A STUDY ON PREVALENCE, DRUG THERAPY, MAJOR COMPLICATIONS & EFFECT ON NEONATES OF GESTATIONAL DIABETES IN DHAKA CITY

Submitted By

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ID: 2011-1-70-030

Department of Pharmacy

East West University

A STUDY ON PREVALENCE, DRUG THERAPY, MAJOR COMPLICATIONS & EFFECT ON NEONATES OF GESTATIONAL DIABETES IN DHAKA CITY

A Project Report to be submitted in the Department of Pharmacy for the Partial Fulfillment of the Degree of Bachelor of Pharmacy.

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DECLARATION BY THE RESEARCH CANDIDATE

I, Tasnia Saleheen Sharna, ID: 2011-1-70-030, hereby declare that the dissertation entitled **"A Study on Prevalence, Drug Therapy, Major Complications & Effect on Neonates of Gestational Diabetes in Dhaka City''** submitted to the Department of Pharmacy, East West University, in the partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Honors) is a genuine & authentic research work carried out by me. The contents of this dissertation, in full or in parts, have not been submitted to any other institute or University for the award of any degree or Diploma of Fellowship.

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CERTIFICATION BY THE SUPERVISOR

This is to certify that the dissertation, entitled **"A Study on Prevalence, Drug Therapy, Major Complications & Effect on Neonates of Gestational Diabetes in Dhaka City"** is a bona fide research work done by Tasnia Saleheen Sharna (ID: 2011-1-70-030), in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy under my supervision.

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ENDORSEMENT BY THE CHAIRPERSON

This is to certify that the dissertation, entitled **"A Study on Prevalence, Drug Therapy, Major Complications & Effect on Neonates of Gestational Diabetes in Dhaka City"** is a bona fide research work done by Tasnia Saleheen Sharna (ID: 2011-1-70-030), under the guidance of **Nishat Nasrin**, Senior Lecturer, in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy.

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DEDICATION

This research paper is dedicated to my beloved parents for their unconditional support.

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List of Abbreviations

GDM	Gestational diabetes Mellitus
HAPO	Hyperglycemia and Adverse Pregnancy Outcomes
hCG	human Chorionic Gonadotrophin
NOD	Non-Obese diabetic
TC	Total cholesterol
IL	Interleukin
AA	Arachidonic acid
TNF	Tumor Necrosis Factor
TG	Triglyceride
SOD	Superoxide Dismutase.
ORAC	Oxygen radical absorbance capacity
LA	Linoleic acid
OGTT	Oral Glucose Tolerance Test
Th Cells	T helper cells
TARS	Thiobarbituric Acid-Reactive Substances
IFN	Interferon

Abstract

The increased rate of prevalence and associated risk of Gestational Diabetes Mellitus (GDM) is an important issue to consider in the global world lately. The consequences fall on both the mother and the neonate and it may increase the rate of child mortality and morbidity if the condition is avoided or ineffectively treated. The aim of the present study was to determine the prevalence and examine the treatment therapy and the associated major complications of GDM. This prospective study included 150 pregnant women, more than 24 weeks' gestation, with or without GDM from different hospitals in Dhaka City. They were surveyed with a standard, structured questionnaire. The prevalence of GDM was found in 49 (32.69%) out of 150 patients surveyed. About 6.12% of them had preeclampsia; 4.08% had postpartum hypo/hypertension; 6.12% had preterm deliveries, and all of them (100%) underwent cesarean section. Of all the 49 patients with GDM, 16.33% gave birth to babies with Macrosomia, about 34.69% with Jaundice and approx. 28.57% with Respiratory Distress Syndrome (RDS). Majority of the patients were under treatment with Insulin (46.93%) and Metformin (30.61%). The incidence of gestational diabetes mellitus has become quite a common scenario among people around the world especially in Asia and Africa because of lack of awareness of the risk factors and consequences of this condition. The current situation can only be overcome by letting general people know about GDM and its effects on both mother and baby. However, in this study, the prevalence rate was found to be quite higher than usual due to the error in sampling, which happened because the study was carried out in such settings where most of the patients had Diabetes Mellitus. So if further studies to be conducted, it should be designed in such a way that more population can be included to bring a better outcome in future.

Key Words: *Gestational Diabetes Mellitus, GDM, Bangladesh, Macrosomia, Insulin, Metformin, Awareness, Morbidity, Child Mortality, Exercise, Mealplan, Pregnancy*

CHAPTER ONE

INTRODUCTION

1.1 Introduction

Gestational Diabetes Mellitus (GDM) is a common condition affecting ~7% of all pregnancies. The detection of GDM is important because of its associated maternal and fetal complications. Treatment with medical nutrition therapy, close monitoring of glucose levels, and insulin therapy if glucose levels are above goal can help to reduce these complications.

Gestational diabetes mellitus (GDM) is defined as glucose intolerance that begins or is first detected during pregnancy. GDM affects ~7% of all pregnancies, resulting in > 200,000 cases per year. Depending on the population sample and diagnostic criteria, the prevalence may range from 1 to 14%. Of all pregnancies complicated by diabetes, GDM accounts for ~90% (Setji *et al.*, 2005).

1.2 History of Gestational Diabetes Mellitus (GDM)

The history of GDM dated back to 1964 when O'Sullivan proposed specific criteria to interpret the glucose tolerance level in pregnancy to identify women at a higher risk for developing diabetes after delivery. The criteria was later modified by the National Diabetes Data Group (NDDG) in 1979 and Carpenter and Coustan in view of the change from using venous whole blood samples to plasma or serum samples and the technique in analyzing blood glucose levels. The Carpenter and Coustan criteria were lower than the NDDG criteria and therefore resulted in a higher prevalence of GDM. In 2000, the American Diabetes Association (ADA) recommended the use of the Carpenter and Coustan criteria for diagnosis of GDM. Despite this recommendation, various authorities had their own diagnostic threshold which resulted in a lot of confusions to the physicians and their patients. In 2008, the result of "Hyperglycemia and Adverse Pregnancy Outcomes (HAPO)" study was published. This major observational study provided us valuable information regarding the risks of adverse outcomes associated with various degrees of maternal glucose intolerance. Based on the result of this study, the IADPSG proposed a new diagnostic criteria in 2010. However, controversies and debates continued (Cheung and Wong, 2012).

1.3 Diabetes

Diabetes Mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The chronic hyperglycemia of diabetes is associated with long-term damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels.

Several pathogenic processes are involved in the development of diabetes. These range from autoimmune destruction of the β-cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action. The basis of the abnormalities in carbohydrate, fat, and protein metabolism in diabetes is deficient action of insulin on target tissues. Deficient insulin action results from inadequate insulin secretion and/or diminished tissue responses to insulin at one or more points in the complex pathways of hormone action. Impairment of insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of the hyperglycemia.

Symptoms of marked hyperglycemia include polyuria, polydipsia, weight loss, sometimes with polyphagia, and blurred vision. Impairment of growth and susceptibility to certain infections may also accompany chronic hyperglycemia. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or the nonketotic hyperosmolar syndrome.

Long-term complications of diabetes include retinopathy with potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints; and autonomic neuropathy causing gastrointestinal, genitourinary, and cardiovascular symptoms and sexual dysfunction. Patients with diabetes have an increased incidence of atherosclerotic cardiovascular, peripheral arterial and cerebrovascular disease. Hypertension and abnormalities of lipoprotein metabolism are often found in people with diabetes.

The vast majority of cases of diabetes fall into two broad etiopathogenetic categories. In one category, type 1 diabetes, the cause is an absolute deficiency of insulin secretion. Individuals at increased risk of developing this type of diabetes can often be identified by serological evidence of an autoimmune pathologic process occurring in the pancreatic islets and by genetic markers.

In the other, much more prevalent category, type 2 diabetes, the cause is a combination of resistance to insulin action and an inadequate compensatory insulin secretory response. In the latter category, a degree of hyperglycemia sufficient to cause pathologic and functional changes in various target tissues, but without clinical symptoms, may be present for a long period of time before diabetes is detected. During this asymptomatic period, it is possible to demonstrate an abnormality in carbohydrate metabolism by measurement of plasma glucose in the fasting state or after a challenge with an oral glucose load.

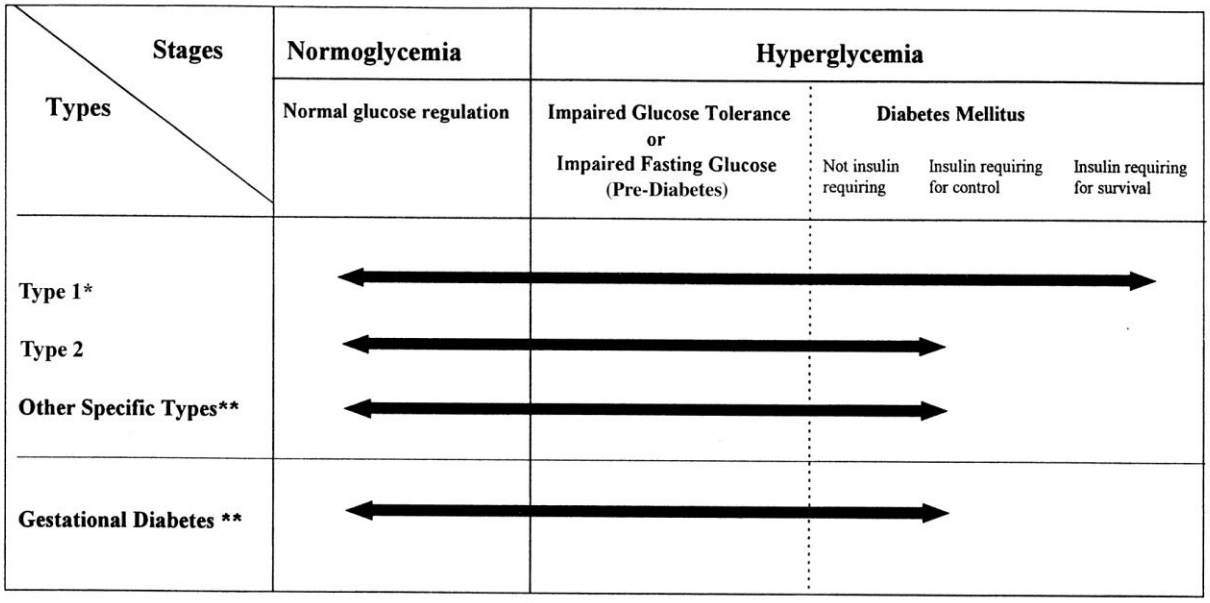

Figure 1.1 Disorders of glycemia: etiologic types and stages. Even after presenting in ketoacidosis, these patients can briefly return to normoglycemia without requiring continuous therapy (i.e., "honeymoon" remission); in rare instances, patients in these categories (e.g., Vacor toxicity, type 1 diabetes presenting in pregnancy) may require insulin for survival (American Diabetes Association, 2003)

The degree of hyperglycemia (if any) may change over time, depending on the extent of the underlying disease process (Figure 1.1). A disease process may be present but may not have progressed far enough to cause hyperglycemia. The same disease process can cause impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT) without fulfilling the criteria for the diagnosis of diabetes. In some individuals with diabetes, adequate glycemic control can be achieved with weight reduction, exercise, and/or oral glucose-lowering agents. These individuals therefore do not require insulin. Other individuals who have some residual insulin secretion but

require exogenous insulin for adequate glycemic control can survive without it. Individuals with extensive β-cell destruction and therefore no residual insulin secretion require insulin for survival. The severity of the metabolic abnormality can progress, regress, or stay the same. Thus, the degree of hyperglycemia reflects the severity of the underlying metabolic process and its treatment more than the nature of the process itself.

It has been clearly established in recent years that diabetes mellitus is a genetically and clinically heterogeneous group of disorders that share glucose intolerance in common. The evidence in favor of this heterogeneity is overwhelming:

i. There are more than 30 distinct, mostly rare, disorders in which glucose intolerance is a feature;
ii. Ethnic variability in prevalence and clinical features;
iii. Genetic heterogeneity in diabetic animal models;
iv. Clinical variability between thin, ketosis-prone, insulin-dependent diabetes and obese, nonketotic, insulin-resistant diabetes;
v. Genetic and immunologic studies that show "juvenile" and "adult-onset" diabetes to be distinct entities; and
vi. Demonstration that a type of mild diabetes in young people, which is inherited in an autosomal dominant fashion, is clearly different from the classic acute-onset diabetes of juveniles.

This collective evidence has been used to divide the class of diabetes mellitus into three distinct types, in each of which subtypes have been identified. Heterogeneity within the diabetic syndrome has important implications for research and for the clinical management of diabetes: *first*, that different genetic and environmental etiologic factor can result in similar diabetic phenotypes; and *second*, that the distinct disorders grouped together under the rubric diabetes may differ markedly in pathogenesis, natural history, and responses to therapy and prophylactic measures (American Diabetes Association, 2003).

1.4 Types of Diabetes

There are two major types of diabetes, called type 1 and type 2. Type 1 diabetes was also formerly called insulin dependent diabetes mellitus (IDDM), or juvenile onset diabetes mellitus. In type 1 diabetes, the pancreas undergoes an autoimmune attack by the body itself, and is rendered incapable of making insulin. Abnormal antibodies have been found in the majority of patients with type 1 diabetes. Antibodies are proteins in the blood that are part of the body's immune system. The patient with type 1 diabetes must rely on insulin medication for survival. Type 2 diabetes, formerly called non-insulin-dependent (NIDDM) or adult-onset results from the body's ineffective use of insulin.

1.4.1 Type I: Insulin-Dependent Diabetes Mellitus

The first subclass of diabetes, type I or insulin-dependent diabetes mellitus (IDDM), is usually characterized clinically by abrupt onset of symptoms, insulinopenia and dependence on injected insulin to sustain life, and proneness to ketosis. Classically, this type of disease occurs in juveniles, and it was formerly termed juvenile diabetes. However, it can be recognized and become symptomatic for the first time at any age; hence, diagnosis based on age at onset is inappropriate. In addition to the ketosis-prone stage, this type of diabetes can also be recognized in a preketosis-prone stage. For example, prospective testing in siblings of insulin-dependent diabetics has disclosed patients with normal fasting plasma glucose (FPG) levels but with abnormal glucose tolerance who progress rapidly to the ketotic form, usually within 2 yr after recognition, but occasionally after longer periods of time.1 IDDM appears to be heterogeneous in terms of genetics and environmental factors that precipitate the disease.2 Genetic determinants are thought to be important in most patients, as expressed by the associated increased or decreased frequency of certain histocompatibility antigens (HLA) on chromosome 6.3 ' 4 Abnormal immune responses and autoimmunity are also thought to play an etiologic role, and islet cell antibodies are frequently present at diagnosis in this type of diabetes (National Diabetes Data Group, 1979).

1.4.2 Type II: Noninsulin-Dependent Diabetes Mellitus

The second subclass of diabetes, type II or noninsulin-dependent diabetes mellitus (NIDDM), frequently presents with minimal or no symptoms referable to the metabolic aberrations of diabetes. Patients with NIDDM are not dependent on insulin for prevention of ketonuria and are not prone to ketosis. However, they may require insulin for correction of symptomatic, or persistent, fasting hyperglycemia if this cannot be achieved with the use of diet or oral agents. Such patients may develop ketosis under special circumstances, such as severe stress precipitated by infections or trauma. There may be normal levels of insulin, mild insulinopenia, or above normal levels of insulin associated with insulin resistance. The whole range of insulin responses to glucose from onset diabetes and variations of this phrase should be abandoned as classifying terms. NIDDM also has a genetic basis, which appears to be stronger than in IDDM, as evidenced by a more frequent familial pattern of occurrence. Indeed, included within this type are families in whom diabetes presents in children, adolescents, and adults in which autosomal dominant inheritance has been well established (formerly referred to as maturity-onset-type diabetes of the young, or, MODY1. Environmental factors superimposed on genetic susceptibility are undoubtedly involved in onset of the NIDDM types. Intake of excessive calories leading to weight gain and obesity is probably an important factor in its pathogenesis. Although small changes in weight may be important, NIDDM has been subdivided according to the absence or presence of obesity, as 60% to 90% of all NIDDM patients are obese in Western societies. Hyperglycemia and glucose intolerance are usually improved by weight loss. In persons with this type of diabetes, characteristic aggregation of HLA types and islet cell antibodies have not been found (National Diabetes Data Group, 1979)

TABLE 2
Classification of diabetes mellitus and other categories of glucose intolerance

Class	Former terminology	Associated factors	Clinical characteristics	Diagnostic criteria
		Clinical Classes		
Diabetes Mellitus (DM)				
Insulin-dependent type (IDDM), Type I	Juvenile diabetes, juvenile-onset diabetes, juvenile-onset-type diabetes, JOD, ketosis-prone diabetes, brittle diabetes	Evidence regarding etiology suggests genetic and environmental or acquired factors, association with certain HLA types, and abnormal immune responses, including autoimmune reactions.	Persons in this subclass are dependent on injected insulin to prevent ketosis and to preserve life, although there may be preketotic, non-insulin-dependent phases in the natural history of the disease. In the preponderance of cases, onset is in youth, but IDDM may occur at any age. Characterized by insulinopenia. Islet cell antibodies are frequently present at diagnosis in this type.	Diagnosis of diabetes in adults should be based on: (1) unequivocal elevation of plasma glucose concentration together with the classical symptoms of diabetes. or (2) elevated fasting plasma glucose concentration on more than one occasion. or (3) elevated plasma glucose concentration after an oral glucose challenge on more than one occasion. Diagnosis of diabetes in *children requires* either (1) or (2) *and* (3). See Table 5 for diagnostic plasma glucose standards. See text for recommended procedure for performance of the oral glucose tolerance test. Additional criteria for NIDDM: See text and Table 6 for standards of obesity.
Noninsulin-dependent types (NIDDM), Type II 1. Nonobese NIDDM 2. Obese NIDDM	Adult-onset diabetes, maturity-onset diabetes, maturity-onset-type diabetes, MOD, ketosis-resistant diabetes, stable diabetes	There are probably multiple etiologies for this class, the common outcome being derangement of carbohydrate metabolism. Evidence on familial aggregation of diabetes implies genetic factors, and this class includes diabetes presenting in children and adults in which autosomal dominant inheritance has been clearly established (formerly termed the MODY type, maturity-onset diabetes in the young). Environmental factors superimposed on genetic susceptibility are probably involved in the onset of the NIDDM types. Obesity is suspected as an etiologic factor and is recommended as a criterion for dividing NIDDM into two subclasses, according to the presence or absence of obesity.	Persons in this subclass are not insulin-dependent or ketosis-prone, although they may use insulin for correction of symptomatic or persistent hyperglycemia and they can develop ketosis under special circumstances, such as episodes of infection or stress. Serum insulin levels may be normal, elevated, or depressed. In the preponderance of cases, onset is after age 40, but NIDDM is known to occur at all ages. About 60–90% of NIDDM subjects are obese and constitute a subtype of NIDDM; in these patients, glucose tolerance is often improved by weight loss. Hyperinsulinemia and insulin resistance characterize some patients in this subtype.	
Other types, including diabetes mellitus associated with certain conditions and syndromes: 1. Pancreatic disease 2. Hormonal 3. Drug or chemical induced 4. Insulin receptor abnormalities 5. Certain genetic syndromes 6. Other types	Secondary diabetes	This subclass contains a variety of types of diabetes, in some of which the etiologic relationship is known (e.g., diabetes secondary to pancreatic disease, endocrine disease, or administration of certain drugs). In others, an etiologic relationship is suspected because of a higher frequency of association of diabetes with a syndrome or condition (e.g., a number of the genetic syndromes). See Table 3 for a list of these conditions and syndromes.	In addition to the presence of the specific condition or syndrome, diabetes mellitus is also present.	In order to place an individual in the subclass Other Types, two diagnostic determinations must be made, the presence of diabetes (as described above) and the presence of the associated condition or syndrome.
Impaired Glucose Tolerance (IGT)				
Nonobese IGT Obese IGT IGT associated with certain conditions and syndromes, which may be (1) pancreatic disease, (2) hormonal,	Asymptomatic diabetes, chemical diabetes, subclinical diabetes, borderline diabetes, latent diabetes	Mild glucose intolerance in subjects in this class may be attributable to normal variation of glucose tolerance within a population. In some subjects, IGT may	Nondiagnostic fasting glucose levels and glucose intolerance of a degree between normal and diabetic. Some studies have shown increased preva-	Diagnosis is based on the oral glucose tolerance test after determining that fasting plasma glucose is <140 mg/dl. See Table 5 for diagnostic criteria and

NATIONAL DIABETES DATA GROUP

TABLE 2 (Continued)

Class	Former terminology	Associated factors	Clinical characteristics	Diagnostic criteria
		Clinical Classes		
(3) drug or chemical induced, (4) insulin receptor abnormalities, (5) certain genetic syndromes		represent a stage in the development of NIDDM or IDDM although the majority of persons with IGT remain in this class for many years or return to normal glucose tolerance. See Table 3 for a list of associated conditions and syndromes.	lence of arterial disease symptoms and electrocardiographic abnormalities and increased susceptibility to atherosclerotic disease associated with known risk factors including hypertension, hyperlipidemia, adiposity, and age. Clinically significant renal and retinal complications of diabetes are absent.	text and Table 6 for standards of obesity.
Gestational Diabetes (GDM)	Gestational diabetes	Glucose tolerance with onset during pregnancy is thought to be due to complex metabolic and hormonal changes which are incompletely understood. Insulin resistance may be responsible in part for gestational diabetes.	Glucose intolerance that has its onset or recognition during pregnancy. Thus, diabetics who become pregnant are not included in this class. Associated with increased perinatal complications and with increased risk for progression to diabetes within 5–10 yr after parturition. Requires reclassification after pregnancy terminates into PrevAGT, DM, or IGT.	Diagnosis is based on the oral glucose tolerance test. See Table 5 for the 1964 diagnostic standards of O'Sullivan and Mahan which are widely used in North America. Different criteria are employed in other parts of the world.

Class	Former terminology	Description
		Statistical Risk Classes
Previous Abnormality of Glucose Tolerance (PrevAGT)	Latent diabetes, prediabetes	This class is restricted to those persons who now have normal glucose tolerance but who have previously demonstrated diabetic hyperglycemia or impaired glucose tolerance either spontaneously or in response to an identifiable stimulus. Individuals who have been gestational diabetics and returned to normal glucose tolerance after parturition form an obvious subclass of PrevAGT. Another small but important group of individuals in this class are former obese diabetics whose glucose tolerance has returned to normal after losing weight. Clinical studies have shown that many patients under acute metabolic stress due to trauma or injury experience transient hyperglycemia. Apart from studies of former gestational diabetics, there has been little systematic investigation of the later liability of persons who have exhibited glucose intolerance to develop diabetes. However, it is likely that this is increased and that there is utility in including all those with a history of glucose intolerance, now normal, in this separate class "Previous Abnormality of Glucose Tolerance."
Potential Abnormality of Glucose Tolerance (PotAGT)	Prediabetes, potential diabetes	This class includes persons who have never exhibited abnormal glucose tolerance but who are at substantially increased risk for the development of diabetes. Individuals who are at increased risk for IDDM include (in decreasing order of risk): persons with islet cell antibodies; monozygotic twin of an IDDM diabetic; sib of an IDDM diabetic, especially one with identical HLA haplotypes; offspring of an IDDM diabetic. Individuals who are at increased risk for NIDDM include (in decreasing order of risk): monozygotic twin of an NIDDM diabetic; first degree relative of an NIDDM diabetic (sib, parent, and offspring); mother of a neonate weighing more than 9 lb; obese individuals; members of racial or ethnic groups with a high prevalence of diabetes, e.g., a number of American Indian tribes. The degree of risk for any of these circumstances is not well established as yet.

Figure 1.2 Classification of Diabetes Mellitus and other categories of Glucose Intolerance (National Diabetes Data Group, 1979)

1.4.3 Other Types of Diabetes

In this subclass, diabetes forms part of certain other conditions and syndromes that often have many clinical features not generally associated with the diabetic state. In some instances the co-occurrence of glucose intolerance and the other features is known to be etiologically related. In others, the frequency of co-occurrence indicates that there is an, as yet unknown, causal relationship. Thus, this subclass has been divided according to the known or suspected etiologic relationships. For example, diabetes may be secondary to

i. pancreatic disease or removal of pancreatic tissue,
ii. endocrine diseases such as acromegaly, Cushing's syndrome, pheochromocytoma, glucagonoma, somatostatinoma, and primary aldosteronism, or
iii. The administration of certain hormones, drugs, and chemicals that cause hyperglycemia.

Diabetes may also be associated with defects of insulin receptors, which may be caused by either abnormalities in numbers or affinity of insulin receptors or antibodies to receptors with or without associated immune disorders. Diabetes (or carbohydrate intolerance) is found in increased frequency with a large number of genetic syndromes. Finally, this class contains room for certain special types of diabetes that occur only under specific, well-described environmental and clinical conditions, e.g., diabetes associated with malnourished populations (National Diabetes Data Group, 1979).

1.4.4 Genetic Defects in Insulin Action

There are unusual causes of diabetes that result from genetically determined abnormalities of insulin action. The metabolic abnormalities associated with mutations of the insulin receptor may range from hyperinsulinemia and modest hyperglycemia to severe diabetes. Some individuals with these mutations may have acanthosis nigricans. Women may be virilized and have enlarged, cystic ovaries. In the past, this syndrome was termed type A insulin resistance. Leprechaunism and the Rabson-Mendenhall syndrome are two pediatric syndromes that have mutations in the insulin receptor gene with subsequent alterations in insulin receptor function and extreme insulin resistance. The former has characteristic facial features and is usually fatal in infancy, while the latter is associated with abnormalities of teeth and nails and pineal gland hyperplasia.

