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INTRODUCTION

1.1 OVERVIEW

Millions of people worldwide are suffering from diabetes and the prevalence is rising. China being on the top, India follows by a total of 63 million diabetics by 2012. The worldwide population of diabetics being around 371 million is projected to be 552 million till 2030 (International Diabetes Federation, 2013).

Type 2 diabetes may result from genetic predisposition, programming during pregnancy, childhood growth and factors related to daily life (Yajnik, 2001, 2002, 2003). Lifestyle related factors to type 2 diabetes are urbanization, living standards and fatty, fast foods. Some factors like sedentariness, have resulted from the replacement of manual activities to computers and television which make people lethargic. Type 2 diabetes as an epidemic is characterized by quick rate of increase and starts at a relatively young age and lower body mass index (Chan et al., 2004).

As cognitive dysfunction is not yet identified as one of the major complications but the association of diabetes with cognition is recognized (Patla et al, 2014). Diabetic encephalopathy was used in 1950 to describe brain dysfunction in the settings of diabetes (De Jong, 1950). Over the past few years, understanding of possible mechanisms and pathways has increased. Some reviews describe vascular and metabolic contributors to cognitive decline and dementia (Banks, Owen, Erickson, 2012; Kodl & Seaquist, 2008, Whitmer, 2007, Van den Berg et al, 2006; Biessels et al , 2006; Ryan et al, 2006). There is evidence from longitudinal and cross-sectional studies that diabetes is associated with risk of cognitive impairment, increased risk of vascular and Alzheimer's dementia in older adults (American Diabetes Association, 2013; Biessels et al, 2006; Cukierman, Gerstein, Williamson, 2005; McCrimmon, Ryan, Frier, 2012). Critical reviews have identified limitations in quality and representativeness of assessment and challenges in neuropsychological evaluation and need for consistency in tests which are used to compare populations (Jacobson, 2011; Strachan, Deary, Ewing, Frier, 1997).
So far, research on Health Related Quality of Life (HRQoL) has encompassed those aspects of overall quality of life that can affect either physical or mental health. This has led to the development and refinement of a number of generic and disease-specific HRQoL measures (Feinstein, 1994; Greenfield & Nelson, 1992; Guyatt et al, 1989; Guyatt, Kirshner, Jaeschke, 1992; Guyatt, Feeny, & Patrick, 1993; Patrick, Erickson, 1988; Shipper, Clinch, Powell, 1990). Generic measures of HRQoL are appropriate and desirable for particular applications in diabetes. Diabetes-specific measures may not capture the HRQoL issues related with comorbidities (Jacobson, De Groot, Samson, 1994; Anderson et al, 1997; de Visser et al, 2002), which contributes to the burden on type 2 diabetes. Thus, the actual choice of HRQoL measure should vary on various factors like purpose of measurement, health attributes relevant to the target population, in addition to the evidence of construct validity (Hays, Anderson, Revicki, 1993) of the measure in the target population. The contribution of the determinants of health to overall HRQoL in type 2 diabetes specifically has been assessed in past research, but generally the focus has tended to be on demographic, treatment related factors, and less emphasis on behavioural and social determinants of health. A more holistic approach to studying the determinants of health in type 2 diabetes would help to get better idea of the factors influencing diabetic patients. In the present study the researcher has looked at all the 3 aspects mental, physical and social of the HRQoL.

As recommended by the WHO the social aspect of HRQoL is as important as the physical and mental. In 2008, the WHO Commission on Social Determinants of Health issued its final report (Currie et al, 2012). The report made recommendations on necessary action on the social determinants of health across all sectors of society. Handling social determinants of health has been considered as a fundamental approach to the work of WHO in the 12th draft of WHO’s general programme of work 2014 – 2019. The World Conference on Social Determinants of Health also generated interest on social determinants of health in the South-East Asia Region. The Secretariat supported health ministries and partners in most countries including India in holding meetings to strengthen their response to social determinants of health and change in outlook towards health inequity in their respective countries. WHO in India has begun work on a study of hurdles to access to health services for particular chronic diseases services in order to analyse the wider social determinants of health.
influencing access to health care in population. This study has put up a theme of Rio Political Declaration “further reorient health sector towards reducing health inequities” and focuses towards universal health coverage, and non-communicable diseases (WHO, 2012).

