A STUDY ON GESTATIONAL DIABETES MELLITUS AND ITS EFFECT ON NEONATES IN BANGLADESH

Submitted By

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This dissertation is submitted to the Department of Pharmacy, East West University in the partial fulfillment of the requirements for the Degree of Bachelor of Pharmacy.

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Declaration by the Research Candidate

I, **Mst. Meoyatul Zannat**, ID: 2011-1-70-054, hereby declare that the dissertation entitled "A STUDY ON PREVALENCE, DRUG THERAPY, MAJOR COMPLICATIONS & EFFECT ON NEONATES OF GESTATIONAL DIABETES IN BANGLADESH'' submitted by me to the Department of Pharmacy, East West University and in the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy, under the supervision and guidance of **Nishat Nasrin**, Senior Lecturer, Department of Pharmacy, East West University, Dhaka, Bangladesh.

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Certificate 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 BANGLADESH’’ submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bonafied record of original and genuine research work carried out by **Mst. Meoyatul Zannat**, ID: 2011-1-70-054 under my supervision and guidance.

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Certificate 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 BANGLADESH’’ submitted to the Department of Pharmacy, East West University for the partial fulfillment of the requirement for the award of the degree Bachelor of Pharmacy is a bonafied record of original and genuine research work carried out by **Mst. Meoyatul Zannat**, ID: 2011-1-70-054, under the supervision and guidance of **Nishat Nasrin**, Senior Lecturer, Department of Pharmacy, East West University and no part of this project has been submitted to other degree.

Dr. Shamsun Nahar Khan

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This Research paper is

Dedicated

To my beloved Parents

Table of Content

List of Tables

List of Figures

List of Abbreviation

ADA	American Diabetes Association
AFN	Assembly of First Nations
CDA	Canadian Diabetes Association
FNW	First Nation Women
GDM	Gestational Diabetes Mellitus
GCT	Glucose Challenge Test
HAPO	Hyperglycemia and Adverse Pharmacy Outcomes
MODY	Maturity Onset Diabetes of the Young
NIDDM	Non Insulin Dependent Diabetes Mellitus
OGTT	Oral Glucose Tolerance Test
PCOS	Polycystic Ovary Syndrome
RCTs	Randomized Controlled Trials
T2D	Type 2 Diabetes
WHO	World Health Organization

Abstract

Gestational Diabetes Mellitus (GDM) is a common metabolic disorder that occurs during pregnancy. GDM can cause significant problems, including maternal complications, perinatal complications, and metabolic disorders in offspring of mothers with GDM. The primary management method for women with GDM is nutritional therapy. Some women with GDM require diet therapy alone, while some women require both diet therapy and insulin therapy. The present study was aimed to assess the prevalence of (GDM) among the pregnant women in different districts of Bangladesh, and to find out the consequences or effects of GDM on pregnancy. The data were collected from 150 pregnant women from hospital located in Tongi, Narayanganj and Naogaon using a structured questionnaire. The prevalence of GDM was 18.67%. This present study also shows that, most of the patients (64%) had a history of diabetes in their family, very few patients (29%) had knowledge about diabetes in the past and they mostly took Insulin (57.14%) and Metformine HCl (42.86%) for managing GDM. All of the patients underwent caesarean section (100%) and 35.71% gave birth to a macrosomic baby. Among the patients, about 57% of them have had knowledge about GDM and 86% of them did exercise regularly. Most of the women (64.29%) had no other complication during their pregnancy period but 17.86% had pre-eclampsia during gestational period. Almost 64.29% of the babies were full term and 34.71% were not full term. Among them, premature babies were 60% and 40% were postmature. Diabetes prevention initiatives should be given high priority to avoid high rates of GDM in the future. But the gigantic problem of GDM cannot be solved by Government alone, so public awareness is the best way to reduce the prevalence and risk factors associated with GDM.

Key words: Gestational Diabetes Mellitus (GDM), Prevalence, Macrosomia, Maternal Morbidities.

1.1 Overview

Gestational diabetes mellitus (GDM) is defined by glucose intolerance of variable severity with onset of first recognition during pregnancy. Hyperglycemia during pregnancy is found to be associated with various maternal and perinatal adverse outcomes. Their offspring will have a lifelong increase risk of glucose intolerance, obesity and metabolic syndrome whereas the mothers will have a higher risk of metabolic syndrome and diabetes in the future. The detection of GDM during pregnancy provides an opportunity to identify women at risk of short term and long term complications. We now have evidence that early diagnosis and intervention can reduce the adverse perinatal outcomes. Throughout all these years, there is still no consensus on the optimal diagnostic cut-off until the recent recommendation by the International Association of Diabetes and Pregnancy Study Groups (IADPSG). The purpose of this review is to provide a recent update and discuss the current controversies on GDM (WHO, 2012).

1.2 Historic Evolution of Gestational Diabetes

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 International Association of Diabetes and Pregnancy Study Groups (IADPSG) proposed a new diagnostic criteria in 2010 (WHO, 2012).

1.3 Definition of Diabetes

Diabetes is a disease in which the body is unable to use sugar (or glucose) resulting in too much sugar in the blood (hyperglycemia). Diabetes is a group of diseases marked by high levels of blood glucose resulting from problems in how insulin is produced, how insulin works, or both. People with diabetes may develop serious complications such as heart disease, stroke, kidney failure, blindness, and premature death.

Diabetes places a burden on individual health and the health care system. It is also associated with a range of complications ranging from heart disease to eye disease (CDA, 2005-2009). First Nation diabetics suffer more health consequences from their diabetes and have more activity limitations than others in Canada who have the same disease. Unfortunately, only about 40% of First Nations type 2 diabetics are estimated to have attended a diabetes clinic or have received diabetes education, with only about half of them monitoring their glucose intake every day (AFN, 2007).

1.4 Types of diabetes

There are mainly three types of diabetes: type1 (insulin dependent), type 2 (non-insulin dependent diabetes mellitus (NIDDM) or "adult onset"), and gestational diabetes mellitus (GDM) (ADA, 2000).

1.4.1 Type 1 diabetes

It was previously called insulin dependent diabetes mellitus or juvenile-onset diabetes. Although disease onset can occur at any age, the peak age for diagnosis is in the mid teens. Type 1 diabetes develops when the cells that produce the hormone insulin, known as the beta cells, in the pancreas are destroyed. This destruction is initiated or mediated by the body's immune system and limits or completely eliminates the production and secretion of insulin, the hormone that is required to lower blood glucose levels. To survive, people with type 1 diabetes must have insulin delivered by injection or a pump. In adults, type 1 diabetes accounts for approximately 5% of all diagnosed cases of diabetes. There is no known way to prevent type 1 diabetes. Several clinical trials for preventing type1 diabetes are currently in progress with additional studies being planned (Berger *et al.,* 2002).

1.4.2 Type 2 diabetes

It was previously called non insulin dependent diabetes mellitus or adult onset diabetes because the peak age of onset is usually later than type 1 diabetes. In adults, type 2 diabetes accounts for about 90% to 95% of all diagnosed cases of diabetes. Type 2 diabetes usually begins with insulin resistance, a disorder in which the cells primarily within the muscles, liver, and fat tissue do not use insulin properly. As the need for insulin rises, the beta cells in the pancreas gradually lose the ability to produce sufficient quantities of the hormone. The role of insulin resistance as opposed to beta cell dysfunction differs among individuals, with some having primarily insulin resistance and only a minor defect in insulin secretion, and others with slight insulin resistance and primarily a lack of insulin secretion. The risk for developing type2 diabetes is associated with older age, obesity, family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity (ADA, 2000).

