CLINICAL SIGNIFICANCE OF HBA1C AS A MARKER OF CIRCULATING LIPIDS IN TYPE 2 DIABETIC PATIENTS

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In partial fulfillment of the
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MD
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Under the guidance of
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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation/thesis entitled "**CLINICAL SIGNIFICANCE OF HBA1C AS A MARKER OF CIRCULATING LIPIDS IN TYPE 2 DIABETIC PATIENTS**" is a bonafide and genuine research work carried out by me under the guidance of **Dr. S.S. Devarmani**, **M.D.**, Professor, Department of Medicine, Shri B.M. Patil Medical College, Bijapur

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Dr. Mohamed Ayaz Abdul Assiz

LIST OF ABBREVIATIONS USED

CBC	Complete Blood Count
CETP	Cholesteryl Ester Transfer Protein
CHD	Coronary Heart Disease
CVD	Cardiovascular Disease
DCCT	Diabetes Control and Complications Trial
DPP	Diabetes Prevention Program
FPG	Fasting Plasma Glucose
FBS	Fasting Blood Glucose
HbA1c	Glycosylated Hemoglobin
HDL	High Density Lipoproteins
IFG	Impaired Fasting Glucose
IGT	Impaired Glucose Tolerance

OGTT	Oral Glucose Tolerance Test
LDL	Low Density Lipoproteins
NGSP	National Glycohemoglobin Standardization Program
NHANES	National Health and Nutrition Examination Survey
PG	Plasma Glucose
PPBS	Post Prandial Blood Sugar
R	Pearson Correlation Coefficient
RPG	Random Plasma Glucose
SD	Standard Deviation
TC	Total Cholesterol
T. TGL	Total Triglycerides
WHO	World Health Organization

ABSTRACT

Back ground & Objectives:

Diabetic patients with accompanied (but often unnoticed) dyslipidemia are soft targets of cardiovascular deaths. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality. Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. This investigation is an attempt to evaluate the diagnostic value of HbA1c in predicting diabetic dyslipidemia in type 2 diabetes patients**.**

Methods:

This study was carried out in B.L.D.E.U's Shri B.M. Patil Medical College Hospital and Research Centre, Bijapur during the period from January 2011 to June 2012. A total of 167 patients (108 males & 59 females) with type 2 Diabetes Mellitus who satisfied the inclusion & exclusion criteria were included in the study.

The sera of the selected subjects were analyzed for HbA1c, fasting blood sugar (FBS), post prandial blood sugar (PPBS), total cholesterol, triglycerides, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels.

Results:

A significant and direct correlation exists between HbA1c and serum levels of total cholesterol ($r = 0.524$), LDL ($r = 0.430$) and total triglyceride levels ($r = 0.620$) respectively. At the same time, this study also reveals a significant inverse relationship between HbA1c and HDL levels($r = -0.866$).

Conclusions:

The findings of this study illustrate the valuable additional information that can be provided by HbA1c about the levels of circulating lipids, besides its primary role in monitoring long-term glycemic control. This study also emphasizes that persons with high levels of HbA1c should be evaluated for diabetic dyslipidemia and managed accordingly.

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INTRODUCTION

"By the end of this decade, every fifth Indian will be a diabetic and every fifth Diabetic in the world will be an Indian"[1]

Diabetes mellitus is the single, most important metabolic disease recognized worldwide as one of the leading causes of death and disability[2]. The problem has reached pandemic proportions. Type 2 diabetes is the commonest form of diabetes constituting almost 90% of diabetic population. Prevalence of diabetes in the adults worldwide was estimated to be 4.0% in 1995 and expected to be 5.4% by the year 2025. Its incidence is higher in developing countries than developed countries.[3]

Today, India leads in the world with its largest number of diabetic subjects as compared with any given country. It has been estimated that presently 19.4 million individuals are affected by diabetes and these numbers are expected to increase to 57.2 million by the year 2025 (one-sixth of the world total)[4]. World Health Organization (WHO) has already declared India as the global capital of diabetes. In 1970s, the prevalence of diabetes among urban Indians was reported to be 2.1%, and this has now risen to 12.4%[5]. There is an economic paradox of wealthier being healthier in developed countries and wealthier being not healthier in developing countries. Shockingly, WHO has revised the predicted number of diabetics in India to be nearly 80 million by 2030.[6]

There is a high risk of cardiovascular disease (CVD) in people with type 2 diabetes, while cardiovascular deaths represent the top killer in this population[7].Hyperglycemia is the apparent feature of diabetes due to diagnostic dependency of patients on blood

glucose measurements. However, most of the individuals may also carry unnoticed dyslipidemia, characterized by increased levels of triglycerides and LDL and decreased HDL. Individuals with coexisting diabetes and metabolic syndrome (dyslipidemia + hyperglycemia + hypertension) have the highest prevalence of CVD[8].

Besides enduring multiple complications of chronic hyperglycemia, diabetic patients tend to be soft targets of deadly cardiovascular disease (CVD). Quantitatively, subjects with diabetes have more than two-fold increased risk for cardiovascular death compared with persons without diabetes[9, 10]. The synchronous occurrence of diabetes and cardiovascular events is evident from the findings of a cohort of acute coronary syndrome patients showing that few patients (16.4%) had normal glucose tolerance and the remaining were either diabetic or had impaired glucose tolerance[11].Furthermore, the role of hyperglycemia in CVD is supported by a direct correlation between fasting blood glucose (FBG) and cardiovascular events[12].Even isolated postprandial hyperglycemia has been suggested to be a cardiovascular risk factor[13]. It has been noticed that glucose fluctuations (glucose swing) during postprandial periods exhibit a more specific triggering effect on oxidative stress than chronic hyperglycemia[14].

Glycated haemoglobin (HbA1c) is an important indicator of long-term glycemic control with the ability to reflect the cumulative glycemic history of the preceding 2–3 months. Recently, elevated HbA1c has been regarded as an independent risk factor for coronary heart disease (CHD) [15]and stroke[16] in subjects with or without diabetes.

AIMS &OBJECTIVES

To examine the relationship between glycemic control and serum lipid profile and evaluate the relevance of HbA1c as an indicator of circulating lipids in male & female type 2 diabetic patients.

REVIEW OF LITERATURE

HISTORICAL REVIEW OF DIABETES MELLITUS

The earliest known record of diabetes was mentioned on the 3rd Dynasty Egyptian papyrus (1552 BC) by physician Hesy-Ra; it mentions polyuria as a symptom[78]. The first described cases are believed to be of type 1 diabetes. Indian physicians around the same time identified the disease and classified it as *madhumeha* or *honey urine* noting that the urine would attract ants[19].

The term "diabetes" or "to pass through" was first used in 230 BCE by the Greek Appollonius of Memphis[18]. The first complete clinical description of diabetes was given by the Ancient Greek physician Aretaeus of Cappadocia during 1st century AD, who noted the excessive amount of urine which passed through the kidneys and gave the disease the name “diabetes.”[78] He described it as "the melting down of flesh and limbs into urine" during 1st century AD.[19] In 164 AD, the Greek physician Galen of Pergamum mistakenly diagnoses diabetes as an ailment of the kidneys.[19, 78]

Type 1 and type 2 diabetes where identified as separate conditions for the first time by the Indian physicians Sushruta and Charaka in 400-500 AD with type 1 associated with youth and type 2 with being overweight.[78] Diabetes mellitus appears to have been a death sentence in the ancient era. Hippocrates makes no mention of it, which may indicate that he felt the disease was incurable.[78]

In medieval Persia, Avicenna (980–1037) provided a detailed account on diabetes mellitus in *The Canon of Medicine*, "describing the abnormal appetite and the collapse of sexual functions," and he documented the sweet taste of diabetic urine. Like Aretaeus before him, Avicenna recognized primary as well as secondary diabetes. He also described diabetic gangrene, and treated diabetes using a mixture of lupine, trigonella (fenugreek), and zedoary seed, which produces a considerable reduction in the excretion of sugar. This treatment is still prescribed in modern times. Avicenna also "described diabetes insipidus very precisely for the first time", though it was later Johann Peter Frank (1745–1821) who first differentiated between diabetes mellitus and diabetes insipidus.[80]

Upto the 11th century, diabetes was commonly diagnosed by "water tasters," who drank the urine of those suspected of having diabetes as the urine of people with diabetes was thought to be sweet-tasting.[19, 81]

In the 15th century, Paracelsus identified diabetes as a serious general disorder.[17] The term "mellitus" or "from honey" was added by the Britain John Rolle in the late 1700s to separate the condition from diabetes insipidus which is also associated with frequent urination.[18] It was in 1776 that Matthew Dobson confirmed that the sweet taste comes from an excess of a kind of sugar in the urine and blood.[17, 81]

The French physician, Priorry, during the late 1850s, used to advise diabetic patients to eat extra large quantities of sugar as a treatment modality.[17] In 1869, Paul Langerhans, a German medical student, announced in a dissertation that the pancreas contains two systems of cells; one set that secretes the normal pancreatic juice[17,18].

The function of the other was unknown. Several years later, these cells were identified as the "islets of Langerhans."[17]

In 1870s, Paris was under siege by Germany during the Franco-Prussian War. As a result, food was rationed in Paris. During this time, the French physician, Bouchardat, noticed that there was disappearance of glycosuria in his diabetic patients because of rationing. So he formulated the idea of individualized diets for his diabetic patients.[18]

The discovery of a role for the pancreas in diabetes is generally ascribed to Joseph von Mering and Oskar Minkowski, who in 1889 while working at the University of Strasbourg, Austria, found that dogs whose pancreas was removed, developed all the signs and symptoms of diabetes and died shortly afterwards.[79, 82]

In the late 18th century, the Italian diabetes specialist, Catoni, isolated his patients under lock and key in order to get them to follow their diets.[18]

During the early 19th century, chemical tests were developed to indicate and measure the presence of sugar in the urine. During this period, the French researcher, Claude Bernard, studied the workings of the pancreas and the glycogen metabolism of the liver.[17,18] The Czech researcher, I.V. Pavlov, discovered the links between the nervous system and gastric secretion, thus making an important contribution to science's knowledge of the physiology of the digestive system.[18]

During the 1900-1915s, many "fad" diabetes diets were recommended. They included the "oat-cure" (in which the majority of diet was made up of oatmeal), the milk diet, the rice cure, "potato therapy" and even the use of opium![19]

In 1908, German scientist, Georg Zuelzer developed the first injectible pancreatic extract to suppress glycosuria. However, extreme side effects were found to this treatment.[19]

In 1910, Sir Edward Albert Sharpey-Schafer suggested that people with diabetes were deficient in a single chemical that was normally produced by the pancreas—he proposed calling this substance *insulin*, from the Latin *insula*, meaning island, in reference to the insulin-producing islets of Langerhans in the pancreas.[19, 78]

During the time period from 1910-1920, the physicians Frederick Madison Allen and Elliot P. Joslin, emerged as the two leading diabetes specialists in the United States. Joslin believed diabetes to be "the best of the chronic diseases" because it was "clean, seldom unsightly, not contagious, often painless and susceptible to treatment."[17] In 1913, after three years of extensive studies on diabetes, Frederick Allen published *"Studies Concerning Glycosuria and Diabetes"*; a book that was significant for the revolution in diabetes therapy which was developed from it. Allen in 1919 also published "*Total Dietary Regulation in the Treatment of Diabetes"*. [17] In this article he cited the exhaustive case records of 76 out of the 100 diabetes patients he had observed. He became the director of diabetes research at the Rockefeller Institute in the same year. During 1919-1920, Frederick Allen established the first treatment clinic in the USA, 'the Psychiatric Institute' in New Jersey, to treat patients with

diabetes, high blood pressure and Bright's disease. The wealthy and desperate patients of this time flocked to this clinic.

Another one of the eminent personalities in the field of diabetes was Dr. Frederick Banting. [17] He was born near Alliston, Ontario on November 14, 1891. His parents, who were devout Methodist, initially tried to pressurise their son into joining the ministry. But instead of relenting into parental pressures, Banting, in 1912, enrolled for medicine at the University of Toronto.

On July 1, 1920, Dr. Banting opened his first office in the city of London, Ontario. He received his first patient on July 29th; his total earnings for his first month of work were only $4.00. Dr. Banting conceived of the idea of insulin after reading Moses Barron's "*The Relation of the Islets of Langerhans to Diabetes with Special Reference to Cases of Pancreatic Lithiasis*"[17,18] in the November issue of *Surgery, Gynecology and Obstetrics* of the same year. For the next year, with the assistance of Dr. Best, Dr. Collip and Professor Macleod, Dr. Banting continued his research using a variety of different extracts on de-pancreatized dogs. On December 30, 1921, Dr. Banting presented a paper entitled "The Beneficial Influences of Certain Pancreatic Extracts on Pancreatic Diabetes", summarizing his work to this point at a session of the American Physiological Society at Yale University.[19] Among the attendees were Allen and Joslin. But, little praise or congratulation was received by Banting for the same.

One of Dr. Collip's insulin extracts was first tested on a human being, a 14-year-old boy named Leonard Thompson, in Toronto on January 23, 1922.[17] The treatment was

considered a success by the end of the following February. On May 21st of 1922, Mr. James Havens was declared to be the first American successfully treated with insulin. 9 days later, .i.e., on 30th of May, Eli Lilly and Company and the University of Toronto enter a deal for the mass production of insulin in North America.[19]

For their efforts, on October 25, 1923, Dr. Banting and his colleague Prof. Macleod were awarded the Nobel Prize in Physiology or Medicine. Dr. Banting shared his award with Dr. Best & Prof. Macleod shared his award with Dr. Collip. Banting and Best made the patent available without charge and did not attempt to control commercial production.[18] Insulin production and therapy rapidly spread around the world, largely as a result of this decision. Banting is honored by World Diabetes Day which is held every year on his birthday, November 14. In 1934, Dr. Banting is knighted, thereby becoming Sir Frederick Banting. On February 21 1941, Sir Frederick Banting was killed in an airplane crash over Newfoundland while en route to England.

Sir Harold Percival (Harry) Himsworth was the first person to clearly make the distinction between what is now known as type 1 diabetes and type 2 diabetes, and this was published in January 1936.[83]

During 1940's, the link was found between diabetes and its long-term complications involving the organs like the kidneys and eyes.[18] This was followed by the development of the long acting insulin NPH in the 1940s.[78] It was also during this period that the American Diabetes Association was founded by 28 physicians.[17]

Identification of the first of the sulfonylureas occurred in 1942.[78] In 1944, standard insulin syringe was developed, helping to make diabetes management more uniform.[78] In 1946, Dr. Best co-founded a diabetes association under the name of Diabetic Association of Ontario.[18] Later, in 1953, it was formally established as the Canadian Diabetes Association. In the same year, Nova Scotia and Alberta establish provincial diabetes organizations. In 1956, L'Association Diabète Quebec was established.[17]

In 1950's insulin zinc proportions were developed by Hallas – Moller and coworkers as lente (slow acting) insulin.[19] In 1955, oral drugs are introduced to help lower blood glucose levels. The initial phenformin was withdrawn worldwide (in the U.S. in 1977) due to its potential for sometimes fatal lactic acidosis and metformin was first marketed in France in 1979, but not until 1994 in the US.[78]

Sir Frederick Sanger identified the amino acid sequence of insulin in beef, pork and sheep in 1956 for which he received a Nobel Prize. The amino acid sequence of insulin in humans was identified only in the 1960's.[84]

In 1959, two major types of diabetes were recognized; type 1 (insulin-dependent) diabetes and type 2 (non-insulin-dependent) diabetes.[20]

During the 1960's, apart from identifying the amino acid sequence in humans, the purity of insulin was improved. The method of testing for urinary sugar levels at home increased the level of control of diabetes in people during the same period.[79] The first pancreas transplant was performed at the University of Manitoba in the year 1966.[84]

The radioimmunoassay for insulin, was discovered by Rosalyn Yalow and Solomon Berson for which Yalow received the 1977 Nobel Prize in Physiology or Medicine[84]. In 1980, U.S. biotech company Genentech developed biosynthetic human insulin. The insulin was isolated from genetically altered bacteria, which produce large quantities of insulin[20]. The purified insulin was distributed to pharmacies for use by diabetes patients. Initially, this development was not regarded by the medical profession as a clinically meaningful development. The first insulin pen delivery system was introduced in 1986[19]

In 1988, Dr. Gerald Reaven identified the constellation of symptoms now called metabolic syndrome[20].