The present research focuses on cognitive functioning and health related quality of life (HRQoL) in type 2 diabetic adults. The first chapter deals with introduction of the research topic, and a detailed explanation of all the concepts used in the study, followed by the statement of the problem. The significance and objectives are focused along with the rationale.

1.2 DIABETES: A METABOLIC DISORDER

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycaemia resulting from defects in insulin secretion, insulin action, or both (WHO, 1999). Patients with high blood sugar typically experience excessive thirst (polydipsia), excessive hunger (polyphagia) or frequent urination (polyuria). Majority of the type 2 diabetes patients initially may be having pre-diabetes. Their glucose levels are higher than normal and the cells in the body become resistant to insulin but levels not high enough to diagnose diabetes.

The degree of hyperglycaemia as measured by the glycated haemoglobin (HbA1c) or glucose levels (mg/dL) are specific measures to know diabetes control of a patient. Some pathogenic processes are involved in the development of diabetes, which range from autoimmune destruction of the β-cells of the pancreas with consequent insulin deficiency and gives rise to resistance to insulin action. The abnormalities in carbohydrate and protein metabolism in diabetes are deficient action of insulin on target tissues. Type 2 diabetes includes 90–95% of those with diabetes (Ramchandran et al, 2001), also referred as non-insulin-dependent diabetes mellitus (NIDDM) or adult onset diabetes. It encompasses individuals who have insulin resistance and relative insulin deficiency.

Diabetes is classified as a metabolic disorder. Metabolism is the way our bodies use digested food for energy and growth. Most of what we eat is broken down into glucose. Glucose in the blood is the main source of body fuel. When food is
digested, the glucose enters the bloodstream. Body cells use the glucose for energy, but glucose cannot enter the cells without insulin as insulin makes it possible for cells to take in the glucose. Insulin is a hormone which is produced by the pancreas. After food intake, the pancreas releases an enough quantity of insulin to release the glucose in blood cells. In diabetic patients quantity of glucose in the blood is elevated (hyperglycemia) as the body does not produce enough insulin or doesn’t produce insulin at all, which results in excessive glucose building.

1.3 CAUSES AND RISK FACTORS RELATED TO DIABETES

Urbanisation and industrialisation have produced advancement on the social and economic front in developing countries such as India ultimately resulting in dramatic lifestyle changes leading to lifestyle related diseases. The shift from a traditional to modern lifestyle, consumption of fatty foods along with a high level of stress compounds the ailment further. Studies from various parts of India reveal a rising trend in the prevalence of type 2 diabetes in the urban areas. A National Survey in 2000 observed that the prevalence of diabetes in urban India in adults was 12.1%. Recent data has illustrated the impact of socio-economic change in rural India; as a result the prevalence has risen from 2.4% to 6.4% in last 15 years. The risk of developing type 2 diabetes increases with age, obesity, lack of physical activity and nutritional change (fast foods) due to urbanization (Garduno, Khokhar, 2011). It is associated with a strong genetic predisposition (Arora et al, 2011); however the genetics of type 2 diabetes are complex and not clearly defined. Contribution of genes and environment is under debate. The tendency of Indians in regard to higher body fat and central adiposity compared with other races may be programmed in utero. Infections, environmental pollution and crowded living conditions in Indian cities may increase cardiovascular risk by stimulating fat cells. The impact of physical and mental stress along with lifestyle changes have a strong effect of increasing incidence of type 2 diabetes amongst individuals with a strong genetic background. Lot of patients with type 2 diabetes are obese, and the obesity itself causes some degree of insulin resistance. Few patients may have body fat distributed predominantly in the abdominal region even if they are not categorised as obese. This form of diabetes may go undetected because the hyperglycaemia develops gradually and at earlier stages is often not severe enough for the patient to notice any of the classic symptoms of
diabetes. Nevertheless, such patients are at high risk of developing vascular and cognitive complications. The insulin secretion is defective in these patients or insufficient to compensate for insulin resistance. Prevention of diabetes and coronary heart disease in India can be approached throughout the life cycle approach (Yajnik, 2001). As discussed, susceptibility to type 2 diabetes could be due to genetic factors, intrauterine programming, accelerated childhood growth and lifestyle factors (Yajnik 2001, 2002, 2003). Rise in migration of rural to urban population, change in food habits and lack of physical activity lead to the obesity epidemic. All these factors contribute to the rising epidemic of diabetes. Maternal and fetal undernutrition contributes to the diabetes epidemic in India. The Diabetes Unit, King Edward Memorial Hospital, Pune, has contributed a number of observations on the evolution of the insulin resistance syndrome during the life course. The insulin resistance syndrome evolves continuously over an individual's lifetime, thereby calling for a life-course model for its management (Yajnik, 2004). Specifically the unit has studied the relationships between size, body composition and nutrition in mothers and offspring (Yajnik, 2005). Some common risk factors in Indians quoted by few researchers above, are listed below-