Alterations in the structure and function of the insulin receptor cannot be demonstrated in patients with insulin-resistant lipoatrophic diabetes. Therefore, it is assumed that the lesion(s) must reside in the postreceptor signal transduction pathways (National Diabetes Data Group, 1979).

1.4.5 Diseases of the Exocrine Pancreas

Any process that diffusely injures the pancreas can cause diabetes. Acquired processes include pancreatitis, trauma, infection, pancreatectomy, and pancreatic carcinoma. With the exception of that caused by cancer, damage to the pancreas must be extensive for diabetes to occur; adrenocarcinomas that involve only a small portion of the pancreas have been associated with diabetes. This implies a mechanism other than simple reduction in β-cell mass. If extensive enough, cystic fibrosis and hemochromatosis will also damage β-cells and impair insulin secretion. Fibrocalculous pancreatopathy may be accompanied by abdominal pain radiating to the back and pancreatic calcifications identified on X-ray examination. Pancreatic fibrosis and calcium stones in the exocrine ducts have been found at autopsy (National Diabetes Data Group, 1979).

1.4.6 Endocrinopathies

Several hormones (e.g., growth hormone, cortisol, glucagon, epinephrine) antagonize insulin action. Excess amounts of these hormones (e.g., acromegaly, Cushing's syndrome, glucagonoma, pheochromocytoma, respectively) can cause diabetes. This generally occurs in individuals with preexisting defects in insulin secretion, and hyperglycemia typically resolves when the hormone excess is resolved.

Somatostatinoma- and aldosteronoma-induced hypokalemia can cause diabetes, at least in part, by inhibiting insulin secretion. Hyperglycemia generally resolves after successful removal of the tumor (National Diabetes Data Group, 1979).

1.4.7 Drug- or Chemical-Induced Diabetes

Many drugs can impair insulin secretion. These drugs may not cause diabetes by themselves, but they may precipitate diabetes in individuals with insulin resistance. In such cases, the classification is unclear because the sequence or relative importance of β-cell dysfunction and insulin resistance is unknown. Certain toxins such as Vacor (a rat poison) and intravenous pentamidine can permanently destroy pancreatic β-cells. Such drug reactions fortunately are rare. There are also many drugs and hormones that can impair insulin action. Examples include nicotinic acid and glucocorticoids. Patients receiving α-interferon have been reported to develop diabetes associated with islet cell antibodies and, in certain instances, severe insulin deficiency (National Diabetes Data Group, 1979).

1.4.8 Infections

Certain viruses have been associated with β-cell destruction. Diabetes occurs in patients with congenital rubella, although most of these patients have HLA and immune markers characteristic of type 1 diabetes. In addition, coxsackievirus B, cytomegalovirus, adenovirus, and mumps have been implicated in inducing certain cases of the disease (National Diabetes Data Group, 1979).

1.4.9 Uncommon Forms of Immune-Mediated Diabetes

In this category, there are two known conditions, and others are likely to occur. The stiff-man syndrome is an autoimmune disorder of the central nervous system characterized by stiffness of the axial muscles with painful spasms. Patients usually have high titers of the GAD autoantibodies, and approximately one-third will develop diabetes.

Anti-insulin receptor antibodies can cause diabetes by binding to the insulin receptor, thereby blocking the binding of insulin to its receptor in target tissues. However, in some cases, these antibodies can act as an insulin agonist after binding to the receptor and can thereby cause hypoglycemia. Anti-insulin receptor antibodies are occasionally found in patients with systemic lupus erythematosus and other autoimmune diseases. As in other states of extreme insulin resistance, patients with anti-insulin receptor antibodies often have acanthosis nigricans. In the past, this syndrome was termed type B insulin resistance (National Diabetes Data Group, 1979).

1.4.10 Other Genetic Syndromes Sometimes Associated with Diabetes

Many genetic syndromes are accompanied by an increased incidence of diabetes mellitus. These include the chromosomal abnormalities of Down's syndrome, Klinefelter's syndrome, and Turner's syndrome. Wolfram's syndrome is an autosomal recessive disorder characterized by insulin-deficient diabetes and the absence of β-cells at autopsy. Additional manifestations include diabetes insipidus, hypogonadism, optic atrophy, and neural deafness (American Diabetes Association, 2003).

1.5 Screening

Screening procedures identify pregnant women who are at sufficient risk to warrant a diagnostic test, the oral glucose-tolerance test. Screening of all pregnant women by measurement of serum or plasma glucose between 24 and 28 weeks of gestation has been recommended widely. However, some women have clinical characteristics that indicate such a low risk of gestational diabetes that screening may not be warranted. Other women have high-risk characteristics that warrant screening early in pregnancy. Accordingly, screening for gestational diabetes should include an assessment of the clinical characteristics of all pregnant women to determine the risk of gestational diabetes and serum glucose screening in women who do not have a low-risk clinical profile. The initial clinical assessment should be made at the first antepartum visit. Women with high-risk clinical characteristics should then undergo glucose screening as soon as possible. A 50-g oral glucose-challenge testis usually recommended for this purpose, followed by an oral glucose-tolerance test if the serum glucose concentration at screening is sufficiently high. However, if the suspicion of overt hyperglycemia is very high (e.g., if polyuria and polydipsia are present), measurement of serum glucose during fasting may be sufficient to confirm the diagnosis of diabetes. Women who are found to be at average or low clinical risk at the initial clinical evaluation should be reassessed between 24 and 28 weeks of gestation, along with women at high risk who have not already received a diagnosis of gestational diabetes by that time.

At 24 to 28 weeks, women with low-risk clinical characteristics do not need further testing. The risk in these women is low, although the effect of not performing glucose screening has not been

evaluated thoroughly. Women with any clinical characteristic placing them at risk should undergo glucose testing. In most populations, a two-step testing procedure will limit the number of full glucose-tolerance tests that are performed; step 1 is the 50-g, one-hour glucose-challenge test, and step 2 an oral glucose-tolerance test performed in women whose one-hour glucose-challenge test indicates an increased risk of gestational diabetes. The frequency of positive screening tests and their specificity for the detection of gestational diabetes vary according to the cutoff point selected for the serum glucose concentration at one hour. In some groups (e.g., some Native American peoples), the rates of diabetes and gestational diabetes are so high that proceeding directly to the full oral glucose-tolerance test may be appropriate (Kjos and Buchanan, 1999).

1.6 Diagnosis

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance resulting in hyperglycemia of variable severity, with onset or first recognition during pregnancy. It does not exclude the possibility that unrecognized glucose intolerance may have antedated but has been previously unrecognized. Women who become pregnant and who are known to have diabetes mellitus which antedates pregnancy do not have gestational diabetes but have "diabetes mellitus and pregnancy" and should be treated accordingly before, during, and after the pregnancy. Gestational diabetes generally has few symptoms and it is most commonly diagnosed by screening during pregnancy. Diagnostic tests detect inappropriately high levels of glucose in blood samples (Al-Noaemi and Shalayel, 2011).

1.6.1 WHO Diagnostic Criteria for Hyperglycemia and GDM

In the early part of pregnancy (e.g. first trimester and first half of second trimester) fasting and postprandial glucose concentrations are normally lower than in normal, non-pregnant women. Elevated fasting or postprandial plasma glucose levels at this time in pregnancy may well reflect the presence of diabetes which has antedated pregnancy. The occurrence of higher than usual plasma glucose levels at this time in pregnancy mandates careful management and may be an indication for carrying out an oral glucose tolerance test (OGTT). Nevertheless, normal glucose tolerance in the early part of pregnancy does not by itself establish that gestational diabetes will not develop later. It may be appropriate to screen pregnant women belonging to high-risk

populations during the first trimester of pregnancy in order to detect previously undiagnosed diabetes mellitus. Formal systematic testing for gestational diabetes is usually done between 24 and 28 weeks of gestation. To determine if gestational diabetes is present in pregnant women, a standard OGTT should be performed after overnight fasting (8-14 hours) by giving 75 g anhydrous glucose in 250- 300 ml water. Plasma glucose is measured fasting and after 2 hours. Pregnant women who meet WHO criteria for diabetes mellitus or impaired glucose tolerance (IGT) are classified as having GDM. After the pregnancy ends, the woman should be re-classified as having either diabetes mellitus, or IGT, or normal glucose tolerance based on the results of a 75 g OGTT six weeks or more after delivery. The following table (**Table 1)** summarizes the 2006 WHO recommendations for the diagnostic criteria for diabetes and intermediate hyperglycemia (Al-Noaemi and Shalayel, 2011).

Diabetes	
Fasting plasma glucose,	≥7.0mmol/l (126mg/dl) or
2–h plasma glucose *	≥11.1mmol/l (200mg/dl)
Impaired Glucose Tolerance (IGT)	
Fasting plasma glucose	<7.0mmol/l (126mg/dl)
2–h plasma glucose*	≥7.8 and <11.1mmol/l (140mg/dl or 00mg/dl)
Impaired Fasting Glucose (IFG)	
Fasting plasma glucose	6.1 to 6.9 mmol/L (110mg/dl to 125 mg/dl)
2–h plasma glucose*	< 7.8 mmol/dl (140mg/dl)

* Venous plasma 2-h after ingestion of 75gm oral glucose load (OGTT)

Table 1 Diagnostic criterion for diabetes and intermediate hyperglycemia (Al-Noaemi and Shalayel, 2011).

1.7 Treatment

1.7.1 Glucose Monitoring

Self-monitoring of blood glucose is recommended for women with GDM. The goal of monitoring is to detect glucose concentrations elevated enough to increase perinatal mortality. The Fourth International Workshop-Conference on Gestational Diabetes Mellitus recommends maintaining the following capillary blood glucose values: preprandial glucose < 95 mg/dl, 1-hour postprandial glucose < 140 mg/dl, and 2-hour postprandial glucose < 120 mg/dl. ACOG guidelines are the same except that the 1-hour postprandial glucose value is considered acceptable at either 130 or 140 mg/dl. Jovanovic-Peterson *et al.* suggest guidelines that are a little stricter: fasting glucose < 90 mg/dl and 1-hour postprandial glucose < 120 mg/dl.

One prospective study of 668 patients (334 with GDM and 334 control subjects) found that women with GDM who had a mean blood glucose level between 87 and 104 mg/dl had incidence rates of intrauterine growth retardation (IUGR) and large for gestational age (LGA) infants comparable to the control group. However, women who had mean blood glucose values < 87 mg/dl had a higher incidence of infants with IUGR, whereas women who had mean blood glucose values > 104 mg/dl had a higher incidence of LGA infants. This study suggests that although it is important to treat hyperglycemia in GDM, it is also important not to overtreat because this can increase the risk of IUGR.

It is important for women to check postprandial glucose levels because these have been shown to correlate more with macrosomia than do fasting levels. The Diabetes in Early Pregnancy Study found that third-trimester postprandial glucose levels were the strongest predictor of percentile birth weight. In women with GDM who require insulin therapy, adjustments of their insulin regimens based on postprandial, rather than preprandial, glucose levels decreased the incidence of neonatal hypoglycemia, macrosomia, and cesarean delivery for cephalopelvic disproportion (Setji *et al*, 2005).

1.7.2 Medical Nutrition Therapy (MNT)

The goals of MNT are to provide adequate nutrition for the mother and fetus, provide sufficient calories for appropriate maternal weight gain, maintain normoglycemia, and avoid ketosis. In general, there is not an increased energy requirement during the first trimester of pregnancy.

However, most normal-weight women require an additional 300 kcal/day in the second and third trimester.

In normal-weight women with GDM, the recommended daily caloric intake is 30 kcal/kg/day based on their present pregnant weight. In women with GDM who are overweight (BMI > 30 kg/m^2), a 33% calorie restriction of their estimated energy needs is recommended (~25 kcal/kg/day based on their present pregnant weight). This level of calorie restriction is not associated with an elevation of free fatty acids or ketonuria. Some authors recommend further calorie restriction for women who are morbidly obese. However, caution must be taken to avoid ketosis, which can be seen with more aggressive calorie restriction.

Ketonemia in mothers with diabetes during pregnancy has been associated with lower IQ levels and impaired psychomotor development in their children. Monitoring with prebreakfast ketone measurements is recommended for patients who are on a hypocaloric or carbohydrate-restricted diet.

Carbohydrates should be distributed throughout the day. Eating three small- to moderate-sized meals and three snacks per day is recommended. Limiting carbohydrates to 40% of the total daily caloric intake has been shown to decrease postprandial glucose levels. Further limitation of carbohydrates at breakfast to 33% may be required to meet the desired postprandial glucose goals because insulin resistance is greatest in the morning. In addition, carbohydrate restriction to < 42% in patients with GDM resulted in a decreased incidence of LGA infants, a decrease in cesarean deliveries for macrosomia and cephalopelvic disproportion, and a decreased need for insulin therapy compared to patients on a diet with higher carbohydrate content (45-50%). Consuming carbohydrates with a low glycemic index also results in lower postprandial glucose levels, especially late in gestation (Setji *et al*, 2005).

1.7.3 Exercise

The role of exercise in women with GDM has been controversial in the past because maternal exercise on a bicycle ergometer has been associated with fetal bradycardia. Subsequent small studies have shown small transient increases in fetal heart rate after maternal exercise. There were no fetal complications in either study.

Durak *et al*. found that uterine activity, defined as contractions with an external tocometer deflection of > 15 mmHg above baseline for > 30 seconds, varied in response to different types

of aerobic exercise, even at comparable levels of exertion. The bicycle ergometer, treadmill, and rowing ergometer led to uterine activity in 50, 40, and 10% of exercise sessions, respectively. The recumbent bicycle and upper body ergometer did not lead to any increase in uterine activity. Therefore, the authors concluded that the recumbent bicycle and upper body ergometer were the safest forms of aerobic exercise for pregnant women. In addition, they recommended teaching women to palpate their uterus during exercise to detect subclinical contractions and to discontinue the exercise if contractions occur.

A potential benefit of exercise in women with GDM is improved glycemic control. One small trial randomized women with GDM to diet and exercise with an arm ergometer versus diet alone for 6 weeks. Researchers found that the diet-and-exercise group had a significant decrease in glycated hemoglobin levels and in both fasting and 1-hour plasma glucose levels during a glucose challenge test compared to the diet-alone group. Another trial, in which women with GDM were randomized to a partially home-based exercise program, did not find any reduction in blood glucose level, although the women did have an improvement in cardiovascular fitness. Based on the potential benefits of exercise in women with GDM, the ADA recommends starting or continuing a program of moderate exercise in women without medical or obstetrical contraindications (Setji *et al*, 2005).

1.7.4 Insulin

Insulin therapy is the most commonly used treatment when MNT fails to maintain blood glucose levels at the desired ranges or when there is evidence of excessive fetal growth. Small studies have demonstrated a decrease in macrosomia as well as related morbidities including operative deliveries and birth trauma in women with GDM who were treated with insulin.

A large, prospective, population-based study of almost 2,500 women with GDM compared the effect of intensive versus conventional management of GDM. The women randomized to the intensive management group were given memory reflectance meters and instructed to monitor their blood glucose seven times per day (fasting, preprandial, 2-hour postprandial, and bedtime). The women in the conventional management group were instructed to monitor four times per day (fasting and 2-hour postprandial) in addition to weekly fasting and 2-hour postprandial glucose measurements during clinic visits. Both groups were treated with diet and insulin as needed to

reach the following goals: overall mean blood glucose 90-100 mg/dl, fasting blood glucose 60-90 mg/dl, and postprandial blood glucose < 120 mg/dl. Overall, 66% of the women in the intensive management group were treated with insulin versus 36% of women in the conventional management group.

This study demonstrated a decreased rate of macrosomia, cesarean section, fetal metabolic complications, shoulder dystocia, neonatal intensive care unit days, and respiratory complications in the intensive management group. Another important consideration of this study is that GDM was defined as only one or more abnormal OGTT values, rather than the current standard of two or more abnormal glucose levels. Other studies have also shown improvement in rates of macrosomia and other maternal and fetal complications by treating women who do not meet the criteria for GDM but who have evidence of impaired carbohydrate tolerance as determined by an abnormal screening 50-g glucose challenge test and/or one or more abnormal results on OGTT.

Because there are no data demonstrating an optimal insulin regimen, the type and dose of insulin must be tailored to meet each patient's requirements. Human insulin is currently recommended by the ADA. However, one study of 42 women with GDM diagnosed at 14-32 weeks of gestation found that insulin lispro was as effective as regular insulin in controlling glucose levels with fewer episodes of hypoglycemia. Anti-insulin antibody levels were similar in the two groups. Additionally, the results of umbilical cord blood in four patients who received continuous intravenous insulin lispro and dextrose infusions intrapartum to assess placental insulin transfer did not detect any insulin lispro. Although insulin lispro appears to be safe in pregnancy if started after 14 weeks of gestation, it is considered to be in Pregnancy Category B by the Food and Drug Administration (FDA), and the official recommendation of the ADA is to use human insulin until further studies verify the safety of insulin lispro.

The short-term efficacy of insulin aspart was evaluated in a small study of 15 women with GDM during standardized meal tests. Although this study found that insulin aspart was effective in decreasing postprandial glucose concentration, further studies need to be done to ensure the safety of this medication in pregnant women. Insulin aspart is considered to be in Pregnancy Category C by the FDA.

The use of insulin glargine in humans has only been reported in case reports. There have been no clinical trials evaluating the use of insulin glargine in pregnancy. It is currently considered to be in Pregnancy Category C by the FDA (Setji *et al*, 2005).

1.7.5 Oral Agents

Currently, oral hypoglycemic agents are not recommended by the ADA or ACOG. The older sulfonylureas chlorpropamide and tolbutamide could cross the placenta, stimulate the fetal pancreas, and cause fetal hyperinsulinemia. However, the transfer of glyburide, a second-generation sulfonylurea, across the human placenta was insignificant in experimental models.

This finding led to a clinical trial of 404 women with GDM randomized to either glyburide or insulin therapy at 11-33 weeks of gestation. There were no significant differences in glycemic control or adverse fetal outcomes. In addition, glyburide was not detected in the cord serum of any infants in the glyburide group.

Smaller studies have also supported the safety of glyburide use in pregnancy. In one of these trials, women with GDM who were treated with glyburide had fewer asymptomatic hypoglycemic episodes compared to women with GDM treated with insulin, although the clinical significance of these hypoglycemic episodes is unknown.

Thus, although glyburide appears to be safe in pregnancy based on the above studies, it is important to recognize that these studies in aggregate are small and not adequately powered to detect clinically important, relatively rare outcomes in pregnancy. Furthermore, glyburide is considered to be in Pregnancy Category C by the FDA, and therefore it is not currently recommended by the ADA or ACOG until larger studies confirm its safety. Another potential concern with the use of glyburide in GDM is possible impairment of myocardial ischemic preconditioning.

Metformin has also been used to treat pregnant women with GDM. A retrospective cohort study found an increased prevalence of preeclampsia and perinatal mortality in women treated with metformin. However, the women in the metformin group were more obese and older, and their treatment was begun later in gestation. Recent studies involving women with polycystic ovary syndrome or women with type 2 diabetes who continue metformin in pregnancy have found no adverse pregnancy outcomes.

Although previous studies have been small, there is an ongoing prospective, randomized controlled trial in New Zealand and Australia comparing metformin with insulin in women with GDM. This study will help to answer questions about the safety of metformin during pregnancy. Metformin is listed as Pregnancy Category B by the FDA (Setji *et al*, 2005).

1.8 Risk Factors

Risk factors for developing GDM include:

- a previous diagnosis of GDM during an earlier pregnancy;
- family history of diabetes;
- previous delivery of a heavy or 'high birth weight' baby (weighing over 4000 grams or 8 pounds, 13 ounces)
- age – the risk for GDM increases with age and is highest for women 35 years old and older;
- obesity (measured as Body Mass Index (BMI) over 30 kg/m2);
- polyhydramnios (too much amniotic fluid in the womb);
- use of corticosteroids (i.e. drugs used for arthritis);
- previous unexplained stillbirth;
- history of polycystic ovary syndrome; and
- acanthosis nigricans (disorder in which there are darkened patches of skin) (National Aboriginal Health Organization, 2009)

1.9 Effects of Gestational Diabetes

Gestational diabetes creates risks for both the mother and the baby. These risks vary from additional stress on the mother and baby during delivery to the development of type 2 diabetes later in life. GDM is a temporary condition that can have long-term effects.

1.9.1 Effects of GDM on the Mother

• Women with GDM are at risk of delivering a heavy (high birth weight) baby which can lead to increases in birth trauma and may increase the need for caesarian section delivery.

• Women who have had GDM are at increased risk of developing type 2 diabetes

• Up to 70% of First Nations women with GDM in their first pregnancy will develop type 2 diabetes later on compared to about 40% of non-First Nations women.

• Some studies have found that Aboriginal women with GDM are more likely to have high blood pressure during pregnancy

• There has not been enough research to determine if treating GDM can reduce the risk of type 2 diabetes later in life. A diagnosis of GDM may mean that a woman is more carefully monitored and allows for earlier detection of and treatment for type 2 diabetes (National Aboriginal Health Organization, 2009).

1.9.2 Effects of GDM on the Infant

• Gestational diabetes can cause the baby to have a high birth weight. High birth weight is considered to be a baby weighing more than 4000 grams at birth (or 8 pounds, 13 ounces).

• Infants born to mothers with GDM have three times the risk of shoulder dystocia which can cause temporary or permanent nerve damage in the shoulder. Shoulder dystocia occurs when the baby's shoulder gets stuck behind the mother's pubic bone.

• Newborns born to a mother with GDM are at increased risk for dangerously low blood sugar levels (hypoglycemia) after birth, excessive blood insulin levels (hyperinsulinemia), low levels of calcium in the blood (hypocalcemia), too many red blood cells (polycythemia), and yellowing of the skin and eyes (jaundice caused by hyperbilirubinemia)

• Babies born to mothers with GDM are at greater risk of becoming obese and having long-term glucose intolerance or developing early onset type 2 diabetes (National Aboriginal Health Organization, 2009)

1.10 Genetics of GDM: Familial Clustering

Surprisingly, there has been relatively little research in the area of GDM genetics per se. An essential first step in genetics research has been the determination of evidence for a genetic basis for the disease. This can come in the form of twin concordance studies or estimates of familial

risk or heritability. However, performing such studies in a prospective fashion is fraught with numerous difficulties, primarily the need to identify women who will become pregnant. Studies are also difficult to perform in a retrospective fashion. The clinical definition for GDM has evolved over the years and differs slightly among countries. Furthermore, there has not been consistent screening for GDM, leading to possible bias in ascertainment, e.g., missed cases. Finally, there are difficulties in ascertaining families with multiple cases of GDM, which is partly related to the relatively low prevalence of GDM. There has been, to our knowledge, only one unpublished attempt to estimate familiarity of GDM. In 1999, Williams and colleagues used the statewide medical record system in the state of Washington to identify and link sisters diagnosed with GDM using *International Classification of Diseases, Ninth Revision* (ICD-9), coding. Based on their initial screening, they estimated that the sibling risk ratio for GDM was 1.75 (M. Williams, personal communication), suggesting some evidence for a genetic basis for GDM. This risk, likely an underestimate, is significantly lower than the estimated sibling risk ratio for type 2 diabetes, which ranges from 2 to 4.

The question of a genetic basis for GDM, however, is also closely tied to the debate of whether GDM is a unique disease state or whether pregnancy with its associated metabolic derangements simply provides us with a crystal ball with which to identify women who are susceptible to hyperglycemia and subsequent development of diabetes. If genetic variants associated with type 1 or type 2 diabetes are also associated with GDM, from a purely genetic perspective, it would be difficult to argue a unique genetic predisposition for GDM. This does not take into account the possibility of unique environmental exposures related to pregnancy that may interact with genetic variants to alter disease risk. Also, this does not negate the importance of using genetic information to improve treatment for GDM and minimize the deleterious effect of hyperglycemia on fetal outcomes.

There are studies that have examined the familial clustering of GDM and type 1 and type 2 diabetes. Examples include the studies of Dorner *et al.*, who showed increased familial aggregation of diabetes on the maternal side of offspring with type 1 diabetes whose mothers had GDM. Similarly, there is evidence for clustering of type 2 diabetes and impaired glucose tolerance in families with a GDM and evidence for higher prevalence of type 2 diabetes in

mothers of women with GDM. Thus, there is evidence of some link between both autoimmune and non-autoimmune forms of diabetes and GDM (Watanabe *et al.*, 2007).

1.11 Lactogenesis in Women with Previous GDM

Breastfeeding provides important health benefits to both women and their offspring. Health benefits of lactation for women include a lower risk of breast and ovarian cancer and possibly protection against type 2 diabetes. For the offspring, breastfeeding confers protection against both undernutrition and overnutrition during early childhood and may lower risk of developing obesity, hypertension, cardiovascular disease, and diabetes later in life. Postnatal feeding is one of several critical or sensitive developmental periods (fetal life, adiposity rebound in childhood, and adolescence) hypothesized to result in "metabolic programming" of future chronic disease risk.

Lactation may be more difficult for women with GDM because both maternal diabetes and obesity can delay the onset of lactogenesis. Furthermore, medical management of their newborns that involves provision of supplemental milk feedings may interfere with maternal milk production. In obese women, lactogenesis may be impaired because of lower physiological levels of prolactin in response to suckling. Delayed milk production may lead to lower rates of breastfeeding and shorter duration among obese women. A small sample of women with GDM were observed to have no marked delays based on similar concentration of lactose in the colostrums of GDM women compared with control women at 40 –50 h postpartum. However, GDM women had more difficulty expressing colostrum from their breasts during the first 2 days of lactation (Gunderson, 2007).

1.12 Human Placenta and GDM

The placenta is a complex fetal organ that fulfills pleiotropic roles during fetal growth. It separates the maternal and fetal circulation, with which it is in contact through different surfaces, i.e., the syncytiotrophoblast exposes the placenta to the maternal circulation and the endothelium is in contact with fetal blood. Because of this unique position, the placenta is exposed to the regulatory influence of hormones, cytokines, growth factors, and substrates present in both circulations and, hence, may be affected by changes in any of these. In turn, it can produce molecules that will affect mother and fetus independently.