In 1989, the Banting Museum and Education Centre in London, Ontario was inaugurated; Her Majesty Queen Elizabeth & the Queen Mother lighted the Flame of Hope.[17, 18]

Identification of the first thiazolidinedione as an effective insulin sensitizer was during the 1990s[19]. In 1993, Diabetes Control and Complications Trial (DCCT) report was published. The DCCT results clearly demonstrated that intensive therapy (i.e., more frequent doses and self-adjustment according to individual activity and eating patterns) delayed the onset and progression of long-term complications in individuals with type 1 diabetes[17,18].

In 1995, DES launched its first education awareness campaign. In the same year, the Canadian Diabetes Association launched its web site. It turned out to be an award-winning source of diabetes-related information for people all over the world[20].

In the year 1996, the 75th Anniversary of the discovery of insulin was celebrated around the world. As part of the celebration, the Canadian Diabetes Association presented a symposium entitled "75 Years of Progress in Diabetes Care, Management and Treatment." By this time, the advent of insulin analogues which had vastly improved absorption, distribution, metabolism, and excretion characteristics were found to be clinically meaningful[17, 18].

During 1998, the United Kingdom Prospective Diabetes Study (UKPDS) was published. UKPDS results clearly identified the importance of good glucose control and good blood pressure control in the delay and/or prevention of complications in type 2 diabetes[20]. The clinical practice guidelines for the management of diabetes in Canada were released by the Canadian Diabetes Association during the same year[17]. Guidelines for the Nutritional Management of Diabetes were released in the year 1999. In 2001, the Diabetes Prevention Program was launched in USA[17].

In 2003, the names Insulin Dependent Diabetes Mellitus (IDDM) for Type 1 & Non-Insulin Dependent Diabetes Mellitus (NIDDM) for Type 2 Diabetes were formally dropped[20]. Clinical Guidelines by American Diabetes Association were issued in the same year. The Human Genome Project was also started in 2003[18]. The first genome-wide association studies for diabetes were initiated in 2007.[21]

During 2008, the Canadian Diabetes Association released their updated clinical practice guidelines on management of Diabetes.[17] The American Diabetes Association released their updated clinical Practice Guidelines on management of Diabetes also in the same year and it was again updated in the year 2012.[22]

ETIOLOGY OF DIABETES MELLITUS[21]

Diabetes mellitus (DM) comprises a group of metabolic disorders that share the common phenotype of hyperglycemia. DM is currently classified on the basis of the pathogenic process that leads to hyperglycemia. Type 1 DM is characterized by insulin deficiency and a tendency to develop ketosis, whereas type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and excessive hepatic glucose production.

Other specific types include DM caused by genetic defects [maturity-onset diabetes of the young (MODY)], diseases of the exocrine pancreas (chronic pancreatitis, cystic fibrosis, hemochromatosis), endocrinopathies (acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, hyperthyroidism), drugs (nicotinic acid, glucocorticoids, thiazides, protease inhibitors), and pregnancy (gestational DM).

Table 1 : ETIOLOGIC CLASSIFICATION OF DIABETES MELLITUS[22]

I. TYPE 1 DIABETES (² -cell destruction, usually leading to absolute insulin deficiency)
A. Immune mediated
B. Idiopathic
II. TYPE 2 DIABETES (may range from predominantly insulin resistance with relative insulin deficiencyto a predominantly secretory defect with insulin resistance)
III. OTHER SPECIFIC TYPES
A. Genetic defects of ² -cell function
1. Chromosome 12, HNF-1a (MODY3) 2. Chromosome 7, glucokinase (MODY2) 3. Chromosome 20, HNF-4a (MODY1) 4. Chromosome 13, insulin promoter factor-1 (IPF-1; MODY4) 5. Chromosome 17, HNF-1b (MODY5) 6. Chromosome 2, NeuroD1 (MODY6) 7. Mitochondrial DNA 8. Others
B. Genetic defects in insulin action
1. Type A insulin resistance 2. Leprechaunism 3. Rabson-Mendenhall syndrome 4. Lipoatrophic diabetes 5. Others

C. Diseases of the exocrine pancreas
1. Pancreatitis 2. Trauma/pancreatectomy 3. Neoplasia 4. Cystic fibrosis 5. Hemochromatosis 6. Fibrocalculous pancreatopathy 7. Others
D. Endocrinopathies
1. Acromegaly 2. Cushing's syndrome 3. Glucagonoma 4. Pheochromocytoma 5. Hyperthyroidism 6. Somatostatinoma 7. Aldosteronoma 8. Others
E. Drug or chemical induced
1. Vacor 2. Pentamidine 3. Nicotinic acid 4. Glucocorticoids 5. Thyroid hormone 6. Diazoxide 7. ² -adrenergic agonists 8. Thiazides 9. Dilantin 10. Gamma-Interferon 11. Others

F. Infections
1. Congenital rubella 2. Cytomegalovirus 3. Others
G. Uncommon forms of immune-mediated diabetes
1. “Stiff-man” syndrome 2. Anti-insulin receptor antibodies 3. Others
H. Other genetic syndromes sometimes associated with diabetes
1. Down syndrome 2. Klinefelter syndrome 3. Turner syndrome 4. Wolfram syndrome 5. Friedreich ataxia 6. Huntington chorea 7. Laurence-Moon-Biedl syndrome 8. Myotonic dystrophy 9. Porphyria 10. Prader-Willi syndrome 11. Others
IV. **GESTATIONAL DIABETES MELLITUS**

Patients with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, of itself, classify the patient.

CATEGORIES OF INCREASED RISK FOR DIABETES

In 1997 and 2003, The Expert Committee on Diagnosis and Classification of Diabetes Mellitus[23,24] recognized an intermediate group of individuals whose glucose levels do not meet criteria for diabetes, yet are higher than those considered normal. These people were defined as having impaired fasting glucose (IFG) [FPG levels 100 mg/dl (5.6 mmol/l) to 125 mg/dl (6.9mmol/l)], or impaired glucose tolerance (IGT) [2-h values in the OGTT of 140 mg/dl (7.8 mmol/l) to 199 mg/dl (11.0 mmol/l)].

Individuals with IFG and/or IGT have been referred to as having pre-diabetes, indicating the relatively high risk for the future development of diabetes. IFG and IGT should not be viewed as clinical entities in their own right but rather risk factors for diabetes as well as cardiovascular disease. They can be observed as intermediate stages in any of the disease processes listed in **Table 1**. IFG and IGT are associated with obesity (especially abdominal or visceral obesity), dyslipidemia with high triglycerides and/or low HDL cholesterol, and hypertension. Structured lifestyle intervention, aimed at increasing physical activity and producing 5–10% loss of body weight, and certain pharmacological agents have been demonstrated to prevent or delay the development of diabetes in people with IGT; the potential impact of such interventions to reduce mortality or the incidence of cardiovascular disease has not been demonstrated to date.

It should be noted that the 2003 ADA Expert Committee report reduced the lower FPG cut-off point to define IFG from 110 mg/dl (6.1 mmol/l) to 100mg/dl (5.6 mmol/l), in part to ensure that prevalence of IFG was similar to that of IGT. However, WHO and many other diabetes organizations did not adopt this change in the definition of IFG.

As HbA1c is used more commonly to diagnose diabetes in individuals with risk factors, it will also identify those at higher risk for developing diabetes in the future. When recommending the use of the HbA1c to diagnose diabetes in its 2009 report, the International Expert Committee[25]stressed the continuum of risk for diabetes with all glycemic measures and did not formally identify an equivalent intermediate category for HbA1c. The group did note that those with HbA1c levels above the laboratory "normal" range but below the diagnostic cut-off point for diabetes (6.0 to <6.5%) are at very high risk of developing diabetes. Indeed, incidence of diabetes in people with HbA1c levels in this range is more than 10 times that of people with lower levels [26-29]. However, the 6.0 to <6.5% range fails to identify a substantial number of patients who have IFG and/or IGT. Prospective studies indicate that people within the HbA1c range of 5.5–6.0% have a 5-year cumulative incidence of diabetes that ranges from 12 to 25%[26-29].

Analyses of nationally representative U.S. data from the NHANES indicate that theHbA1c value that most accurately identifies people with IFG or IGT falls between 5.5and 6.0%. In addition, linear regression analyses of these data indicate that among the nondiabetic adult population, an FPG of 110 mg/dl (6.1 mmol/l)

corresponds to an HbA1c of 5.6%, while an FPG of 100mg/dl (5.6 mmol/l) corresponds to an HbA1c of 5.4%. Finally, evidence from the DPP, wherein the mean HbA1c was 5.9% (SD 0.5%), indicates that preventive interventions are effective in groups of people with HbA1c levels both below and above 5.9%[30]. For these reasons, the most appropriate HbA1c level above which to initiate preventive interventions is likely to be somewhere in the range of 5.5–6%. As was the case with FPG and 2-h PG, defining a lower limit of an intermediate category of HbA1c is somewhat arbitrary, as the risk of diabetes with any measure or surrogate of glycemia is a continuum, extending well into the normal ranges.

To maximize equity and efficiency of preventive interventions, such an HbA1c cut-off point should balance the costs of "false negatives" (failing to identify those who are going to develop diabetes) against the costs of "false positives" (falsely identifying and then spending intervention resources on those who were not going to develop diabetes anyway).Compared to the fasting glucose cut-off point of 100 mg/dl (5.6 mmol/l), an HbA1c cut-off point of 5.7% is less sensitive but more specific and has a higher positive predictive value to identify people at risk for later development of diabetes.

A large prospective study found that a 5.7% cut-off point has a sensitivity of 66% and specificity of 88% for the identification of subsequent 6-year diabetes incidence[31]. Receiver operating curve analyses of nationally representative U.S. data (NHANES 1999-2006) indicate that an HbA1c value of 5.7% has modest

sensitivity (39-45%) but high specificity (81-91%) to identify cases of IFP (FPG >100 mg/dl) (5.6 mmol/l) or IGT (2-h glucose >140 mg/dl).

Other analyses suggest that an HbA1c of 5.7% is associated with diabetes risk similar to the high-risk participants in the DPP. Hence, it is reasonable to consider an HbA1c range of5.7 to 6.4% as identifying individuals with high risk for future diabetes and to whom the term pre-diabetes may be applied if desired. Individuals with an HbA1c of 5.7–6.4%should be informed of their increased risk for diabetes as well as cardiovascular disease and counseled about effective strategies, such as weight loss and physical activity, to lower their risks. As with glucose measurements, the continuum of risk is curvilinear, so that as HbA1c rises, the risk of diabetes rises disproportionately.

Accordingly, interventions should be most intensive and follow-up should be particularly vigilant for those with HbA1c levels above 6.0%, who should be considered to be at very high risk. However, just as an individual with a fasting glucose of 98 mg/dl (5.4 mmol/l) may not be at negligible risk for diabetes, individuals with HbA1c levels below 5.7% may still be at risk, depending on level of HbA1c and presence of other risk factors, such as obesity and family history.

Table 2 : CATEGORIES OF INCREASED RISK FOR DIABETES*

FPG 100 mg/dl (5.6mmol/l) to 125mg/dl (6.9mmol/l) [**IFG**]
2-h PG in the 75-g OGTT 140 mg/dl (7.8mmol/l) to 199 mg/dl (11.0 mmol/l) [**IGT**]
HbA1c 5.7–6.4%

**For all three tests, risk is continuous, extending below the lower limit of the range and becoming disproportionately greater at higher ends of the range*

DIAGNOSIS

Table 3 : CRITERIA FOR THE DIAGNOSIS OF DIABETES[22]

1. HbA1c ≥6.5%	The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.*
OR	
2. FPG ≥ 126 mg/dl (7.0 mmol/l)	Fasting is defined as no caloric intake for at least 8 h.*
OR	
3. 2-h plasma glucose ≥ 200mg/dl (11.1mmol/l) during an OGTT	The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.*
OR	
4. RPG ≥ 200 mg/dl (11.1 mmol/l).	In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis

**In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.*

Screening with a fasting plasma glucose level is recommended every 3 years for individuals over the age of 45, as well as for younger individuals who are overweight (body mass index e 25 kg/m^2) and have one or more additional risk factors.

The metabolic syndrome, the insulin resistance syndrome, and syndrome X are terms used to describe a commonly found constellation of metabolic derangements that includes insulin resistance (with or without diabetes), hypertension, dyslipidemia, central or visceral obesity, and endothelial dysfunction and is associated with accelerated cardiovascular disease.[21]

GLYCOSYLATED HEMOGLOBIN

History

Hemoglobin A1c was first separated from other forms of hemoglobin by Huisman and Meyering in 1958 using a chromatographic column.[32] It was first characterized as a glycoprotein by Bookchin and Gallop in 1968.[33] Its increase in diabetes was first described in 1969 by Samuel Rahbar et. al.[34] The reactions leading to its formation were characterized by Bunn and his co-workers in 1975.[35] The use of hemoglobin A1c for monitoring the degree of control of glucose metabolism in diabetic patients was proposed in 1976 by Anthony Cerami, Ronald Koenig and coworkers.[36]

General Consideration

Hemoglobin A (Hb A) constitutes 90% hemoglobin of adults and children above 6 months age. When Hb A is passed through a chromatographic column it separates into Hb A_O, the major component and minor components – Hb A_1A, HbA_1B and HbA_1C collectively called Hb A_1.[37] HbA1c is the most abundant of the minor hemoglobin components. This is structurally identical to Hb A, except for a hexose group linked to the N-terminal amino acid (valine) of the beta chain. Hence, this is called "Glycosylated hemoglobin" or HbA1c

Structure and Biosynthesis[35, 37, 38]

Biosynthesis of HbA1c involves post – translational, non-enzymatic slow glycosylation of Hb A within the RBC, occurring continuously throughout its 120days life span in the circulation.

Formation of HbA1c is a two stage process. (**Figure 1**)

Stage (1): Initially, the formation of a weak attachment between the glucose and the amino group of Hb A by the way of an Aldamine (Schiff base); called PreHbA1c.

Stage (2): There is a molecular rearrangement of Aldamine (Amadori reaction) with the formation of a ketamine in which the glucose molecule is finally attached to the Hemoglobin to form HbA1c.

State (1) – seems to be rapid and reversible and

Stage (2)- slow and irreversible.