- **Age**- The incidence of diabetes increases with age. Indians develop diabetes at least 10 years earlier than the western population. An early diagnosis of diabetes gives enough time for development of the chronic complications of diabetes.

- **Family history**- The prevalence of diabetes increases with a family history of diabetes. The risk of a child developing diabetes with a parental history is high. Indians have a high genetic risk for diabetes as observed in Asian Indians who have migrated to other countries.

- **Obesity**- The association of obesity with type 2 diabetes is well known. An excess body fat concentrated at the abdomen increases risk. The rising prevalence of overweight and obesity in India has a correlation with the increasing prevalence of obesity-related co-morbidities; hypertension, the metabolic syndrome, type 2 diabetes mellitus and cardiovascular disease (Gupta et al, 2002; Gupta & Misra, 2007).

- **Physical inactivity and sedentary living**- Physical inactivity is an independent factor for the development of type 2 diabetes. The availability of
transport and a shift in occupations combined with the multimedia has reduced the physical activity in all groups of populations.

- **Insulin resistance** - Asian Indians have a high prevalence of insulin resistance syndrome that may underlie tendency to develop diabetes and atherosclerosis. Important reasons could be their excess body fat and adverse body fat patterning including abdominal adiposity even when the body mass index is within the currently defined normal limits (Misra, 2004).

- **Urbanisation** - Countries like India are undergoing rapid urbanisation. Urbanisation is linked with increasing obesity, decreasing physical activity, unhealthy diet. All these factors contributing towards sedentary life style lead to complications of diabetes.

### 1.4 COMPLICATIONS RELATED TO DIABETES

Chronic hyperglycaemia is associated with dysfunction and failure of various organs especially the eyes, kidneys, nerves and heart. As long-term complications of diabetes develop, they can eventually be disabling. Some of the complications of diabetes identified by American Heart Association are as follows:

- **Heart and blood vessel disease** - Diabetes increases the risk of various cardiovascular problems, including coronary heart disease and heart attack. The risk of stroke is higher for people with diabetes, than for people without the disease according to the American Heart Association.

- **Nerve damage (neuropathy)** - Excess sugar can injure blood vessels especially in the legs. This can cause tingling, numbness or pain that gradually spreads. Poorly controlled blood sugar can minimise the sensation in affected limbs.

- **Kidney** - Diabetes can damage the kidney as well. Severe damage can lead to irreversible kidney failure requiring dialysis or a kidney transplant.

- **Eye** - Diabetes increases the risk of cataracts and glaucoma. It can damage the blood vessels of the retina (diabetic retinopathy), leading to blindness.

- **Foot** - Nerve damage in the feet, increases the risk of various foot complications. Left untreated, cuts can become serious infections.