Table1.1 Clinical characteristics of patients with Type1 and Type2 diabetes mellitus

Features	Type 1	Type 2
Age of onset	Usually less than 20 years	Usually greater than 30 years
Body mass	Low (wasted) to normal	Obese
Plasma insulin	Low or absent	Normal to high initially
Plasma Glucagon	High, can be suppressed	High, resistant to suppression
Plasma glucose	Increased	Increased
Insulin sensitivity	Increased	Reduced
Therapy	Insulin	Weight loss, thiazolidinediones, metformin, sulfonylureas, insulin

(Guyton and Hall, 2006)

1.4.3 Gestational Diabetes Mellitus (GDM)

A third type of diabetes exists which affects only women and is called gestational diabetes mellitus (GDM). It is a form of glucose intolerance diagnosed during the second or third trimester of pregnancy. During pregnancy, increasing blood glucose levels increase the risk for both mother and fetus and require treatment to reduce problems for the mother and infant. Treatment may include diet, regular physical activity, or insulin.

Shortly after pregnancy, 5% to 10% of women with gestational diabetes continue to have high blood glucose levels and are diagnosed as having diabetes, usually type 2. The risk factors for gestational diabetes are similar to those for type 2 diabetes. The occurrence of gestational diabetes itself is a risk factor for developing recurrent gestational diabetes with future pregnancies and subsequent development of type2 diabetes. Also the children of women who had gestational diabetes during pregnancies may be at risk of developing obesity and diabetes. GDM is a temporary type of diabetes. Most women with GDM will return to normal glucose levels after delivery of the baby. If a woman does not return to normal glucose levels she will be rediagnosed with type2 diabetes and will no longer be considered to have GDM (Smith et al., 2005). In some cases this may mean that glucose intolerance began before pregnancy but was only diagnosed during pregnancy (Berger et al., 2002). In some communities, women are screened for GDM before they are screened for type 2 diabetes. For this reason some women are unaware of their diabetic status until they have GDM that does not go away after the delivery of their baby. In general, GDM occurs in 2% to 4% of all pregnancies in Canada (Health Canada, 2001). However, rates for First Nations women have been reported to range from 8% up to 18% (CDA, 2005-2009). According to the 2002-2003 Regional Health Survey, one in eight First Nations women reported having gestational diabetes (First Nations Centre, 2005). Heavier women are at greater risk for developing gestational and type 2 diabetes. Women who have had GDM and their infants are at increased risk of developing type 2 diabetes, with the infants further at risk of and having high birth weight. Babies born with a high birth weight are at increased risk of developing diabetes even if the mother did not have diabetes (AFN, 2007).

First Nations women are at increased risk of developing GDM and rates of GDM among native groups in North America are on the rise. First Nations ancestry is considered to be an independent risk factor for GDM. This means that women with First Nations ancestry are more likely to develop GDM (Dyck *et al.,* 2002).

1.4.4 Prediabetes

In addition to types 1, types 2 and Gestational Diabetes another type of diabetes exists which is called Predaidetes. Prediabetes is a condition in which individuals have high blood glucose or hemoglobin A1C levels but not high enough to be classified as diabetes. People with prediabetes have an increased risk of developing type 2 diabetes, heart

disease, and stroke, but not everyone with prediabetes will progress to diabetes. The Diabetes Prevention Program, a large prevention study of people at high risk for diabetes, showed that lifestyle intervention that resulted in weight loss and increased physical activity in this population can prevent or delay type 2 diabetes and in some cases return blood glucose levels to within the normal range. Other international studies have shown similar results (Smith et al., 2005).

1.4.5 Secondary diabetes

Diabetes, which may occasionally develop as consequences of other diseases or drug therapy. Some causes of secondary diabetes; Pancreatic disease (pancreatitis, surgery, carcinoma), Endocrine disease (acromegally, Cushing's Syndromes), Drugs (steroids, contraceptives, diuretics). But this condition is very rare (WHO, 1999).

1.5 Causes of Gestational Diabetes Mellitus (GDM)

Almost all women have some degree of impaired glucose intolerance as a result of hormonal changes that occur during pregnancy. That means that their blood sugar may be higher than normal, but not high enough to have diabetes. During the later part of pregnancy (the third trimester), these hormonal changes place pregnant woman at risk for gestational diabetes. During pregnancy, increased levels of certain hormones made in the placenta (the organ that connects the baby by the umbilical cord to the uterus) help shift nutrients from the mother to the developing fetus. Other hormones are produced by the placenta to help prevent the mother from developing low blood sugar. They work by resisting the actions of insulin.

Over the course of the pregnancy, these hormones lead to progressive impaired glucose intolerance (higher blood sugar levels). To try to decrease blood sugar levels, the body makes more insulin to get glucose into cells to be used for energy. Usually, the mother's pancreas is able to produce more insulin (about three times the normal amount) to overcome the effect of the pregnancy hormones on blood sugar levels. If, however, the pancreas cannot produce enough insulin, blood sugar levels will rise, resulting in gestational diabetes (Oster *et al.,* 2009).

1.6 Risk Factors of Gestational Diabetes Mellitus

Mild insulin resistance late in pregnancy is normal, but the presence of one or more risk factors increases the chance of this normal insulin resistance progressing. Other 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
- 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) (CDA, 2009; Godwin *et al*., 1999)

Being obese or overweight before pregnancy and gaining excessive weight during pregnancy can also increase the risk of gestational diabetes. Research has shown that both pre-gestational diabetes and gestational diabetes contribute to the high prevalence of diabetes in First Nations populations. This pattern is also seen in non First Nations populations (Oster *et al.,* 2009).

1.7 Effects of Gestational Diabetes Mellitus

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. Diabetes can affect the developing fetus throughout the pregnancy. In early pregnancy, a mother's diabetes can result in birth defects and an increased rate of miscarriage. Many of the birth defects that occur affect major organs such as the brain and heart.

During the second and third trimester, a mother's diabetes can lead to over nutrition and excess growth of the baby. Having a large baby increases risks during labor and delivery. For example, large babies often require planned or emergency caesarean deliveries, and if he or she is delivered vaginally, they are at increased risk for complications such as trauma to the baby.

In addition, when high blood sugar from the mother causes high insulin levels (hyperinsulinemia) in the baby, the baby's blood sugar can drop very low after birth, because it won't be receiving the high blood sugar (Harris *et al.,* 1997)

1.7.1 Effects of Gestational Diabetes Mellitus 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.
- There has not been enough research to determine if treating GDM can reduce the risk of type2 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.
- Some studies have found that Aboriginal women with GDM are more likely to have high blood pressure during pregnancy (Dyck *et al.,* 2002).

1.7.2 Effects of Gestational Diabetes Mellitus 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 type2 diabetes (Berger *et al.,* 2002; CDA, 2009).

1.8 Signs and Symptoms of Gestational Diabetes Mellitus

In most cases, the only sign of gestational diabetes is an abnormally high blood glucose level though a small number of pregnant women with this condition will also experience increased thirst and urination. Since there are no obvious signs that are observable during a regular physical exam, most pregnant women will have their blood glucose levels tested at about 24 weeks. If blood glucose appears high, then specific tests for gestational diabetes will be utilized (CDA, 2009).

1.9 Detection and Diagnosis of Gestational Diabetes Mellitus

A growing body of evidence suggests that elevated blood glucose levels during pregnancy may contribute to worse birth outcomes even at levels that until recently were considered normal. These data have prompted new guidelines from the American Diabetes Association (ADA) that advocate universal screening for GDM using less stringent diagnostic criteria than have been used in the past. The current screening guidelines are-

-Screen for undiagnosed type2 diabetes at the first prenatal visit in those with risk factors, using standard diagnostic criteria.