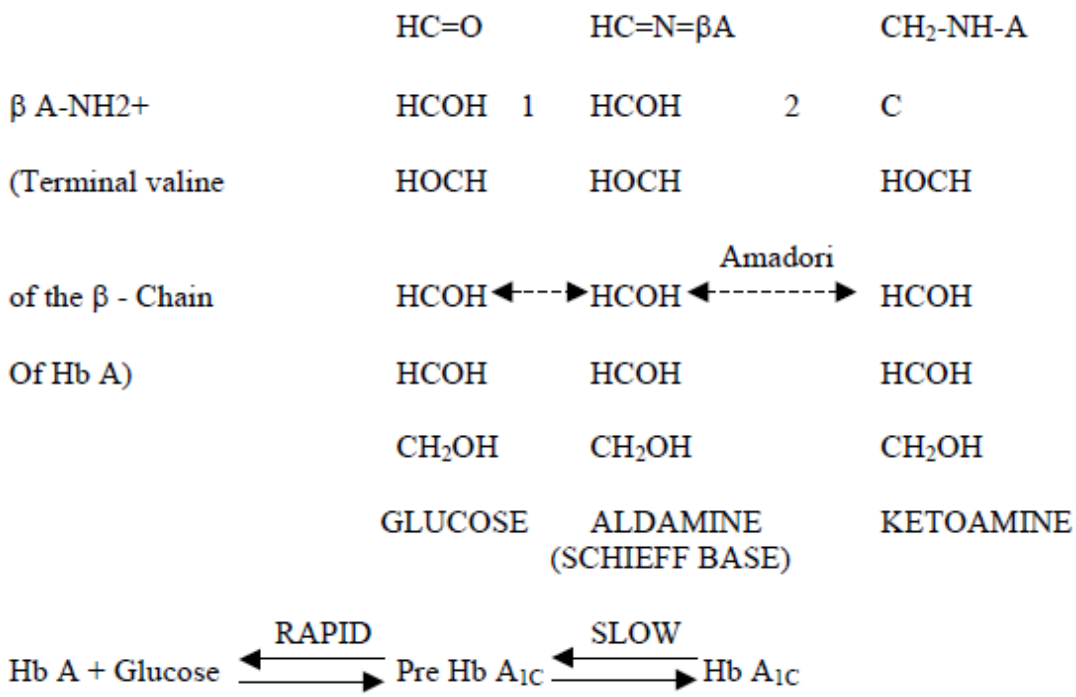


Figure 1: Schematic representation of the adduction of the glucose to the amino terminal of the beta chain of Hemoglobin to form HbA1c.

Relation HbA1c to Diabetic Hyperglycemia[35, 37, 39]

From structural and biosynthetic information available this is clear that HbA1c is formed slowly and almost irreversibly by the condensation of glucose and Hb in RBC. With simultaneous accumulation of HbA1c, it is evident that the amount of this component should be a reflection of average glucose concentration seen by the RBCs during their life span. Direct evidence for this relationship derives from atleast three lines of evidence which include

1. A reduction of HbA1c levels after diabetic patients are brought under optimal blood glucose control.
2. A plethora of studies which demonstrate a relationship between HbA1c levels and a variety of indices of diabetic glycemia and
3. Excellent correlations between clinical evaluation of the patients level of control and HbA1c level.

Clinical Significance of HbA1c

HbA1c is a widely used marker of chronic glycemia, reflecting average blood glucose levels over a 2 to 3-month period of time. The test plays a critical role in the management of the patient with diabetes, since it correlates well with both microvascular and, to a lesser extent, macrovascular complications and is widely used as the standard biomarker for the adequacy of glycemic management.

Prior Expert Committees have not recommended use of the HbA1c for diagnosis of diabetes, in part due to lack of standardization of the assay. However, HbA1c assays are now highly standardized so that their results can be uniformly applied both temporally and across populations. In their recent report[25], an International Expert Committee, after an extensive review of both established and emerging epidemiological evidence, recommended the use of the HbA1c test to diagnose diabetes, with a threshold of e6.5%, and ADA affirms this decision. The diagnostic HbA1c cut-off point of 6.5% is associated with an inflection point for retinopathy prevalence, as are the diagnostic thresholds for FPG and 2-h PG [25].

The diagnostic test should be performed using a method that is certified by the NGSP and standardized or traceable to the DCCT reference assay. Point-of-care HbA1c assays are not sufficiently accurate at this time to use for diagnostic purposes.

There is an inherent logic to using a more chronic versus an acute marker of dysglycemia, particularly since the HbA1c is already widely familiar to clinicians as a marker of glycemic control. Moreover, the HbA1c has several advantages to the FPG, including greater convenience, since fasting is not required, evidence to suggest greater preanalytical stability, and less day-to-day perturbations during periods of stress and illness.

These advantages, however, must be balanced by greater cost, the limited availability of HbA1c testing in certain regions of the developing world, and the incomplete correlation between HbA1c and average glucose in certain individuals. In addition, the HbA1c can be misleading in patients with certain forms of anemia and hemoglobinopathies, which may also have unique ethnic or geographic distributions. For patients with a hemoglobinopathy but normal red cell turnover, such as sickle cell trait, an HbA1c assay without interference from abnormal hemoglobins should be used. For conditions with abnormal red cell turnover, such as anemias from hemolysis and iron deficiency, the diagnosis of diabetes must employ glucose criteria exclusively.

The established glucose criteria for the diagnosis of diabetes remain valid (see **Table 3**).It is likely that in such cases the health care professional would also measure an HbA1c test as part of the initial assessment of the severity of the diabetes and that it would (in most cases) be above the diagnostic cut-off point for diabetes. However, in rapidly evolving diabetes, such as the development of type 1diabetes in some children, HbA1c may not be significantly elevated despite frank diabetes. Just as there

is less than 100% concordance between the FPG and 2-h PG tests, there is not full concordance between HbA1c and either glucose-based test.

Analyses of NHANES data indicate that, assuming universal screening of the undiagnosed, the HbA1c cut-off point of e6.5% identifies one-third fewer cases of undiagnosed diabetes than a fasting glucose cut-off point of e126 mg/dl (7.0 mmol/l).However, in practice, a large portion of the population with type 2 diabetes remains unaware of their condition. Thus, it is conceivable that the lower sensitivity of HbA1c at the designated cut-off point will be offset by the test's greater practicality, and that wider application of a more convenient test (HbA1c) may actually increase the number of diagnosis made.

Conditions leading to falsely abnormal values for theHbA1c limitation of the Assay[40-42]

I. Conditions leading to false elevation of HbA1c

A. Chromatographic abnormalities

1. Hyperlipidemia (due to lactescence)
2. Elevated temperature and or buffer pH.
3. Negatively charged Hb variants, such as HbF
4. Acute hyperglycemia ("Fast Glycosylation")

B. Other post translational modification of Hb

1. Aspirin (acetylation)
2. Antibiotics (Penicilloylation)
3. Alcohol (5-deoxy-xylulose-1-PO_4)
4. Uremia (Carbamylation)

II. Conditions leading to falsely low HbA1c values

A. Chromatographic abnormalities

1. Low temperature and/or buffer pH.
2. Positively charged Hb variants, such as HbS or HbC.

B. Altered RBC dynamics

1. Increased destruction of RBCs – Hemolytic Anemia.
2. Active erythropoiesis as in pregnancy
3. Recent blood transfusion.

Methods for measuring Glycosylated Hemoglobin[35, 43-45]

1. Chromatographic method (Kynoch and Lehmann)
2. Colorimetric Method (Fluckiger and Winterhalter).
3. Electrophoretic method
4. Radio Immuno Assay.

Among these, chromatographic method has been widely used to estimate HbA1c. It is a simple and rapid method (microchromatography). It has better resolution and more precision. It requires small amount of sample and no special equipment. Its cost and use of cyanide as buffer are the main disadvantages.

Ion exchange chromatographic method has been used in this study. The principle and the procedures of the method are dealt below.

Principle

Whole blood is mixed with a lysing reagent to prepare a hemolysate. This is then mixed with a weakly binding cation exchange resin. The non-glycosylated hemoglobin binds to resin leaving Glycosylated Hemoglobin (HbA1c) free in the supernatant. The HbA1c% is determined by measuring the absorbance of the HbA1c fraction and of the total Hb.

Reagents and apparatus

1. Ion exchange Resin (Bio-Rex 70)
2. Hemolysing Reagent

   0.3 g white saponin

   0.5 g potassium cyanide

   Dissolved in a Buffer pH 6.7 to make 1 litre
3. Control (lyophilized).
4. Apparatus – Plastic Tubes and Resin Separators.

Specimen

Whole blood is collected in EDTA bulb. Heparin may also be used. HbA1cin blood is found to be stable for one week at 2-8^{O}C.

Equipment Required

1. Spectrophotometer/photocolorimeter
2. Cuvettes
3. Test tubes
4. Vortex Mixer
5. Pipettes and Micropipette.

Reagent Preparation

Reagents 1 and 2 are ready to use. HbA1c control (3) is dissolved in 1 ml. of deionized water by inverting / swirling. Reconstituted control is stable for 30 mins only at Room temp or 15 days at -20 ^{0}C.

Procedure

Assay Temperature : 23 ± 2^{0}C

Wave length : 415 nm (Hg 405 nm)

Step 1: Hemolysate preparation

1. 0.5ml of lysing reagent (2) is pipetted into a test tube.
2. To it 0.1ml of well mixed whole blood sample is to be added.
3. Mixed and allowed to stand at room temperature for 5 minutes.

Step 2: Hb A_1C Separation and Assay.

1. 3.0 ml of Ion Exchange Resin (1) is pipetted into the plastic tube which was mixed well before use.
2. 1.0ml of the hemolysate is added (from step 1)
3. The resin separator is positioned in the plastic tube so that the rubber sleeve is approximately 2 cms above the liquid level.
4. Plastic tube is placed on cortex mixer and is mixed for 5 minutes.
5. The resin separator is pushed down in the plastic tube until the resin is firmly packed.
6. The supernatant is poured directly into a cuvette and absorbance is measured against deionized water within 60 minutes.

Step: 3 Total Hemoglobin (THB) Assay

1. 5.0ml of deionized water is pipetted into test tube.

2. 0.02ml of hemolysate (from step 1) is pipetted into it.

3. Mixed and absorbance is read against deionized water within 60 minutes.

Calculations

$$\text{HbA1c\%} = \frac{\text{Absorbance of HbA1c}}{\text{Absorbance of THb}} \times 10 \times \text{Temp. factor (Ff)}$$

Tf for Assay at $23 \pm 20^{C} = 1.0$

Tf for Assay at $300^{C} = 0.7$

Finally, the pooled information is analyzed using appropriate statistical methods.

The interpretation of HbA1c test in this study is as follows:

Normal	-	4 - 6%
Good Control	-	6.1 - 7%
Fair Control	-	7.1 - 8%
Poor Control	-	>8%

LIPOPROTEIN ABNORMALITIES IN DIABETES

Diabetic patients have 2 to 3 times increased risk of coronary artery disease as compared to the non diabetic[46]. The causes for it are multiple, which include dyslipidemia, hypertension, obesity and smoking. Dyslipidemia which is usually present in diabetic, in the form of increased triglycerides and decreased HDL cholesterol levels, is 2 to 3 fold common in diabetics than in the non diabetics and confers much of accelerated and increased early risk of coronary artery disease (CAD), cerebrovascular disease, peripheral vascular disease and sudden cardiac death. The frequency of hypercholesterolemia and the LDL hyperlipoproteinemia is equal or higher in diabetics. However the qualitative abnormalities of LDL cholesterol increase the affinity of endothelium towards them. Thus comparable levels of LDL are more atherogenic and much lower levels of LDL contribute to coronary risk in diabetics which is now given more importance in diabetics. The clinical trials such as Cholesterol and Current Event study (CARE) and the Scandinavian Simvastatin Survival Study[47] have shown significant reduction in macrovascular disease by lowering the LDL with the statins.

The atherogenic component of the serum total cholesterol is the LDL cholesterol which is directly related to CAD incidence[48]. The level of HDL cholesterol is inversely related to coronary heart disease incidence consistent with its putative role in cholesterol removal. Coronary heart disease incidence is independently related to with each of these lipoprotein components. Use of the total to HDL cholesterol ratio was recommended in Framingham study because this ratio was easy to calculate and

was found to be more efficient for detecting coronary candidates than reliance of the LDL cholesterol as recommended by the US Expert panel reports.

Blood triglyceride concentration continues to be debatable as a CAD risk factor. Both fasting and non fasting triglycerides levels were associated with CAD risk in the Framingham study; the debate centers around whether total triglycerides are significantly associated with CAD risk after adjustment by HDL cholesterol in prediction. Analysis of lipid research clinics and Framingham data show significant impact on the triglyceride levels after HDL cholesterol adjustment and these correlations are consistently demonstrated if logarithmic transformations for the lipids are used. In addition the residual effect of triglyceride after consideration of HDL cholesterol appears to be greater in women than in men.

Abnormal postprandial lipoprotein metabolism in diabetes[49]

Patients with type 1 diabetes mellitus with very good glycemic control can have normal postprandial lipid levels. However, as glycemic control worsens because of inadequate insulin, lipoprotein lipase activity decreases, and postprandial hyperlipidemia can result. In patients with type 2 diabetes, the underlying insulin resistance can be associated with mild reductions in lipoprotein lipase, but overproduction of VLDL is a major problem. Increased VLDL competes with chylomicrons for lipoprotein lipase, resulting in postprandial hyperlipidemia in most patients with type 2 diabetes. The fasting triglyceride level is, therefore, a predictor of the severity of postprandial hyperlipidemia.

Evidence has been accumulating to support the atherogenicity of postprandial triglyceride-rich lipoproteins[50, 51] When TGL rich lipoproteins are increased, increase exchange of HDL & LDL cholesteryl esters for TGL in chylomicrons and VLDL can reduce HDL levels and generate small, dense LDL. These exchanges are mediated by a plasma protein called cholesteryl ester transfer protein (CETP).

It is now thought that disordered metabolism of VLDL and/or chylomicrons may be proatherogenic. Chylomicron remnants and VLDL or its remnants enter the subendothelial space of the vessel wall where the atherogenic process is initiated. The size of the triglyceride-rich particles in the bloodstream is critical, because very large particles cannot penetrate into the subendothelial space (**Figure 2**).[52]

The number of triglyceride-rich particles also influences the risk for atherosclerotic cardiovascular disease, inasmuch as a larger number of particles increase the likelihood that they will enter and remain in the vessel wall. For any triglyceride level, more particles mean smaller, more atherogenic particles. The cholesterol content of the triglyceride-rich lipoproteins is important, because persons with more cholesterol-enriched particles will be at greater risk for atherosclerotic cardiovascular disease.[53] This association is well documented by the increased risk of atherosclerosis in patients with dysbetalipoproteinemia who are homozygous for apolipoprotein E and in whom the accumulation of chylomicron and VLDL remnants occurs owing to reduced binding of apolipoprotein E on the chylomicron and VLDL remnants to hepatic receptors.[54]

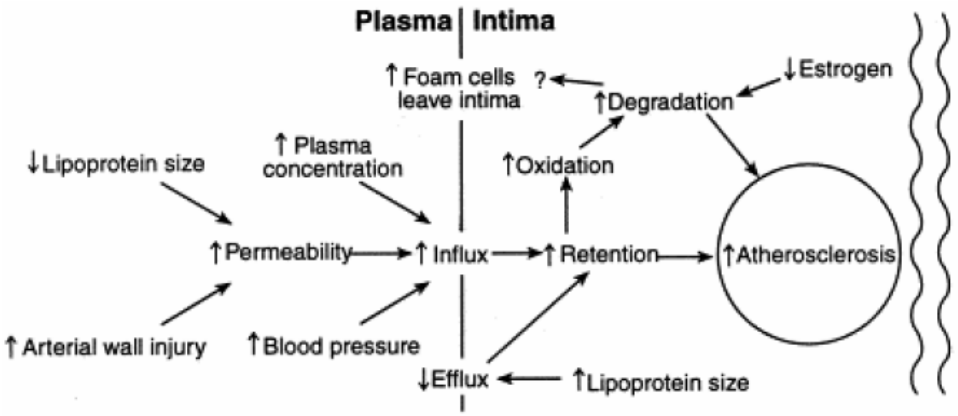


Figure 2 The plasma concentration of very-low-density lipoprotein, intermediate-density lipoprotein, and low-density lipoprotein cholesterol is linearly related to the flux of these particles into the arterial wall, suggesting that variation in plasma lipoprotein concentration directly affects the extent of delivery of lipoproteins to the arterial intima. Portrayed here are the known determinants of arterial intimal permeability, influx, efflux, degradation, and retention of plasma lipoproteins and their relation to atherosclerosis.[52]

National cholesterol education program (NCEP) and the Adult treatment plan III[55] maintains that CAD patients be treated intensively. Its major new feature is that a focus on primary prevention in a person with multiple risk factors. This report also calls for more aggressive lowering of LDL cholesterol. The important features of these guidelines include that complete lipoprotein profile, total cholesterol, LDL cholesterol, HDL cholesterol and triglyceride as the preferred initial test rather than screening for total cholesterol and HDL alone.