- **Alzheimer's** - Type 2 diabetes may increase the risk of Alzheimer's and vascular dementia. The poor the blood sugar control, the greater the risk. One
theory is that cardiovascular problems caused by diabetes could contribute to dementia by blocking blood flow to the brain or causing strokes. Other possibilities are that too much insulin in the blood leads to brain-damage and lack of insulin in the brain may deprive brain cells of glucose.

1.5 TYPES OF DIABETES

1. **Type 1 Diabetes (IDDM)** - It is referred as insulin-dependent diabetes mellitus or juvenile diabetes. People usually develop type 1 diabetes in childhood or teenage years due to lack of insulin production. Patients with type 1 diabetes have to take insulin injections for their entire life. They must also ensure proper blood-glucose levels. If untreated it may be fatal, but the disease can be controlled with injectable insulin. Other options such as insulin pumps do exist, but are not so common being very expensive.

2. **Type 2 Diabetes (NIDDM)** - The body does not produce enough insulin for proper functioning, or the cells in the body do not react to insulin in this type of insulin, this condition is called insulin resistance. It can be controlled by losing weight, following a healthy diet, doing plenty of exercise, and monitoring their blood glucose levels. Type 2 diabetes is typically a progressive disease, which might get worse and the patient might probably end up taking injectable insulin though treated on tablet earlier. Overweight people have a higher risk of developing it, compared to those with a healthy body weight. People with a lot of visceral fat also known as central obesity are at risk. Being overweight, physically inactive and consuming junk food contribute to the risk of developing type 2 diabetes.

3. **Gestational Diabetes (GDM)** - This type affects women during pregnancy. The gestational diabetes is diagnosed during pregnancy. If women have high levels of sugar, and are unable to produce enough insulin it results in high levels of glucose. The majority of gestational diabetic patients need to take blood-glucose-controlling tablets or insulin. Undetected or uncontrolled gestational diabetes increases the risk of complications during childbirth. In some cases, the diabetes during pregnancy continues even after pregnancy and may be continued as type 2 diabetes.
There is an increasing trend in the number of women suffering from type 2 diabetes. They are more at risk of complications in diabetes because of certain social, cultural, and economic trends. The quality of life (QoL) may deteriorate especially in women due to some factors like dual responsibility of job and family, lack of proper diet and exercise, and lack of support. In a study (Rubin, Peyrot, 1998) on issues related to diabetes, it was seen that men were satisfied than women with diabetes treatment, and took lesser leaves than women.

1.6 CONCEPTS USED IN THE PRESENT STUDY

The concepts used in the study are explained in detail below. The operational definitions of variables are briefed in Chapter 3 on methodology.

1.6.1 Cognitive Functioning

Cognition is the information processing view of an individual's psychological functions (Coren, Lawrence, James, 1999). Cognitive functioning is any mental process that involves symbolic operations like perception, memory, executive functioning and thinking; it also includes awareness, attentiveness and the capacity for judgment (Lycan, 1999).

Cognitive process gained importance year's back, with Aristotle and his interest in the working of the mind and how they affect the human experience. Aristotle worked on cognitive areas related to memory and mental imagery. He found great importance in ensuring that his studies were based on empirical evidence (Matlin, 2009). Years later, as cognitive psychology became a upcoming field in Europe and America, other scientists like Wilhelm Wundt who opened his first laboratory for experimental psychology in 1879, William James in the 19th century, offered their contributions to the study of cognition.

Mild cognitive impairment (MCI), is a brain function syndrome involving the onset and evolution of cognitive impairment beyond expected age and education of the individual that are not significant enough to interfere with daily activities. However, people with MCI are at an increased risk of eventually developing
Alzheimer's. It represents an important phase on the path from normal cognitive function to dementia. It is characterized by impairment in memory, language or other cognitive domains, with activities of daily living being intact. A lack of consensus on the definition for and measurement of MCI has made it difficult to ascertain prevalence estimates for MCI (Winblad et al, 2004). A recent study explored the different prevalence estimates obtained when utilizing different definitions for categorizing MCI (Kochan et al, 2010). MCI is more common than Alzheimer's disease and its potential impact on population health is also high.