-Screen women with GDM for persistent diabetes at 6–12 weeks postpartum, using OGTT, non pregnancy diagnostic criteria.

-All pregnant women are screened for GDM.

-For the pregnant women with a high risk of developing GDM, it is recommended that GDM screening be omitted and diagnostic testing (75 g OGTT) carried out from the first.

-Women with a history of GDM should have lifelong screening for the development of diabetes or prediabetes at least every 3 years.

-Screening is carried out using the following two-step methods

i) In the first trimester, a casual blood glucose test is carried out. Individual medical institutions may set their own cut-off values.

ii) A 50 g glucose challenge test (GCT) is carried out in the second trimester (weeks 24–28); the cut-off value is 140 mg/dl. This test should be administered to pregnant women who tested negatively on the first trimester casual blood glucose test, or who tested positively on the first trimester casual blood glucose test but were diagnosed as non-GDM on 75 g OGTT.

In women at high risk of developing gestational diabetes, a normal screening test result is followed up with another screening test at 24-28 weeks for confirmation of the diagnosis.

The new guidelines are based in large part on findings from the Hyperglycemia and Adverse Pregnancy Outcomes (HAPO) study and stipulate that an abnormal value for a 75-g OGTT (when the test is performed in the morning after an overnight fast of at least 8 hours) at 24-28 weeks of gestation at any of the three diagnostic cut points (Table 2) measurements is sufficient to make the diagnosis of GDM. It is estimated that implementing these guidelines will increase prevalence of GDM more than 2-fold, from around 7% currently to an estimated 17.8%. This enormous increase in the number of patients with GDM presents diabetes educators and the entire health care team with tremendous opportunities and challenges (JAOG, 2008).

Table 1.2: Diagnosis of Gestational Diabetes Mellitus

Measure Glucose concentration	Glucose concentration threshold - mg/dl	Glucose concentration threshold - mmol/l
Fasting plasma glucose	>92	>5.1
1-h plasma glucose	>180	>10.0
2-h plasma glucose	>153	>8.5

(Metzger *et al.,* 2008).

1.9.1 Self-monitoring of blood glucose

Depending on the degree of hyperglycemic disorder in pregnancy, self-monitoring of blood glucose is carried out by the patient at a frequency of 4–7 times per day. As explained above, the target blood glucose levels are venous plasma glucose values of 100mg/dl or lower before meals and of 120mg/dl or lower 2 hours after meals. In the case that these target values cannot be achieved, the diet and insulin therapies described below are implemented. Furthermore, while the patient is hospitalized, checks should be made to ensure that the difference between blood glucose levels obtained through self-monitoring and by laboratory testing is no more than around 10% (Nakabayashi *et al.,* 2010).

1.10 Management of Gestational Diabetes Mellitus

Gestational diabetes is managed by-

- Monitoring blood sugar levels four times per day before breakfast and 2 hours after meals; monitoring blood sugar before all meals may also become necessary.
- Monitoring urine for ketones, an acid that indicates your diabetes is not under control.
- Following specific dietary guidelines as instructed by your doctor; you'll be asked to distribute your calories evenly throughout the day.
- Exercising after obtaining your health care provider's permission.
- Monitoring weight gain.

- Taking insulin or an oral hypoglycemic medication such as glyburide, metformin, if necessary.
- Controlling high blood pressure (Sugiyama *et al.*, 2006).

1.11 Treatment of Gestational Diabetes mellitus (GDM)

In the majority of GDM cases, the frequency of the various complications that may affect mother or child can be controlled with appropriate diagnosis and management. As mentioned above, control of blood glucose levels during pregnancy is extremely important, and the reasons will be explained below. Conventionally, it is desirable that, in the case that two or more 75g OGTT cut-off values are abnormal, the patient undergoes in-patient education with diet therapy, and if the target blood glucose levels given below are not achieved, the patient should be treated with insulin therapy. In contrast, in the case that only one 75g OGTT cut-off value is abnormal, it is thought to be possible to treat the patient with diet therapy on an outpatient level. In the case of obese women, however, as a general rule in-patient education is thought to be desirable. GDM management policy is an important topic requiring consideration going forward. The JSOG Committee on Nutrient and Metabolism recommends as target blood glucose levels venous plasma glucose values of 100mg/dl or lower before meals and of 120mg/ dl or lower 2 hours after meals. According to two randomized controlled trials (RCTs) concerning the management of GDM that were published recently, amongst the patients who received treatment intervention (diet therapy, self monitoring of blood glucose, insulin therapy) there was a clearly lower incidence of complications for both the mother and newborn than for patients receiving no treatment intervention. The findings of these reports substantiate the need for blood glucose control in GDM (Gonzalez *et al.*, 2005).

1.11.1 Diet and exercise

Patients benefit significantly by receiving dietary counseling to learn to count carbohydrates and plan meals. The ADA recommends that women of normal weight in the second half of pregnancy consume 30-32 kcal/kg body wt. Carbohydrate intake should be ~ 40% of total calories and should be selected from carbohydrate foods with a low glycemic index. In overweight women, this requirement should be reduced to 25kcal/kg. Excessive calorie restriction can be monitored by checking for fasting ketonuria, especially when there is a caloric restriction > 30%. The key strategies for

achieving strict control of blood glucose levels are first of all frequent self monitoring of blood glucose, followed by appropriate diet therapy, which is extremely important. During pregnancy, as pregnant women patients need to consume adequate energy, protein, and minerals. In Japan, according to the diet therapy recommended by the JSOG Committee on Nutrient and Metabolism in 1985, dietary intake for ideal pregnancy weight is 25–30kcal/kg150 kcal for the first half of pregnancy and 25–30kcal/kg350 kcal for the second half of pregnancy, with "150 kcal" and "350kcal" the additional calorie intake recommended for pregnant women according to the dietary reference intakes prescribed by the Ministry of Health and Welfare. Under the nutritional guidelines recommended by the Ministry of Health, Labor and Welfare in 2010, an additional calorie intake of 50kcal, 250kcal, 450kcal is recommended for pregnant women during the first, second, and third trimester, respectively. Thus using these recommendations, it is reasonable to regard the currently recommended calorie intake for pregnant women as 25–30kcal/kg50kcal, 25–30kcal/kg250kcal, and 25–30kcal/kg450kcal for the first, second, and third trimester, respectively. In the case that the target blood glucose levels described above cannot be achieved eating three meals a day, dividing each meal in a ratio of 2:1 or 1:1 and eating 4–6 meals per day can be effective (Knopp *et al.,* 1998)

1.11.2 Insulin

For decades, human insulins were the only insulin options available for the treatment of GDM. The recent advent of newer insulin analogs that mimic physiological insulin action calls for more information regarding the safety and applicability of their use in GDM.

The insulin analogs lispro and aspart have proven to be more effective than regular human insulin in achieving goal glucose levels and reducing the risk of fetal macrosomia. Using analogs has the advantage of dosing 5-10 minutes before meals, versus 30-45 minutes before meals with regular insulin. Because these analogs are rapid acting and have a short duration of action, they better control postprandial glycemia and are associated with less postprandial hypoglycemia than regular insulin. Lispro and aspart have not been found to cross the placenta (Pettitt *et al.,* 2003).