In diabetes, the placenta undergoes a variety of structural and functional changes. Their nature and extent depend on a range of variables including the quality of glycemic control achieved during the critical periods in placental development, the modality of treatment, and the time period of severe departures from excellent metabolic control of a nondiabetic environment.

One of the characteristic features of a placenta in GDM is its increased weight, which is accompanied by enlarged surface areas of exchange on the maternal (syncytiotrophoblast) and fetal (endothelium) side. Teleologically, it may appear paradoxical that in a situation of maternal nutritional oversupply, the placenta increases its surface, thus potentially contributing to enhanced maternal fetal transport, but this reflects the prime importance of adequate oxygen supply to the fetus and the effect of excess growth factors such as insulin, which collectively dictate some of the placental changes even at the cost of adverse side effects (Desoye and Mouzon, 2007).

1.13 Maternal Obesity and Fetal Macrosomia in Infants of GDM Mothers

The infant of a GDM mother may have a variable phenotype based on the interaction of genes and the in utero environment. Additionally, the macrosomic fetus who presents much like the infant of a GDM mother may have the possibility, albeit small, of other genetic or metabolic dysfunctions mimicking GDM. Birth weight alone may not be a sensitive enough measure of fetal growth to assess the effects of GDM on the developing offspring. Consideration should be given to estimation of fetal adiposity, including such simple measures as Ponderal Index (weight/length^3). Last, given the increased prevalence of overweight and obesity in the population, and the independent effect of maternal pregravid obesity on fetal growth/adiposity, maternal obesity in and of itself needs to be addressed if the short- and long-term effects of fetal macrosomia in women with GDM are to be prevented (Catalano *et al.*, 2007).

CHAPTER TWO

LITERATURE REVIEW

2.1 Determination of the Frequency of Screening for Gestational Diabetes Mellitus (GDM) among a Population Receiving Regular Prenatal Care in the United States of America

A research was conducted in Division of General Medicine, Brigham and Women's Hospital, by Solomon *et al.* to determine the frequency of screening for gestational diabetes mellitus (GDM) among a population receiving regular prenatal care among 116678 nurses aged 25-42 years in 1989. The result shows, among a sample of 93 women who reported a pregnancy not complicated by GDM and responded to the supplementary questionnaire, 16 (17%) reported no glucose loading test; 69% of un unscreened women had one or more risk factors for GDM, Among a sample of 114 women who self-reported GDM in a singleton pregnancy and whose medical records were available for review, a physician diagnosis of GDM was confirmed in 107 (94%). Records and supplementary questionnaires indicated that oral glucose tolerance tests (OGTTs) were performed in 96(86%) of these women. Of women with a physician diagnosis of GDM whose OGTT results were available, 25% failed to meet NDDG criteria for this diagnosis, although all had evidence of abnormal glucose homeostasis (Solomon *et al*, 2004).

2.2 Identifying Risk Factors and Pregnancy Outcomes and Examining Maternal and Neonatal Complications Associated with GDM in Bangladesh

A case control study was carried out on Risk factors and pregnancy outcomes among gestational diabetic mothers by Ruhina Tasmin Biswas in BIRDEM and MCHTI hospital from July to October 2004. 106 pregnant women with a diagnosis of GDM and 196 without GDM were included in this study. Data on risk factors and pregnancy outcomes were collected through a face to face interview with the mothers and checking antenatal and delivery records at postnatal word. Study shows that Maternal age >25 years, pregnancy BMI >23 kg/m^2, positive family history of diabetes were found to be independent risk factor for GDM in multivariate analysis. Women who were diagnosed in the first half of the pregnancy were most likely to be treated with insulin. Prevalence of hypertension was higher in GDM compared to Non-GDM (12.3% vs. 4.1%). Anaemia was less prevalent in the GDM group. Preterm delivery, caesarean section, birth weight >3.5 kg were seen to be independently associated with GDM. No significant difference was found in maternal, fetal or neonatal complications either according to time of diagnosis of

GDM or type of treatment they received. Only the occurrence of hypoglycemia in the neonates born to mothers with GDM has been seen to be higher in the women who were diagnosed early (75.8% vs. 52%) and also who received insulin (74.5% vs. 36.7%). Hypertension in pregnancy appeared to be significantly associated with the women who were diagnosed of GDM in early stage of pregnancy. Women who were treated with insulin had higher prevalence of birth weight more than 3.5 kg (Biswas, 2006).

2.3 Observing the Perinatal Outcome of Patients with Gestational Diabetes Mellitus in Israel

A prospective, population-based study is conducted on perinatal complications following gestational diabetes mellitus, by Hod *et al*. in 1996. This study compared the perinatal outcome of patients with gestational diabetes mellitus (n=470) (diabetic with regard to the parameters specified above) and a contemporaneous control group (nondiabetic, n=250). The result came that the diabetic and control groups were matched in their demographic characteristics. Patient compliance reduced the rate of macrosomia (14.4%) and neonatal hypoglycemia (3.4%) but not to the levels of the control group (5.2% and 1.2% respectively). The level of fasting plasma glucose on the oral glucose tolerance test had no effect on perinatal outcome. Intensified (insulin) treatment reduced the rate of macrosomia and large-for-gestational age infants in the subgroups with intermediate and high levels of fasting plasma glucose on the oral glucose tolerance test (9.5%/14.2% and 12.2%/24.2% respectively), again not to levels of the control group (5.2%/10.8%). Obese patients were found to have more perinatal complications than lean patients. Intensified (insulin) treatment has proved to be beneficial in terms of reducing the rate of perinatal complications in the obese patients, but not to the corresponding levels of the control group. Such treatment had no effect on the lean patients (Hod *et al.*, 1996).

2.4 Screening for Gestational Diabetes Mellitus and its Prevalence in Bangladesh

A cross-sectional study was done in HDRCRP (Health & Disease Research Center for Rural Peoples) by Jesmin *et al*. 2014 on gestational diabetes which included 3447 women who

consecutively visited the antenatal clinics with an average gestation age of 26 weeks. GDM was defined according to WHO criteria (fasting plasma glucose [FPG] ≥ 7.0 mmol/L or 2-h ≥ 7.8 mmol/L) and the new ADA criteria (FPG ≥ 5.3 mmol/L or 2-h ≥ 8.6 mmol/L OGTT). We also calculated overt diabetes as FPG ≥ 7.0 mmol/L. The result said that the Prevalence of GDM was 9.7% according to the WHO criteria and 12.9% according to the ADA criteria in this study population. Prevalence of overt diabetes was 1.8%. Women with GDM were older, higher educated, had higher household income, higher parity, parental history of diabetes, and more hypertensive, compared with non-GDM women. Conclusion: This study demonstrates a high prevalence of GDM in Bangladesh. These estimates for GDM may help to formulate new policies to prevent and manage diabetes (Jesmin *et al*., 2014).

2.5 Observation of Maternal Gestational Diabetes, Birth Weight, and Adolescent Obesity in the United States of America

A survey was conducted by Gillman *et al*, including 7981 girls and 6900 boys, 9 to 14 years of age, who are participants in the growing up today study, 1996. Here, mean birth weight was 3.4 kg for girls and 3.6 kg for boys. Among the 465 subjects whose mothers had GDM, 17.1% were at risk for overweight and 9.7% were overweight in early adolescence. In the group without maternal diabetes, these estimates were 14.2% and 6.6%, respectively. In multiple logistic regression analysis, controlling for age, gender, and Tanner stage, the odds ratio for adolescent overweight for each 1-kg increment in birth weight was 1.4 (95% confidence interval: 1.2–1.6). Adjustment for physical activity, television watching, energy intake, breastfeeding duration, mother's BMI, and other maternal and family variables reduced the estimate to 1.3 (1.1–1.5). For offspring of mothers with GDM versus no diabetes, the odds ratio for adolescent overweight was 1.4 (1.1–2.0), which was unchanged after controlling for energy balance and socioeconomic factors. Adjustment for birth weight slightly attenuated the estimate (1.3; 0.9–1.9); adjustment for maternal BMI reduced the odds ratio to 1.2 (0.8–1.7) (Gillman *et al*, 1996).

2.6 Prospective Study of Gestational Diabetes Mellitus Risk Related Maternal Recreational Physical Activity Before and During Pregnancy

A study conducted by Dempsey on Prospective study of gestational diabetes mellitus risk related maternal recreational physical activity before & during pregnancy. Here, authors examined the relation between recreational physical activity before and during pregnancy and risk of gestational diabetes mellitus in a prospective cohort study. In 1996–2000, 909 normotensive, nondiabetic women in Seattle and Tacoma, Washington, were questioned during early gestation about physical activity performed during the year before and 7 days prior to the interview during pregnancy. Compared with inactive women, women who participated in any physical activity during the year before experienced a 56% risk reduction. Women spending ≥4.2 hours/week engaged in physical activity experienced a 76% reduction in gestational diabetes mellitus risk, and those expending ≥21.1 metabolic equivalent-hours/ week experienced a 74% reduction compared with inactive women. Physical activity during pregnancy was also associated with reductions in gestational diabetes mellitus risk. Women who engaged in physical activity during both time periods experienced a 69% reduced risk. Findings suggest that efforts to increase maternal physical activity may contribute to substantial reductions in gestational diabetes mellitus risk (Dempsey, 2004).

Significance of the study

Gestational Diabetes Mellitus (GDM) is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. It is an important dimension of the syndrome of Diabetes Mellitus. Similar to other members of the Western world and Asian race, Bangladeshi women are also considered to be at a high risk for developing gestational diabetes (Begum, 2008).

The increased rate of the prevalence of GDM in Bangladesh, along with the recent world is quite alarming and the consequences are quite dangerous if the condition is not treated effectively.

In our country majority of the female population lack the slightest knowledge about GDM let alone have concerns to manage its effects. Although the reasons for GDM are not fully understood by the scholars yet, the idea of its impact is noted down by many. If patients with GDM do not follow their physicians' instructions regarding treatment therapy, meal plan, and physical exercise; and act accordingly, they themselves may experience various complications such as: Abortion, Miscarriage, Preeclampsia, Postpartum Depression, Stillbirth, Postpartum Hypo/hypertension, Caesarean deliveries etc.

Neonates are also at an increased risk of low blood glucose (hypoglycemia), jaundice, high red blood cell mass (polycythemia) and low blood calcium (hypocalcemia) and magnesium (hypomagnesemia). GDM also interferes with maturation, causing immature babies prone to respiratory distress syndrome due to incomplete lung maturation and impaired surfactant synthesis (Rahman *et al.* 2009).

The most dangerous issue in this regard is that many of the physicians in our country, mostly from rural areas are not aware of the fact that GDM exists. This is very crucial because in Bangladesh, almost all the patients rely on their respective doctors and so if they are not enlightened with the idea of GDM, it is quite unsure that the patients will be accurately diagnosed and will get effective treatment. The rate of child mortality and morbidity will significantly increase with the increased rate of GDM prevalence.

One of the major reasons for choosing this topic for the study was to create awareness about GDM on mass level and discuss the recent issues associated with this term so that preventive

measures can be taken to decrease the prevalence rate of GDM and the idea of impacts of GDM can be established among the people of Bangladesh.

Aims and Objectives of the Study

The aims and objectives of this study were to:

- Estimate the prevalence of Gestational Diabetes Mellitus (GDM), its risk factors,
- Determine the most common drug therapy followed among the population inside the city of Dhaka,
- Observe the major complications associated during pregnancy period and its effect on the neonate, and
- Determine the knowledge level of Gestational Diabetes Mellitus among the general population.

CHAPTER THREE

METHODOLOGY

3.1 Type of the study

It was a prospective study.

3.2 Study Area

The survey was conducted in some hospitals in different areas inside Dhaka City.

3.3 Study Population

In this study a total number of 150 pregnant women were surveyed with a questionnaire in order to determine the prevalence, major drug therapy, major complications & effects of Gestational Diabetes Mellitus (GDM) on neonates specifically. Other important variables such as – meal plan, exercise profile, knowledge and management of Gestational Diabetes Mellitus (GDM) etc were also observed. The study was carried out in Azimpur Maternity Hospital, Azimpur; BSMMU Hospital, Shahbag; Monowara Hospital, Shiddheswari and Dr. Muttalib Clinic, Bijoy Nagar.

3.4 Study Period

The duration of the study was about six months starting from January to June in 2015.

3.5 Inclusion Criteria

Pregnant women with and without Diabetes having gestational period of six months or more were included for this study.

3.6 Exclusion Criteria

Women without pregnancy and having gestational period less than six months were excluded

3.7 Questionnaire Development

The questionnaire was developed based on studying different relevant journals of Gestational Diabetes Mellitus (GDM). The survey questionnaire form has the following major parts:

- Personal Information
- Disease Information

- Pregnancy History
- Nutrition
- Exercise Profile
- Diagnosis
- General Knowledge about Gestational Diabetes Mellitus (GDM)
- Post natal effects

3.8 Sampling Technique

In this study purposive sampling was followed.

3.9 Data Analysis

After collecting, the data were checked and analyzed with the help of Microsoft Excel 2007. The result was shown in bar, pie and column chart and calculated the percentage of the prevalence rate of GDM and other aspects and risk factors of this study.

CHAPTER FOUR

RESULT

4.1 Prevalence of Gestational Diabetes Mellitus (GDM) (N=150)

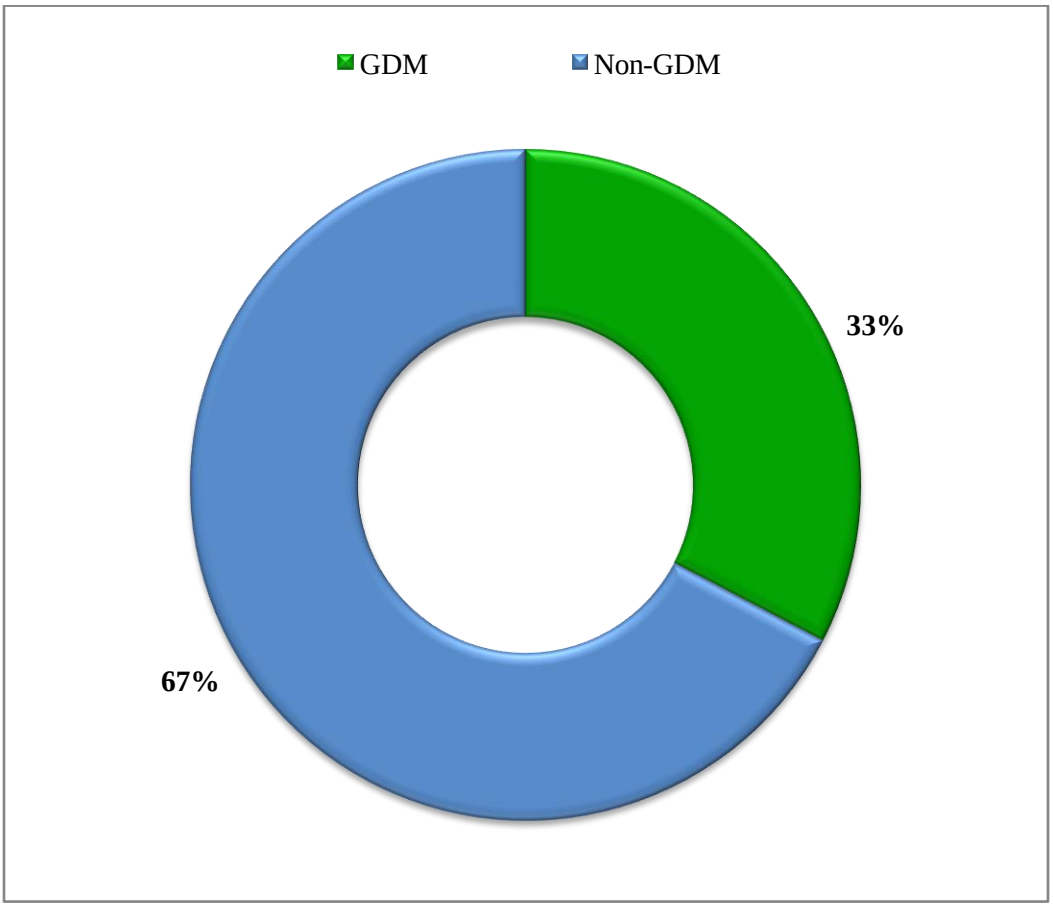

Figure 4.1 Prevalence of Gestational Diabetes Mellitus (GDM)

A total of 150 pregnant women were surveyed for this study. And 33% of them had Gestational Diabetes Mellitus (GDM). However 67% of the patients responded negatively.

*N.B. All the questions from here on where subjected to only 49 patients who had GDM

4.2 Age Distribution among the patients (N=49)

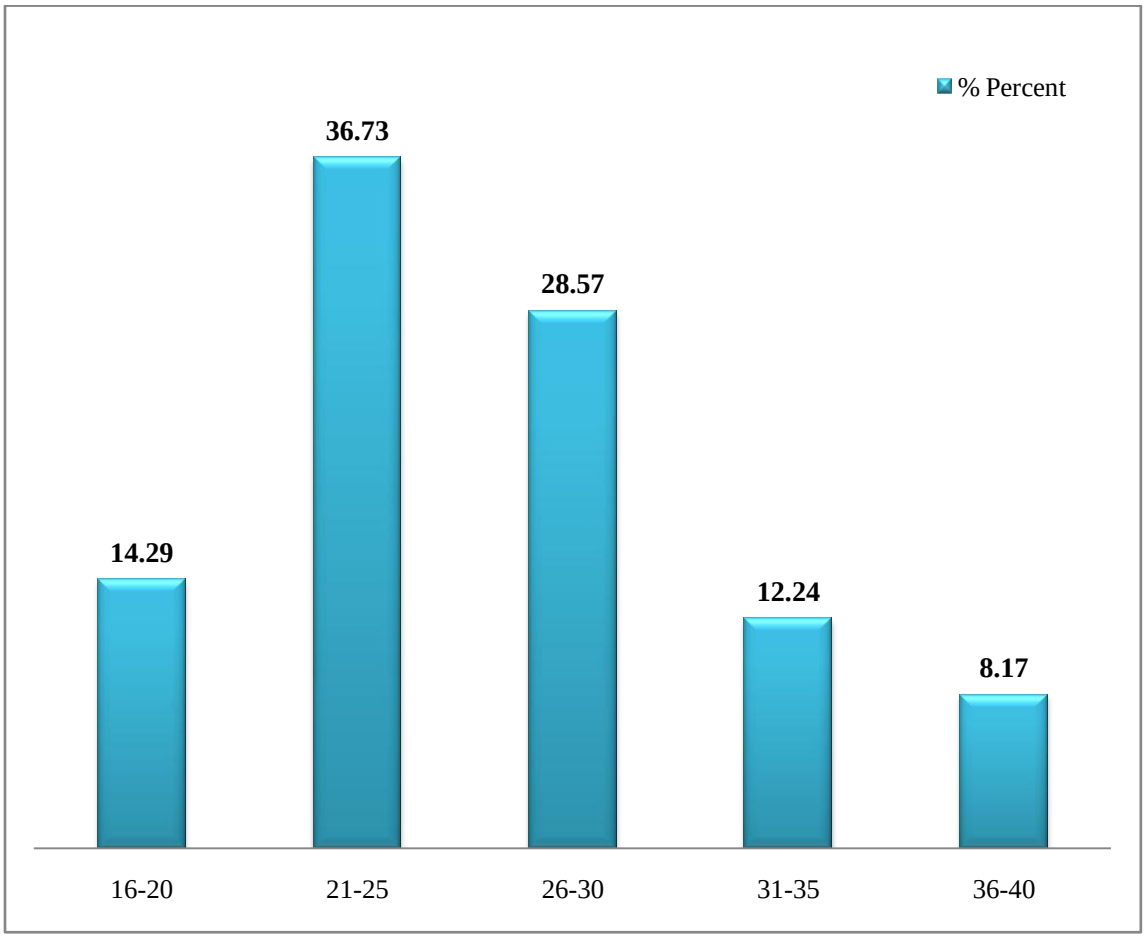

Figure 4.2 Age Distribution among the patients

The above figure shows the age distribution of patients. Out of 49 pregnant women with Gestational Diabetes Mellitus (GDM), majority were from the 21-25 years age range. The least amount of respondents was from the age group of 16 to 20 years.

4.3 Educational Qualification (N=49)

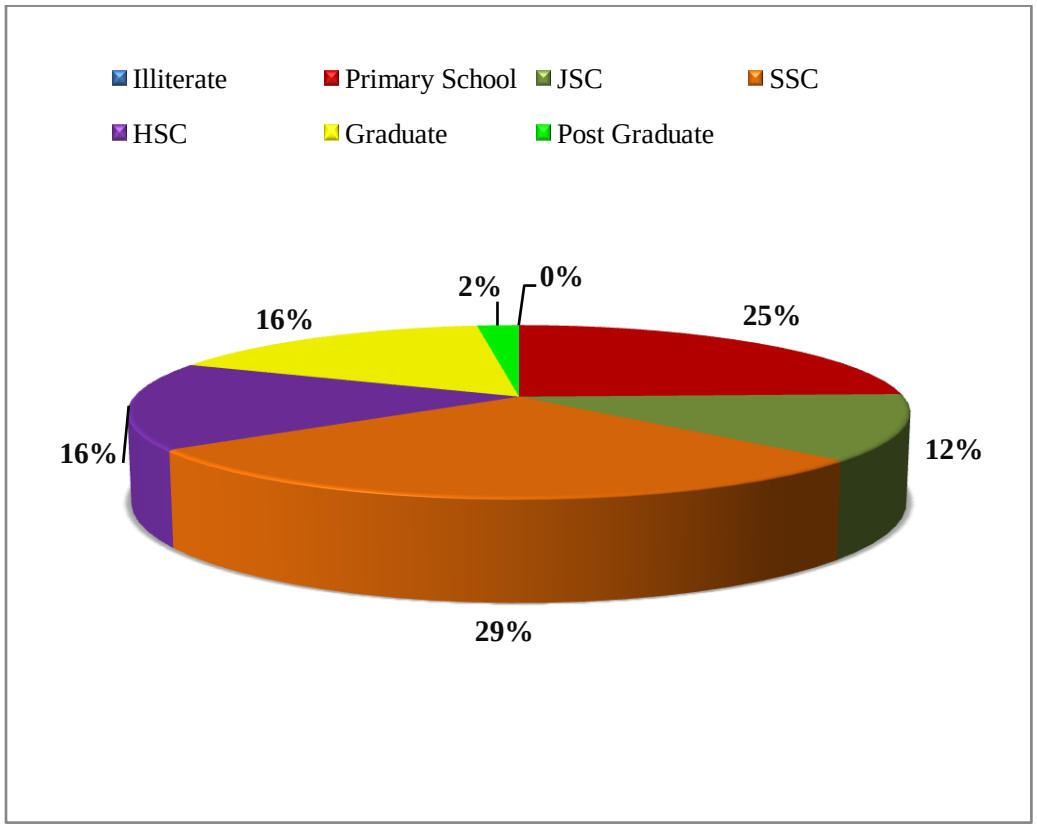

Figure 4.3 Educational Qualification

From the above graph it can be said that, among all the GDM patients, maximum respondents (29%) had a minimum qualification of SSC level. Very few had completed their Post graduation (2%) and none of them (0%) were illiterate.

4.4 Occupational Status (N=49)

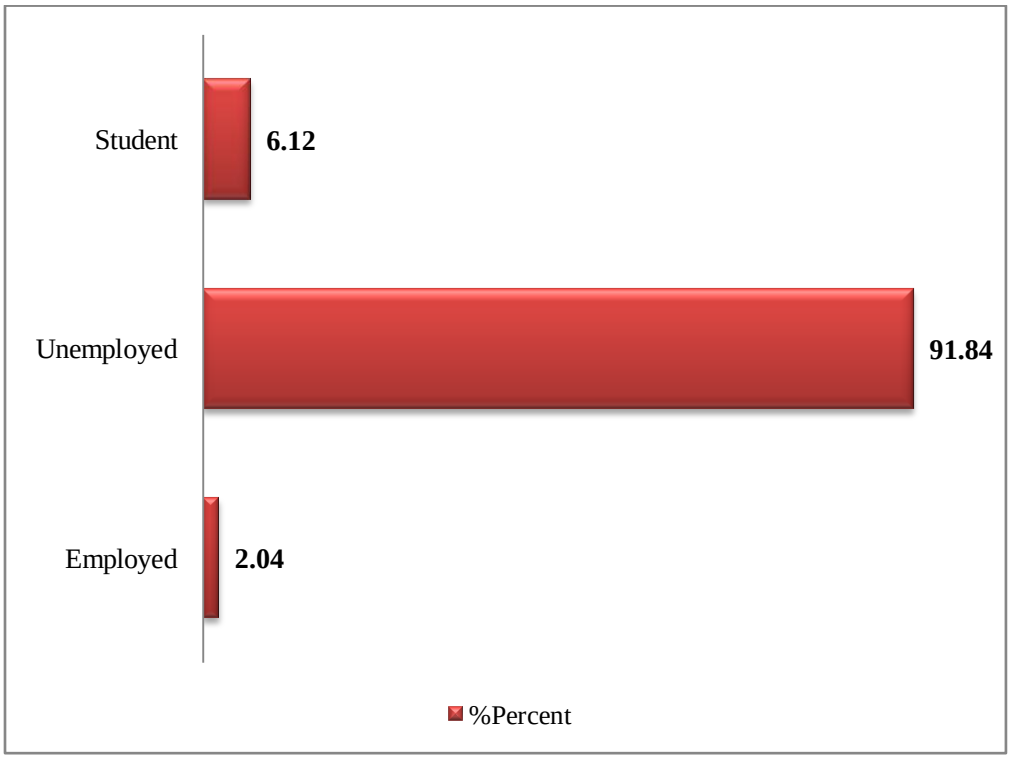

Figure 4.4 Occupational Status

Among all the patients with GDM surveyed, majority (91.84%) said that they were unemployed and only one patient was employed (2.04%).