1.6.2 Health Related Quality of Life

The term Quality of Life (QoL) is used to evaluate the general well-being of people and societies. It is used in a various contexts, including development, healthcare, and politics. The indicators of the QoL include wealth, employment, environment, physical and mental health, education, recreation and social belonging.

The term QoL overlaps but is not similar with terms like well-being, social indicators, and way of life (Andrews, 1980). Many investigators in this area have adopted the phrase 'level of well-being' as one that seems to express the QoL concept most precisely. QoL has various definitions and is complex. Overall, it involves perceptions, attitudes and beliefs about psychological and other interpersonal living dimensions (Kraut, 2011). Hornquist (1982) defines quality of life as “a broad spectrum of dimensions of human experience, ranging from those associated with the necessities of life, to those associated with achieving a sense of fulfilment and personal happiness”.

There are various models of QoL, but one conceptual model plays a very important role in explaining the focus of an individual on his QoL. This model suggested by Baker and Intagliata (1982). It focuses on relationship between external environment, individual experience and quality of life responses. It suggests that there are four different foci of interest as related to QoL assessment. Researchers concerned with Focus 1, labelled as 'environmental system' are those who concentrate on the objective indicators of QoL. With Focus 2, the 'experienced environment' the interest shifts to perceived attributes of the environment, with recognition that everyone does not see the world in the same way. Focus 3, called the 'bio-psycho system', represents
the actual degree of mental and physical health of the individual and his or her attitudes, values, and aspirations. Finally, Focus 4 concentrates on 'behavioural outcomes', particularly respondent behaviour in response to the questionnaires and interviews assessing QoL.

HRQoL is a multidimensional concept that includes self-reported measures of physical and mental health. In modern concept, HRQoL is thought to encompass three fundamental domains: physical, mental and social functioning. A proper measure of HRQoL captures all of these domains and summarizes them in a single metric.

1.6.3 Diabetes Control (HbA1c)

HbA1c is the glycated haemoglobin, a form of haemoglobin which is measured primarily to identify the average plasma glucose concentration over prolonged period of time. When blood glucose levels are high, the molecules attach to the haemoglobin in RBCs. The longer the hyperglycaemia in blood, higher the rate of glucose binding to red blood cell that increases the glycated haemoglobin.

Once a haemoglobin molecule is glycated, it remains that way. A build-up of glycated haemoglobin within the red cell reflects the average level of glucose to which the cell has been exposed. Glycated haemoglobin is measured to assess the effectiveness of treatment by monitoring long-term serum glucose regulation. The HbA1c level is average blood glucose concentration for around three months. It is used to see the control of diabetes in patients and lower the levels better is the control. As the life span of red blood cells is 90-120 days, it reflects the average blood glucose values for the previous 2-3 months and is directly proportional to the concentration of plasma glucose in the blood over the life span of the red blood cells (Goldstein et al., 2004). Normal range of HbA1c is 3.5-5.5%.

The Expert Committee (Wild et al, 2004) from the American Diabetes Association (ADA, 2003) recommended criteria for diagnosis (WHO, 1999) of diabetes. The American Diabetes Association Standards of Care list the following as criteria for a diagnosis of diabetes: 1) HbA1c > 6.5%; 2) fasting plasma glucose >126 mg/dL; or 3) two-hour plasma glucose > 200 mg/dL during a oral glucose tolerance
test (OGTT); 4) symptoms of diabetes and a random plasma glucose > 200 mg/dL (ADA, 2013).

The HbA1c test is a best measure to check diabetes control and the levels to predict the likelihood of complications in diabetes. For day to day analysis, a glucose level is the best guide. The HbA1c level changes slowly over a period so it can be used as a 'quality control' measure.

The method most commonly used to measure HbA1c is High Performance Liquid Chromatography (HPLC) sometimes referred to as High-Pressure Liquid Chromatography. HPLC is a chromatographic technique used to separate a mixture of compounds in analytical chemistry and biochemistry with the purpose of identifying, quantifying or purifying the individual components of the mixture. HPLC is considered as a technique of analytical chemistry (as opposed to a gravimetric technique).