Insulin therapy decreases the frequency of fetal macrosomia and perinatal morbidity. A study by Jovanovic *et al.* demonstrated in 19 women with GDM on either lispro or regular insulin that there was decreased hypoglycemia, improved postprandial glycemia,

and lower hemoglobin in the third trimester in the lispro group. Traditionally, longer acting insulins, such as NPH insulin have been used extensively to treat GDM. Sources suggest if the fasting blood glucose is > 90 mg/dl, then NPH at a dose of 0.2units/kg per day should be initiated at bedtime. Next, if both fasting and preprandial levels are elevated, a rapid-acting analog should be added with meals. There are few data in the literature on the use of the long-acting insulin analog glargine in women with GDM. Graves *et al.* have described the treatment of four patients with GDM with glargine, which resulted in no poor outcomes and adequate glycemic control (Jovanovic *et al.,* 1997).

1.11.3 Glyburide

This sulfonylurea has been identified in the past several years as an alternative to insulin therapy for the treatment of GDM. Its primary action is to enhance insulin secretion. Glyburide does not significantly cross the placenta. Several studies have found that glyburide serves as a suitable alternative to insulin for treatment of GDM with similar perinatal outcomes. A survey performed by the American College of Obstetricians and Gynecologists found that 13% of obstetricians and maternal-fetal medicine specialists were using glyburide as a first line agent in the treatment of women with GDM who failed to achieve glucose control with diet. A disadvantage to taking glyburide is that it sometimes takes greater than one week to observe the effect of titration. However, it is inexpensive and less invasive than insulin and has been found to be as effective as insulin therapy for GDM treatment. Langer *et al*. found that glyburide was as effective as insulin for the treatment of GDM in 404 patients, despite severity of disease when fasting plasma glucose on a glucose tolerance test was between 95 and 139 mg/dl. More than 80% of GDM patients were found to achieve the established levels of control with glyburide; 71% of patients required an average dose of 10 mg of glyburide daily. There was no significant difference in neonatal birth weight, metabolic complications, and composite outcome between the two groups. Chmait *et al.* studied 69 patients with GDM who failed dietary therapy and were then treated with glyburide. Treatment failure was defined as inadequate glycemic control on 10 mg of glyburide twice daily. The failure rate was 18.8%. Glyburide success was predicted if dietary failure occurred after 30 weeks or fasting blood glucose levels were < 110 mg/dl and 1-hour postprandial levels were > 140 mg/dl. This study was done in a predominantly (87%) Hispanic population.

Markers for advancement to insulin include inadequate glycemic control, severe restriction of carbohydrates and calories (as demonstrated by ketonuria) necessary to meet glycemia goals, and a fetus that is large for gestational age. Glyburide is contraindicated in those with an allergy to sulfa. The main risk of taking glyburide, as with insulin, is hypoglycemia (Langer *et al.*, 2000).

1.11.4 Metformin

The biguanide metformin during pregnancy has mostly been studied in the first 12 weeks of gestation for patients with polycystic ovary syndrome (PCOS). Preliminary studies have shown that in women with PCOS, metformin may be safe and may reduce risk of miscarriage and development of GDM when used for the entire pregnancy. Metformin may also have a role in therapy for GDM; a multicenter trial is underway in New Zealand to address this question (Glueck *et al.*, 2004).

1.12 Factors that can be ameliorated before and after pregnancy

In the case of women with diabetes complications, and especially in the case that diabetic retinopathy is present, the patient needs to undergo evaluation and treatment by an ophthalmologist. For example, if the patient was being treated before pregnancy for proliferative retinopathy using photo-coagulation therapy, pregnancy is possible. In addition, it is necessary to educate the patient about points to be careful about with regard to further pregnancies. Obesity is an important risk factor for GDM, and so prior to pregnancy not only is it necessary for patients to take special care with their lifestyle, especially diet, but it is also vital that women suffering from infertility be checked for glucose intolerance. For women with carbohydrate intolerance as a complication of obesity, it is also necessary that the patient make lifestyle improvements after the birth. GDM patients are encouraged to undergo 75g OGTT testing 6–12 weeks postpartum for reevaluation. In the case that a hyperglycemic disorder is confirmed, the patient is referred to a diabetes specialist for future follow up. Many GDM patients drop out of medical care at the obstetric/gynecological level, and so patient education is also thought to be important. Since obese women are at a high risk for developing a hyperglycemic disorder in pregnancy in the future, nutritional guidance and appropriate diet therapy should be considered (Yogev *et al.*, 2004).

1.12.1 Timing and route of delivery

There are no data supporting delivery of women with GDM before 38 weeks' gestation in the absence of objective evidence of maternal or fetal compromise. Data are not available to indicate whether or not there is greater risk of perinatal morbidity/mortality in the infants of women with well controlled GDM if pregnancy is allowed to proceed past 40 weeks' gestation. Nevertheless, it is reasonable to intensify fetal surveillance when pregnancy is allowed to continue beyond 40 weeks' gestation. Some evidence indicates that delivery past 38 weeks can lead to an increase in the rate of large-for-gestational-age infants without reducing the rate of cesarean deliveries. Amniocentesis for assessment of fetal lung maturity is not indicated in well controlled patients who have indications for induction of labor or cesarean section as long as there is reasonable certainty about the estimation of gestational age. When delivery is necessary at an earlier gestational age for the well-being of mother or fetus, delivery should be affected without regard to lung maturity testing. Delivery of a large-for-gestational-age fetus in the setting of GDM is associated with an increased risk of birth injury compared with the non diabetic population. Strategies to reduce the risk of birth injury include a liberal policy toward cesarean delivery when fetal overgrowth is suspected. However, no controlled trials are available to support this approach. In planning the timing and route of delivery, consideration of fetal size using clinical and ultra sound estimate on off weight, despite inherent inaccuracies, is frequently used. Using ultra sound estimated fetal weight or abdominal circumference to make decisions regarding timing and route of delivery may be associated with a lower rate of shoulder dystocia, but larger studies are needed to determine if this approach affects the rate of neonatal injury (Yogev *et al.,* 2004).

1.12.2 Gestational Diabetes Mellitus and insulin resistance

Two forms of insulin resistance exist in women who develop GDM. The first is the physiological insulin resistance of late pregnancy. Evidence presented suggests the post receptor mechanisms that contribute to the insulin resistance of normal pregnancy appear to be multi factorial, but are exerted in skeletal muscle at the subunit of the insulin receptor and at the level of insulin receptor substrate-1. In addition, increased free intra cytoplasmic p85 subunit of phosphatidylinositol 3-kinase appears to be involved. These alterations in insulin signaling may contribute to reduced insulin mediated glucose uptake in skeletal muscle, a major tissue for whole body glucose disposal. Insulin resistance

abates soon after pregnancy, and the signaling changes have returned to normal within 1 year postpartum in women with normal glucose tolerance. These findings suggest that the insulin resistance is driven by pregnancy induced factors, with placental growth hormone and tumor necrosis factor currently being the most likely candidates. The second form of insulin resistance in GDM is a more chronic form that is present before pregnancy and is exacerbated by the physiological changes that lead to insulin resistance during pregnancy. Thus, most women with GDM have a combination of acquired and chronic insulin resistance and are therefore, as a group, slightly more insulin resistant than normal women during late pregnancy. Phosphorylation of insulin receptor tyrosine results in the transmission of the insulin signal to enable glucose uptake. Evidence presented identified a significant decrease in maximal insulin receptor tyrosine phosphorylation in muscle as one potential mechanism for the additional insulin resistance in obese women. Evidence was also presented for a role of increased serine phosphorylation of the insulin receptor and insulin receptor substrate-1, competitively inhibiting insulin receptor substrate-1 tyrosine phosphorylation and further inhibiting downstream insulin signaling (Langer *et al.*, 2000).