4.5 Diabetes in Past Pregnancy (N=49)

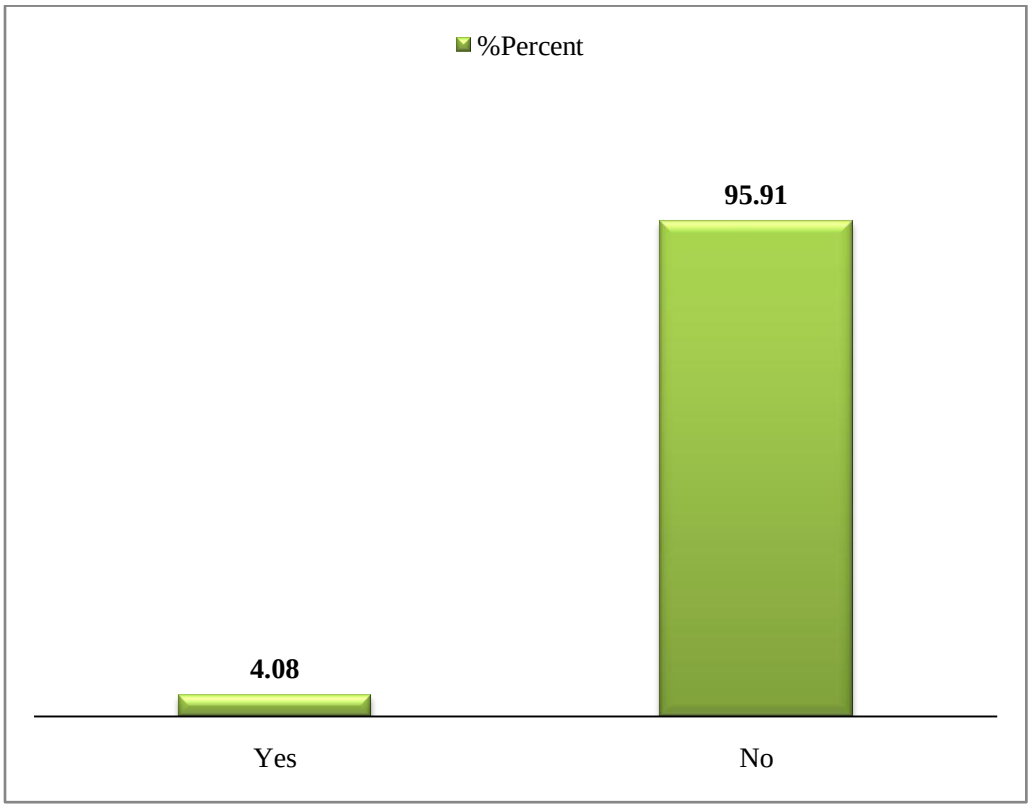

Figure 4.5 Diabetes in Past Pregnancy

The above figure shows that whether the 49 respondents with Gestational Diabetes Mellitus (GDM), who were being surveyed, had had Diabetes in their past pregnancy. Most of them (95.91%) said they did not have Diabetes in their previous gestational period. However, only a few of them (4.08%) responded positively.

4.6 Family History (N=49)

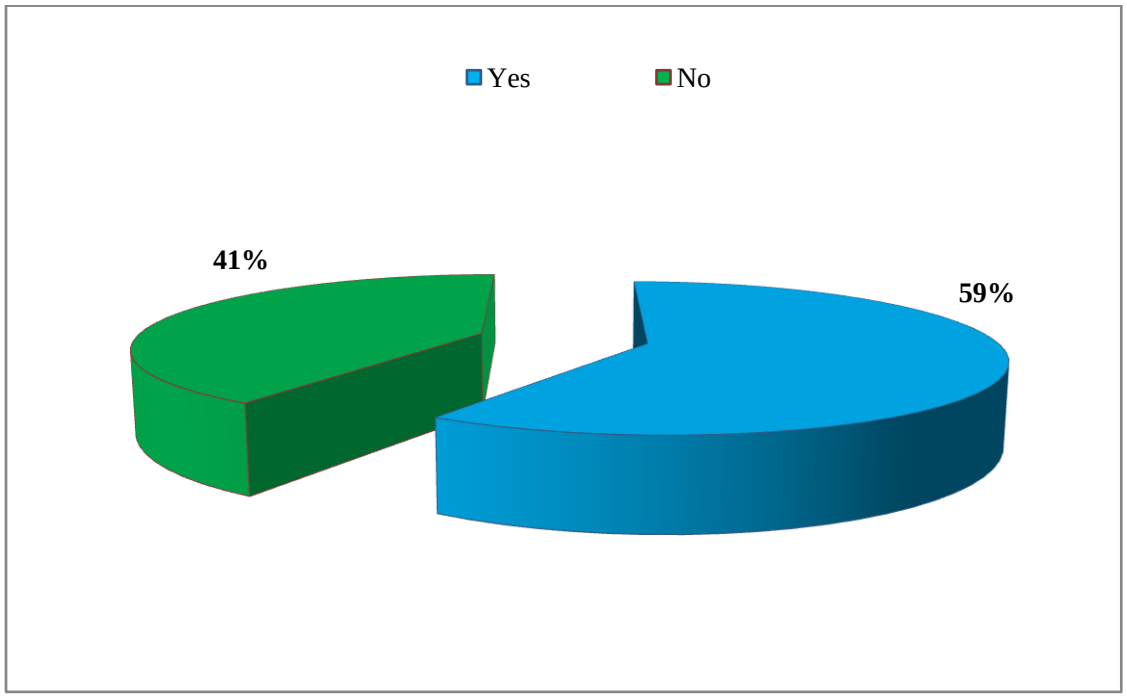

Figure 4.6 Family History of Diabetes

From the above figure it can be said that, most of the patients (59%) with GDM had one or more histories of Diabetes in their family. However, 29 (41%) of them responded negatively in this case.

4.7 Person with Diabetes in Family (N=29)

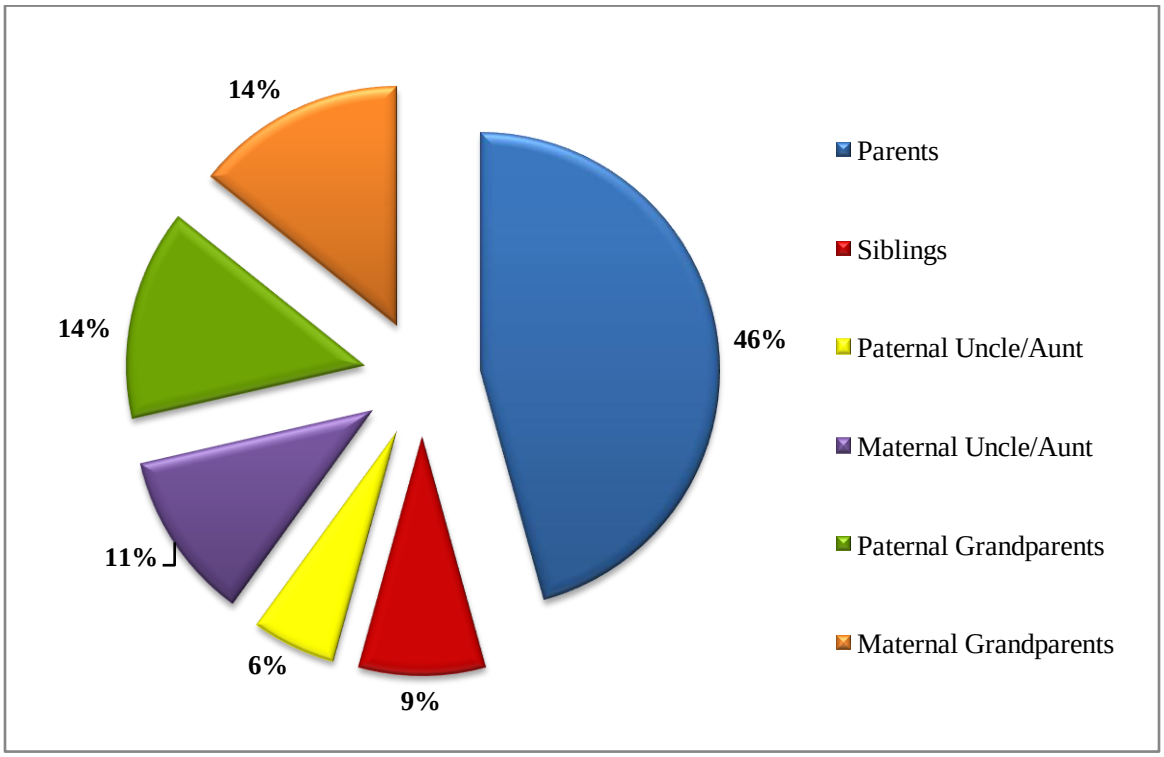

Figure 4.7 Person with Diabetes in family

The figure above shows the percentage of people with Diabetes who were related as family to the patients of this study. It is clearly understood that most of the respondents' (46%) parents had Diabetes. Other family members also had Diabetes but the least were reported to be the patients' paternal relations (Uncle/Aunt).

4.8 Diabetes Education (N=49)

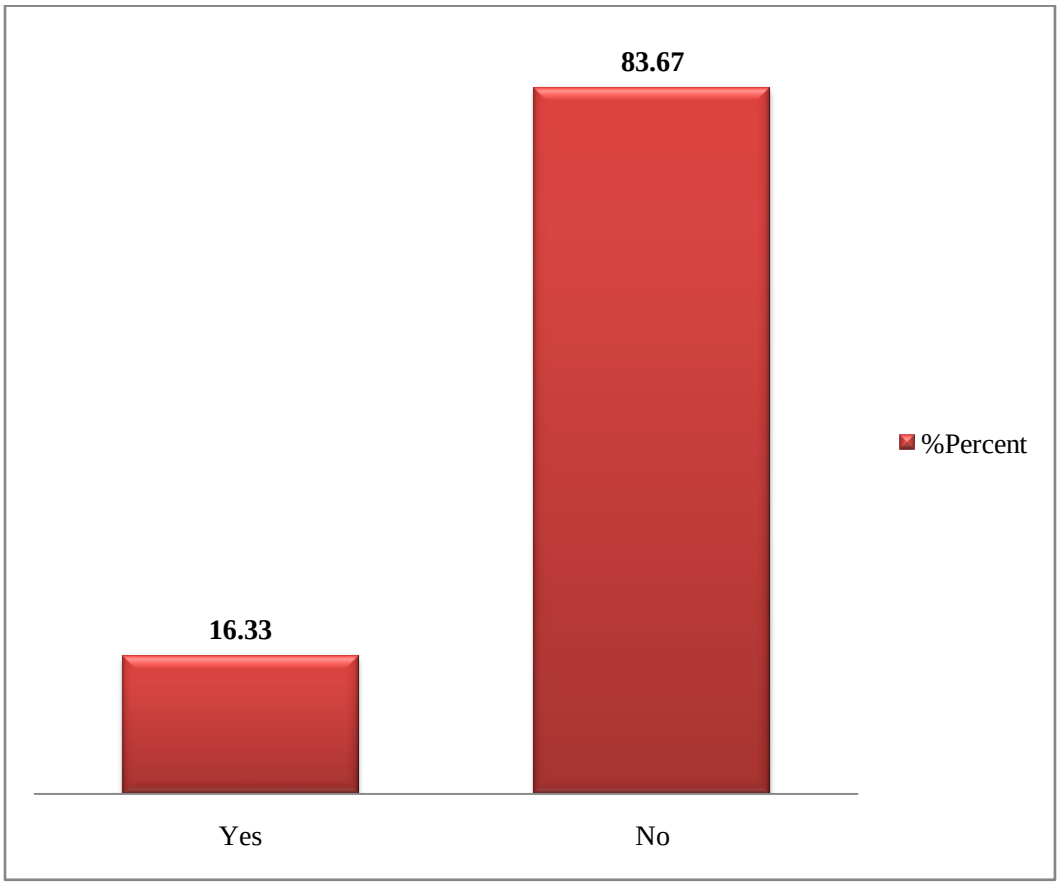

Figure 4.8 Diabetes Education

In this study, a total of 49 patients were found to have Gestational Diabetes Mellitus (GDM) and when they were asked whether they have had any education regarding GDM in the past, most of them (83.67%) answered negatively and only 16.33% of the patients replied with a 'Yes'.

4.9 Suffering with Any Other Medical Problem Apart from GDM (N=49)

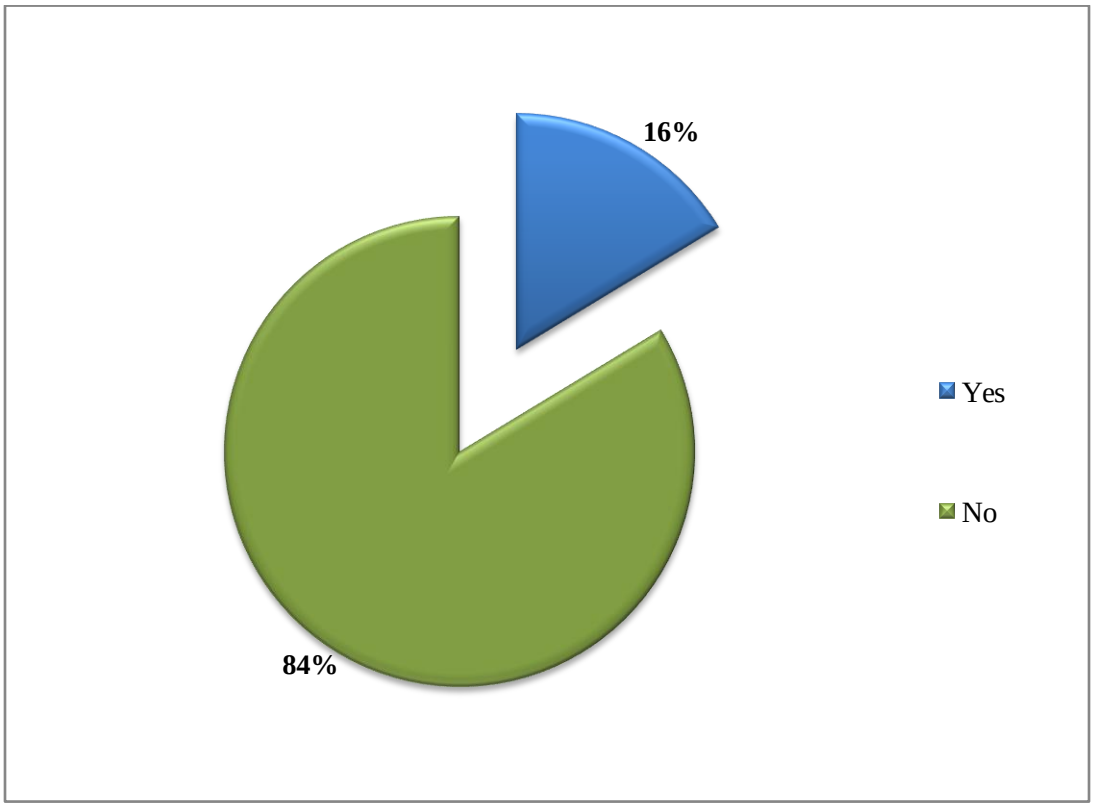

Figure 4.9 Suffering with any other medical problem apart from GDM

Out of 49 patients with GDM, 84% replied with a 'No' and confirmed that they were not suffering with any other medical problems apart from GDM. However, 16% of the respondents have said they were facing some difficulties which were not symptoms of GDM.

4.10 Types of Other Medical Problems Patients Suffered with (N=8)

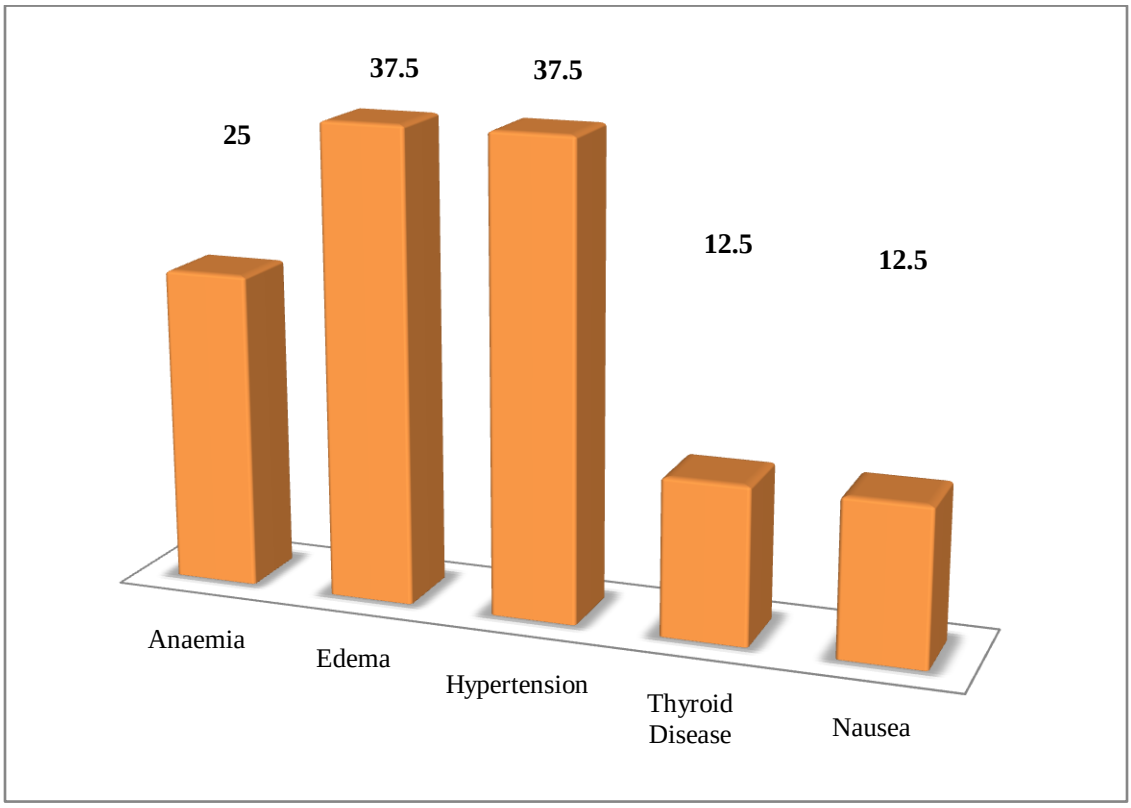

Figure 4.10 Types of other medical problems patients suffered with

Among 49 patients with GDM, 8 said that they were having some other medical problems apart from GDM during their pregnancy period. Among them 37.5% had Anaemia; 37.5% had Hypertension and the least amount of patients had Nausea and Thyroid Disesase.

4.11 Medications Prescribed (N=49)

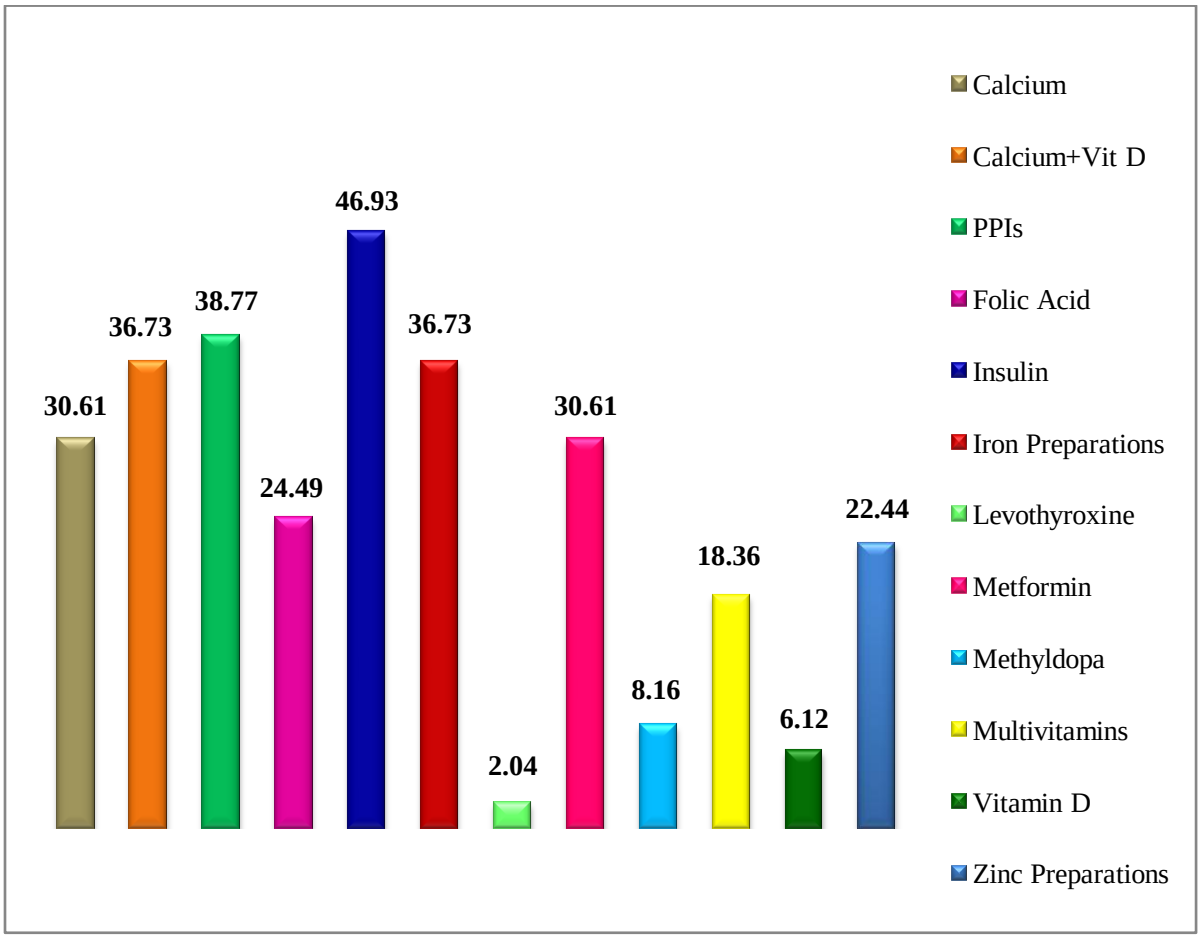

Figure 4.11 Medications prescribed

In patients with GDM, numerous drugs are prescribed according to their physiological requirements. And in this survey, majority (46.93%) of the patients was prescribed to take Insulin by their physicians. The patients also took Calcium (30.61), Iron (36.73%), Zinc preparations (22.44%), Multivitamins (18.36%) and Vitamin D preparations (6.12%) for fetuses' overall growth purpose. And few (2.04%) were asked to take Levothyroxine for their Thyroid disease conditions and Methyldopa (8.16%) for Hypertension etc.

4.12 Pregnancy Period (N=49)

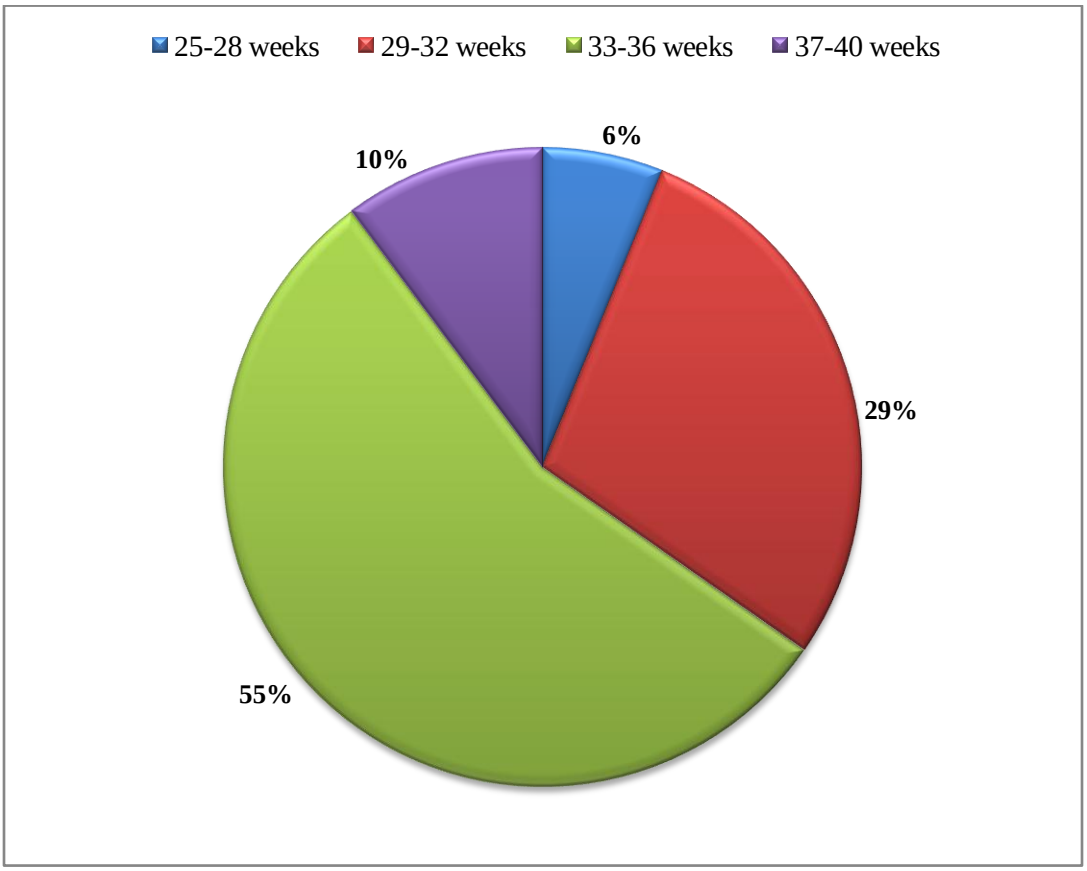

Figure 4.12 Pregnancy Period

In this study maximum patients (55%) with GDM were from the group of 33-36 weeks of gestational period. Very few (6%) were in their 25-28 weeks of pregnancy duration.