1.6.4 Mode of Treatment

There are two modes of treatment which type 2 diabetic patients may undergo.

- **Oral Hypoglycaemic Agents** (OHA) - OHA’s are anti-diabetic medications which treat diabetes mellitus by lowering glucose levels in the blood. They are administered orally hence termed as oral hypoglycemics. The dosage and drug varies depending on individual patients.

- **Injectable Insulin** - This mode of treatment refers to insulin which needs to be injected in body in order to control blood sugar. Insulin is an essential hormone, for the body to control and use glucose. There are many kinds of insulin to treat diabetes. Classification is based on how fast they start to work and how long their effects last. The types of insulin are:
  - Rapid-acting
  - Short-acting
  - Intermediate-acting
  - Long-acting
  - Pre-mixed
The doctor prescribes the type of insulin that is best for an individual depending on some factors listed below:

- Body's response to insulin, i.e. how long it takes insulin to be absorbed in the body and remain active in the body varies from individual to individual.
- Lifestyle choices like the type of food intake and exercise followed
- Willingness about multiple injections per day
- Age

1.7 THE PRESENT STUDY

This section covers rationale of the study, statement of the problem, objectives, and significance of the present study.

1.7.1 Rationale of the Study

Cognitive dysfunction and dementia have been observed to be complications in diabetes. Few studies have evidenced that phenotypes associated with obesity or alterations on insulin homeostasis are at a risk for developing cognitive decline and vascular dementia. In recent years, more interest has been developed to see the effect of diabetes on brain. Like cerebrovascular disease, diabetes is implicated in the development of other neurological co-morbidities. Not so well recognized complications of diabetes are cognitive dysfunction and dementia. The dysfunction represents serious health issue and is rising in prevalence worldwide. Diabetes is implicated as risk factor for dementia of vascular type as well as Alzheimer's disease.

Vascular dementia is a decline in thinking skills caused by conditions that reduce blood flow to the brain, depriving brain cells of oxygen and nutrients. The brain has one of the body's richest networks of blood vessels and is vulnerable. Thinking problems also may begin as mild changes that worsen gradually as a result of multiple minor strokes or other conditions like diabetes that affect smaller blood vessels, leading to cumulative damage. Vascular brain changes exist with changes linked to other types of dementia, including Alzheimer's disease and dementia with lewy bodies.
Vascular dementia is widely considered to be most common cause of dementia after Alzheimer’s disease, accounting for 20% of cases (Alzheimers Association, 2014). Many experts believe that vascular dementia remains undiagnosed even though it is recognized as common. Symptoms can vary widely, depending on the severity of the blood vessel damage and the part of the brain affected. Memory loss may be a significant symptom depending on the specific brain areas where blood flow is reduced. Changes in thinking and perception may include confusion, disorientation, trouble speaking or understanding speech and vision loss.

Current clinical practice of diabetes in India is based entirely on the Western model, which may not be wholly appropriate in view of different biological, cultural, racial and economic conditions. An urgent need was felt by the researcher to study cognitive decline associated with type 2 diabetes in India. India being diabetes capital of the world, it was felt necessary to confirm the findings in local population. Early diagnosis will help improve cognitive health and avoid patients leading towards dementia. In turn this will also help to improve their diabetic control. The contribution of diabetes control, mode of treatment and gender in cognitive functioning and HRQoL was assessed. These 3 factors play a major role in the sense that HbA1c gives an average of around 3 months’ blood sugar, mode of treatment gives an idea about which treatment affects the HRQoL specifically and gender implies to analyzing gender differences across the scores.

Cognitive decline and related dementia may shorten life expectancy, so based on the various patho-physiological mechanisms proposed to underlie cognitive impairment, a wide range of management strategies can be implemented to treat it, including control of risk factors, treatment of cognitive disorder, cognitive behavioral therapy, cognitive retraining and caregiver support. Recent attempts to reverse or delay progression of cognitive impairment due to cerebrovascular disease have given grounds for hope of treatment of cognitive impairment.