The LDL cholesterol levels

< 100 mg /dl – optimal
100-129 mg/dl – near optimal
130-159 mg/dl – border line high
160-189 mg/dl – high
e 190 mg/dl – very high

Total cholesterol levels

< 200 mg/dl – desirable
200-239 mg/dl – borderline high
e 240 mg/dl – high

HDL cholesterol levels

< 40 mg/dl – low levels
d 60mg/dl – border line high

Triglyceride levels

< 150 mg/dl – normal levels
150-199 mg/dl – border line high
200-499 mg/dl – high levels
e 500 mg / dl – very high levels

Thus the new NCEP guidelines remain same for total cholesterol and identifies LDL cholesterol of < 100mg/dl as optimal and raises HDL levels from < 35 mg/dl to < 40 mg/dl and lowers desirable triglyceride levels from < 200 mg/dl to < 150 mg/dl and that LDL cholesterol is the primary target of the therapy.

The ATP III continues to identify LDL as primary of therapy and has put forth the following criteria.

Table – 4

RISK CATEGORY	LDL GOAL
CAD and its equivalents	< 100 mg/dl
>=2 risk factors	< 130 mg/dl
No risk factors or 1 risk factor	< 160 mg/dl

Risk factors include cigarette smoking, hypertension, or on antihypertensive therapy, low HDL of < 40 mg/dl, family history of premature CAD, age > 45 in men, that of > 55 in women.

RELATION BETWEEN HbA1c, SERUM LIPIDS & CHD

Elevated HbA1c has been regarded as an independent risk factor for CHD[15] and stroke [16] in subjects with or without diabetes. Ravipati et al.[56]observed a direct correlation between HbA1c and the severity of CAD in diabetic patients. Vaag [57] has suggested that improving glycemic control in patients with type 2 diabetes may be more important than treating dyslipidemia for the prevention of both microvascular and macrovascular complications. Nakamura et al.[58] have observed significant elevation of soluble form of receptor for advanced glycation end products (sRAGE) in type 2 diabetic patients with CAD. They also demonstrated significant association between sRAGE and HbA1c as well as serum lipids.

Giansanti et al.[59] also observed significantly higher levels of hypercholesterolemia and hyperlipidemia in type 2 diabetic patients with CVD as compared to diabetic patients without CVD.

Patients with type 2 diabetes often exhibit an atherogenic lipid profile (high TG and low HDL cholesterol) which greatly increases their risk of CVD compared with people without diabetes. Recently, patients with type 2 diabetes carrying apolipoprotein E 4 genotype were found to have a greater cardiovascular risk owing to metabolic variation in lipid metabolism leading to higher cholesterol and LDL[60]. Interestingly, attempts to reduce cardiovascular risks resulted in the improvement of HbA1c even in the absence of any specific intervention targeted at improving glycemic control.

HA Khan et al showed in his study that clearly suggested that HbA1c endures the ability of predicting serum lipid profile in both male and female diabetic patients & that the dual biomarker capacity of HbA1c (glycemic control as well as lipid profile indicator) may be utilized for screening high-risk diabetic patients for timely intervention with lipid lowering drugs[61].

MATERIALS AND METHODS

SOURCE OF DATA

Patients with type 2 diabetes mellitus who presented to B.L.D.E.U's Sri B.M. Patil Medical College, Hospital and Research Centre Bijapur, from January 2011 to June 2012.

Sample size:

With the prevalence rate of type 2 Diabetes mellitus taken as 12.4%[62], 95% confidence interval & 5% margin of error, the calculated sample size (n) is 167 using the statistical formula

$$n = \frac{(1.96)^2\, p(1-p)}{d^2}$$

Where, n = Sample size

p = Prevalence rate

d = Margin of error

Statistical method:

Data will be analyzed using the following statistical methods:

- Diagrams
- Mean ±SD
- Correlation tests like Pearson correlation coefficient (r)
- Significance tests like Z-test. F-test, $Ç^2$ test (if necessary)

METHOD OF COLLECTION OF DATA

The study will be carried out on consecutive 167 patients coming to B.L.D.E.U's Shri B.M. Patil Medical College Hospital and Research Centre, Bijapur presenting with type 2 Diabetes Mellitus.

INCLUSION CRITERIA

Patients presenting with type 2 Diabetes Mellitus with/ without dyslipidemia

EXCLUSION CRITERIA

Patients who had

- A change in diet or diabetic treatment within 6 weeks.
- Treatment for dyslipidemia.
- Recent blood loss.
- Hemolytic anemia.
- Hemoglobinopathy such as sickle-cell disease.
- Donated blood recently.

STUDY DESIGN

After obtaining the necessary approval and clearance from the ethical committee of our teaching hospital cum research centre, this prospective study was carried out on a total of 167 patients, suffering from type 2 diabetes mellitus, who satisfied the inclusion and the exclusion criteria and presented to our hospital during the time period from January, 2011 to June, 2012. A detailed clinical history of each of the included subjects was taken and physical examination was done using a pre-approved standardised proforma. Following this, venous blood of the each of the subject was drawn after ensuring that the subject had underwent at least 8 hours of overnight fasting. The collected blood sample was sent to the central laboratory of our hospital for testing the levels of FBS, PPBS, HbA1c & lipid profile (Total Cholesterol, Total TGL, LDL & HDL). The reports of these investigations were collected. Later on, the entire collected data (comprising of the details obtained from history taking, physical examination & the investigation reports) was meticulously compiled and co-relation was calculated using the formula of Pearson co-relation coefficient between HbA1c, FBS, PPBS and Lipid Profile. The obtained results were analyzed and inferences were drawn from them.

INVESTIGATIONS

BLOOD TESTS

- FASTING BLOOD SUGAR (FBS)
- POST PRANDIAL BLOOD SUGAR (PPBS)
- GLYCATED HEMOGLOBIN (HbA1c)
- LIPID PROFILE (TC, TGL, LDL, HDL)
- COMPLETE BLOOD COUNT (CBC)
- URINE ROUTINE
- BLOOD UREA
- BLOOD CREATININE

FUNDOSCOPIC EXAMINATION

ELECTROCARDIOGRAM

OBSERVATIONS AND RESULTS

This study was carried out in B.L.D.E.U's Shri B.M. Patil Medical College Hospital and Research Centre, Bijapur during the period from January 2011 to June 2012. A total of 167 patients with type 2 Diabetes Mellitus who satisfied the inclusion & exclusion criteria were included in the study.

Clinical Profile of the involved subjects:

At the very onset, let us start with the clinical profile of the subjects taken into the study. **Table 5** gives an outline of the minimum value & maximum value of the various parameters of the subjects involved in the study, their mean and standard deviation.

Table 5: Clinical profile of the subjects taken into the study

n = 167	Minimum	Maximum	Mean	Std. Deviation
Age of Subjects (years)	36	86	57.03	9.586
Duration of Diabetes (months)	6	348	65.81	62.373
Systolic BP (mm/Hg)	88	230	132.85	14.693
Diastolic BP (mm/Hg)	50	110	78.54	8.818
Pulse Pressure (mm/Hg)	30	120	54.31	9.942
Mean Arterial Pressure (mm/Hg)	62.6	150	96.64	10.091
Height (cm)	135	184	160.55	10.117
Weight (kg)	41	87	63.05	10.391
BMI (kg/m^2)	16.29	33.26	24.392	2.884
FBS (mg/dl)	64	394	147.59	63.696
PPBS (mg/dl)	56	457	223.82	76.725
HbA1c (%)	5.00	14.80	8.126	1.736
Total Cholesterol (mg/dl)	65	317	176.90	41.229
LDL (mg/dl)	21	231.9	109.85	39.076
HDL (mg/dl)	17	43	32.27	4.449
Total Triglycerides (mg/dl)	37	408.5	176.18	75.568
Blood Urea (mg/dl)	13	119	26.80	10.552
S.Creatinine (mg/dl)	0.6	4.5	.997	.386
E.S.R (mm/Hr)	5	140	18.10	17.684

Table 6 shows the distribution of subjects according to age and gender. Out of the total 167 subjects, 108 of them were male and 59 of them were female. Most number of subjects was from the 51-60 year age group.

Table 6 : Distribution of Subjects according to Age and Gender

Age of the subjects	Gender		Total
	M	F	
<50 yrs of age	34	15	49
51-60 yrs of age	41	23	64
61-70 yrs of age	22	20	42
>70 yrs of age	11	1	12
Total	108	59	167

Table 7 : Distribution of Subjects according to BP and Gender

BP	Gender		Total
	M	F	
Normal	4	6	10
Prehypertension	77	40	117
Isolated Systolic Hypertension	27	13	40
Total	108	59	167

Table 7 shows the distribution of the subjects according to their blood pressure and their gender. Out of the 10 subjects who were normotensive, majority of them were female (60%). Males were found to be the predominant group in the prehypertensive group (65.8%) as well as in the isolated systolic hypertensive group (67.5%).

Figure 3 shows distribution of subjects according to duration of diabetes and gender. Out of the 167 subjects, majority of the subjects (n=134, 87 males & 47 females) had diabetes for 1-5 years and 10 subjects (5 males &5 females) had diabetes for less than 1 year, 6 subjects (3 males & 3 females) for 6-10 years, 4 subjects (10 males & 3 females) for 11-15 years and 13 subjects (10 males and 3 females) had it for more than 15 years.

Figure 4 gives an outline of the distribution of the subjects in accordance with the duration of diabetes and their BP control. In patients with less than 1 year of diabetes (n=10), it was noticed that only 1 patient was normotensive, 8 were in prehypertensive state and 1 had isolated systolic hypertension. In the group of patients having diabetes for a period of 1-5 years (n=134), 9 were normotensive, 102 were prehypertensives, and 23 were isolated systolic hypertensives. Out of the 6 subjects having diabetes for a period ranging from 6 to 10 years, it was found that 4 were prehypertensives and 2 were isolated systolic hypertensives. In the group of subjects having diabetes for a duration of 11-15 years (n=4), 1 was prehypertensive and the rest were having isolated systolic hypertension. In the 13 subjects who had diabetes for a period of greater than 15 years, 2 were prehypertensives and the rest were having isolated systolic hypertensives. None of the subjects in the study group could be categorized into stage 1 or stage 2 hypertension.

Figure 3 : Bar chart showing the distribution of subjects according to duration of diabetes and their gender

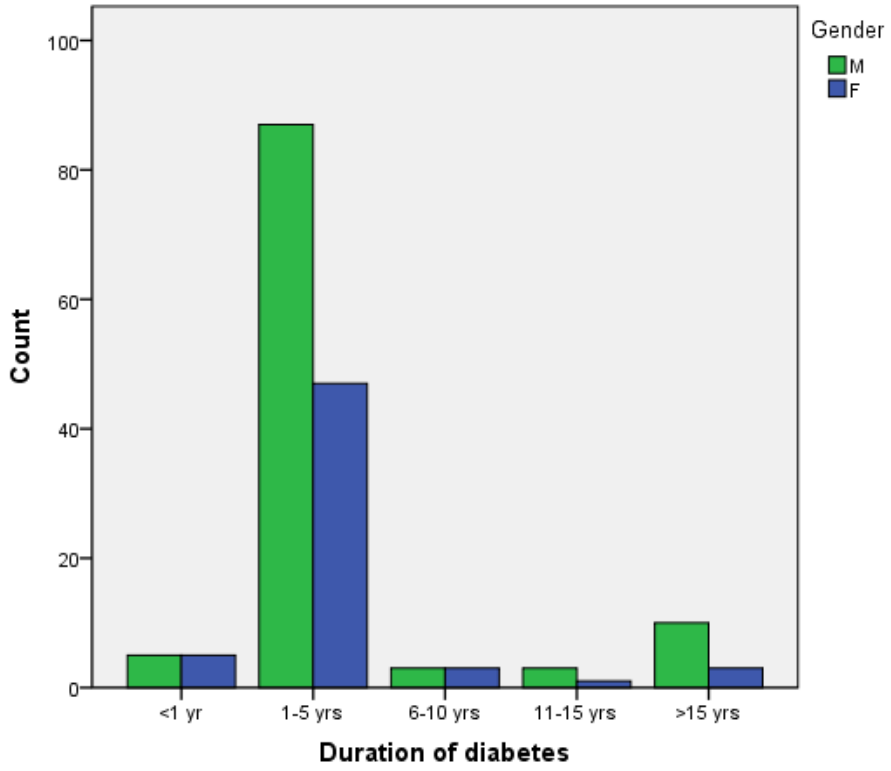


Figure 4 : Bar Chart showing distribution of subjects according to duration of diabetes and BP control

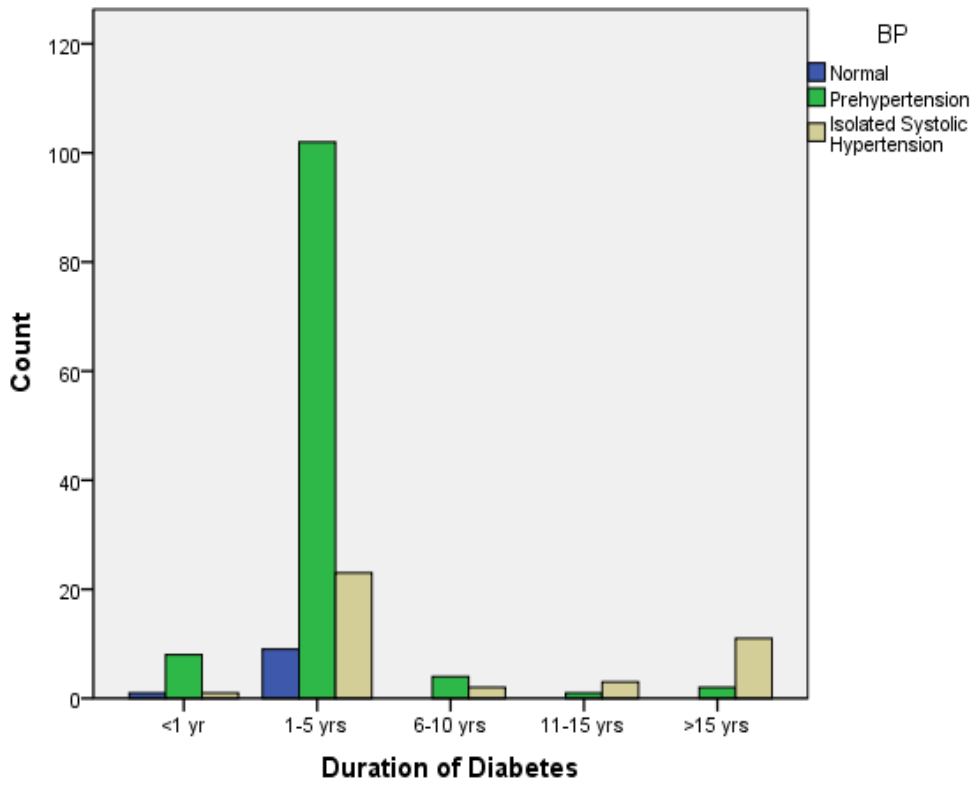


Table 8 : Distribution of Subjects according to BMI and their Age

Body Mass Index	Age of Subjects				Total
	<50 yrs of age	51-60 yrs of age	61-70 yrs of age	>70 yrs of age	
Underweight (<18.5 kg/m2)	2	1	0	0	3
Optimal Weight (18.5-24.9 kg/m2)	20	36	23	11	90
Overweight (25-29.9 kg/m2)	25	24	19	1	69
Obese Class 1 (30-34.9 kg/m2)	2	3	0	0	5
Total	49	64	42	12	167

The distribution of subjects according to body mass index and age of subjects is shown in **Table 8**. It can be seen majority of the subjects were in the optimal weight category (53.9%). The next biggest group of subjects belonged to the overweight category (41.3%). We had only 5 class 1 obese subjects in our study. Overweight individuals were present in all age groups.

