain diseases or formulating a treatment based on more or less specified observations and knowledge. Also several studies have revealed that about 50% of diagnosis is unpredictable due to uncertainty in clinical database. The basis for a valid diagnosis, a sufficient number of experienced cases, is accomplished only in the middle of a physician’s career and is therefore not yet present at the end of the academic formation. Emotional problems and fatigue degrade the doctor’s performance. The training procedure of doctors, in particular specialists, is a lengthy and expensive one. Medical science is one of the most rapidly growing and changing fields of science. New results exclude the older treats. New therapies and new drugs are introduced day by day. Even unidentified
diseases turn up every now and then. So a physician should constantly try hard to keep his/herself up to date.

Computers have been employed widely in the medical sector. From local and global patient and medicine databases to emergency networks, or as digital archives, computers have served well in the medical sector. Meanwhile, in the case of medical diagnosis, regarding the complexity of the task, it has not been realistic yet to expect a fully automatic, computer-based, medical diagnosis system. A computer system never gets tired or bored, can be updated easily in a matter of seconds, and is rather cheap and can be easily distributed. Again, a good percentage of visitors of a clinic are not sick or at least their problem is not serious, if an intelligent diagnosis system can refine that percentage, it will set the doctors free to focus on more serious cases (Moein et al 2008).

1.2 THESIS OBJECTIVE

The main objective of this thesis is to develop accurate, near perfect, easy to use method, cost effective procedures and methods for supporting medical practitioners. The advancement in computer technology has encouraged the researchers to develop a predictive method for assisting medical experts, psychologists, special educators and occupational therapists in better assessment of diabetes disease.

In this thesis various techniques like neural network, genetic algorithm and fuzzy techniques is proposed to predict diabetes mellitus in conjunction with its types and complications. The neural network technique considers the initial diabetic information that is designed for the prediction of diabetes. The information is fed as input to the neural network design where
additional training takes place. A multi layer feed forward network of backpropagation algorithm is applied to reduce errors within the network.

In this thesis, the fuzzy relation between symptoms and risks factors for diabetic patient, primarily based on the expert’s medical information and the clinical analysis opinion are taken to identify numerous complications that cause diabetes. Genetic algorithm is employed to compute the best fitness value for evaluating the prediction accuracy of diabetes.

A new predictive method using data clustering techniques is proposed in this thesis to identify the diabetic disease and its types from the clinical diabetic database. This technique uses a collection of clustered data set that is more precise than the normal method. The proposed method can serve as a supportive method to aid medical experts and to train medical students and nurses to diagnose diabetic disease.

In this thesis questionnaire method developed by a panel of diabetes healthcare experts is carried out among persons with diabetes in a small city Erode-Tamilnadu-South India with the objective of understanding their perceptions, attitudes and practices in relation to their disease and its management. The study design is an initial listing followed by a qualitative survey using a structured questionnaire. Nearly one thousand and fifty patients were selected for a detailed face-to-face interview lasting several hours at the SRC diabetic centre, Erode. The selection was based purely based on patient's readiness to be interviewed, and type of treatment they are given. Interviews were conducted by appropriately trained experts in the language understood by patients. The questionnaire consisted of both, option lists, as well as open ended questions depending on the information being elicited. Information collected was recorded on structured forms and it is used for developing the proposed method.
OVERVIEW OF THE THESIS

Chapter 1 gives a brief introduction about diabetic mellitus along with the techniques that are been implemented for predicting hidden knowledge from clinical database using neural networks, backpropagation learning algorithm, genetic algorithm and fuzzy techniques.

Chapter 2 discusses the literature review on various techniques related to the research study.

Chapter 3 describes the diabetes diseases along with its causes, symptoms and different types of diagnostic tests, range of diabetic mellitus, types of diabetes and various complications due to diabetes.

Chapter 4 presents the implementation of the neural network architecture by training the data to predict the diabetic disease; if any error occurs while training the data then the layers are passed into the backpropagation algorithm to minimize errors in the network. The Performance of the training algorithm obtained using Matlab is analyzed.

Chapter 5 gives a brief introduction about fuzzy relational equation, which relates between symptoms and risk factors of diabetic patient based on the expert’s medical knowledge that are taken to identify the various complications that cause diabetes and the results are evaluated.

Chapter 6 employs the genetic algorithm to compute the best fitness value for evaluating the prediction accuracy of the diabetes and the simulation result obtained using Matlab is analyzed.
Chapter 7 employs data clustering techniques like K-means clustering and Fuzzy C-Means (FCM) clustering for predicting diabetes and its types from clinical diabetic database. The performance of the K-means clustering and FCM clustering techniques for clinical diabetic database is presented using Matlab and compared.

Chapter 8 provides the conclusion of the work proposed in this thesis.

Chapter 9 gives the future scope of the work proposed in this thesis, followed by references, appendix and publications.