4.13 Twins/Triplets (N=49)

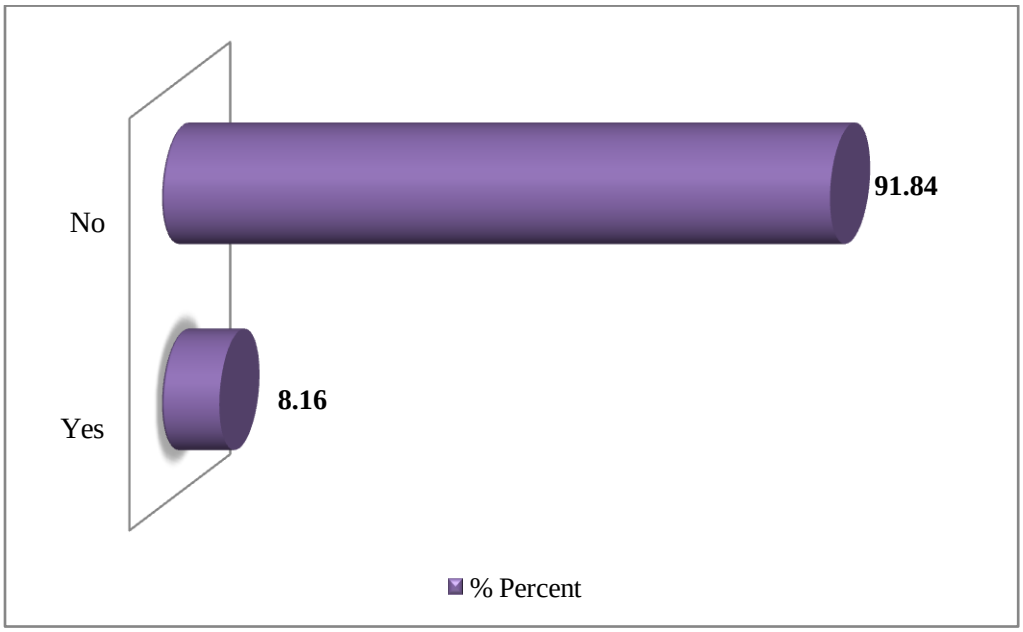

Figure 4.13 Twins/Triplets

The above figure refers to the percentage of patients with GDM who were about to have twins or triplets during the study period. Only 8.16% of the respondents stated that they were pregnant with twins.

4.14 Current No. of Children (N=49)

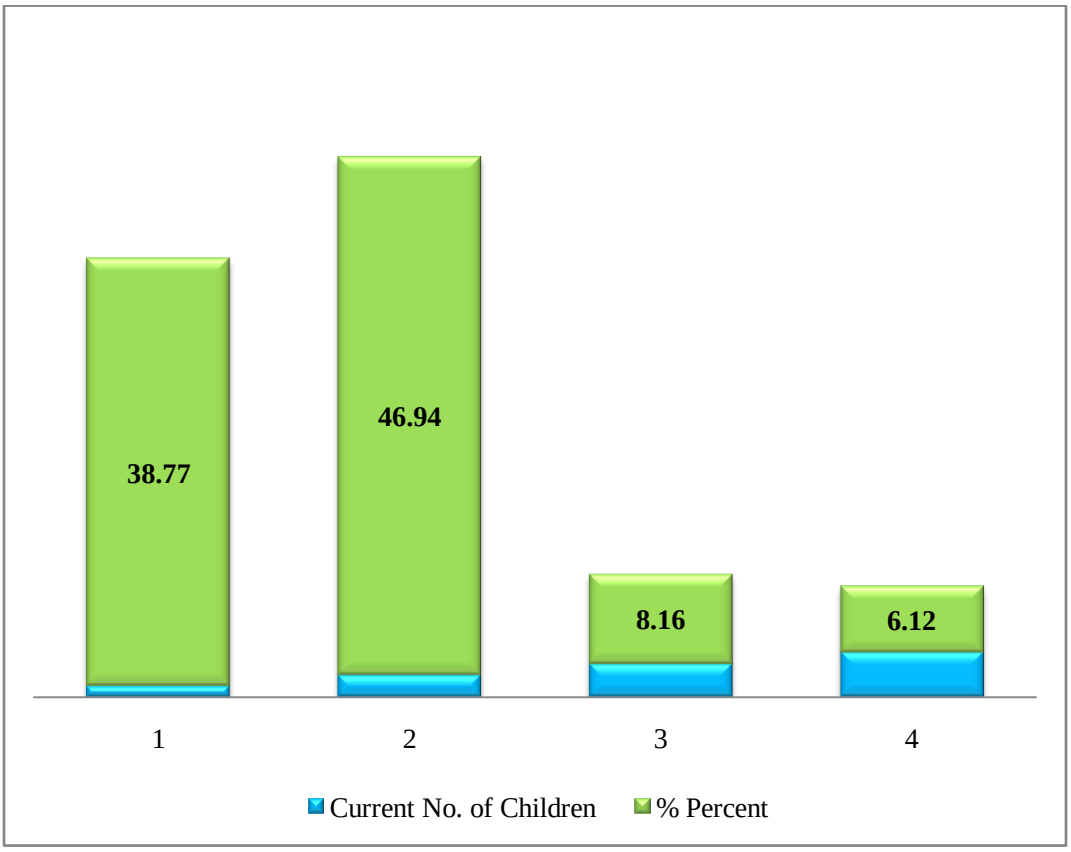

Figure 4.14 Current No. of Children

Among 49 patients who were being surveyed, 46.94% stated that they had already 2 children and only 6.12% said that they had 4 children at the time of the study.

4.15 Children's Term Status (N=49)

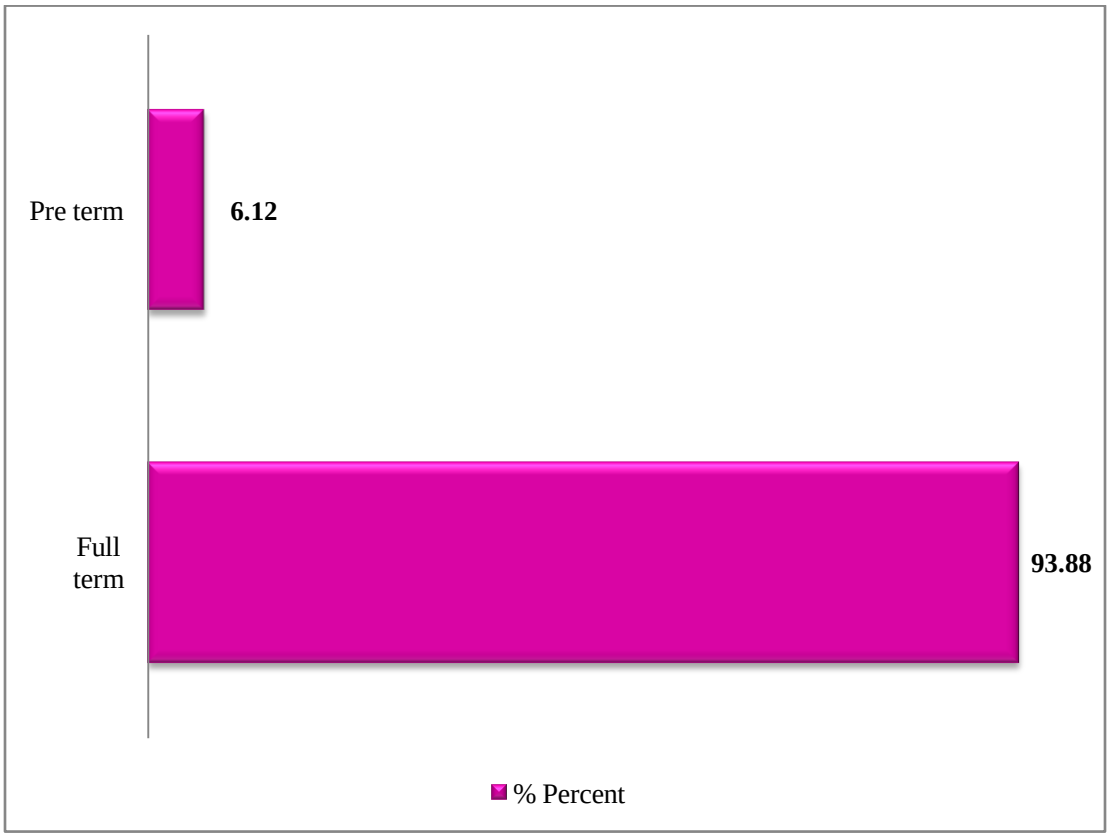

Figure 4.15 Children's Term Status

From the figure above, it is clearly understood that 93.88% of the patients with GDM had full term delivery. Only a few (6.12%) had preterm babies.

4.16 Age of First Pregnancy (N=49)

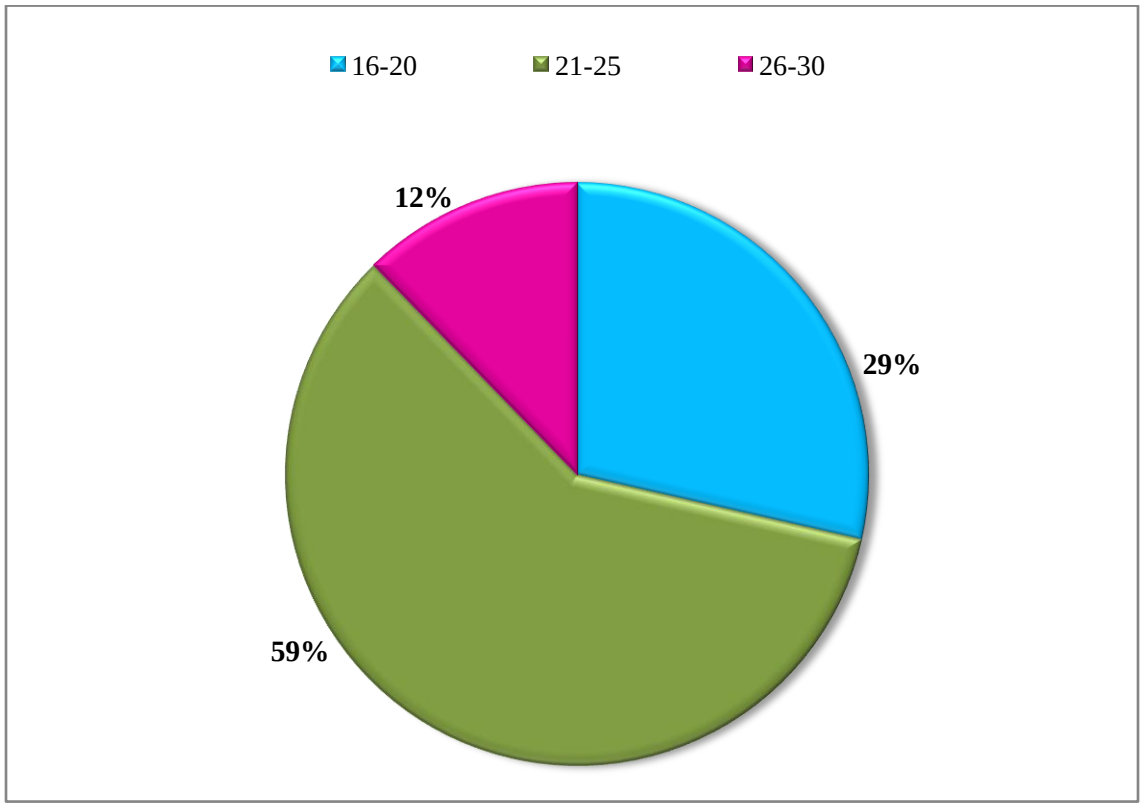

Figure 4.16 Age of First Pregnancy

The pie-chart above depicts that 59% of the patients with GDM have had their first baby when they were in their early 20s (21-25years). Only 12% of them had delayed conception at their late 20s to early 30s (26-30years).

4.17 Complications in Past Delivery (N=49)

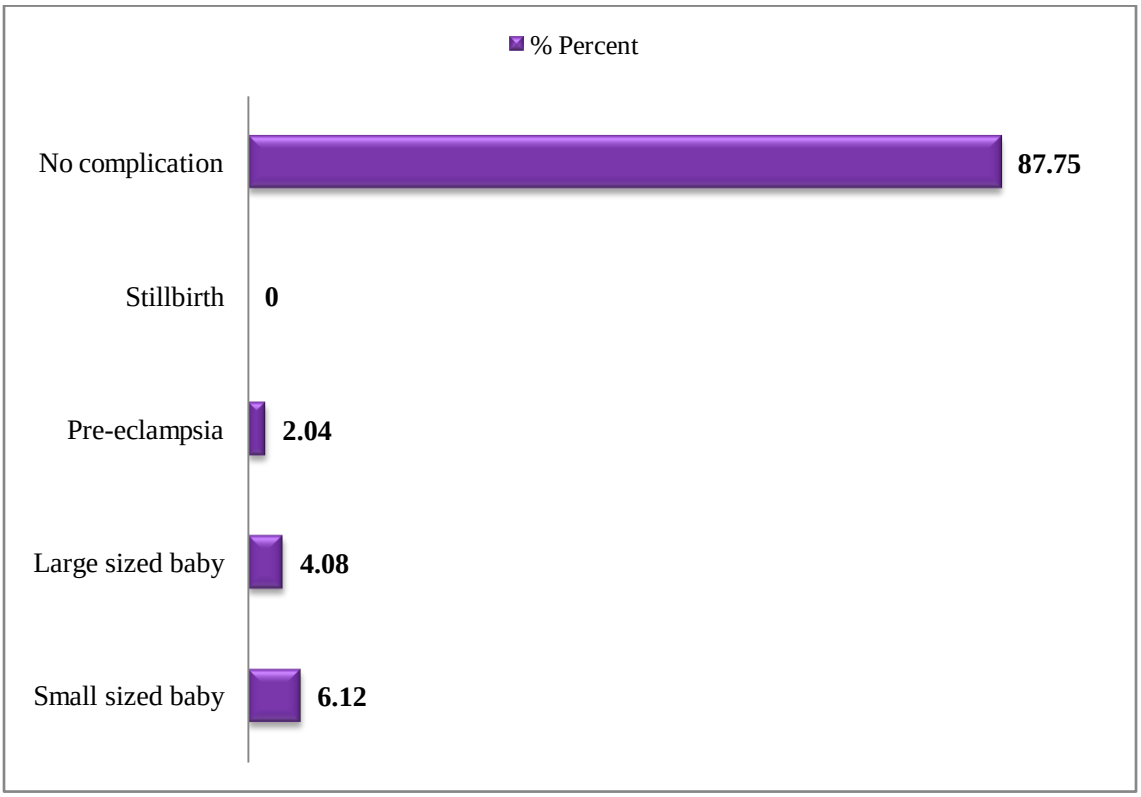

Figure 4.17 Complications in Past Delivery

The figure above shows the percentage of different complications the patients had in their prior pregnancy (s). Majority (87.75%) of them had no complications. But there were few who suffered with Pre-eclampsia (2.04%) and had babies of larger sized (4.08%) than usual.

4.18 GDM in the Past (N=49)

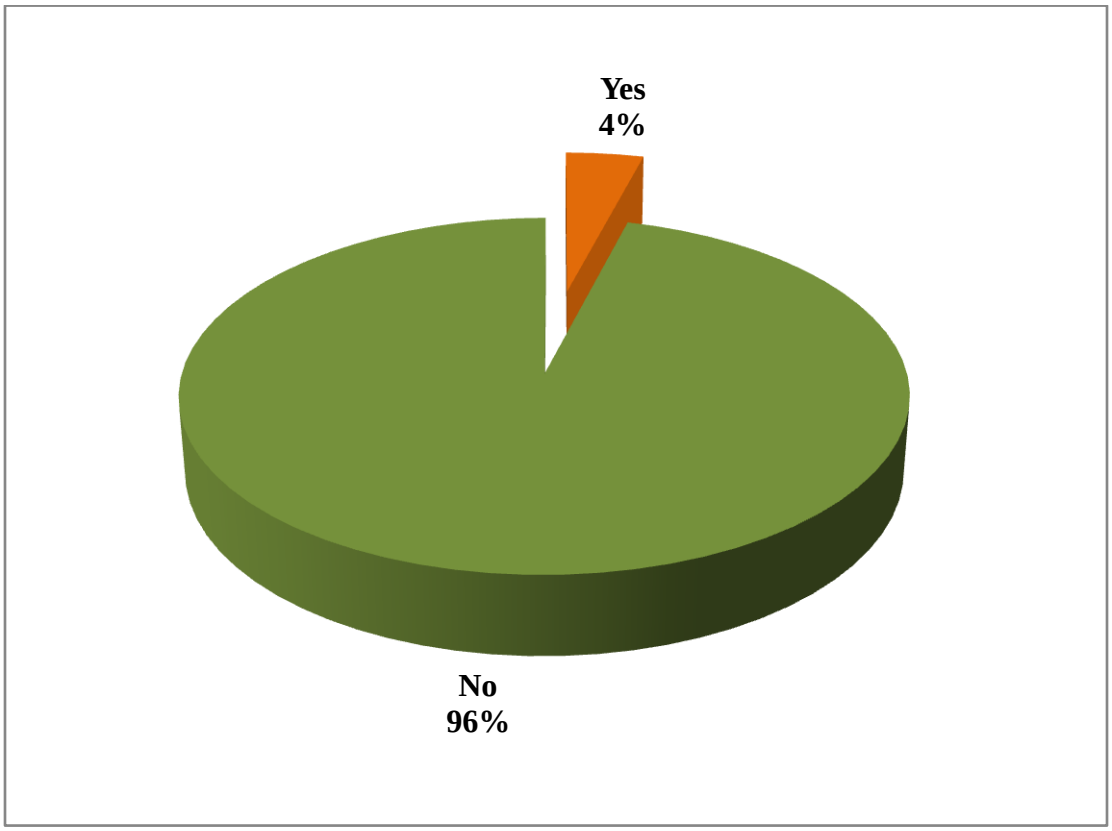

Figure 4.18 GDM in the past

Among 49 patients with GDM, 96% stated that they did not have GDM in their past pregnancies. Only a few (4%) said that they had GDM in their past.

4.19 Treatment in the Past GDM (N=2)

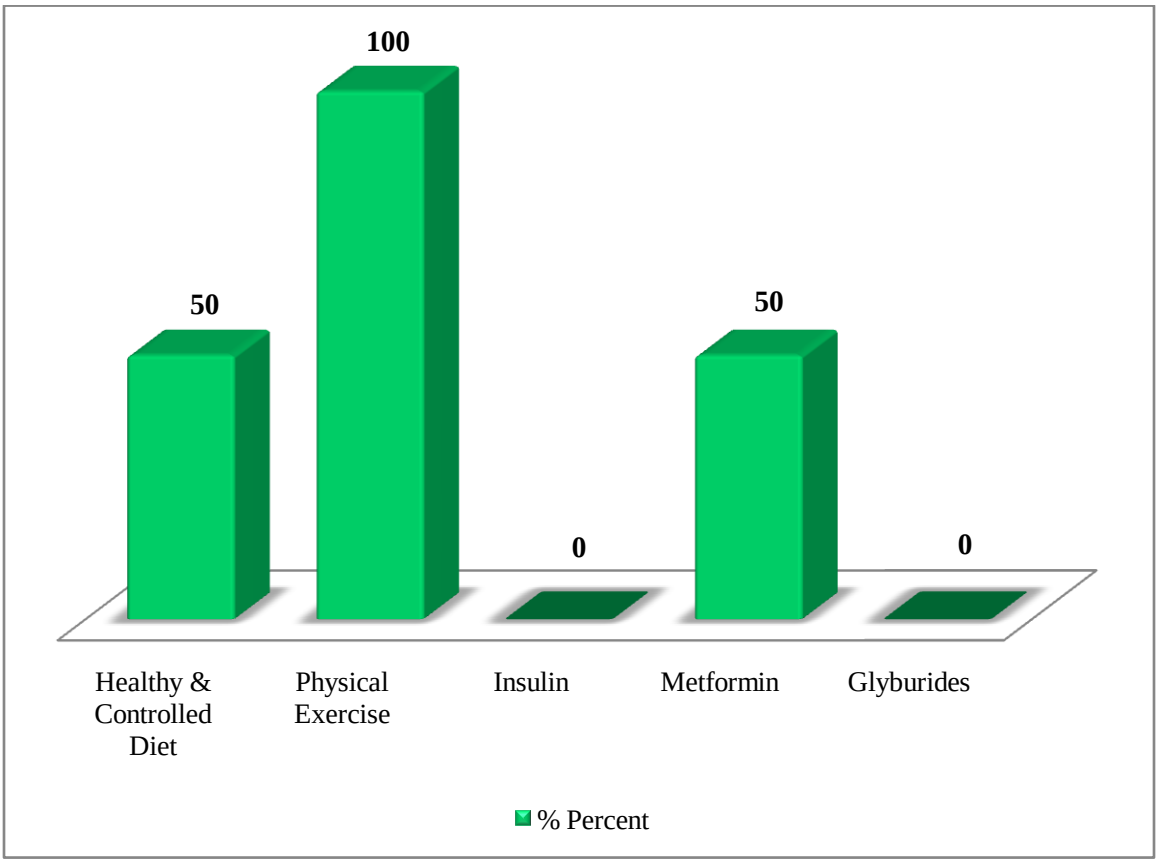

Figure 4.19 Treatment of GDM in patients with past GDM history

Out of 49 patients, only 2 (4.08%) said that they had previous history of GDM and both of them (100%) were treated with physical exercise. 50% of the patients were treated with Healthy & Controlled Diet and 50% with Metformin drugs.

4.20 Impact of GDM on Pregnancy/Neonate (N=49)

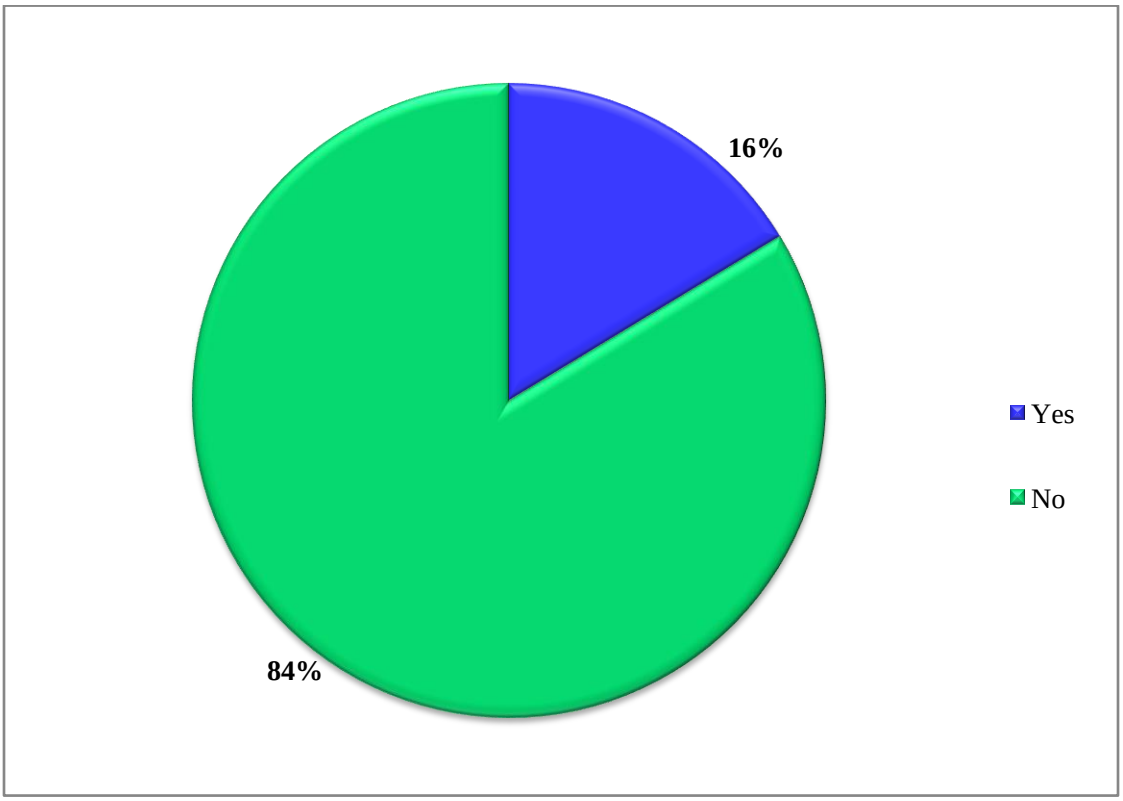

Figure 4.20 Impact of GDM on Pregnancy/Neonate

Among 49 patients with GDM surveyed, most of them (84%) said they know how Diabetes can affect the pregnancy or the neonate adversely. Although 16% of the patients stated that they had no clue in this regard.