1.12.3 Gestational Diabetes Mellitus and pancreatic β-cell function

Compared with women with normal glucose tolerance, those with GDM have lower insulin secretion for their degree of insulin resistance. Over the long term (i.e., years), insulin secretion deteriorates in relation to chronic insulin resistance, leading to progressive hyperglycemia and predominantly type 2 diabetes. In a Latino population of women with prior GDM, this deterioration has been slowed or arrested by treatment of insulin resistance, which takes advantages of short term insulin sensitivity secretion changes to reduce insulin secretory demands on cells. In the Diabetes Prevention Program, lifestyle intervention and therapy with metformin also improved insulin sensitivity and preserved cell function in women with or without previous GDM. Whereas most women who develop GDM have evidence for cell dysfunction related to chronic insulin resistance, an important minority do not. Some of these women appear to have autoimmune β-cell dysfunction. Evidence was presented for the presence of cytoplasmic islet cell antibodies and antibodies directed against GAD 65, the membrane tyrosine phosphatase, and insulin in some women with GDM. These auto antibodies have also been used to identify individuals at high risk for the development of auto immune

diabetes in other settings, such as in first degree relatives of subjects with classic type1diabetes.The frequency of such autoimmunity tends to parallel the frequency of type1diabetes in a given ethnic group. These findings suggest that auto- immune β-cell problems and related hyperglycemia represent a specific biological subtype of GDM that is distinct from insulin resistance and type 2 diabetes. Women with this subtype of GDM have clinical characteristics that are typically considered to impart a low risk of GDM (lean, Caucasian). Autoimmune GDM should be suspected in such patients. They may experience relatively rapid metabolic deterioration during or after pregnancy, so they require more aggressive follow up. No specific disease modifying therapies are currently available for autoimmune GDM (Crowther *et al.,* 2005).

1.12.4 Genetics of Gestational Diabetes Mellitus

Monogenic forms of diabetes such as maturity onset diabetes of the young (MODY; autosomal dominant inheritance) and mitochondrial diabetes (maternal inheritance, often with other clinical manifestations) appear to contribute in a relatively minor way to GDM. These conditions generally have a young age at onset and relatively mild hyperglycemia, at least initially, so they may be detected by the routine glucose screening that is commonly practiced in pregnancy. The genes involved in these subtypes of diabetes and GDM appear to have important effects on β-cell function, and patients often do not have evidence of chronic insulin resistance. Clinical suspicion of these sub types is based on lack of clinical evidence for insulin resistance, coupled with a suggestive family history. Diagnosis requires genotyping that has recently become available for clinical practice. The contribution of genetics to other forms of GDM is not well established. The sparse data that are available suggest modest heritability but are confounded by incomplete case ascertainment. None the less, the autoimmune and insulin resistant forms of diabetes outside of pregnancy, diseases for which GDM is often a precursor, are heritable, and some contributory genetic variants have been defined. Evidence was presented that some of the variants may contribute to GDM or its physiological phenotypes (insulin resistance, β-cell dysfunction), but the studies to date are relatively small, as are the potential genetic contributions (Seino *et al.,* 2010).

1.12.5 The placenta in Gestational Diabetes Mellitus

The placenta serves as the primary interface between the mother and fetus. Alterations in placental transport functions can modify the impact of maternal metabolic abnormalities

of GDM on the developing fetus. Evidence presented that was obtained from human term placentas studied in vitro indicates that placental glucose transport and metabolism are normal in GDM pregnancies, despite increased glucose fluxes from mother to fetus that result from increased glucose concentrations on the maternal side. Transfer and metabolism of other maternal nutrients (e.g., lipids, amino acids, micronutrients) in GDM are not yet well characterized. The placenta is a rich source of steroids, lipid derived molecules, and peptides that can directly affect maternal metabolism and fetal development. Increased expression and production of cytokines such as TNF, interleukin-6, and leptin by placentas from women with GDM could be relevant to the development of exaggerated insulin resistance in pregnancies complicated by GDM. Evidence was presented that insulin from the fetus can modify placental gene expression, glycogen deposition, and vascular expansion. These findings reveal a potential role of the fetus in regulating placental function but do not indicate whether fetal influences mitigate or exaggerate the impact of GDM on fetal development (Seino *et al.*, 2010).

1.13 Management of Gestational Diabetes Mellitus during labor and delivery

Timing and mode of delivery in the case of diabetes or GDM alone, caesarean section is not indicated, but at the present time it cannot be said that there is sufficient data to support this. For example, it has been reported that in the case of a GDM patient undergoing insulin therapy where fetal development is thought to be within the normal range, there is no difference in the caesarean section rate between women for whom labor is induced at 38 weeks and those for whom labor is not induced. Moreover, it has also been reported that there is no difference in the incidence of macrosomia or caesarean section between insulin-treated GDM patients for whom labor is induced at 38–39 weeks and insulin- treated GDM patients who electively waited for labor and childbirth to take their natural course. Although in general the rate of caesarean section for GDM patients is high, there are some reports that this is due to the concern of physicians about shoulder dystocia occurring as the result of macrosomia, which has a high rate of frequency amongst GDM patients. However, much of the data is from the United States, and the average birth weight of infants born in the United States is higher than that in Japan. Thus it is thought to be impossible to use overseas data as the Japanese standard from the standpoint of infant birth weights. So far, in the case that the GDM patient has good blood glucose control and fetal development is thought to be within the normal range, as a

general rule it is considered that the pregnancies of GDM patients may be managed in the same manner as those of normal glucose-tolerant women. In the case that birth weight is estimated at 4, 000g or higher, an elective caesarean section is considered. However, in the case that the patient has poor blood glucose control, induced delivery at 38 weeks onward is considered.

When carrying out insulin therapy, special care is needed as the amount of insulin required during pregnancy, during delivery, and after birth differs tremendously. Thus, insulin requirements at the end of pregnancy increase by approximately two-fold. During first stage labor the required amount decreases, while in second-stage labor it increases slightly and after birth decreases rapidly. Accordingly, attention needs to be paid to such changes in required insulin amounts during pregnancy and the amount of insulin administered reduces by half following delivery. In particular, since it becomes difficult for the patient to eat during first and second stage labor, especially careful management of blood glucose levels is necessary in the case that labor and delivery are prolonged. In many cases at Mie University, at the onset of labor the patient is administered an electrolyte fluid containing 5% glucose at a rate of 100–120ml/hr, then administered insulin intravenously via an infusion pump. Depending on the individual case, blood glucose is measured at intervals of 1–2 hours. Insulin administration begins with a dosage of 0.5units/hr and the insulin dosing rate is determined based on fluctuations in blood glucose levels (Seino *et al.*, 2010).

1.14 Post pregnancy Management of Gestational Diabetes (GDM)

GDM is increasingly recognized as a general risk factor for the development of Type2 Diabetes (T2D). According to a systematic review of studies, up to 60% of women with GDM had progressed to T2D during 10 years of post pregnancy follow up. Although the majority of women with GDM will be normoglycemic in the immediate postpartum period, studies suggest that 11% to 33% will display evidence of impaired glucose tolerance, and 1% to 8% will have frank diabetes, at 6 to 12 weeks post delivery. In many cases, these individuals likely had some degree of glucose intolerance, pre-diabetes or even undiagnosed T2D, that preceded the pregnancy, but their condition was not recognized until the postpartum screen. Even when postpartum glucose levels are within normal limits, women with a history of GDM are at much higher risk of developing GDM in subsequent pregnancies. Guidelines advocate careful post pregnancy surveillance to

monitor for T2D. Screening for impaired glucose tolerance is recommended at 6 to 12 weeks following delivery and then at a minimum of every 3 years thereafter. Despite this guidance, evidence indicates that only half of women with GDM receive appropriate post-partum screening for T2D in most populations. Barriers to screening may be patient related (e.g. lack of awareness regarding risk status), provider-related (e.g. uncertainty regarding recommended screening intervals) or system-related (e.g. lack of communication between obstetric and postpartum providers, or limited access to the health care system).The American Diabetes Association further recommends that women with a history of GDM found to have prediabetes should receive lifestyle interventions or metformin to prevent diabetes. Diabetes educators have the potential to play a vitally important role in addressing these barriers, both through the education of patients and providers and by serving as a bridge between the prenatal and postnatal care teams (Kim *et al*., 2002).