Figure 5 shows the distribution of the study subjects, based on their BMI and their blood pressure levels. It can be seen that majority of the study subjects (70%) were in the prehypertensive group irrespective of their BMI levels. Only a meager percent (6%) of the subjects had a normal blood pressure reading. All subjects belonging to the obese class 1 category were found to be prehypertensives.

Table 9 shows the distribution of subjects according to the duration of diabetes and their glycated hemoglobin levels. It can be seen that irrespective of the duration of diabetes, most of the subjects had a high HbA1c level (n=74). This was followed by subjects who had a fair control of their diabetes as indicated by their HbA1c levels ranging from 7.1-8% (n=52)

Figure 5 : Bar graph showing the distribution of subjects according to BMI & BP

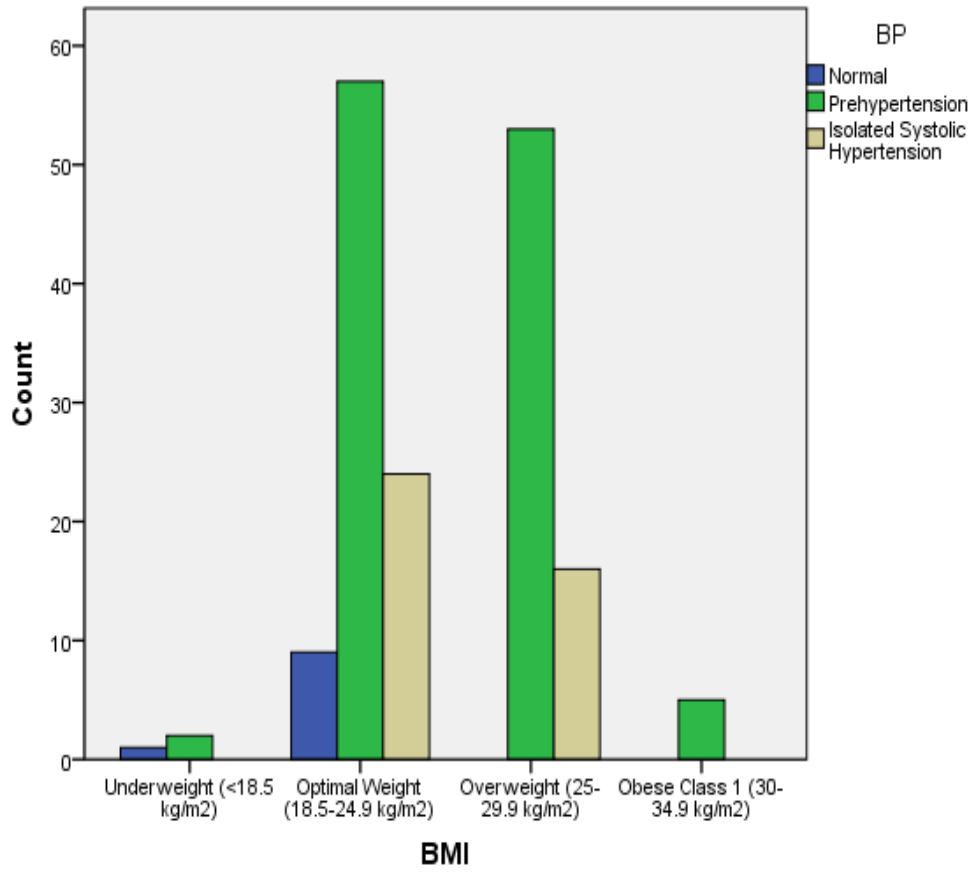


Table 9 : Distribution of subjects in accordance with duration of diabetes and levels of HbA1c

Duration of diabetes	HbA1c				Total
	Normal (4-6%)	Good Control (6.1-7%)	Fair Control (7.1-8%)	Poor Control (>8%)	
<1 yr	1	2	2	5	10
1-5 yrs	10	25	42	57	134
6-10 yrs	1	0	1	4	6
11-15 yrs	0	0	2	2	4
>15 yrs	0	2	5	6	13
Total	12	29	52	74	167

Correlation between HbA1c and FBS, PPBS, Total Cholesterol, LDL, HDL, Total Triglycerides

The following scatter diagrams (**figure 6** to **figure 11**) depict the correlation between HbA1c and the various main parameters of the study which included FBS, PPBS, Total Cholesterol, LDL, HDL & Total Triglycerides.

Pearson correlation coefficient (r) was calculated to find out the correlation between the various variables and the scatter diagram was plotted.

The correlation between HbA1c and FBS (**Figure 6**) as well as between HbA1c and PPBS (**Figure 7**) was found to be positive. (r = 0.579 and r = 0.602 respectively). Similarly, a positive correlation was found between HbA1c and Total Cholesterol (r = 0.524), HbA1c and Low Density Lipoproteins (r = 0.430) and between HbA1c and Total Triglycerides (r = 0.620) (**Figures 8, 9 & 11** respectively). A negative correlation was found between HbA1c and High Density Lipoprotein (r = -0.866) (**Figure 10**).