4.21 Concerns about Having GDM (N=41)

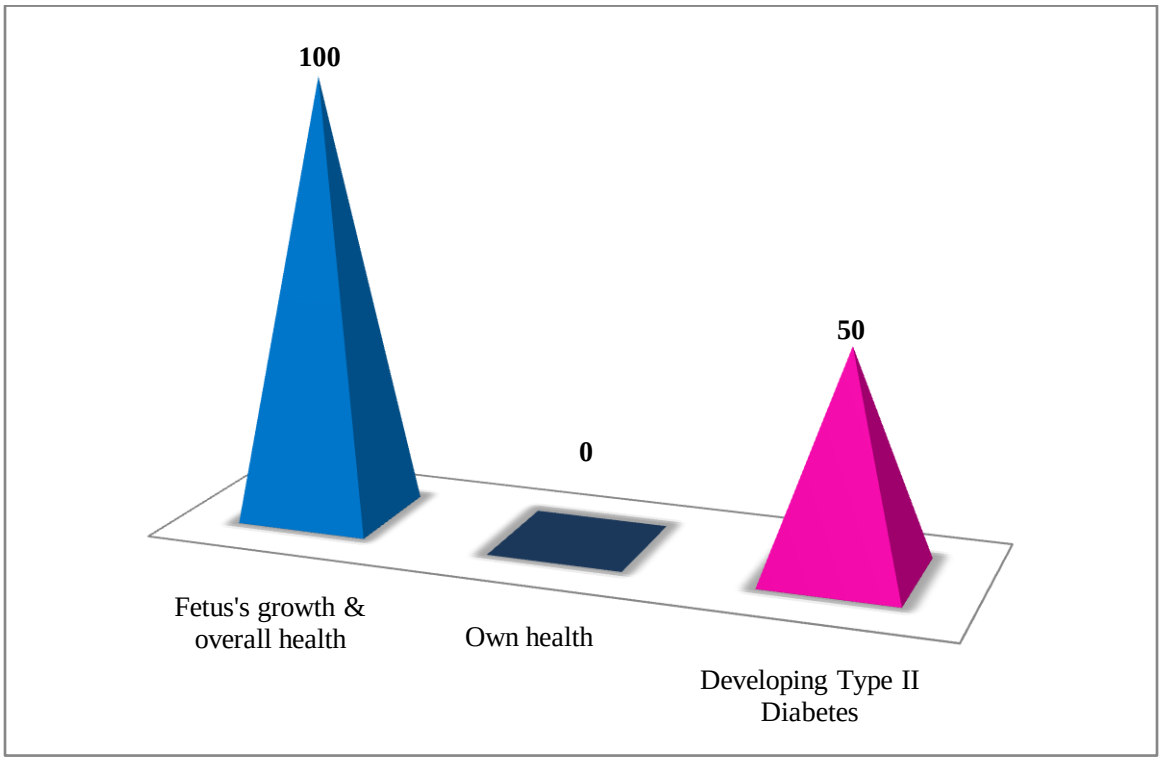

Figure 4.21 Concerns about having GDM

Out of 41 patients with GDM, who had at least a little idea about how Diabetes can affect the neonate, all of them said that they were mostly concerned about the fetus's growth and overall health. And half of them were concerned about their babies becoming Type II Diabetic. However, none of the patients were concerned about their own health at all.

4.22 Pregnancy Weight (Kg) (N=49)

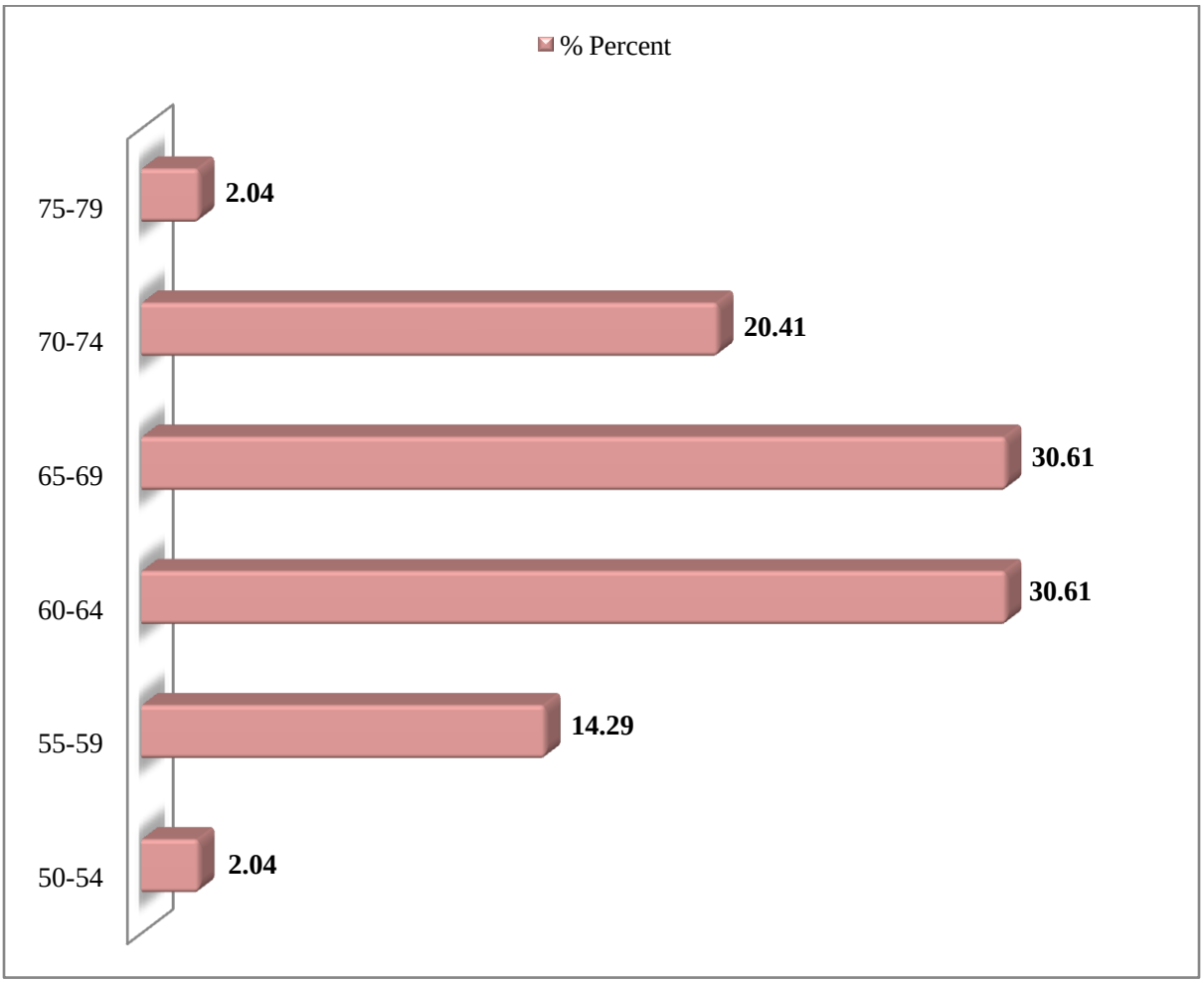

Figure 4.22 Pregnancy Weight (Kg)

Among all the 49 patients with GDM, majority of them (30.61%) had their weights ranging from 60-69 kg. While only few weighed between 50-54 kg range and between 75-70 kg range.

4.23 Pre-Pregnancy Weight (Kg)

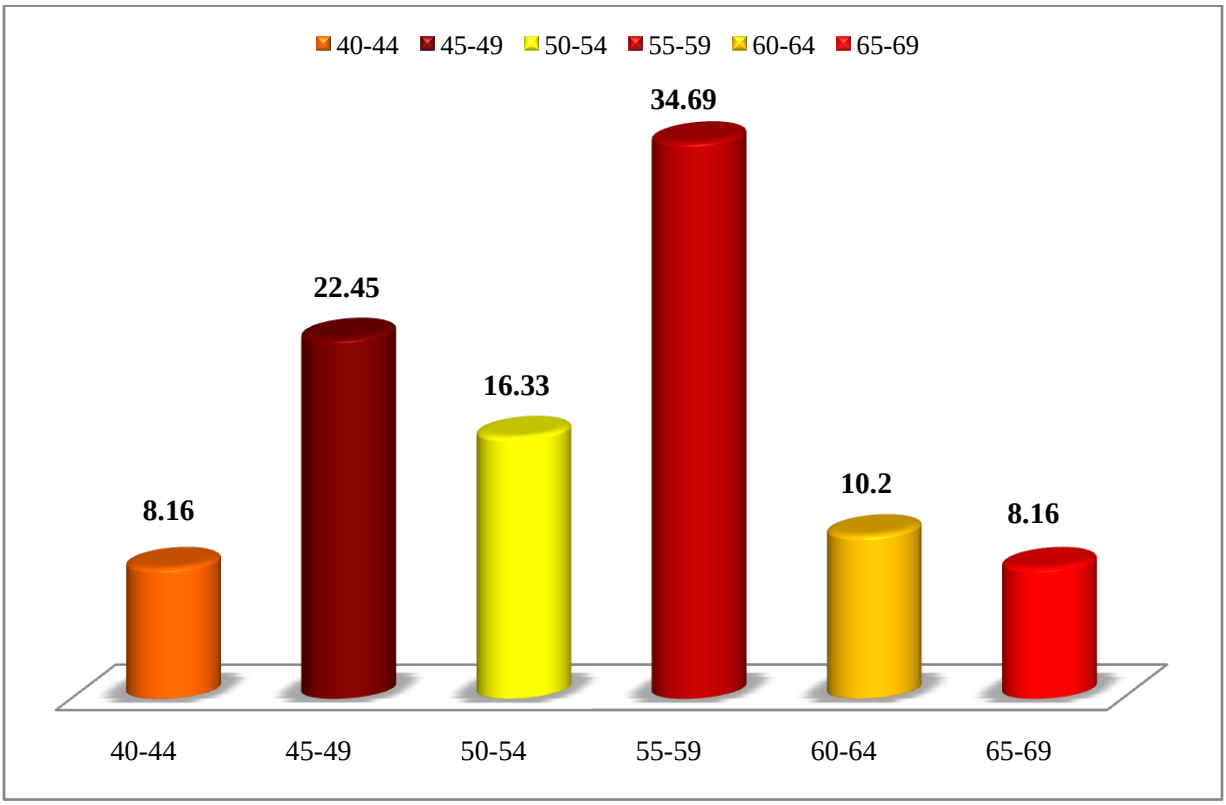

Figure 4.23 Pre-Pregnancy Weight (Kg)

Most of the patients who had GDM (34.69%) weighed around 55-59 Kg during their pre-pregnancy time. And only a few of the respondents (8.16%) were from the 40-44 Kg range and from 65-69 Kg range.

4.24 Frequency of Meal Intake (N=49)

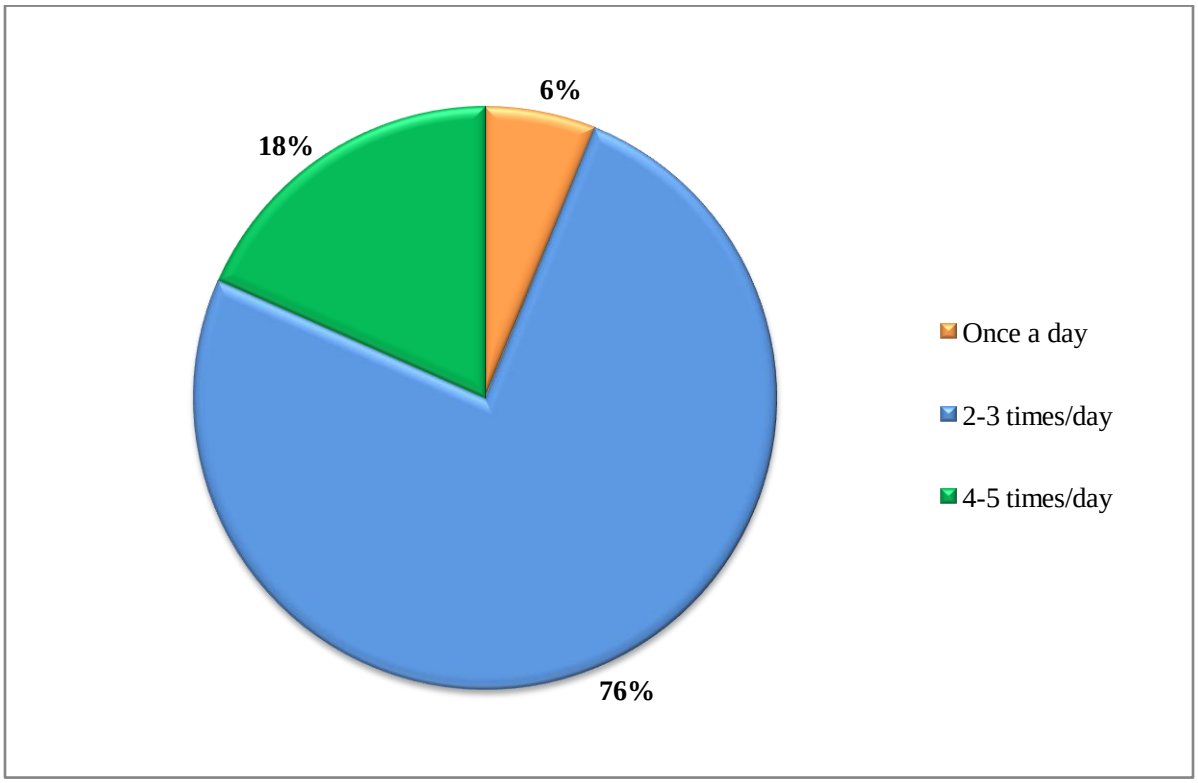

Figure 4.24 Frequency of Meal Intake

A total of 49 patients with GDM were asked that how frequent they take their meals and 76% of them responded with 2-3times/day. Which means majority of the patients were used to having different meals within 8-12 hours interval. Very few (6%) of the respondents said that, they used to eat their meal only once a day.

4.25 Physical Exercise (N=49)

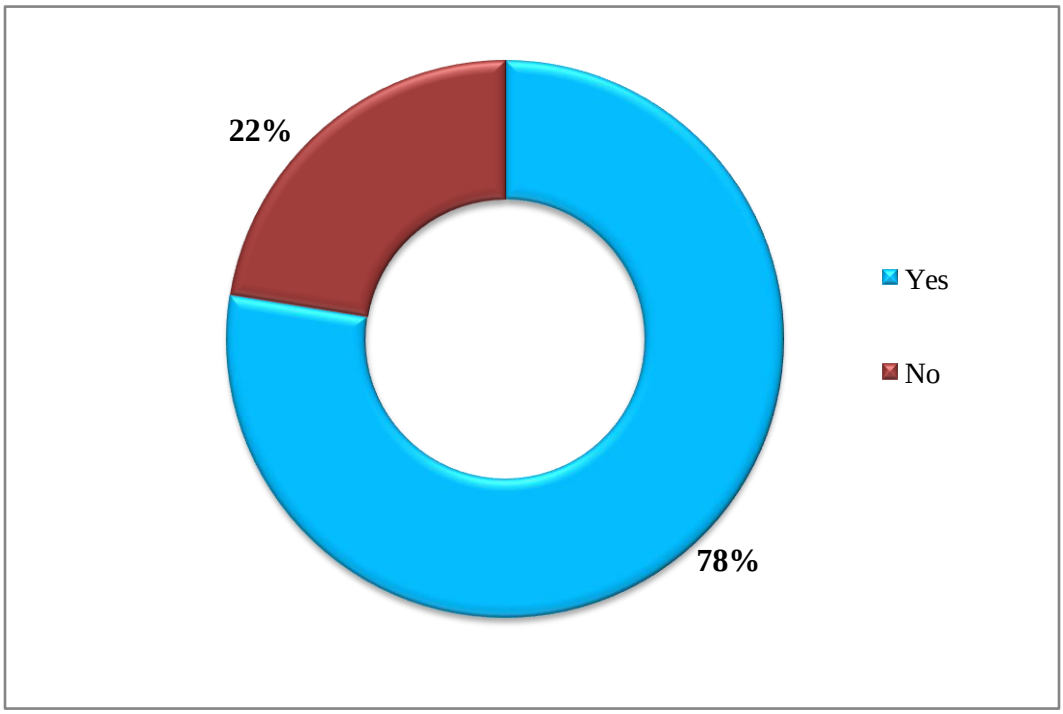

Figure 4.25 Physical Exercise

Out of all the patients with GDM being surveyed, 78% replied that they engaged themselves in physical exercise, when they were asked if they do any sort of physical exercise. However 22% of them responded negatively in this case.

4.26 Reasons for Not Doing Exercise (N=11)

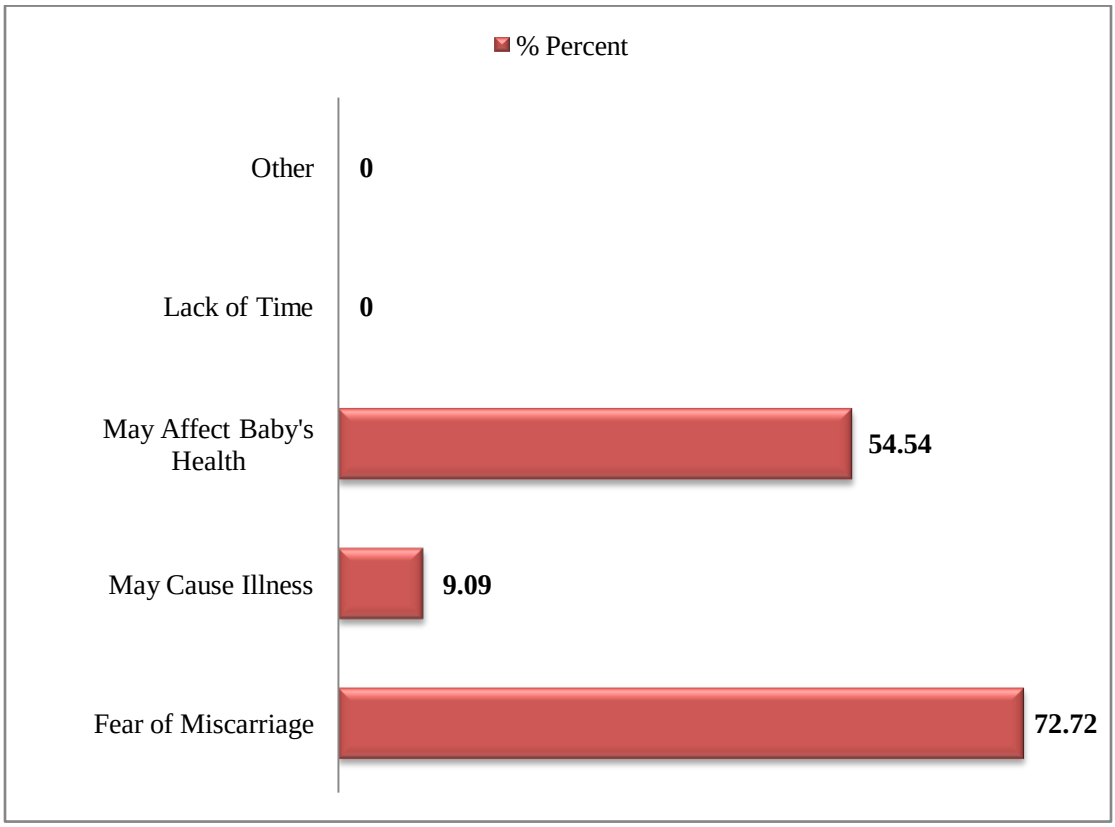

Figure 4.26 Reasons for Not Doing Exercise

Among 49 patients, 11 responded negatively when they were asked if they exercised or not. And of these 11 patients, 72.72% said they did not do any exercise because they feared to experience miscarriages. Another 54.54% said they were afraid of affecting their baby's health by doing exercise.

4.27 Patients' Physical Activity (N=49)

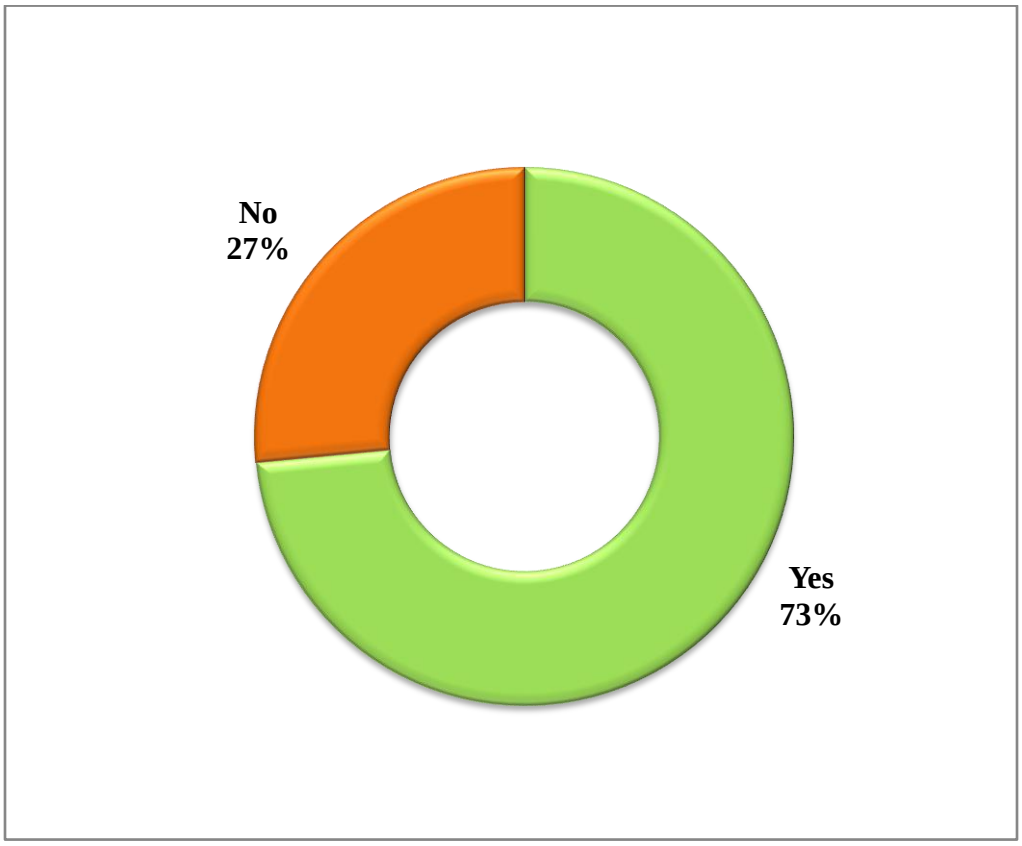

Figure 4.27 Patients' Physical Activity

All the 49 patients with GDM were asked if they thought themselves as physically active or not and most of them replied positively stating they thought they themselves active. But 13 (27%) of those patients responded negatively.

4.28 Why Physically Inactive (N=13)

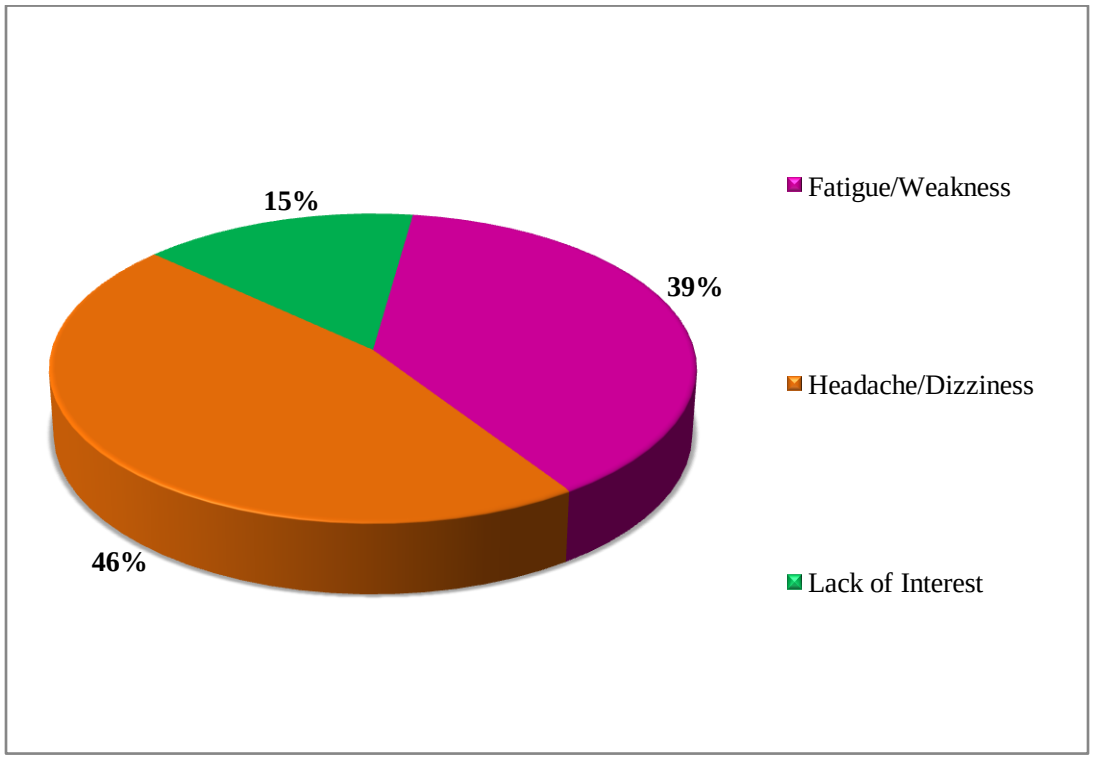

Figure 4.28 Why Physically Inactive

Among the 13 patients, most of them (46%) said they felt inactive because they often had Headache/Dizziness. Also their lack of interest (15%) in doing exercise makes them feel inactive.