1.15 Global Epidemiology of Gestational Diabetes Mellitus (GDM)

There has been some research on gestational diabetes in developed populations. Some of the research findings on GDM are that-

• GDM rates are increasing and are much higher for developed women than other women in Canada.

• The rate of GDM for these women in certain communities in Saskatchewan, Manitoba, Quebec, and Ontario ranges from 9% up to 13% and are up to 4 times higher than the rate for other women .

• Within the Saskatoon Health District, about 4% of pregnant non aboriginal women had GDM and about 6% of Aboriginal women .Outside of the health district, the number of non-Aboriginal pregnant women was lower but almost 23% of Aboriginal women (or about one in four) had GDM. This means that Aboriginal women living outside the Saskatoon Health District were over nine times more likely to have GDM.

• GDM is more common for women in rural areas than urban areas, for women from more accessible communities than less accessible communities, and for women from inland versus coastal communities.

• A study in Alberta found that rural women had more risk factors for GDM, including higher blood sugar levels, higher rates of obesity, greater waist circumferences, and higher rates of self-reported GDM.

• Where a woman lives affects their risk of developing GDM. This is probably due to lifestyle and diet differences in urban, rural, and isolated.

• Normal weight Cree women have been found to have GDM rates as normal women but obese Cree women are at twice the risk. About 15% of Cree women who were overweight before pregnancy had GDM and over 27% of obese women.

• About half of First Nations women diagnosed with GDM in a one pregnancy are diagnosed in subsequent pregnancies.

• Up to 70% of First Nations women with GDM will develop type2 diabetes later in their life.

Studies find that GDM is more common in First Nations populations than the general Canadian and North American populations. Since GDM is a risk factor for the development of type2 diabetes, the high rates of GDM may be contributing to the high rates of type2 diabetes among the First Nations population.

(Berger *et al.,* 2007; Aljohani *et al.,* 2008)

2.1 Prevalence and Pregnancy Outcome of Gestational Diabetes Mellitus Among Bangladeshi Urban Pregnant Women

This was a descriptive type of cross sectional study, conducted in different hospitals in Dhaka city. Initially 960 pregnant women of 24th to 28th weeks were selected purposively. Modified method of Carpenter and Coustan criteria was followed to diagnose GDM. For each GDM case diagnosed, one non GDM pregnant women was taken as control after matching age and parity. Both groups were followed up to 4 weeks after delivery to find out maternal and neonatal mortality and morbidities.

Out of 960 pregnant women 72 were GDM positive (7.5%).There was no maternal mortality but morbidities like hydramnions, pre-eclampsia, urinary tract infection, puerperial sepsis and surgical interventions were more prevalent in GDM compared to non GDM groups. There was one still birth, one perinatal mortality (due to respiratory distress syndrome) and one congenital anomaly observed in neonates of GDM mothers. More pre-term, post-term, low birth weight and macrosomic babies were found among the babies of GDM mothers than non GDM mothers. More babies also suffered from neonatal jaundice and respiratory distress syndrome in GDM groups than non GDM groups (Mannan *et al.,* 2012).

2.2 Prevalence of gestational diabetes mellitus in South Asia

A study was conducted by Conway et al in 1999, on South Indian Population. The purpose of this case study was to determine the prevalence and identify risk factors of GDM in the South Indian population. Result showed that the incidence of gestational diabetes mellitus is approximately 4% of mothers and approximately 40% of women with GDM during their pregnancy will go on to develop Type2 diabetes (Conway *et al.*, 1999).

A subset of the South Asian ethnic group which have been shown to be at high risk for the GDM patients. Among the 980 mothers studied only 7 were diagnosed with GDM (0.71%) and the rate of GDM detected in worldwide women population is 4% every year. Studies conducted by WHO and other organizations like American Diabetes Association are large scale in terms of number of patients, area covered and the time period. The present study is comparatively smaller. But a prevalence of 0.71% of GDM in a time

period of 7 days, in a small population size and covering single area is substantially significant. It also suggests there might be increasing risk. This case study also helped us to identify the causes of GDM is related with family history (genetic), socioeconomic or dietary as opposed to infections, age or weight. 2 out of the 7 affected women (28.6%) had a family history of GDM, which may have influenced their susceptibility. Interestingly, all the patients had undergone at least one stillbirth and two of the patients had two stillbirths. This shows there was consistent pattern of previous history of miscarriage or stillbirths (ADA, 2002).

2.3 Prevalence of gestational diabetes mellitus in Kashmir and Tamil Nadu

Prevalence of gestational diabetes mellitus varies widely. Depending on the population studied and the diagnostic test employed, prevalence may range from 2.4 to 21% of all pregnancies. In India it is difficult to predict any uniform prevalence levels because of wide differences in living conditions, socioeconomic levels and dietary habits. Zargar *et al*. found the prevalence of GDM to be 3.8% in Kashmiri women. In a random survey performed in various cities in India in 2002-2003, an overall GDM prevalence of 16.55% was observed. In another study done in Tamil Nadu, GDM was detected in 17.8% women in urban, 13.8% women in semi-urban and 9.9% women in rural areas (Zargar *et al.*, 2004).

2.4 Prevalence of gestational diabetes mellitus & associated risk factors at a tertiary care hospital in Haryana

This study was carried out during June 2009 to January 2011 in antenatal care clinic at Post Graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana. A total of 607 women (gestational age between 24th and 28th weeks) were enrolled during the study period.GDM was diagnosed in 43 (7.1%) women based on ADA criteria. Of these, 17 women had all three values abnormal on OGTT and 26 women had two abnormal values. A single abnormal value was observed in 66 (10.87%) women, in whom fasting plasma glucose was the most common abnormal value seen in 55 women. Most of the participants were below 26 years of age (463, 76.3%) and highest number of participants were in the age group 21-25 years (353, 58.2%). The mean age of participants was 23.62 ± 3.42 year (range 18-38). The prevalence rate was higher in women aged 26-30 and >30years (11.57 and 34.8%, respectively) compared to women aged 16-20 and 21-25

years (4.54 and 4.53%, respectively) and this observation was found to be statistically significant (Rajput *et al.,* 2013).

2.5 Prevalence of Gestational Diabetes Mellitus (GDM) in Africa

Ethiopia

Seyoum B *et al* conducted a study in 1999 on GDM in rural Ethiopia. This was a well reported study with a low risk of bias. The OGTT was utilized as the diagnostic test based on the WHO 1985 criteria and a GDM prevalence of 3.7% was reported (Seyoum *et al.,* 1999).