Figure 6 Scatter diagram showing correlation between HbA1C and FBS levels

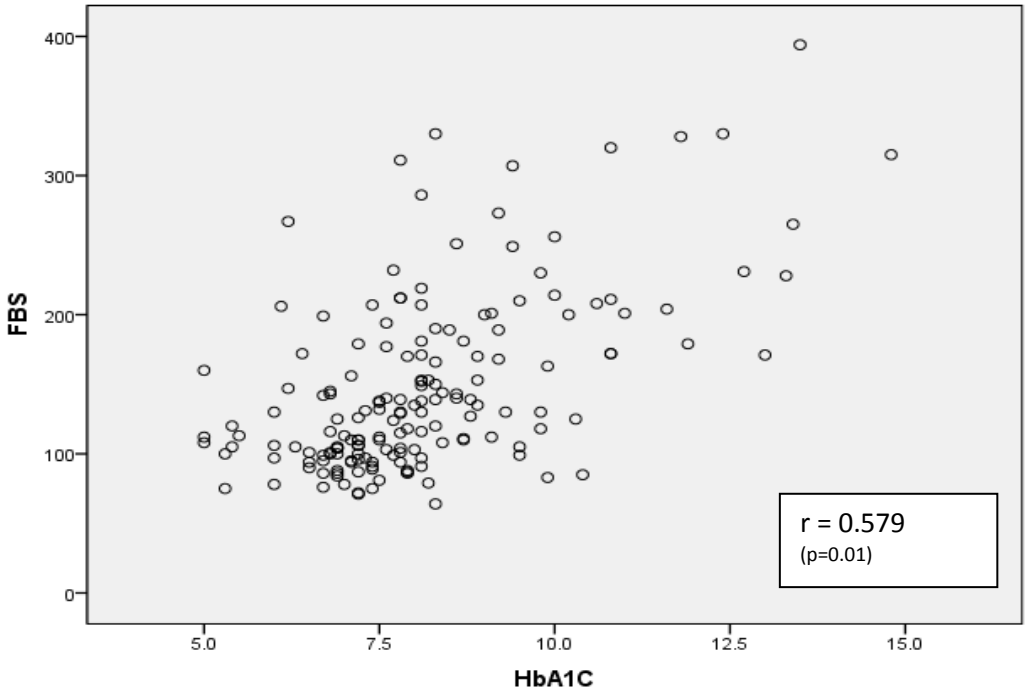


Figure 7 Scatter diagram showing correlation between HbA1C and PPBS levels

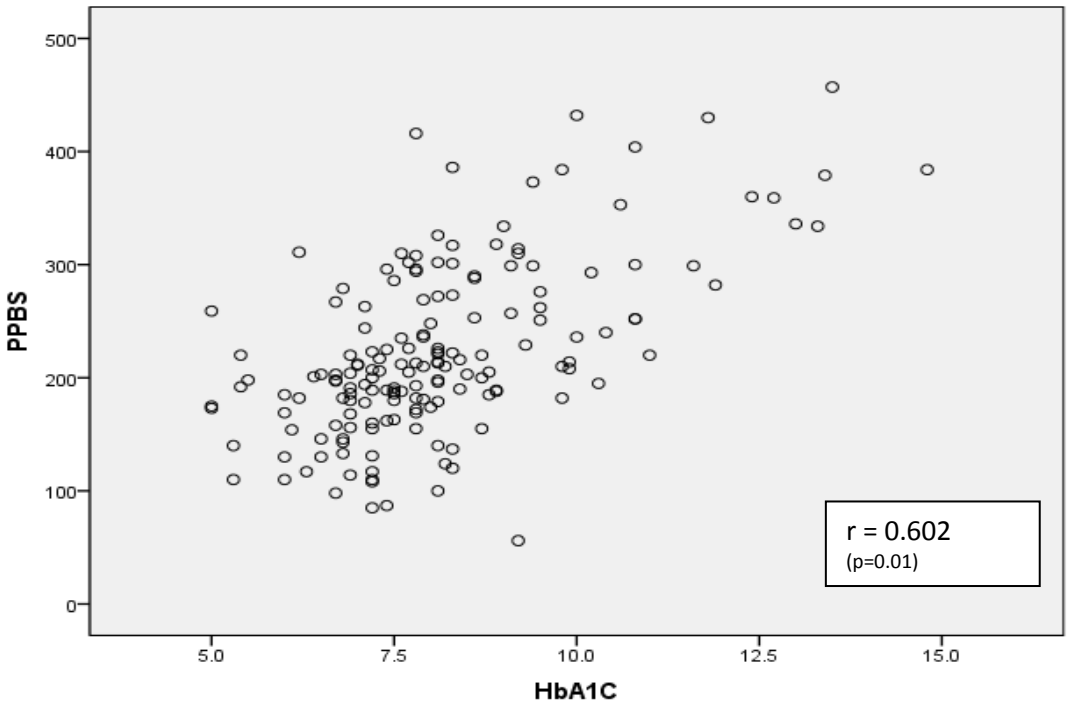


Figure 8

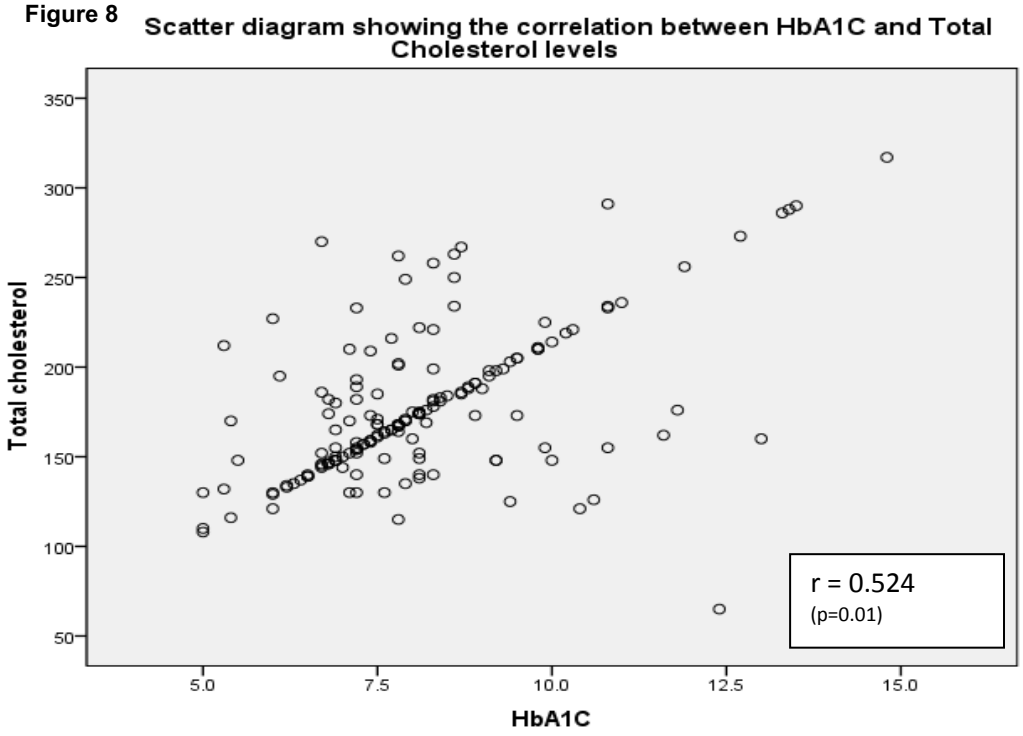


Figure 9

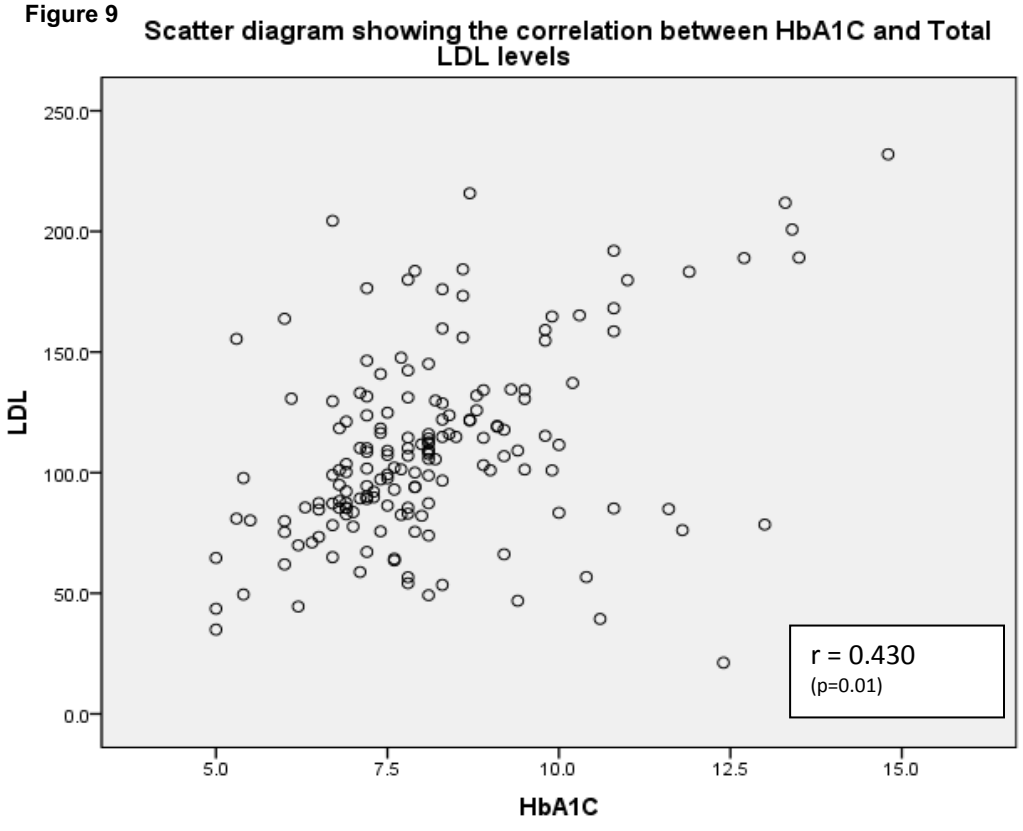


Figure 10 Scatter diagram showing the correlation between HbA1C and HDL levels

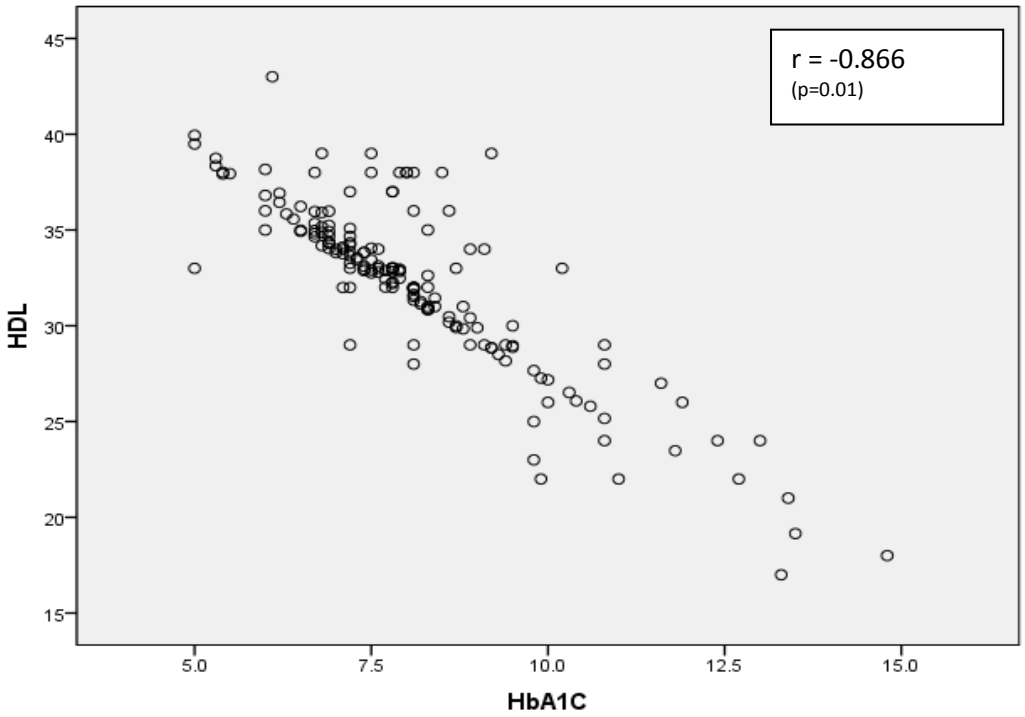
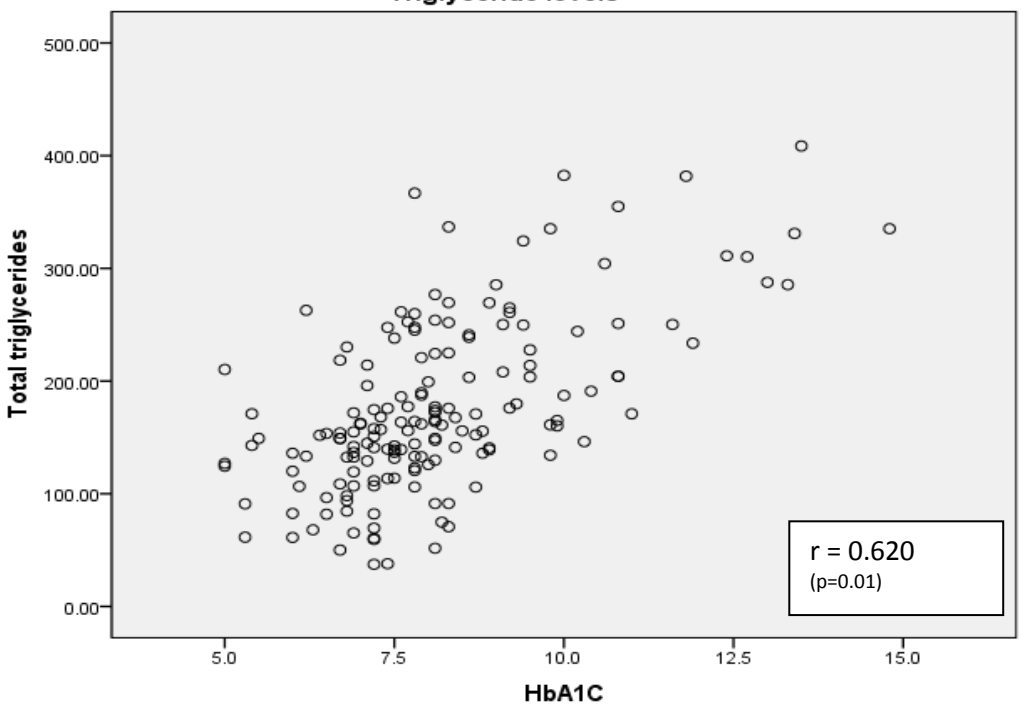


Figure 11 Scatter diagram showing the correlation between HbA1C and Total Triglyceride levels



DISCUSSION

The present study consisted of 167 subjects who were diagnosed earlier with type-2 diabetes mellitus & were already on treatment for their diabetes. But they were not diagnosed earlier with dyslipidemia & thus were not on any lipid lowering agents. The subjects who were taken into the study were attending either the OPD, diabetic clinic or admitted into our hospital & had fulfilled the inclusion & the exclusion criteria.

There were a total of 108 males and 59 female subjects included in our study. The mean age ± standard deviation of the subjects included in the study was 57.03 ± 9.586 years. The age of the subjects ranged between 36 and 86 years. A complete history was taken from all the subjects & physical examination was also done. The blood samples collected from the subjects were sent for testing FBS, PPBS, HbA1c & lipid profile (Total Cholesterol, Total TGL, LDL & HDL) & co-relation between HbA1c, FBS, and Lipid Profile was calculated & results were analyzed.

The significant correlation between HbA1c and FBS & PPBS (**Figure 5** & **6**) is in agreement with earlier reports[63-65]. Diabetes confers a markedly increased risk of CHD events in both women and men [66]. It is important to note that diabetic patients continue to be at an increased risk of CHD if their HDL levels remain suboptimal despite successful reductions of LDL with statin therapy[67]. However, susceptibility to

CVD among type 2 diabetic patients differs markedly according to ethnicity and gender [68] though converse findings also exist [69].

Significant correlations were observed between HbA1cand cholesterol, TG, HDL and LDL in diabetic patients (**Figures 7** to **10**) which is also in agreement with the findings of several other investigators who had reported significant correlations between HbA1cand lipid profiles and thereby suggested the importance of good management of diabetes in controlling dyslipidemia[61,64, 70-72].

Patients of diabetes mellitus, other than withstanding the complications of chronic hyperglycemia, tend to be soft targets of cardiovascular disease (CVD). A major cause of reduction in life expectancy of such patients is associated with cardiovascular complications [85, 86]. Quantitatively, subjects with diabetes have more than two-fold increased risk for cardiovascular death compared with persons without diabetes [8, 9].

From the findings of a cohort of acute coronary syndrome patients (without prior glycemic check up) done by Ramachandran A et al [10], it is clear about the synchronous occurrence of diabetes and cardiovascular events. That study showed that few patients (16.4%) had normal glucose tolerance and the remaining were either diabetic or had impaired glucose tolerance. Furthermore, the role of hyperglycemia in CVD is supported by a direct correlation between fasting blood glucose (FBG) and cardiovascular events[11, 12]. Even isolated postprandial hyperglycemia has been suggested to be a cardiovascular risk factor [13]. It has been noticed that glucose fluctuations (glucose swing) during postprandial periods exhibit a more specific triggering effect on oxidative stress than chronic hyperglycemia [14].

The impact of poor glycemic control is so grave that increased maternal HbA1c could impair fetal long axis cardiac function[87], whereas improving glycemic control can substantially reduce the risk of cardiovascular events in diabetics [88, 89]. It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10%[90]. A study has even suggested that improving glycemic control in patients with type 2 diabetes may be more important than treating dyslipidemia for the prevention of both microvascular and macrovascularcomplications.[57]

Although both FBG and HbA1c have been related to CHD in a similar fashion, the former association has been found to be much weaker.[15] The diabetic patients with poor glycemic control exhibited a significant increase in total cholesterol, LDL and TGL levels as well as a decrease in HDL levels. Selvin et al[15] have demonstrated a linear relationship between CHD andHbA1c in diabetic patients, suggesting that the risk of CHD begins to increase at HbA1c levels even below 7.0%. Grant et al[73] have reported significantly higher CVD risk factors among individuals with HbA1c > 6.0%.

Interestingly, it has been shown that even attempts to reduce cardiovascular risks resulted in the improvement of HbA1c, even if no specific intervention was targeted at improving the glycemic control [91].

It has been reported that HDL cholesterol is inversely associated and that non-HDL cholesterol is directly associated with CHD risk in diabetes patients [74]. Another study on female type 2 diabetic patients has revealed that association between non-HDL cholesterol and CHD risk is apparent in patients with elevated TGL[75]. Moreover,

significantly high serum TGL levels have been found in diabetic patients with CHD as compared to non-diabetic patients [76]. Onat et al[77] have suggested that fasting TGL levels are predictive for future CVD independent of age, diabetes, total cholesterol and HDL.

The above discussion clearly indicates the clinical significance of various lipid parameters including total cholesterol, TGL, HDL and LDL in predisposing diabetic patients to cardiovascular complications. The significant correlation of HbA1c with all these lipid parameters **(Figures 8** to **11**) points towards the usefulness of HbA1c for screening high-risk diabetic patients.

LIMITATIONS OF THE USE OF HbA1c AS A MARKER

The limitations of the use of HbA1c as a marker for additional information on circulating lipids is that it cannot be used in the following conditions:

1. Patients in acute hyperglycemic states
2. Patients in uremic states
3. Patients taking aspirin, antibiotics from penicillin group
4. Patient who regularly consumes alcohol
5. Patient has hemoglobin abnormalities like sickle cell anemia or having any other cause of hemolytic anemia.
6. Patient has recent history of blood loss or of recent blood transfusion
7. Patient is in a state of active erythropoiesis like in pregnancy.
8. Patient already diagnosed with dyslipidemia & undergoing treatment for the same.

CONCLUSION

In conclusion, the findings of this study clearly show that HbA1c, in addition to its role as a reliable biomarker of glycemic control, can also be a good predictor of serum lipid profile in diabetic patients. In this study, HbA1c has showed direct and significant correlations with serum cholesterol, serum triglycerides and LDL levels. HbA1c has also showed an inverse correlation with serum HDL levels. The findings of this study illustrate the valuable additional information that can be provided by HbA1c about the levels of circulating lipids, besides its primary role in monitoring long-term glycemic control. The diabetic patients with HbA1c levels of > 8% tend to have moderate and severe dyslipidemia and therefore should be examined thoroughly for their lipid profile and associated complications. Further studies in other regions are to be conducted to emphasis the role that HbA1c can play as a biomarker for screening of high-risk diabetic patients.

SUMMARY

Glycated hemoglobin (HbA1c) is a routinely used marker for long-term glycemic control. This study was attempted to evaluate the diagnostic value of HbA1c in predicting diabetic dyslipidemia in type 2 diabetes patients**.**

This study was carried out in B.L.D.E.U's Shri B.M. Patil Medical College Hospital and Research Centre, Bijapur during the period from January 2011 to June 2012. A total of 167 patients with type 2 Diabetes Mellitus who satisfied the inclusion & exclusion criteria were included in the study.

The sera of the selected subjects were analyzed for HbA1c, fasting blood sugar (FBS), post prandial blood sugar (PPBS), total cholesterol, triglycerides, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels.

The collected data was analyzed and it was found that a significant and direct correlation existed between HbA1c and serum levels of total cholesterol, LDL and total triglyceride levels respectively. At the same time, this study also revealed a significant inverse relationship between HbA1c and HDL levels.

The findings of this study illustrate the valuable additional information that can be provided by HbA1c about the levels of circulating lipids, besides its primary role in monitoring long-term glycemic control. This study also emphasizes that persons with high levels of HbA1c levels should be evaluated for diabetic dyslipidemia and managed accordingly.

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ANNEXURE I

CONSENT FORM

TITLE OF RESEARCH: **"Clinical significance of HbA1cas a marker of circulating lipids in type 2 diabetic patients."**

GUIDE : **DR. SHASIDHAR S DEVARMANI**

P.G. STUDENT : **DR. MOHAMED AYAZ ABDUL ASSIZ**

PURPOSE OF RESEARCH:

I have been informed that the purpose of this research is to study the relationship between glycemic control and serum lipid profile and evaluate the relevance of HbA1c as an indicator of circulating lipids in male & female type 2 diabetic patients.

PROCEDURE:

I understand that a detailed medical history of mine will be taken & that I shall have to undergo a complete physical examination and be subjected to investigations.

RISKS AND DISCOMFORTS:

I understand that there is no risk involved and I may experience mild pain during the above-mentioned procedures.

BENEFITS:

I understand that my participation in this study will help in determining the relationship between glycemic control and serum lipid profile and evaluate the relevance of HbA1c as an indicator of circulating lipids in male & female type 2 diabetic patients.

CONFIDENTIALITY:

I understand that the medical information produced by the study will become a part of hospital record and will be subjected to confidentiality and privacy regulations of hospital. If the data is used for publications, the identity of the patient will not be revealed.

REQUEST FOR MORE INFORMATION:

I understand that I may be asked for more information if required, for inclusion into study at any time.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or withdraw from the study at any time.

INJURY STATEMENT:

I understand that, in the unlikely event of injury to me anytime during the study, I shall get medical treatment for the same but no further compensations.

CONSENT STATEMENT

I, _____ unreservedly and in my full sense give my complete consent to take part in this study. The risk and benefits as mentioned above have been read by me/explained to me in my vernacular language.