In the present study the researcher aims to measure the 3 aspects of HRQoL - mental, physical and social. The contribution of the determinants of health to overall HRQoL in type 2 diabetes has been studied in past research, but the focus has been on treatment related factors, and not on behavioural and social determinants of health. A
holistic approach to studying the determinants of health in type 2 diabetes would provide a better understanding of the factors influencing diabetic patients.

1.7.2 Statement of the Problem

To study cognitive functioning and health related quality of life in type 2 diabetic adults with special emphasis on diabetes control, mode of treatment and gender.

1.7.3 Objectives

- To develop a tool to measure health-related quality of life.
- To establish validity and reliability of the tool.
- To study the relationship between HbA1c (indicative of diabetes control) and cognitive functioning among type 2 diabetic patients.
- To study the relationship between gender and cognitive functioning among type 2 diabetic patients.
- To study the relationship between HbA1c (indicative of diabetes control) and HRQoL and its domains among type 2 diabetic patients.
- To study the relationship between mode of treatment and HRQoL and its domains among type 2 diabetic patients.
- To study the relationship between gender and HRQoL and its domains among type 2 diabetic patients.

1.7.4 Significance of the Present Study

India is facing perhaps the biggest epidemic of non-communicable diseases (NCD) in the world. As per the World Health Report 2005, (WHO India) NCD's contribute to 52% of the total mortality in India and these figures are expected to increase to 69 per cent by the year 2030 (Roglic et al, 2005).

Since it is feared that diabetes induced cognitive decline will become a major clinical problem worldwide in the future, the mechanism is not well known and so is a growing issue of public health. The second aspect of the study is HRQoL. HRQoL of diabetic patients is being recognized as the ultimate goal of health intervention.
As patients with diabetes have various complications, vascular disorders in the brain are considered to be one of the mechanisms in diabetes-induced cognitive decline. Diabetes related cognitive dysfunction has been recognized in humans, but the pathogenesis of this condition is still in debate. Also, evidence from animal studies demonstrates that altered function of the blood brain barrier (BBB) could be a potential contributing cause. The brain requires protection without compromising its requirement for nutrients like oxygen and glucose. The BBB functions to protect the brain by inhibiting toxins in the peripheral circulation from entering the brain, while allowing the nutrients to enter through the barrier. Furthermore, it mediates waste efflux from brain to blood and maintains a constant environment in the brain. The BBB concept originated with the work of Paul Ehrlich around 1885, who observed that water-soluble dyes injected into the circulatory system stained all organs except for the brain and spinal cord (Hawkins, & Davis, 2005). Clinical studies using magnetic resonance imaging-gadolinium techniques have shown that the BBB exhibits increased permeability (Starr et al., 2003). However, the mechanism of this permeability change is not known.

BBB change is induced by alteration of cerebral microvascular endothelial cell connections, so BBB disruption is a microvascular-associated disease; in other words a small-vessel disease. Representative cerebral small vessel diseases evaluated by magnetic resonance imaging (MRI), like the white matter lesions, are frequently observed in patients with type 2 diabetes compared with non-diabetic patients (Manschot et al, 2007, 2008).

1.8 SUMMARY

This chapter gives an introduction about the research topic. The concepts dealt with are, diabetes control measured in terms of HbA1c; mode of treatment in forms of OHA and OHA + insulin; gender; cognitive functioning; and health related quality of life. The chapter has begun with diabetes as a metabolic disorder, its causes, risk factors and complications related to the disease. Diabetes being a metabolic and non-communicable disorder has its own effects. The epidemic of non-communicable diseases like diabetes is rising in India, leading to cardiovascular diseases, and also to cognitive impairment and poor health related quality of life. The present study was
undertaken to study the role of diabetes control, mode of treatment and gender in
cognitive functioning and HRQoL of type 2 diabetic patients in an Indian setting.

In the next section, types of diabetes are enumerated in detail and the main
concepts are defined and explained. In the final section, the chapter concentrates on
significance, objectives and rationale of the study. The next chapter will cover the
review of related literature.