Morocco

In 2009, a research was performed in urban Morocco by Bouhsain *et a.l* on GDM. The authors reported a relatively high prevalence of GDM; 7.7% using the Carpenter and Coustan's criteria. However, the authors stated that all women who tested positive on a glucose challenge screening test should have then been referred for an OGTT yet only 40% of these women received an OGTT. This suggests that the GDM prevalence could actually have been higher if all women requiring an OGTT were in fact tested. The authors did report that the GDM prevalence was similar to the prevalence of type 2 diabetes in that population. In addition, the risk of potential bias within this study was high (Bouhsain *et al.,* 2009).

Mozambique

By Challis K *et al* Only one case control study of relatively poor reporting quality and moderate risk of bias, was analyzed from Mozambique. The study was conducted in 2002 in an urban/suburban setting and the population group was not stated. Considering the majority of the Mozambican population is black, it is assumed that the cohort consisted of black females. Authors of the study reported a GDM prevalence of 11% amongst women who had late fetal deaths (cases) and 7.3% amongst women who had delivered live newborns (controls). The investigators diagnosed GDM using their own diagnostic criteria which classified glucose readings for diabetes mellitus and IGT as GDM (Challis *et al.,* 2002).

Nigeria

Six Nigerian studies by Kuti MA, Abbiyesuku FM, Akinlade KS, Akinosun OM, & Adedapo KS *et al*, all on urban populations, were evaluated. These studies were conducted between the years 2004–2013. All the studies used the OGTT as the method to detect GDM but different glucose concentrations were employed (50 g, 75 g and 100 g) over a time period of one to three hours.

One study was focussed solely on determining the prevalence of GDM amongst women with risk factors which included history of fetal macrosomia, maternal obesity, previous intrauterine death, first degree relative with diabetes, glycosuria and history of GDM in a previous pregnancy. Another two studies were case control studies whereby women with risk factors for GDM or women who had delivered macrosomic babies were classified as cases, and women without risk factors or women who had delivered normal weight babies served as the controls. Prevalence of GDM was higher amongst the cases in both studies; 6.2% versus 4.6% and 2.5% versus 1.5%. However, Kamanu *et al.,* 2009, who used their own diagnostic criteria as mentioned above, diagnosed GDM based on a 1 hour 50 g OGTT (>7.8 mmol/l/140 mg/dl) and only followed up borderline results with a 75 g 2 hour OGTT. Excluding the two case control studies discussed above, the other four Nigerian studies utilized the WHO diagnostic criteria (two used the WHO 1985 criteria and two used the WHO 1999 criteria). One of these four studies compared the detection rate of the three hour 75 g OGTT using the WHO 1985 criteria to the three hour 100 g OGTT using the NDDG criteria. The 75 g OGTT with WHO 1985 diagnostic criteria yielded a higher GDM prevalence (11.6% versus 4.5%). Conversely, this study found that the incidence of fetal macrosomia was higher (66.7%) amongst women diagnosed with GDM by the 100 g OGTT using the NDDG criteria than amongst women diagnosed with GDM by the 75 g OGTT using the WHO 1985 criteria (23.1%) (Kuti *et al.,* 2011).

South Africa

Four South African studies, conducted between 1979 and 2010, were included in the systematic review. One study focused predominantly on Indian women, two on black women and the other did not state the ethnicity of the women. The study by Jackson and Coetzee, (1979) tested women for GDM because they had one or more risk factors. These risk factors included (i) a parent or sibling with diabetes; (ii) repeated miscarriages; (iii)

obesity; (iv) previous macrosomic infant; (v) glycosuria; (vi) previous hyperglycaemia; (vii) previous infant with a severe congenital anomaly; (viii) previous perinatal death; (ix) polyhydramnios and (x) Indian ethnicity. In addition, this particular study utilized a 2 hour 50 g OGTT and the investigators' own diagnostic criteria.

All but one study employed a two hour OGTT for the diagnosis of GDM. The one study that did not employ an OGTT was interestingly the most recent study in South Africa, conducted in 2010, which tested fasting or random blood glucose levels and referred to an institutional protocol for diagnostic criteria. Ranchod *et al.*, (1991) compared the WHO 1999 criteria and DSPG of EASD criteria; WHO criteria produced a higher GDM prevalence (3.8% versus 1.6%). Overall, the four South African studies produced GDM prevalence figures ranging from 1.6% to 8.8% (Jackson *et al.*, 1979).

Tanzania

One study, published in 1991, was included on GDM prevalence in rural Tanzania. This study involved an OGTT on a small sample of women (n = 189) using the WHO 1985 diagnostic criteria. A prevalence of 0% was determined. Unfortunately, as the full text article could not be obtain, reporting quality and risk of bias for this study could not be assessed (Hall *et al.*, 2011).

Significance of the study

Gestational diabetes is associated with important prenatal and long term health risks and many of the risks increases in relation to the severity of maternal hyperglycemia. Women with impaired glucose tolerance in the first few months postpartum are particularly at high risk for diabetes. In some populations, women who have had GDM comprise a substantial proportion of the overall women population who ultimately develops diabetes. Effective measures to prevent women with GDM from progressing to diabetes could therefore have a significant population health impact (Byth *et al.,* 2003).

Offspring of women with GDM are at an increased risk for obesity and have unexpectedly high prevalence of elevated glucose levels during childhood and adolescence (Metzger *et al.,* 1998).

Hyperglycaemia during pregnancy is found to be associated with various maternal and perinatal adverse outcomes. Their offspring's will have a lifelong increase risk of glucose intolerance, obesity and metabolic syndrome whereas the mothers will have a higher risk of metabolic syndrome and diabetes in the future. The detection of GDM during pregnancy provides an opportunity to identify women at risk of short term and long term complications. We now have evidence that early diagnosis and intervention can reduce the adverse perinatal outcomes throughout all these years, there is still no consensus on the optimal diagnostic cut-off until the recent recommendation by the International Association of Diabetes and Pregnancy Study Groups (Landon *et al.,* 2009).

A number of risk factors have been associated with a greater likelihood of developing gestational diabetes. By and large these are the same factors that predict overt diabetes, and they include advanced maternal age, a family history of diabetes in a first-degree relative, obesity, and glycosuria. In addition, certain outcomes in a previous pregnancy are believed to be predictive, including stillbirth and the birth of a macrosomic baby (Yogev *et al.,* 2004).

The purpose of this Study was to provide a recent update and to discuss the current controversies on GDM. Identifying a high risk group could potentially allow preventive measures before the development of GDM. The future direction should focus on the early prediction and effective preventive measures before the development of GDM, so as to decrease the associated short term and long term complications.

Aims of the study

The aim and objectives of the study were

- To estimate the prevalence of Gestational Diabetes Mellitus along with its risk factors among the population in different districts of Bangladesh.
- To observe the major complication associated during pregnancy and effect on neonates.
- To examine the knowledge about Gestational Diabetes Mellitus among the population.

Methodology

3.1 Type of the study

It was a prospective study.

3.2 Study population

In this study a total number of 150 pregnant women were interviewed with a questionnaire to determine the prevalence, drug therapy, major complications & effects on neonates of gestational diabetes mellitus. The study was carried out on patients in Tongi General Hospital; Popular, Al-Raji and Medistar Hospital in Narayanganj and Naogaon Maternity Hospital.

3.3 Inclusion criteria

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

3.4 Exclusion criteria

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

3.5 Questionnaire development

Questionnaires were developed based on the study of different journal papers of Gestational Diabetes Mellitus. Survey questionnaire form has mainly different parts.

- Personal information
- Disease information
- Pregnancy history
- Nutrition
- Exercise profile
- Diagnosis
- About Gestational Diabetes Mellitus
- Post natal effects

3.6 Sampling Technique

In this study purposive sampling was followed.

3.7 Study period

The duration of the study was about six months that started from January to June 2015.