4.29 Stress level (N=49)

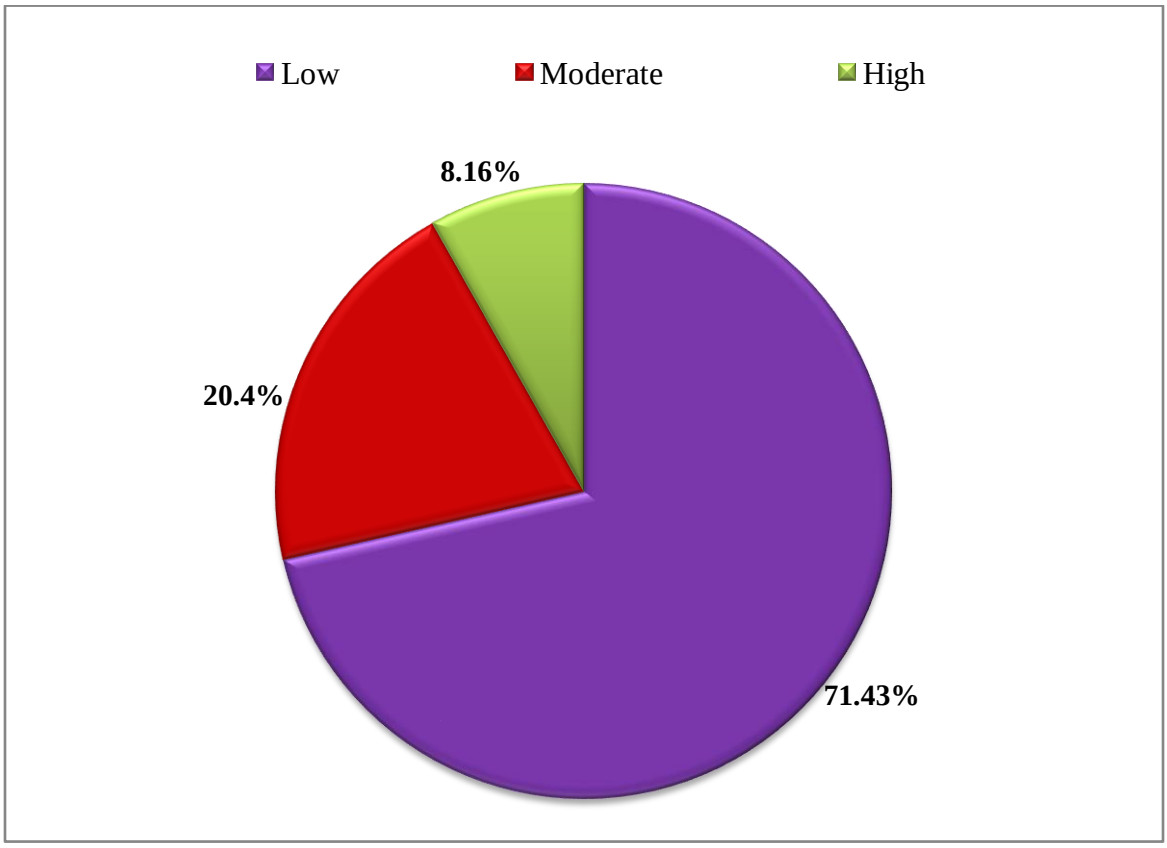

Figure 4.29 Level of stress among patients

All the 49 patients with GDM were asked whether their level of mental stress is low, moderate or high. And 71.43% among them replied to be of low stress level. Only 8.16% agreed that they were very stressful all the time.

4.30 Stress Handling (N=49)

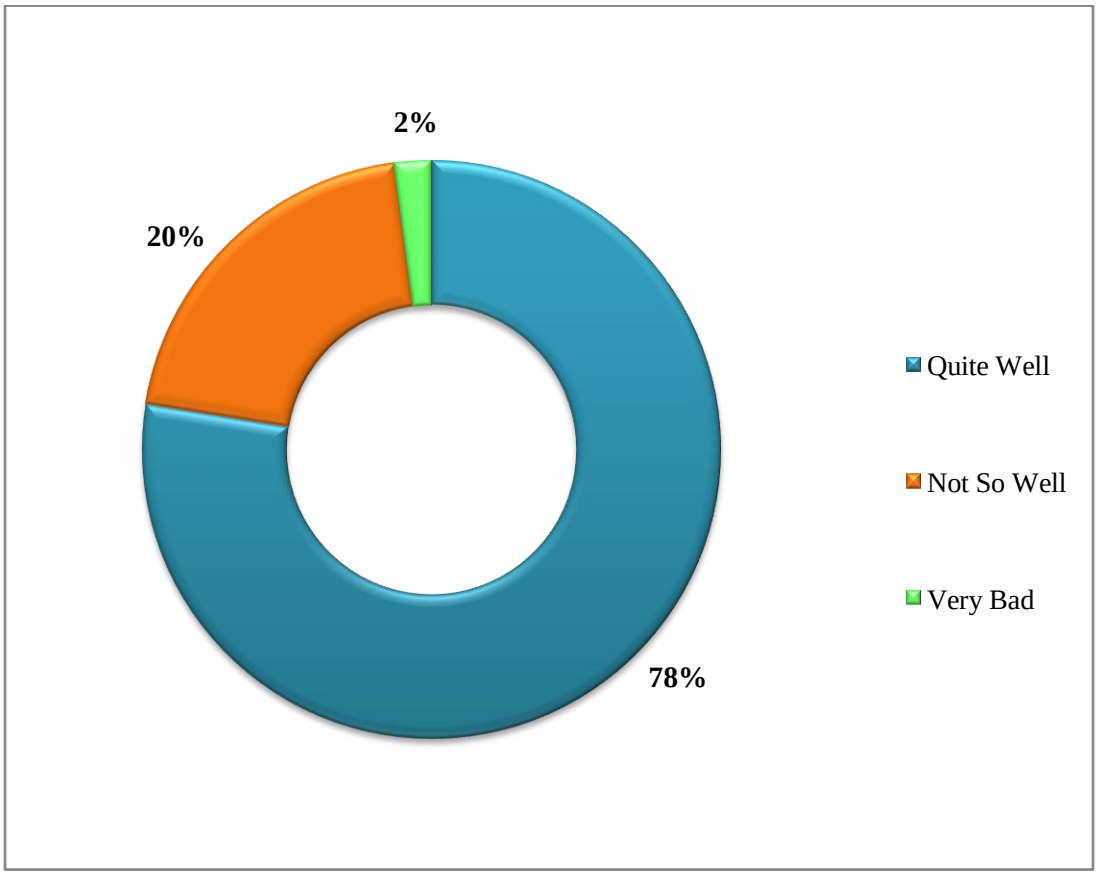

Figure 4.30 Stress Handling

Almost 78% of the 49 patients with GDM were very good at handling their stress. Only 2% of them were found to have very bad at stress handling.

4.31 Knowledge of GDM (N=49)

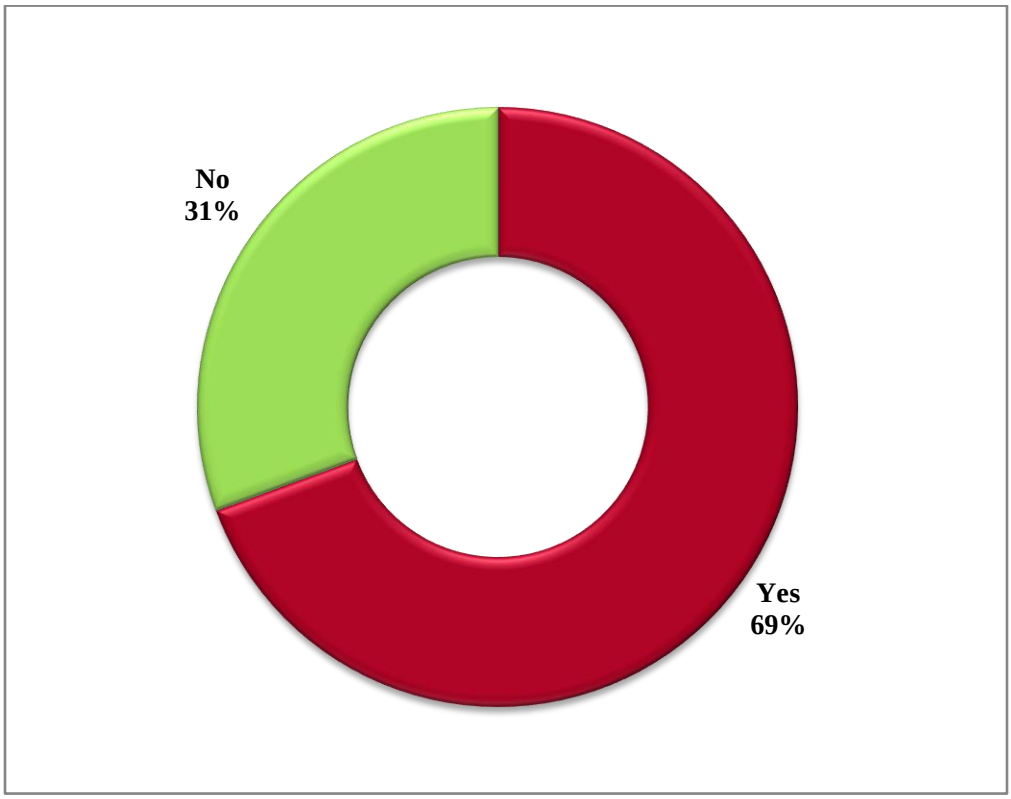

Figure 4.31 Knowledge of GDM

The figure above shows the percentages of patients with GDM regarding their knowledge about Gestational Diabetes Mellitus (GDM). Among 49 subjects, 69% positively replied and stated that they have at least some knowledge about Gestational Diabetes Mellitus (GDM). And 31% of them said that they had no specific idea about this.

4.32 Source of Knowledge about GDM (N=34)

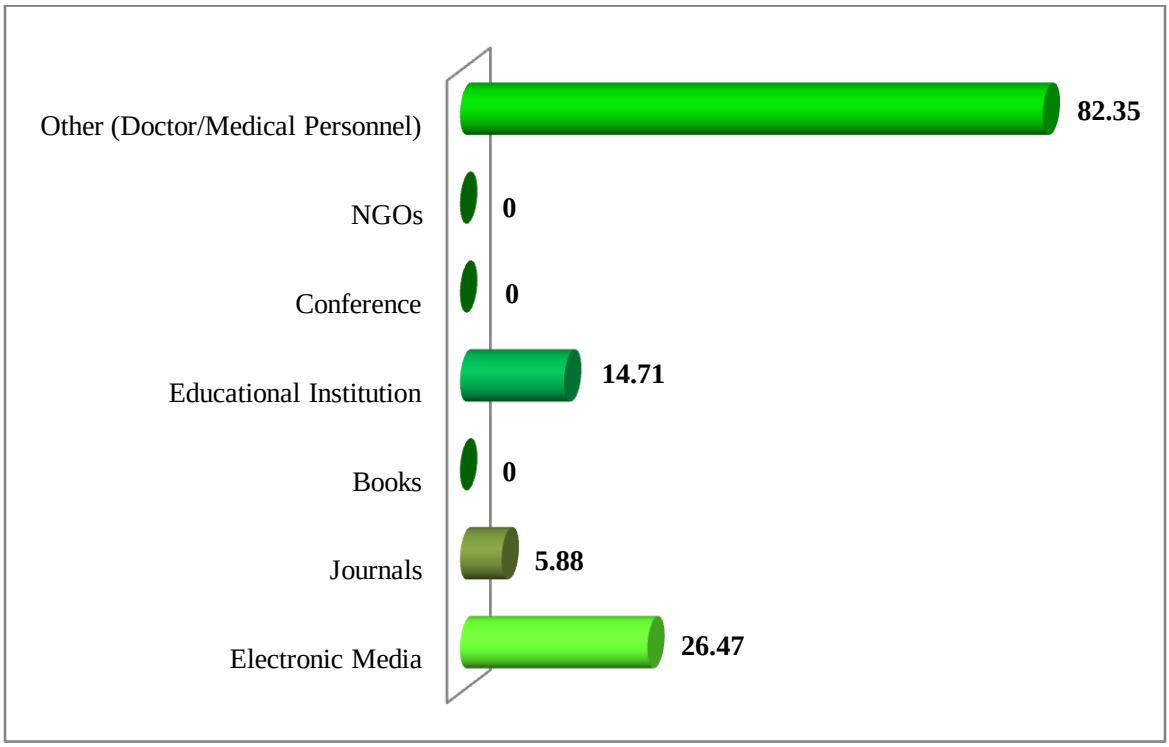

Figure 4.32 Source of Knowledge about GDM

From the above figure it can be said that majority of the patients (82.35%) who had at least a little knowledge about GDM, got to learn it from different Doctors or Medical Personnel. Some of them (26.47%) got the idea from various Electronic Media ore their Educational Institutions (14.71%). Very few patients (5.88%) learnt about GDM through reading different Journals.

4.33 Reasons Behind GDM (N=34)

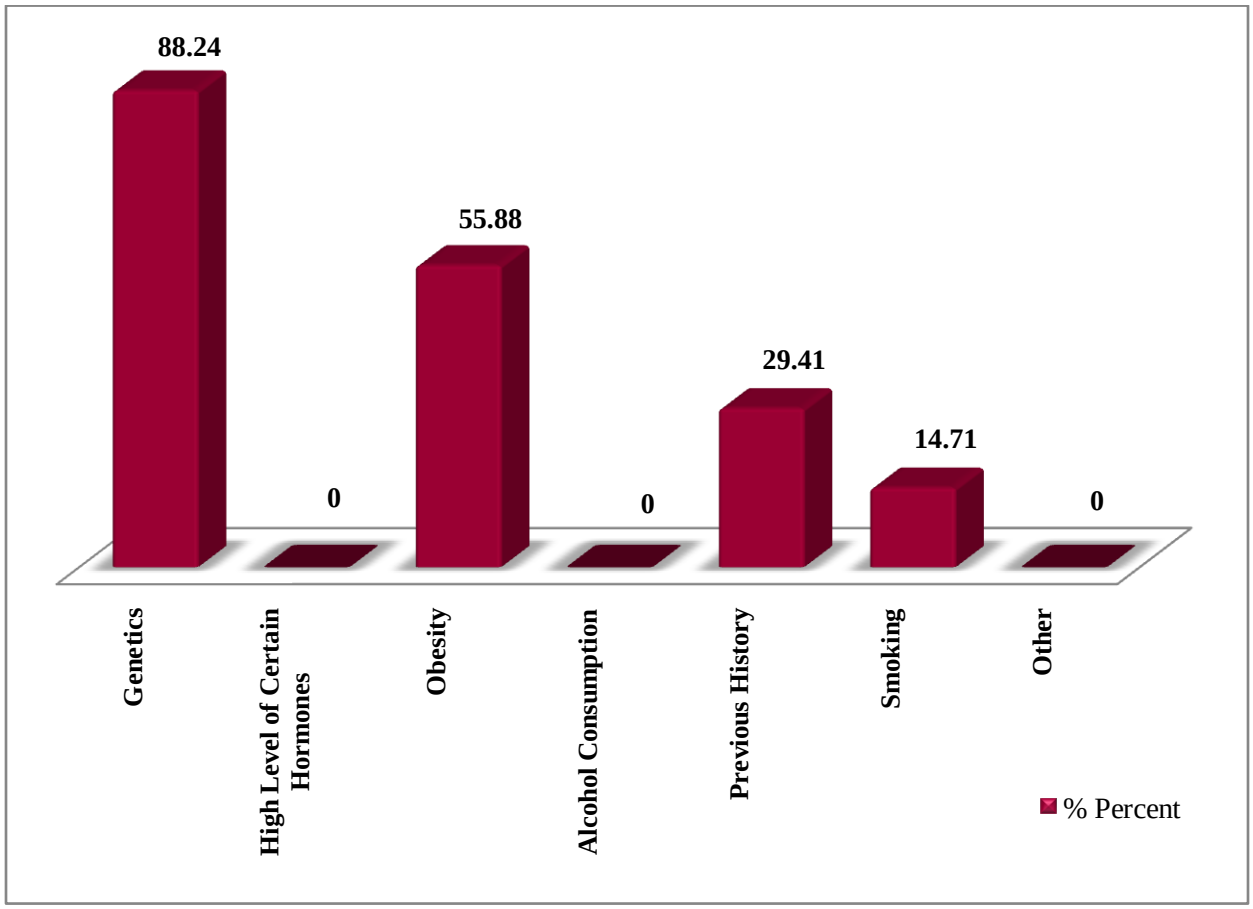

Figure 4.33 Reasons behind GDM

According to the knowledge of the patients regarding GDM, the most common reasons they thought were Genetics (88.24%) and Obesity (55.88%). Previous History of Diabetes (29.41%) or Smoking (14.71%) were also thought by some of the patients as reasons behind GDM.

4.34 Knowledge about GDM Treatment (N=34)

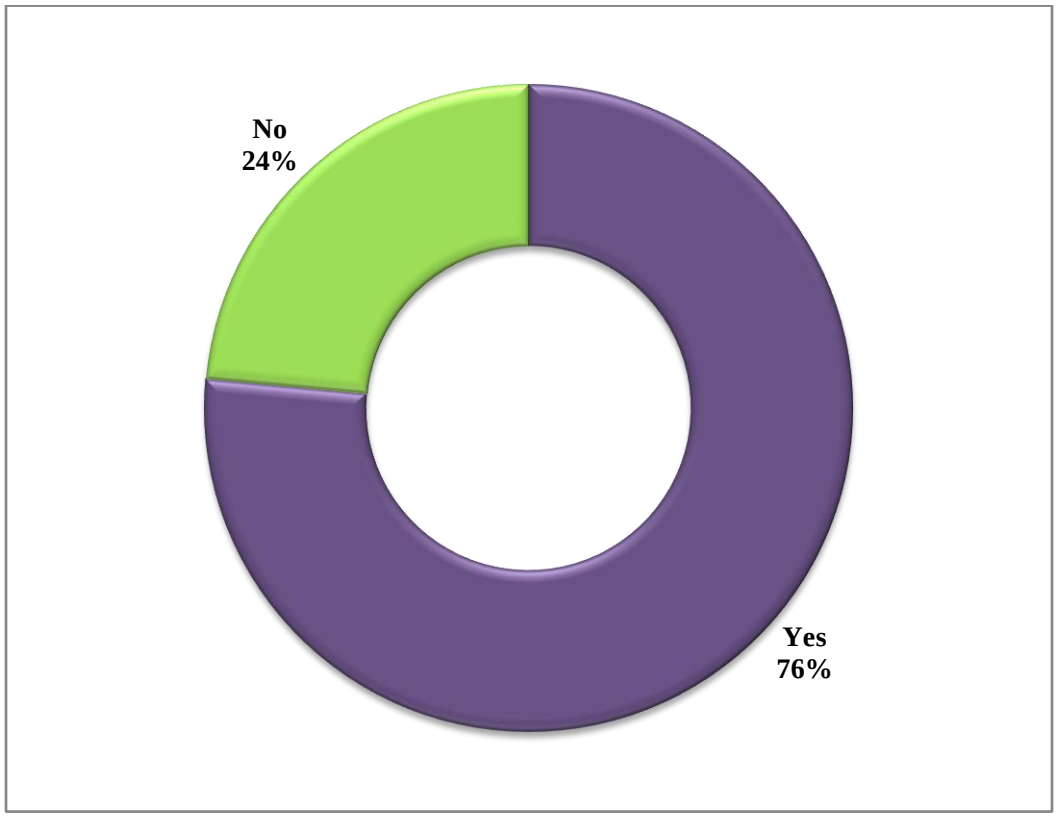

Figure 4.34 Knowledge about GDM Treatment

According to the patients' knowledge, 76% stated that they have the idea about how GDM is treated. But 24% of those patients replied with a negative comment.

4.35 Knowledge about Types of GDM Treatment (N=26)

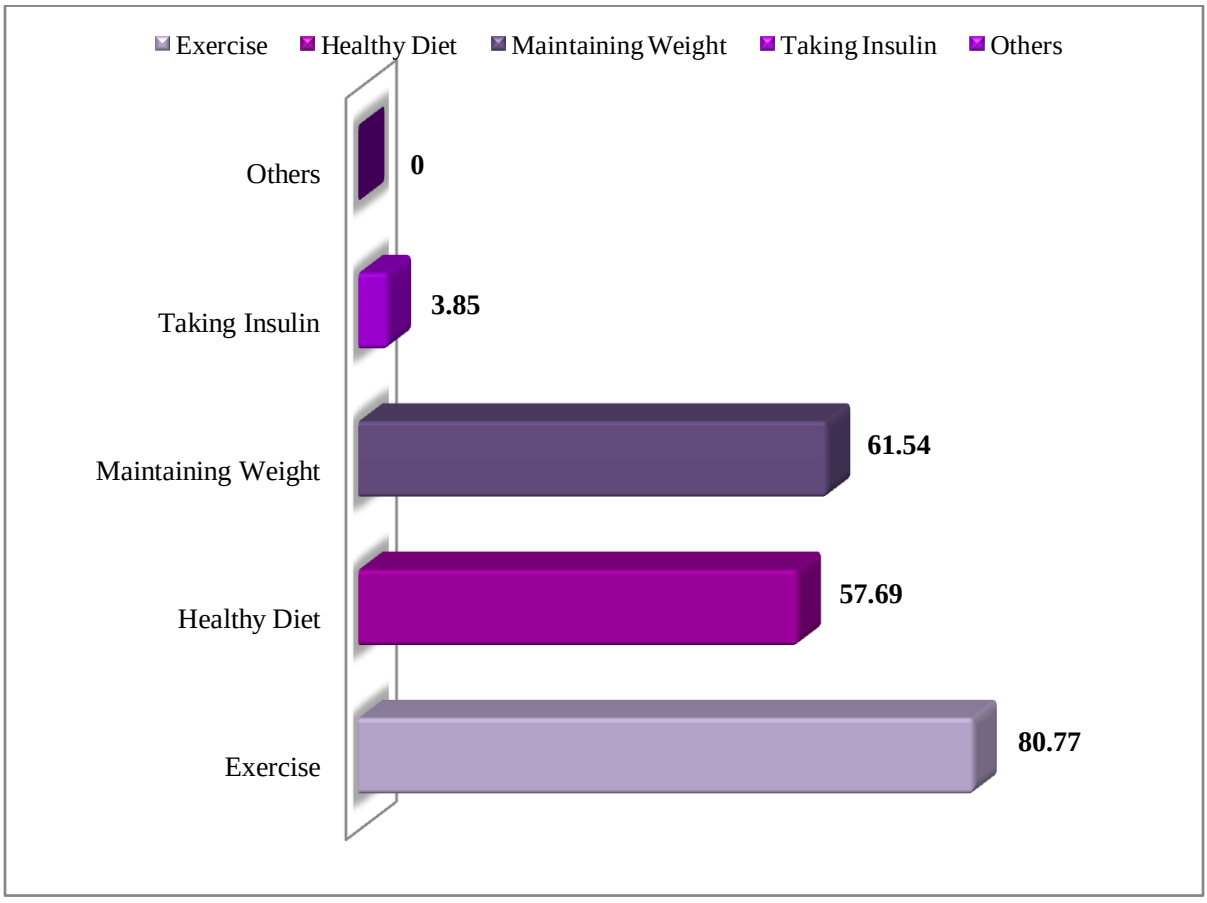

Figure 4.35 Knowledge about different types of GDM treatment

The figure above shows the percentages of patients' knowledge regarding the type of treatment GDM requires. Most of the patients (80.77%) thought doing Physical Exercise is one of the major tools in treating GDM. Maintaining body weight (61.54%) and Healthy Diet (57.69%) were also considered as treatment by some of the patients. However only 3.85% of the patients thought taking Insulin could treat GDM.

4.36 Knowledge about the Options for Diagnosing GDM (N=34)

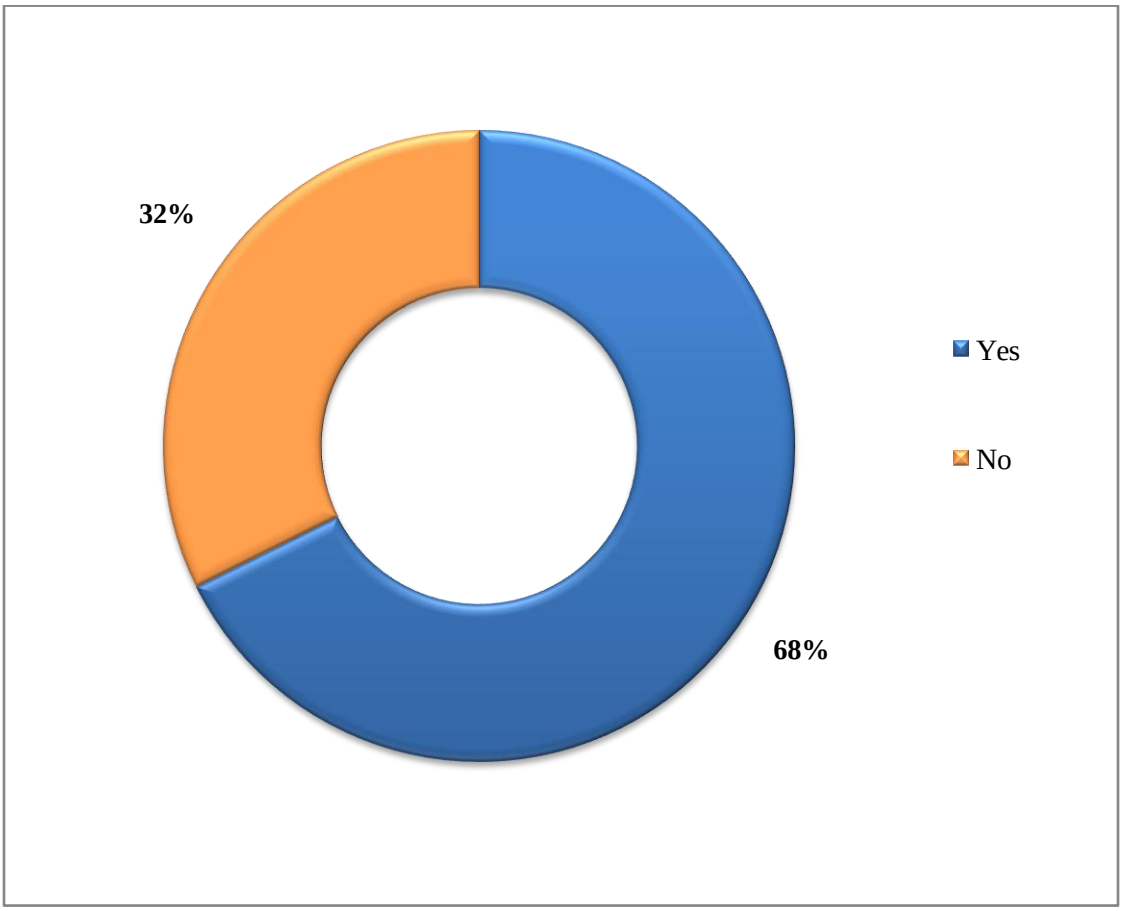

Figure 4.36 Knowledge about the options for diagnosing GDM

Among 34 patients, 23 (68%) stated that they have little knowledge about the diagnosis procedure for Gestational Diabetes Mellitus (GDM). However 11 of the respondents (32%) replied negatively in this regard.