Signature of Patient

ANNEXURE II

BLDEU'S SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, BIJAPUR

"Clinical significance of HbA1c as a marker of circulating lipids in type 2 diabetic patients"

PROFORMA

Serial No. :

Name: IP. No:

Age: Address:

Sex: Date of Admission:

Occupation: Date of Discharge:

Religion: Status at Discharge:

Unit:

Diabetic History

Age of onset:

Total Duration (years):

Mode of Treatment

1. Oral hypoglycemic agents:
   (Sulphonylurea/biguanide)
2. Insulin (Type):
3. Diabetic Diet:

Symptoms Related to Complications

A) Symptoms of Neuropathy

- Postural dizziness:
- Weakness:
- Numbness/parasthesia:
- Pain/hyperaesthesia:
- Bladder incontinence:
- Impotency:

B) Symptoms of Nephropathy

- Oliguria:
- Edema:

C) Symptoms of Retinopathy

- Dimness of vision:
- Blindness:

Chief Complaints & Presenting History (if any)

Past History

- IHD:
- HTN:
- Hyperlipidemia:
- Recent Blood loss:
- Hemolytic anemia:
- Hemoglobinopathies
- Recent Blood Donation

Family History

- DM:
- IHD:
- HTN:
- Hyperlipidemia

Social History

- Diet:
- Change in diet in the past 6 weeks:
- Appetite:
- Smoker:
- Alcoholic:
- Tobacco chewer:
- Sleep pattern:
- Bowel & Bladder Habits:

Treatment History (other than for diabetes)

Physical Examination

General Examination

Height	:	*cm*	Weight	:	*kg*
BP	:	*mmHg*	Pulse Rate	:	*/min*
RR	:	*/min*			

Pallor	:	Icterus	:	Cyanosis	:
Clubbing	:	Lymph Nodes	:	Edema	:

Systemic Examination

1. Cardiovascular System:

2. Respiratory System:

3. Gastrointestinal System:

4. Central Nervous System:

5. Fundoscopic Examination:

PROVISIONAL DIAGNOSIS :

Investigations

FBS	*mg/dl*	HbA1c	%
PPBS	*mg/dl*		

LIPID PROFILE			
T. Chol	*mg/dl*	T. Tgl	*mg/dl*
LDL	*mg/dl*	HDL	*mg/dl*

COMPLETE BLOOD COUNT			
Total WBC counts	*cells/mm^3*		
Differential Count		Hb	*mg/dl*
Neutrophils	*%*	ESR	*mm/1st hr*
Lymphocytes	*%*	Platelets	*lakhs/mm^3*
Eosinophils	*%*		
Basophils	*%*		
Monocytes	*%*		

UREA

CREATININE

URINE ROUTINE	
Sugars	
Protein	
MICROSCOPY	
Epithelial Cells	***/hpf***
Pus Cells	***/hpf***
RBCs	***/hpf***

DIAGNOSIS:

Signature of the guide

Sl. No	OP/IP	Name	Age	Sex	DM d	HTN	SBP	DBP	PP	MAP	Ht	Wt	BMI	FUN	FBS	PPBS	HbA1	T.Ch	LDL	TGL	HDL	T.Ch/HDL	LDL/HDL	B.Ur	S.Crt	ESR
1	302626	MAJ	73	M	15	N	120	72	48	88	172	70	23.66	1	120	137	8.3	205	134.3	204	30	6.83	4.48	31	1.4	8
2	302620	BSP	58	M	2	N	130	80	50	97	158	68	27.24	0	99	251	9.5	174	116	130	32	1.34	3.63	25	0.9	15
3	302619	SAB	60	F	10M	N	132	80	52	97	145	52	24.73	0	138	179	8.1	182	128.7	91	35	1.99	3.68	20	0.8	15
4	28080	MAH	65	F	1	N	156	98	58	117	146	60	28.15	NV2	286	302	8.1	158	94.5	158	32	1.00	2.95	119	4.5	75
5	314306	NEE	60	F	8	N	138	88	50	105	140	58	29.59	1	126	207	7.2	138	49.2	254	38	0.54	1.29	25	0.8	15
6	313861	KAM	45	F	2	N	120	74	46	89	145	52	24.73	0	130	226	8.1	174	109.6	177	29	0.98	3.78	42	1.7	12
7	313862	BHI	54	M	5	N	132	80	52	97	173	60	20.05	0	104	182	7.8	202	142.4	133	33	1.52	4.32	35	1.2	11
8	308188	SAR	65	F	5	Y	142	84	58	103	135	52	28.53	5	149	213	8.1	175	114.2	164	28	1.07	4.08	30	1.1	12
9	296655	SAA	42	M	2	N	136	88	48	104	173	78	26.06	0	170	318	8.9	191	103.1	269	34	0.71	3.03	24	0.8	10
10	308188	SAA	65	F	7	Y	142	84	58	103	167	52	18.65	5	207	272	8.1	222	145.1	224	32	0.99	4.53	27	1.3	15
11	28667	MAL	69	M	11	Y	140	90	50	107	150	66	29.33	5	153	188	8.9	191	134.2	139	29	1.37	4.63	90	2.6	80
12	314011	GUR	50	M	6	N	128	76	52	93	163	67	25.22	0	130	213	7.8	201	131.2	164	37	1.22	3.55	31	1.1	12
13	308	PAR	47	M	6	N	132	80	52	97	154	60	25.30	0	315	384	14.8	317	232	335	18	0.95	12.89	27	0.8	20
14	370	BHH	51	F	8M	N	122	72	50	89	140	41	20.92	0	140	253	8.6	250	173.3	203	36	1.23	4.81	26	0.9	8
15	11877	SUP	45	M	4	N	126	74	52	91	157	62	25.15	0	150	222	8.3	181	114.8	176	31	1.03	3.70	21	0.7	10
16	10002	SHA	67	M	7	N	138	72	66	94	164	73	27.14	0	75	140	5.3	212	155.4	91	38	2.33	4.09	48	1.9	10
17	42305	JAS	46	F	11	N	132	80	52	97	148	61	27.85	0	204	299	11.6	162	85	250	27	0.65	3.15	28	0.9	10
18	42304	MAC	66	F	11	N	148	78	70	101	146	52	24.39	0	179	282	11.9	256	183.3	234	26	1.10	7.05	24	0.7	85
19	1379	BEE	40	M	1	N	120	74	46	89	158	54	21.63	0	135	248	8	160	82.1	199	38	0.80	2.16	19	1	10
20	16244	PSP	62	M	4	Y	186	94	92	125	164	71	26.40	0	127	205	8.8	188	125.9	156	31	1.21	4.06	20	0.7	8
21	30406	MAI	61	M	5	N	126	86	40	99	170	64	22.15	0	171	336	13	288	200.8	331	21	0.87	9.56	16	0.6	15
22	30407	BHA	50	F	10	N	118	76	42	90	148	60	27.39	0	265	379	13.4	160	78.5	288	24	0.56	3.27	28	0.8	10
23	10000	SPK	60	M	2	N	134	80	54	98	157	82	33.27	0	91	100	8.1	214	111.5	382	26	0.56	4.29	46	1.2	15
24	2907	YAM	60	F	3	Y	138	78	60	98	143	51	24.94	0	206	154	6.1	155	85.2	204	29	0.76	2.94	27	0.9	60
25	2703	MAH	57	F	15	Y	148	90	58	109	152	62	26.84	1	172	252	10.8	152	105.7	52	36	2.94	2.94	29	0.7	70
26	2322	KAM	50	F	10	N	122	70	52	87	145	51	24.26	0	256	432	10	195	130.7	107	43	1.83	3.04	18	0.9	10
27	2623	SUD	55	F	15	Y	142	90	52	107	152	60	25.97	0	172	252	10.8	233	168.2	204	24	1.14	7.01	24	0.8	70
28	3921	PAD	65	F	8	N	128	78	50	95	142	52	25.79	0	112	259	5	110	34.9	210	33	0.52	1.06	39	1.4	140
29	3987	GUN	48	M	8	N	126	70	56	89	168	46	16.30	2	330	360	12.4	65	21.2	311	24	0.21	0.88	26	1	40
30	10082	SAP	68	F	5	N	130	84	46	99	151	67	29.38	0	130	185	6	183	123.8	141	31	1.30	3.99	15	0.9	50

Sl. No	OP/IP	Name	Age	Sex	DM dura	HTN	SBP	DBP	PP	MAP	Ht	Wt	BMI	FUNDU	FBS	PPBS	HbA1C	T.Ch	LDL	TGL	HDL	T.Ch/HDL	LDL/HDL	B.Urea	S.Crt	ESR
31	10228	SHP	55	F	8	N	122	70	52	87	162	84	32.01	0	144	190	8.4	227	163.8	136	36	1.67	4.55	18	1	8
32	69502	SHA	45	F	1	N	144	80	64	101	149	58	26.12	0	181	200	8.7	211	159.2	134	25	1.57	6.37	26	0.8	13
33	69494	GUK	38	M	6M	N	134	88	46	103	172	79	26.70	0	118	182	9.8	185	121.5	152	33	1.22	3.68	21	1.2	12
34	4441	VIV	46	M	3	N	128	70	58	89	168	72	25.51	0	273	310	9.2	198	106.8	261	39	0.76	2.74	26	0.7	12
35	4433	YAN	55	M	2	N	132	82	50	99	156	54	22.19	0	116	198	8.1	174	112.2	149	32	1.17	3.51	20	0.9	12
36	69516	UMK	58	F	4	N	124	72	52	89	166	58	21.05	0	103	174	8	262	180	245	33	1.07	5.45	26	0.8	13
37	69483	HAJ	58	F	1	N	122	74	48	90	158	55	22.03	1	307	373	9.4	175	111.8	126	38	1.39	2.94	18	0.6	10
38	4447	YAN	56	F	6	N	128	78	50	95	148	52	23.74	0	212	294	7.8	203	109.1	324	29	0.63	3.76	25	1	10
39	6034	KEG	43	M	3	N	122	70	52	87	160	56	21.88	0	112	299	9.1	198	119	250	29	0.79	4.10	52	1.4	50
40	6081	DAR	45	M	2	Y	134	80	54	98	165	71	26.08	0	181	214	8.1	174	108.9	166	32	1.05	3.40	21	1.1	20
41	7002	SAP	55	M	4	Y	136	72	64	93	168	66	23.38	0	201	220	11	236	179.8	171	22	1.38	8.17	24	0.9	13
42	80477	GHM	59	M	13	N	128	70	58	89	172	69	23.32	0	110	163	7.5	161	99.2	114	39	1.41	2.54	29	1.2	10
43	264156	PBA	53	M	5	N	128	76	52	93	156	61	25.07	0	140	212	7.6	130	64.3	163	33	0.80	1.95	23	0.8	8
44	80999	LAL	36	M	1	N	124	70	54	88	175	68	22.20	0	83	208	9.9	155	101	160	22	0.97	4.59	28	0.7	11
45	7832	MBP	70	M	8	Y	150	90	60	110	165	56	20.57	3+6	129	193	7.8	115	54.2	144	32	0.80	1.69	26	1	10
46	92620	ADN	45	F	3	N	144	96	48	112	158	62	24.84	0	103	188	7.6	286	211.9	286	17	1.00	12.46	26	0.7	15
47	7865	PRM	43	M	1	N	130	80	50	97	170	78	26.99	0	228	334	13.3	164	102.2	139	34	1.18	3.01	27	0.8	35
48	8034	HAM	70	F	2	Y	130	84	46	99	153	67	28.62	0	78	169	6	145	99	50	36	2.90	2.75	29	0.9	50
49	93785	BAH	56	M	6	N	122	74	48	90	176	74	23.89	0	99	197	6.7	273	189	310	22	0.88	8.59	21	0.8	12
50	93786	SUS	50	F	1	N	116	70	46	85	143	46	22.49	0	86	98	6.7	146	78.2	149	38	0.98	2.06	26	0.8	10
51	93793	RMR	52	M	5	Y	138	84	54	102	158	51	20.43	1	231	359	12.7	121	62	120	35	1.01	1.77	28	0.7	12
52	8034	HAM	70	F	4	Y	124	80	44	95	153	64	27.34	NVR+0	78	169	6	234	156.1	239	30	0.98	5.20	29	0.9	50
53	95521	DYA	55	M	2	N	88	50	38	63	170	68	23.53	0	87	108	7.2	155	110.1	59	33	2.61	3.34	16	0.8	65
54	99693	SAA	65	F	8	Y	152	94	58	113	157	66	26.78	2	110	155	8.7	267	215.8	106	30	2.52	7.19	20	0.9	25
55	8557	SAG	65	F	4	Y	140	90	50	107	146	57	26.74	0	110	155	7.2	182	131.6	107	29	1.70	4.54	25	0.9	25
56	102130	BAN	57	M	3	N	128	66	62	87	159	52	20.57	0	200	293	10.2	219	137.2	244	33	0.90	4.16	28	0.8	10
57	105475	MSB	56	M	6	N	132	70	62	91	170	69	23.88	0	130	210	9.8	210	154.8	161	23	1.30	6.73	34	1.4	14
58	105822	SHM	55	M	2	N	128	74	54	92	156	54	22.19	0	112	180	7.5	162	97.7	131	38	1.23	2.57	25	0.9	16
59	111397	MUS	45	M	3	N	122	78	44	93	173	67	22.39	0	95	178	7.1	170	110.2	129	34	1.32	3.24	23	0.9	20
60	106308	VIJ	39	F	6M	N	116	68	48	84	151	49	21.49	0	108	216	8.4	181	116	168	31	1.08	3.74	20	0.7	12

Sl. No	OP/IP	Name	Age	Sex	DM dura	HTN	SBP	DBP	PP	MAP	Ht	Wt	BMI	FUNDU	FBS	PPBS	HbA1C	T.Ch	LDL	TGL	HDL	T.Ch/HDL	LDL/HDL	B.Urea	S.Crt	ESR
61	112507	BRP	80	M	20	Y	150	92	58	111	146	42	19.70	1	110	117	7.2	140	89.1	70	37	2.01	2.41	28	1.2	22
62	115775	YAS	60	M	1	N	140	90	50	107	178	76	23.99	1	200	334	9	188	101	285	30	0.66	3.37	20	0.9	5
63	115670	SSD	74	M	26	Y	142	88	54	106	162	58	22.10	2	201	257	9.1	137	71	152	36	0.90	1.97	25	1	26
64	115703	KAP	71	F	11	N	138	76	62	97	146	48	22.52	1	106	130	6	130	75.3	83	38	1.57	1.98	28	0.9	14
65	139895	VIJ	52	M	5	Y	146	84	62	105	153	52	22.21	0	172	201	6.4	195	119.4	208	34	0.94	3.51	23	0.9	10
66	78229	PBJ	52	M	2	N	124	82	42	96	156	64	26.30	0	160	175	5	116	49.5	143	38	0.81	1.30	19	0.9	12
67	116040	PCS	59	M	5	N	132	78	54	96	155	56	23.31	1	87	238	7.9	130	64.7	127	40	1.02	1.62	22	0.8	12
68	118822	VPA	48	M	3	N	124	70	54	88	172	68	22.99	0	120	192	5.4	170	94.1	190	38	0.90	2.48	27	0.7	14
69	118795	MAB	62	M	3	N	128	72	56	91	145	47	22.35	0	251	290	8.6	263	184.3	241	30	1.09	6.14	19	0.9	10
70	10218	CHN	60	M	8	N	120	90	30	100	165	72	26.45	NV2	189	203	8.5	184	114.8	156	38	1.18	3.02	28	1.1	10
71	10360	KRM	60	M	12	Y	160	94	66	116	170	66	22.84	2+5	208	353	10.6	126	39.4	304	26	0.41	1.52	36	1.2	18
72	121075	NAD	62	M	5	N	138	82	56	101	156	71	29.17	0	100	146	6.8	174	118.4	98	36	1.77	3.29	22	0.7	10
73	10702	RAT	42	M	2	N	120	82	38	95	168	63	22.32	0	125	195	10.3	221	165.2	146	27	1.51	6.12	20	0.8	25
74	127801	KAC	48	F	1	N	124	78	46	93	156	58	23.83	0	85	240	10.4	121	56.7	191	26	0.63	2.18	22	0.8	12
75	128245	DAL	55	M	2	N	128	70	58	89	165	64	23.51	0	116	133	6.8	147	94.9	84	35	1.74	2.71	23	0.9	10
76	128250	SAR	65	F	7	Y	136	80	56	99	148	46	21.00	0	156	244	7.1	130	58.8	196	32	0.66	1.84	20	0.8	9
77	128274	PAA	48	M	2	N	126	74	52	91	170	67	23.18	0	139	185	8.8	189	132	136	30	1.39	4.40	25	0.7	9
78	129692	UME	43	M	1	N	138	86	52	103	153	72	30.76	0	211	300	10.8	234	158.6	251	25	0.93	6.34	28	1	12
79	132204	BRA	56	M	6	N	130	74	56	93	158	57	22.83	1	100	110	5.3	132	81	61	39	2.15	2.08	27	1.1	10
80	132354	GUL	47	M	2	N	128	66	62	87	165	73	26.81	0	311	416	7.8	167	56.7	367	37	0.46	1.53	21	0.9	12
81	132416	SUT	52	F	3	N	126	70	56	89	145	48	22.83	0	190	317	8.3	140	53.5	270	33	0.52	1.62	20	0.8	13
82	133491	SAD	48	M	4	N	132	74	58	93	168	74	26.22	0	138	286	7.5	168	86.3	238	34	0.71	2.54	24	1.1	12
83	136567	SIB	45	M	1	N	124	78	46	93	163	68	25.59	0	320	404	10.8	291	192	355	28	0.82	6.86	23	0.7	10
84	136568	YAL	62	F	4	N	120	72	48	88	172	69	23.32	0	106	189	7.2	130	67.2	141	35	0.92	1.92	28	0.8	12
85	140825	FBP	48	M	1	N	124	70	54	88	152	56	24.24	0	106	131	7.2	152	101.7	82	34	1.85	2.99	33	1.3	10
86	140907	KAA	59	F	5	N	132	78	54	96	158	49	19.63	0	199	267	6.7	144	65	218	35	0.66	1.86	27	1.1	14
87	142733	SAB	55	M	2	N	124	70	54	88	156	75	30.82	0	101	143	6.8	170	97.8	171	38	0.99	2.57	25	0.7	13
88	140857	SVK	46	M	6M	N	138	72	66	94	162	69	26.29	0	105	220	5.4	146	88.2	94	39	1.56	2.26	20	1	14
89	138380	JAY	55	M	7	N	122	70	52	87	155	54	22.48	1	194	310	7.6	154	108.6	61	33	2.54	3.29	28	0.8	16
90	129866	SHU	50	F	1	N	108	60	48	76	164	46	17.10	0	100	110	7.2	149	63.6	261	33	0.57	1.93	33	1.3	10