4.37 Problem for Managing GDM (N=49)

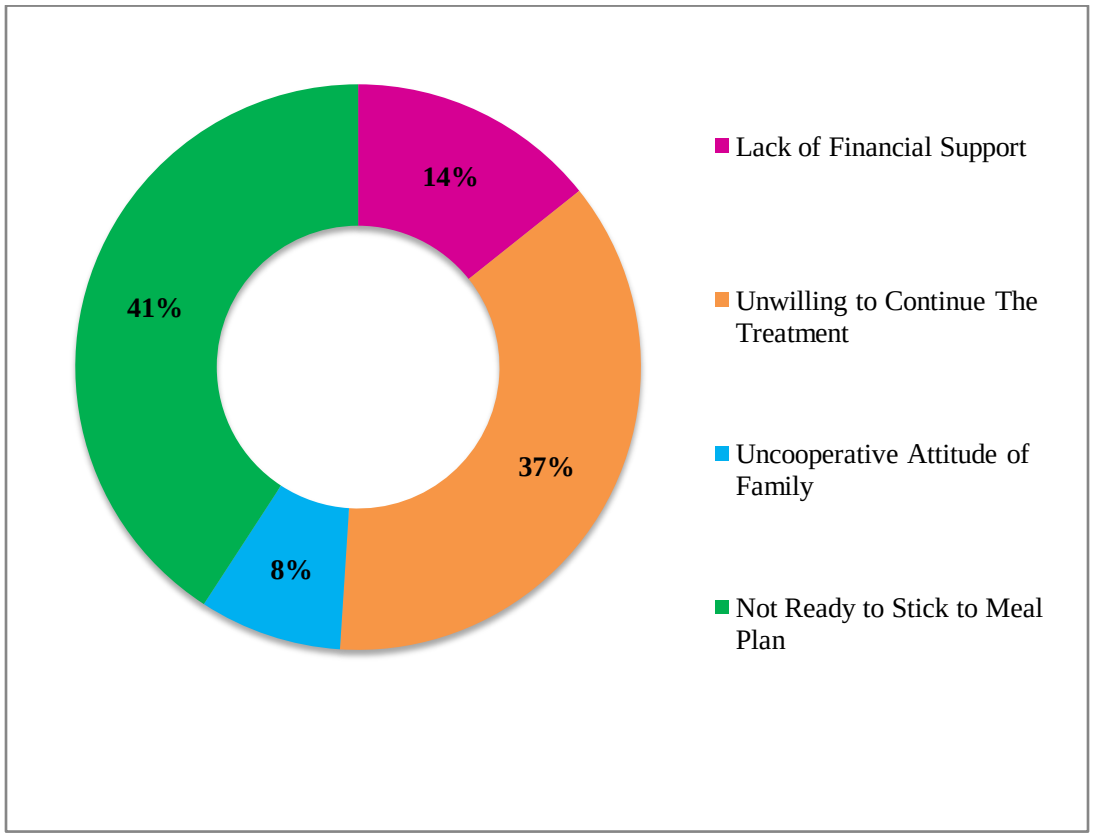

Figure 4.37 Problems for Managing GDM

From the above figure we can see that about 41% of the patients said that they had trouble in sticking to the meal plan, 37% were unwilling to continue the therapy, 14% stated that they faced financial difficulties during the management of GDM. On the other hand, there were few patients (8%) who said that they had to face various obstacles for their families' unsupportive attitude towards them.

4.38 Weight of the Neonate (N=49)

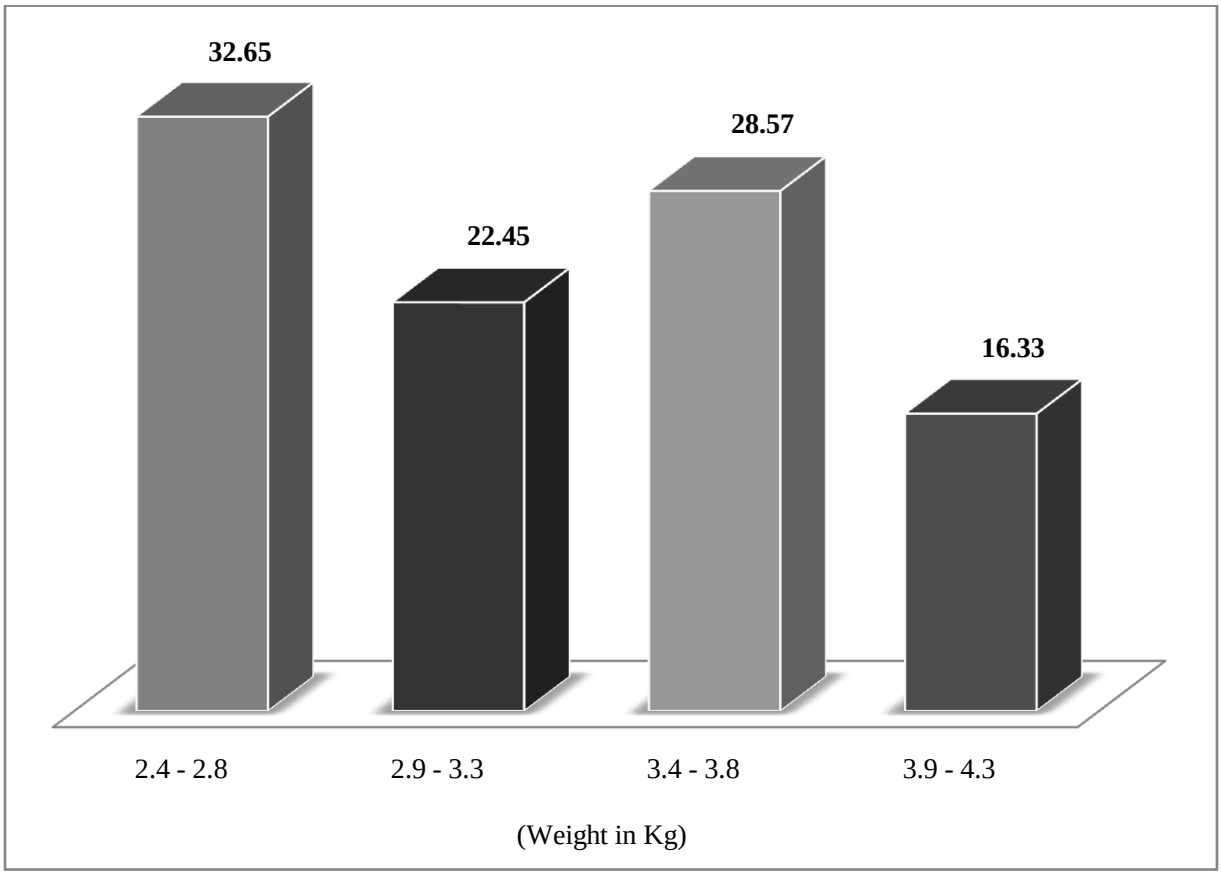

Figure 4.38 Weight of the Neonate (Kg)

From the above graphical presentation, the percentages of the weights of the neonates are observed. All the 49 patients with GDM were asked about their neonates' overall health condition after their delivery. And it was found that most of the neonates (32.65%) weighed between 2.4 to 2.8 Kg. Very few (16.33%) were in the 3.9-4.3 kg group.

4.39 Condition of the Neonate (N=49)

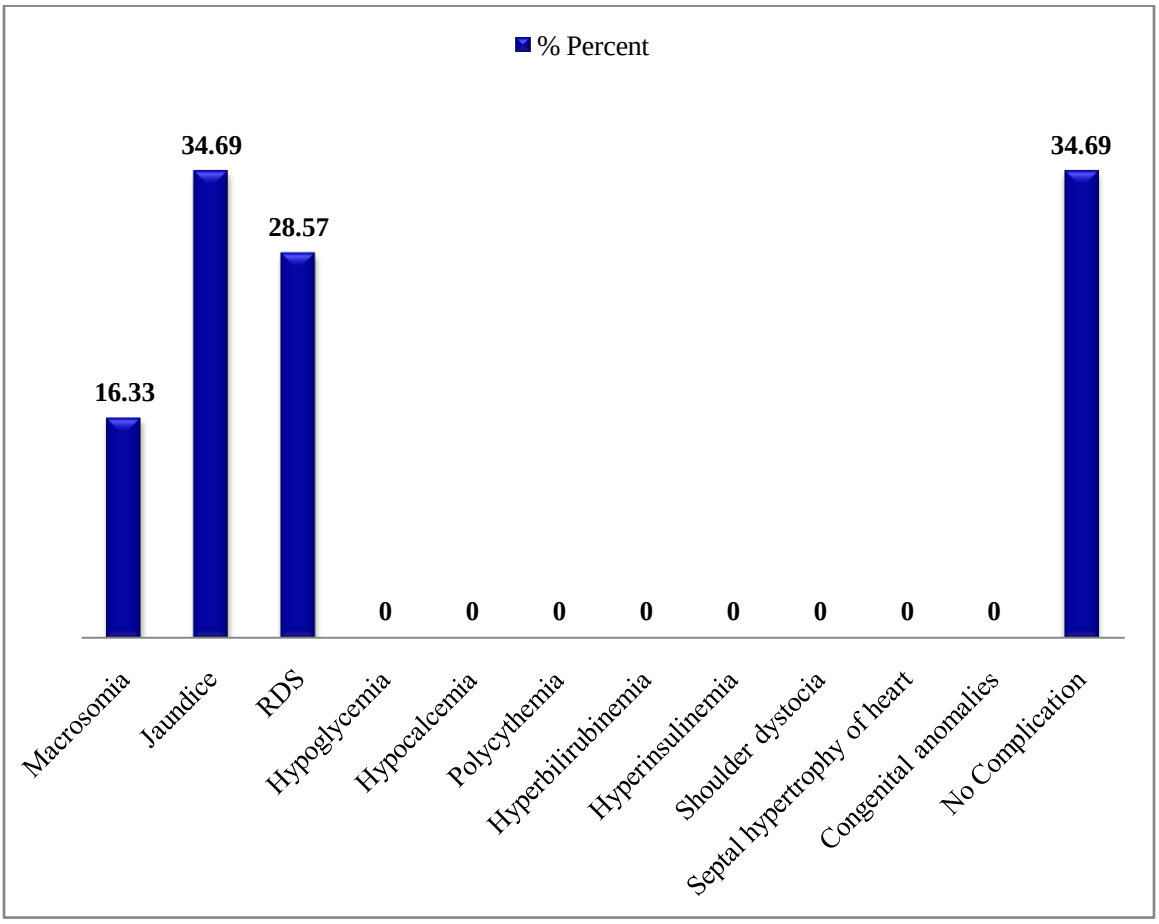

Figure 4.39 Conditions of the Neonate

According to the post natal study, it was found that 34.69% of the neonates had no complications, another 34.69% were found to have jaundice, 28.57% had Respiratory Distress Syndrome (RDS) and about 16.33% of the neonates were macrosomic (≥ 4 Kg in weight).

4.40 Conditions of the Mother (N=49)

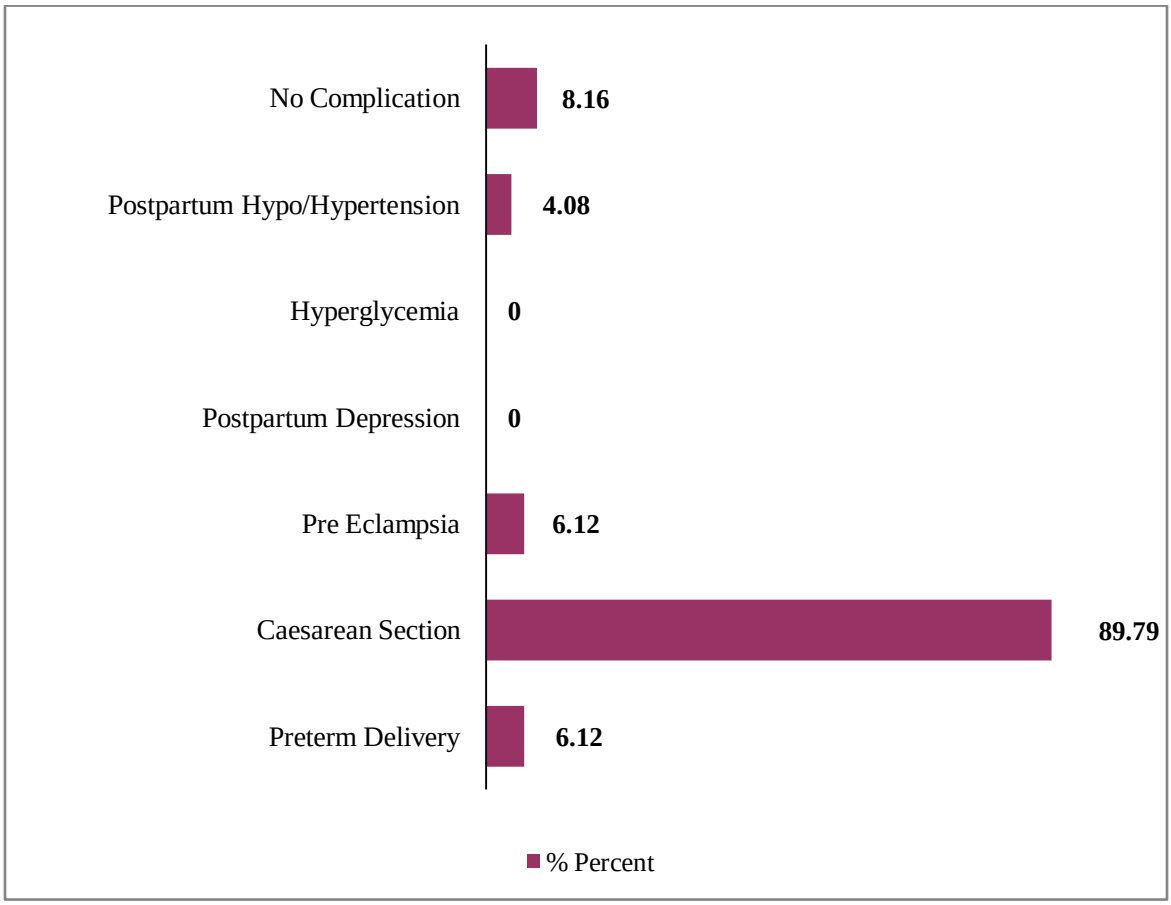

Figure 4.40 Conditions of the Mother

The above figure shows that most of the mothers (89.79%) with GDM went through Caesarean Section (C-Section), 8.16% of the mothers had no complication, 6.12% went through Pre eclampsia, another 6.12% had Preterm delivery and 4.08% were found to have Postpartum Hypo/Hypertension. There was no incidence of Postpartum Depression or Hyperglycemia among these mothers.

4.41 Effects on the Neonate (N=49)

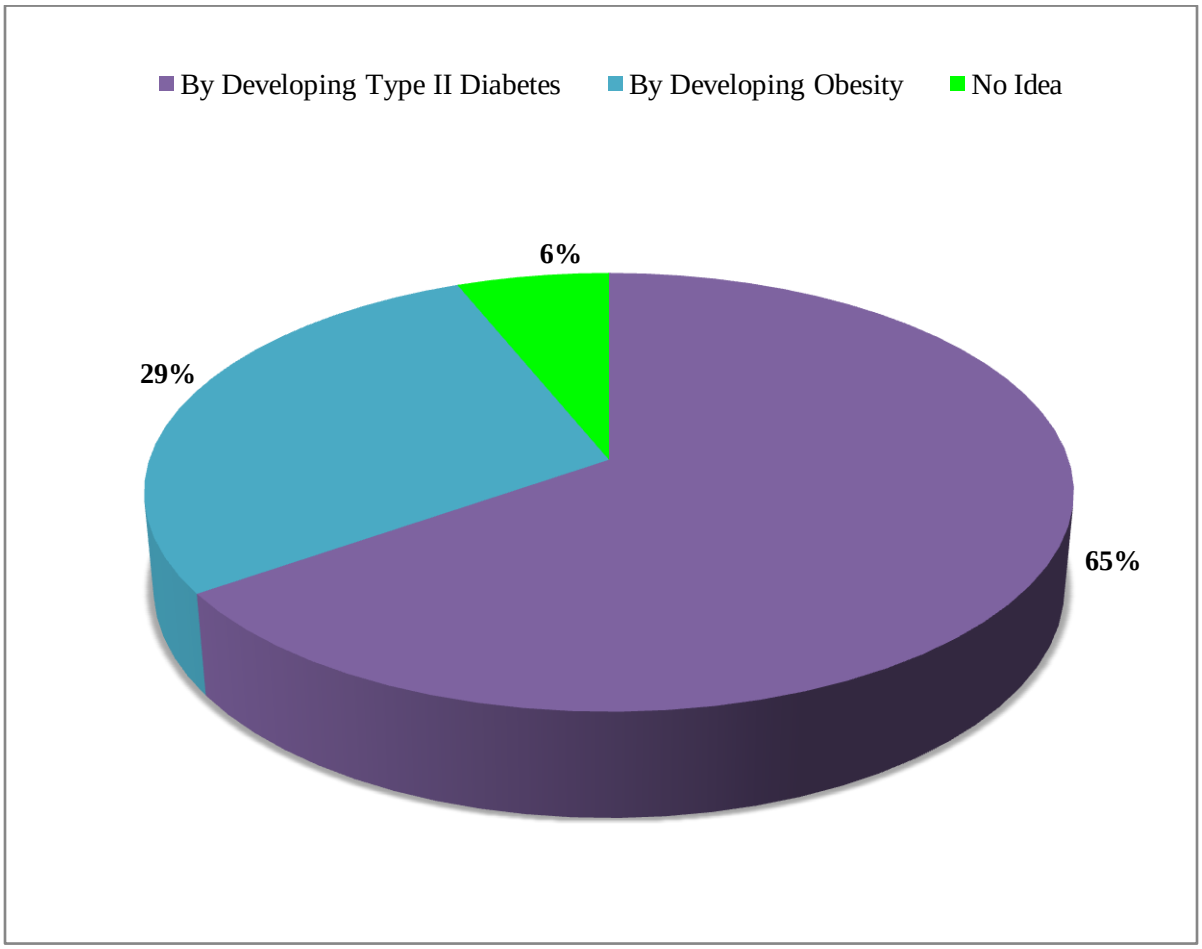

Figure 4.41 Effects on the Neonate

From the above figure it is evident that 65% of the mothers were concerned about their child to develop Type II Diabetes in future. 29% thought their child may develop obesity and the rest (6%) said they had no idea about how their child may get affected with GDM.

CHAPTER FIVE

DISCUSSION & CONCLUSION

Discussion

Diabetes Mellitus is the most common medical complication of pregnancy and it carries a significant risk to the fetus and the mother. Congenital malformations and perinatal morbidity remain common compared with the offspring of non diabetic pregnancies. Diabetic mothers are at risk of progression of micro-vascular diabetic complications as well as early pregnancy loss, pre-eclampsia, polyhydramnios and premature labor. Glycemic control before and during pregnancy is critical and the benefit may result in a viable, healthy offspring. Gestational diabetes mellitus (GDM) which manifests for the first time during pregnancy is common and on the increase, its proper management will reduce the risk of neonatal macrosomia and hypoglycemia. Post-partum evaluation of glucose tolerance and appropriate counseling in women with GDM may help decrease the high risk of subsequent type 2 diabetes in the long-term (Begum, 2008).

The present study was carried out on pregnant women to determine the prevalence of Gestational Diabetes Mellitus (GDM). A total of 150 pregnant women were surveyed and 49 (32.67%) of them were found to be patients of GDM. Prevalence of gestational diabetes mellitus varies widely around the world. Depending on the population studied and the diagnostic test employed, prevalence may range from 2.4 to 21% of all pregnancies (Seshiah *et al.*, 2004). The prevalence of gestational diabetes was found 12.8% in a study conducted in Northern Quebec by Rodrigues *et al* in 1999. The prevalence rate of GDM in our study was quite higher compared to these studies. The major difference occurred in this study, might be due to an error in sampling which occurred because the study was carried out in such settings where most of the patients had Diabetes Mellitus.

Determining the major drug therapy prescribed by the physicians' was an important aspect in our study and we found that, about 46.93% of the patients were prescribed with Insulin and 30.61% with Metformin for the management of Gestational Diabetes Mellitus (GDM). In 2005–06, about 30% of confinements in Australia with gestational diabetes were treated with insulin, with women in older age groups requiring it in about 40% of cases (J Donovan and McIntyre, 2010).

In our study, it was found that approximately 78% of the patients, surveyed with GDM used to do physical exercise during their pregnancy period. In a case controlled study of physical activity

in 155 pregnant women with GDM compared with 386 healthy pregnant controls, physical activity before and during pregnancy was associated with a reduced incidence of GDM (Golbidi and Laher, 2013).

In our study, about 59% of the respondents were found to have at least one person with diabetes mellitus in their family. It has been reported that family history of diabetes is related with higher chances of developing GDM in individuals. Seshiah *et al* observed a significant association between the family history of diabetes mellitus and the occurrence of GDM among pregnant women in South India (Seshiah *et al.*, 2004).

The occurrence of both preeclampsia and preterm delivery was found to be about 6.12% in the present study. And all the respondents (100%) underwent cesarean section (C-section) because their doctors wanted to avoid the risk of any complication associated with normal deliveries and GDM. In Korea, the frequencies of preeclampsia and primary cesarean sections were higher and delivery was earlier in pregnancies complicated by GDM (Jang *et al.* 1997).

The primary respiratory problem in infants of GDM mother is respiratory distress syndrome (RDS). This is caused by surfactant deficiency or by retained fetal lung fluid. In urban areas of Bangladesh, RDS occurs more in infants of diabetic mothers due to the lack of maturity in the type II alveolar cells. (Mannan *et al.*, 2012) In the present study, 28.57% of the neonates were born with RDS.

About 16.33% of the neonates were found to be macrosomic, 34.69% to have jaundice and 28.57% to have Respiratory Distress Syndrome (RDS) in the present study. Birth weight, symmetry index, and chest circumference were greater, and macrosomia and need for phototherapy were more common in offspring of mothers with GDM in Korea (Jang *et al.*, 1997). Langer *et al.* mentioned in a study conducted in Texas, that a 2- to 4-fold increase in metabolic complications and macrosomia/large for gestational age was found in the untreated subjects (Langer *et al.*, 2005). In another study it is reported that, women with GDM, neonates with a birth weight of 4000 g or greater, compared with those with a birth weight of less than 4000 g, had higher frequencies of hypoglycemia (5.3% vs 2.6%), RDS (4.0% vs 1.5%), shoulder dystocia (10.5% vs 1.6%), and Erb's palsy (2.6% vs 0.2%) (Esakoff *et al.*). Normally fetal pancreas is relatively unresponsive to physiological levels of glucose. When maternal

hyperglycemia is present (as in GDM), the fetus responds to elevated glucose levels by beta cell hypertrophy and there is increased production of insulin in utero. Insulin acts as a growth factor in the fetus. This hyperinsulinemia and hyperglycemia lead to an increase in organ size and total adipose tissue mass and subsequent fetal weight gain. Macrosomia is probably the most widely known complication affecting the fetus of diabetic women. A consequence of the increase size of the infant is an increased caesarian section rate also (Mannan *et al.*, 2012)

In a study related to GDM reported that, several possible biologically adverse effects of components in red and processed meats, such as saturated fatty acids and cholesterol, on insulin sensitivity have been proposed and might be relevant to the pathophysiology of GDM. In the present study, the strong association of red meat and processed meat with GDM risk remained significant after further adjustment for other dietary factors, including fatty acids and cholesterol, indicating that components of red meat and processed meat other than these nutrients might be also relevant to the pathogenesis of GDM. For example, nitrites, frequently used as a preservative in processed meats, have been implicated in the development of diabetes. Nitrosamines can be formed by the interaction of amino compounds with nitrites present either in the stomach or within the food product. They have been linked to beta cell toxicity (Zhang *et al.*, 2006). In the present study, all the patients (100%) with GDM followed a meal plan and almost 87% of them said that they took balanced diet. The rest mainly had vegetables, carbohydrates and fibrous food in their meals.

About 72% of the patients with GDM in the current study were found to have low stress level and have handled themselves quite well.

Conclusion

Gestational Diabetes Mellitus (GDM) remains a controversial area. Changes in insulin sensitivity are a key feature of the pregnant state. The evidence that maternal glycaemia has a continuous relationship with neonatal adiposity and further that alteration of maternal glycaemia in turn can lead to changes in birth weight is now clear. GDM often represents diabetes in evolution and, as such, holds great potential as a condition in which to study the pathogenesis of diabetes and to develop and test strategies for diabetes prevention. The current status of GDM in Bangladesh has become a strong potential area for studies to be conducted with a view to determining the exact reasons behind this condition and the preventive measures so that public awareness programs on GDM can be organized for greater good.

CHAPTER SIX

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