Sl. No	OP/IP	Name	Age	Sex	DM dura	HTN	SBP	DBP	PP	MAP	Ht	Wt	BMI	FUNDU	FBS	PPBS	HbA1C	T.Ch	LDL	TGL	HDL	T.Ch/HDL	LDL/HDL	B.Urea	S.Crt	ESR
91	142795	SGP	55	M	4	N	130	74	56	93	169	68	23.81	0	88	210	7.9	249	183.7	162	33	1.54	5.57	25	0.8	12
92	142784	PMK	63	M	4	Y	142	88	54	106	173	70	23.39	1	207	296	7.4	159	75.7	248	34	0.64	2.23	29	0.9	12
93	143968	SHT	40	F	6M	N	128	70	58	89	156	68	27.94	0	86	114	6.9	148	100.3	65	35	2.27	2.87	20	1	9
94	143811	GOP	42	F	1	N	126	78	48	94	148	64	29.22	0	219	326	8.1	174	87.3	277	31	0.63	2.82	25	0.7	10
95	144890	GOV	71	M	10	N	138	88	50	105	165	61	22.41	1	139	296	7.8	168	85.5	248	33	0.68	2.59	28	1.2	12
96	145981	ANA	68	M	5	N	132	80	52	97	178	81	25.56	0	95	198	6.7	150	83.7	162	34	0.93	2.46	26	1	15
97	146130	ANP	47	M	5	N	122	74	48	90	170	75	25.95	0	113	211	7	152	87.2	149	35	1.02	2.49	38	1.5	10
98	146946	SHN	65	F	2	N	112	70	42	84	156	50	20.55	1	137	188	7.5	216	147.6	177	33	1.22	4.47	26	0.7	14
99	147091	SUS	60	F	3	N	128	72	56	91	152	55	23.81	0	99	226	7.7	168	107.3	139	33	1.21	3.25	24	0.9	12
100	12762	MLI	75	M	8	Y	160	100	60	120	148	47	21.46	1	212	308	7.8	233	176.5	112	34	2.09	5.19	28	1.3	25
101	147603	SNH	68	M	3	Y	136	70	66	92	176	81	26.15	0	96	160	7.2	168	83	260	33	0.65	2.52	24	0.6	32
102	149105	SHT	60	F	1	N	118	64	54	82	166	54	19.60	0	97	140	8.1	149	98.8	91	32	1.63	3.09	22	0.8	10
103	149093	MAN	60	F	10	N	138	84	54	102	157	66	26.78	0	147	182	6.2	133	69.9	133	36	1.00	1.94	29	1	23
104	150093	LAP	47	M	1	N	106	72	34	83	175	72	23.51	0	104	191	6.9	148	85.3	142	34	1.04	2.51	18	0.7	8
105	150094	BMK	86	M	20	Y	148	92	56	111	166	64	23.23	5+NVL	94	194	7.1	152	89.3	145	34	1.05	2.63	23	1	12
106	100702	GAK	68	M	4	N	142	90	52	107	158	59	23.63	0	124	205	7.7	157	92.2	157	33	1.00	2.79	21	0.7	14
107	151186	KAJ	55	M	1	N	136	78	58	97	154	62	26.14	0	111	220	8.7	186	129.6	109	35	1.71	3.70	24	0.8	12
108	151291	SAN	52	M	8M	N	118	72	46	87	177	79	25.22	0	76	158	6.7	186	121.9	171	30	1.09	4.06	28	1	12
109	151184	CPL	67	M	3	N	128	80	48	96	165	60	22.04	0	88	156	6.9	150	87.5	133	36	1.13	2.43	35	2	42
110	151183	SMB	42	M	1	N	132	88	44	103	148	56	25.57	0	97	206	7.3	148	92.3	107	34	1.38	2.71	26	1	16
111	151200	SUD	58	F	6	N	120	74	46	89	144	52	25.08	0	100	180	6.9	165	101.4	156	32	1.06	3.17	30	0.8	10
112	151577	ANN	53	F	2	N	128	70	58	89	161	63	24.30	0	115	155	7.8	148	66.2	265	29	0.56	2.28	24	0.9	9
113	152818	KAK	60	M	5	N	136	76	60	96	166	79	28.67	0	105	262	9.5	168	114.5	106	32	1.58	3.58	28	0.9	12
114	152973	HEM	70	M	18	N	148	80	68	103	171	67	22.91	NV2	131	217	7.3	173	101.3	214	29	0.81	3.49	22	0.7	9
115	13114	KAZ	74	M	10	Y	160	100	60	120	158	52	20.83	2	214	236	10	140	87.4	82	36	1.71	2.43	26	0.9	12
116	152575	SHO	51	F	2	Y	138	80	58	99	151	44	19.30	5+1	189	314	9.2	157	89.8	168	34	0.93	2.64	29	1.1	13
117	146052	BAB	60	M	1	N	112	64	48	80	152	47	20.34	NV2	94	130	6.5	148	83.4	187	27	0.79	3.09	22	1	8
118	153245	BKP	59	M	2	N	136	84	52	101	166	78	28.31	0	94	172	7.8	165	103.6	137	34	1.21	3.05	26	1.3	32
119	153401	GUA	69	M	4	N	158	74	84	102	175	70	22.86	0	110	263	7.1	167	110.2	123	32	1.36	3.44	20	0.9	10
120	152973	SHR	45	M	2	N	128	76	52	93	176	87	28.09	0	84	186	6.9	210	133.1	214	34	0.98	3.91	23	0.8	10

Sl. No	OP/IP	Name	Age	Sex	DM dura	HTN	SBP	DBP	PP	MAP	Ht	Wt	BMI	FUNDU	FBS	PPBS	HbA1C	T.Ch	LDL	TGL	HDL	T.Ch/HDL	LDL/HDL	B.Urea	S.Crt	ESR
121	154330	DBG	56	M	1	Y	146	90	56	109	158	66	26.44	5	143	182	6.8	139	84.7	97	35	1.44	2.42	28	0.9	9
122	152370	SIP	71	M	19	N	158	96	62	117	184	82	24.22	1	89	189	7.4	146	85.3	133	34	1.10	2.51	22	1	12
123	154423	BAC	44	M	2	N	130	72	58	91	156	74	30.41	0	90	146	6.5	158	97.2	140	33	1.13	2.95	27	0.8	14
124	154513	VSB	50	M	9M	N	130	84	46	99	167	77	27.61	0	72	85	7.2	140	74	172	32	0.81	2.31	21	0.8	12
125	155556	LSK	68	M	5	N	124	68	56	87	170	68	23.53	1	64	120	8.3	189	146.4	37	35	5.06	4.18	29	1.1	10
126	155526	MJS	44	M	1	N	106	72	34	83	159	61	24.13	0	153	221	8.1	221	176	71	31	3.12	5.68	13	0.8	17
127	156438	PUK	65	F	2	Y	136	80	56	99	155	49	20.40	0	71	200	7.2	210	115.3	335	28	0.63	4.12	28	0.9	9
128	156503	BSS	60	M	5	N	122	74	48	90	168	73	25.86	0	142	203	6.7	270	204.4	154	35	1.75	5.84	29	0.7	12
129	156800	MTR	69	M	10	N	126	66	60	86	156	69	28.35	1	79	124	8.2	154	90.2	151	34	1.02	2.65	23	1.1	10
130	154828	DAN	50	F	2	N	128	72	56	91	152	49	21.21	1	230	384	9.8	176	129.9	75	31	2.35	4.19	28	1	12
131	157404	BRT	80	M	29	Y	148	90	58	109	166	68	24.68	2	104	220	6.9	155	85.4	172	35	0.90	2.44	33	1.3	12
132	153240	BHG	60	F	3	N	132	70	62	91	154	43	18.13	0	78	212	7	144	77.7	163	34	0.89	2.29	27	0.8	10
133	159748	KAV	64	M	6	N	146	92	54	110	176	71	22.92	1	152	196	8.1	174	112.6	147	32	1.18	3.52	32	1	14
134	159711	LSP	68	M	11	N	126	74	52	91	169	73	25.56	0	177	235	7.6	163	93	186	33	0.88	2.82	20	1	10
135	13920	ISH	76	M	20	Y	230	110	120	150	172	67	22.65	6	94	162	7.4	185	124.9	137	33	1.35	3.78	41	1.3	20
136	162339	LAX	62	F	3	N	132	74	58	93	152	58	25.10	0	81	186	7.5	173	116.5	114	34	1.52	3.43	28	0.9	14
137	163240	VAC	60	F	4	N	108	68	40	81	147	51	23.60	0	105	204	6.9	148	82.7	155	34	0.96	2.43	26	1	14
138	162954	PAS	70	F	9	N	152	92	60	112	162	52	19.81	1	139	301	8.3	178	96.7	252	31	0.71	3.12	46	1.2	52
139	161697	SKH	51	M	2	N	142	70	72	94	175	69	22.53	0	91	225	7.4	209	140.9	176	33	1.19	4.27	29	0.9	10
140	165221	DNB	54	M	4	N	120	74	46	89	169	77	26.96	1	145	279	6.8	182	101.1	230	35	0.79	2.89	28	0.9	12
141	166494	TEJ	50	F	2	N	134	66	68	89	166	72	26.13	0	130	229	9.3	199	134.5	180	29	1.11	4.64	29	1.1	21
142	14481	BIR	65	F	5	N	126	84	42	98	160	58	22.66	0	101	169	7.8	164	107	121	33	1.36	3.24	20	1.8	40
143	168346	VRH	56	M	4	N	142	94	48	110	174	78	25.76	0	86	181	7.9	135	75.5	133	33	1.02	2.29	32	1.2	13
144	170493	SRR	48	M	1	N	128	70	58	89	155	61	25.39	0	153	210	8.2	169	105.6	161	31	1.05	3.41	19	0.8	10
145	173725	MAC	60	F	5	N	120	72	48	88	160	52	20.31	1	125	168	6.9	180	121.2	119	35	1.51	3.46	17	0.6	12
146	15193	TUS	50	M	12	Y	150	90	60	110	157	54	21.91	1	232	302	7.7	165	82.5	253	32	0.65	2.58	25	1	5
147	176847	NDE	65	M	6	N	138	82	56	101	162	65	24.77	0	113	198	5.5	148	80.2	149	38	0.99	2.11	21	1	9
148	186302	ANA	63	M	9	N	124	76	48	92	176	84	27.12	0	179	223	7.2	193	123.8	175	34	1.11	3.64	22	0.8	10
149	189463	KAA	61	F	1	N	130	80	50	97	155	58	24.14	0	108	173	5	108	43.6	124	39	0.87	1.12	25	0.9	10
150	190583	JCP	59	M	3	N	116	70	46	85	182	76	22.94	0	75	87	7.4	159	118.3	38	33	4.20	3.58	29	1	12

Sl. No	OP/IP	Name	Age	Sex	DM dura	HTN	SBP	DBP	PP	MAP	Ht	Wt	BMI	FUNDU	FBS	PPBS	HbA1C	T.Ch	LDL	TGL	HDL	T.Ch/HDL	LDL/HDL	B.Urea	S.Crt	ESR
151	190594	DEE	43	M	1	N	122	76	46	91	159	56	22.15	0	171	223	8.1	174	107.7	174	32	1.00	3.37	22	0.8	8
152	193371	MAB	51	F	7	N	144	84	60	104	148	62	28.31	2	330	386	8.3	258	159.8	337	31	0.77	5.15	30	1.1	13
153	16905	SHY	60	M	1	N	160	80	80	107	167	78	27.97	0	394	457	13.5	290	189.1	409	19	0.71	9.95	24	0.7	5
154	17064	ASS	50	M	8	N	152	90	62	111	178	84	26.51	4	267	311	6.2	134	44.5	263	37	0.51	1.20	21	1.1	60
155	199906	AJK	52	M	4	N	138	84	54	102	171	73	24.96	0	132	191	7.5	171	109.1	142	33	1.20	3.31	25	1.3	10
156	199913	NIP	56	M	6	N	122	78	44	93	147	51	23.60	1	163	214	9.9	225	164.7	165	27	1.36	6.10	20	0.8	14
157	202103	BSP	50	M	1	N	124	76	48	92	164	69	25.65	0	105	117	6.3	135	85.6	68	36	1.99	2.38	22	1.4	12
158	17902	BOU	65	F	15	N	156	80	76	105	162	58	22.10	2	328	430	11.8	176	76.2	382	23	0.46	3.31	19	0.8	15
159	207199	RAR	58	M	3	N	126	74	52	91	168	74	26.22	0	249	299	9.4	125	46.9	250	28	0.50	1.68	22	1.1	10
160	17992	SAH	69	F	12	Y	140	80	60	100	173	67	22.39	1	135	189	8.9	173	114.4	141	30	1.23	3.81	28	1.3	20
161	208348	PUI	56	F	3	N	124	72	52	89	153	51	21.79	0	170	269	7.9	171	94	221	33	0.77	2.85	24	0.9	9
162	23281	PUR	50	F	6	N	130	80	50	97	156	54	22.19	0	118	236	7.9	170	100	187	32	0.91	3.13	25	1.1	45
163	272798	NBD	63	M	8	N	136	72	64	93	161	66	25.46	0	97	110	6	129	80	61	37	2.11	2.16	27	0.9	9
164	272809	DOB	51	M	10	N	132	76	56	95	176	78	25.18	0	210	276	9.5	205	130.6	228	29	0.90	4.50	29	1	11
165	24103	VIK	60	M	11	Y	140	80	60	100	163	70	26.35	3	168	56	9.2	148	117.8	176	29	0.84	4.06	23	1.5	15
166	284833	VAJ	74	M	22	N	162	88	74	113	172	76	25.69	1	101	203	6.5	199	122	225	32	0.88	3.81	28	1.1	12
167	284730	BPK	66	M	17	N	124	70	54	88	158	62	24.84	0	166	273	8.3	139	73.4	154	35	0.91	2.10	34	1.3	14