3.8 Data Analysis

Data were registered using Microsoft Access data entry. Control of data entry was secured through both programme appliance and manually. The prevalence rates of GDM and other aspects were analyzed by simple percentages.

4.1 Prevalence of Gestational Diabetes Mellitus (n=150)

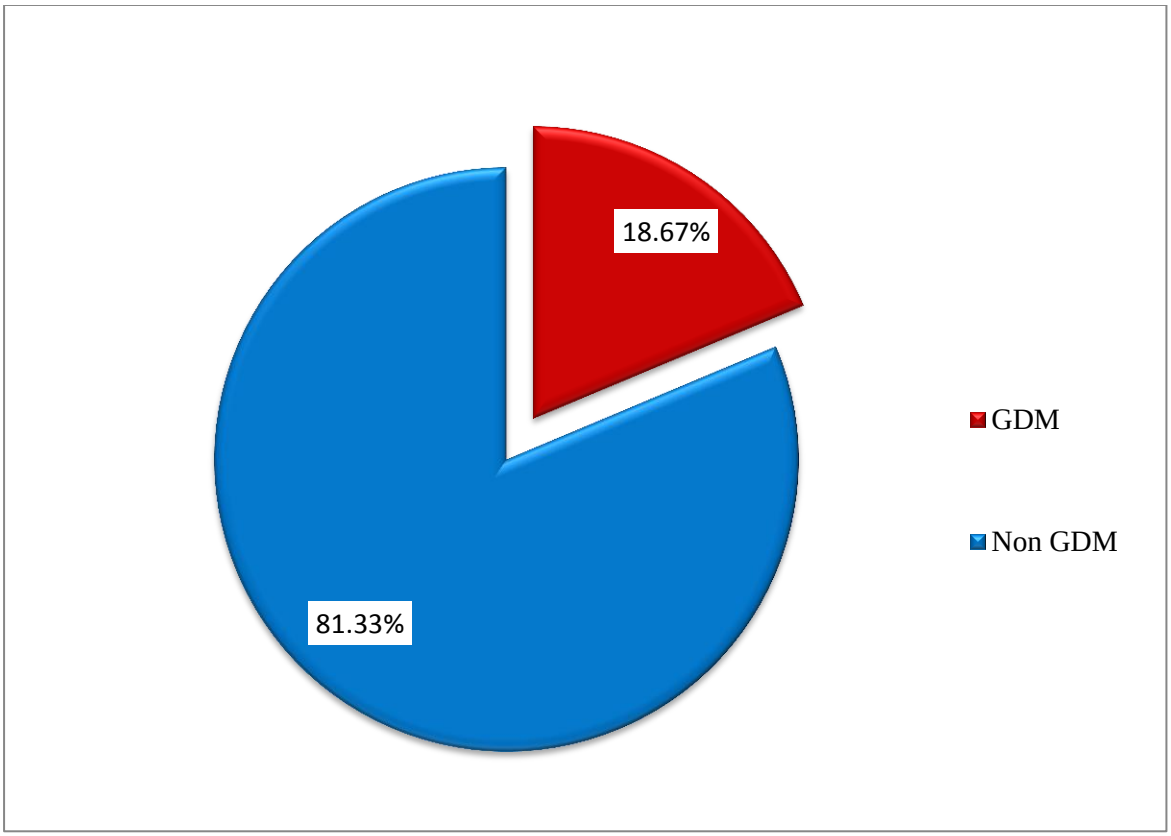

Figure 4.1: Prevalence of gestational diabetes mellitus

The above figure shows the prevalence of Gestational Diabetes Mellitus (GDM). Out of 150 pregnant women surveyed, 28 (18.67%) were found to have gestational diabetes mellitus and 122 (81.33%) women were not affected by Gestational Diabetes mellitus.

4.2 Age Distribution (n=28)

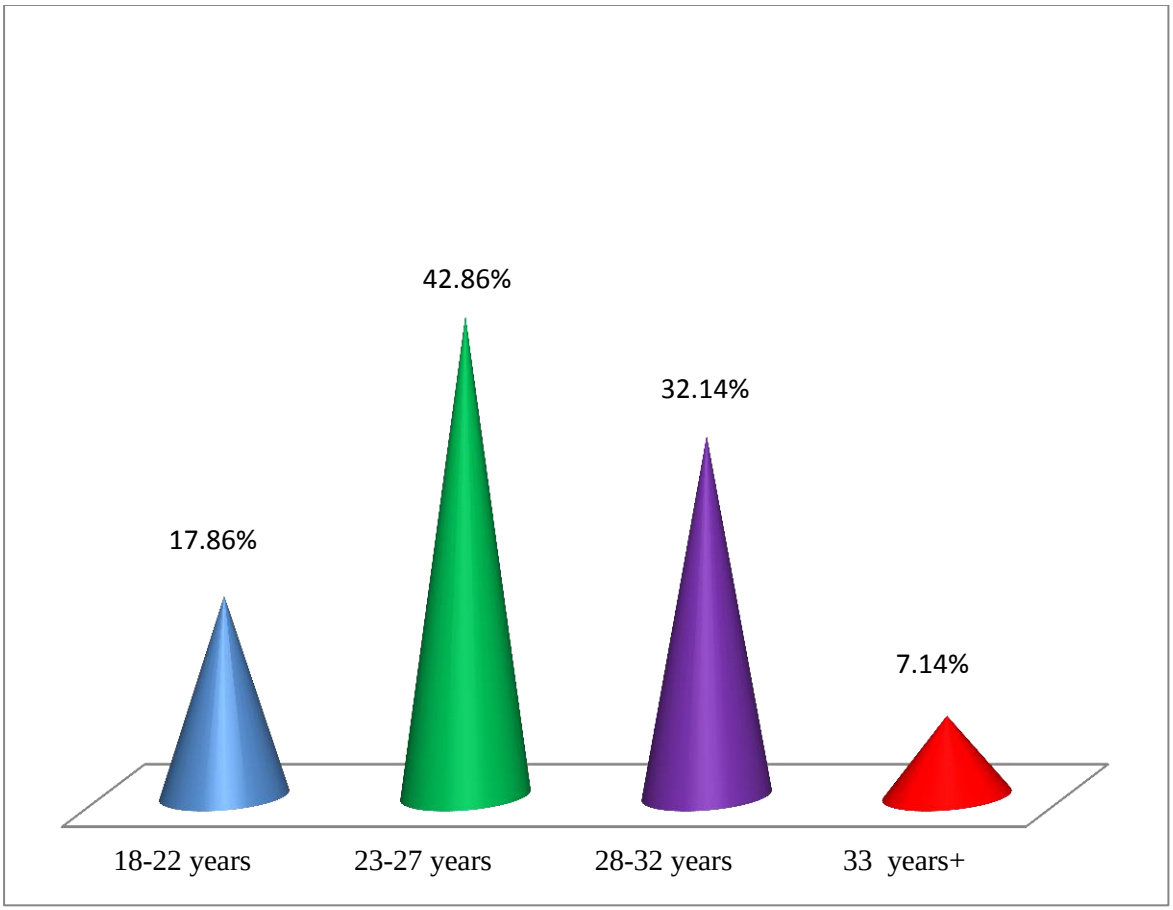

Figure 4.2: Age distribution

In this study, out of 150 patients 28 were found to have GDM. This figure represent the age distribution of GDM patients which observed that the highest percentage of the respondents were in the age group of 23-27 years (42.86%). The least amount (7.14%) of respondents were from the age group of 33years and above.

4.3 Educational Qualification (n=28)

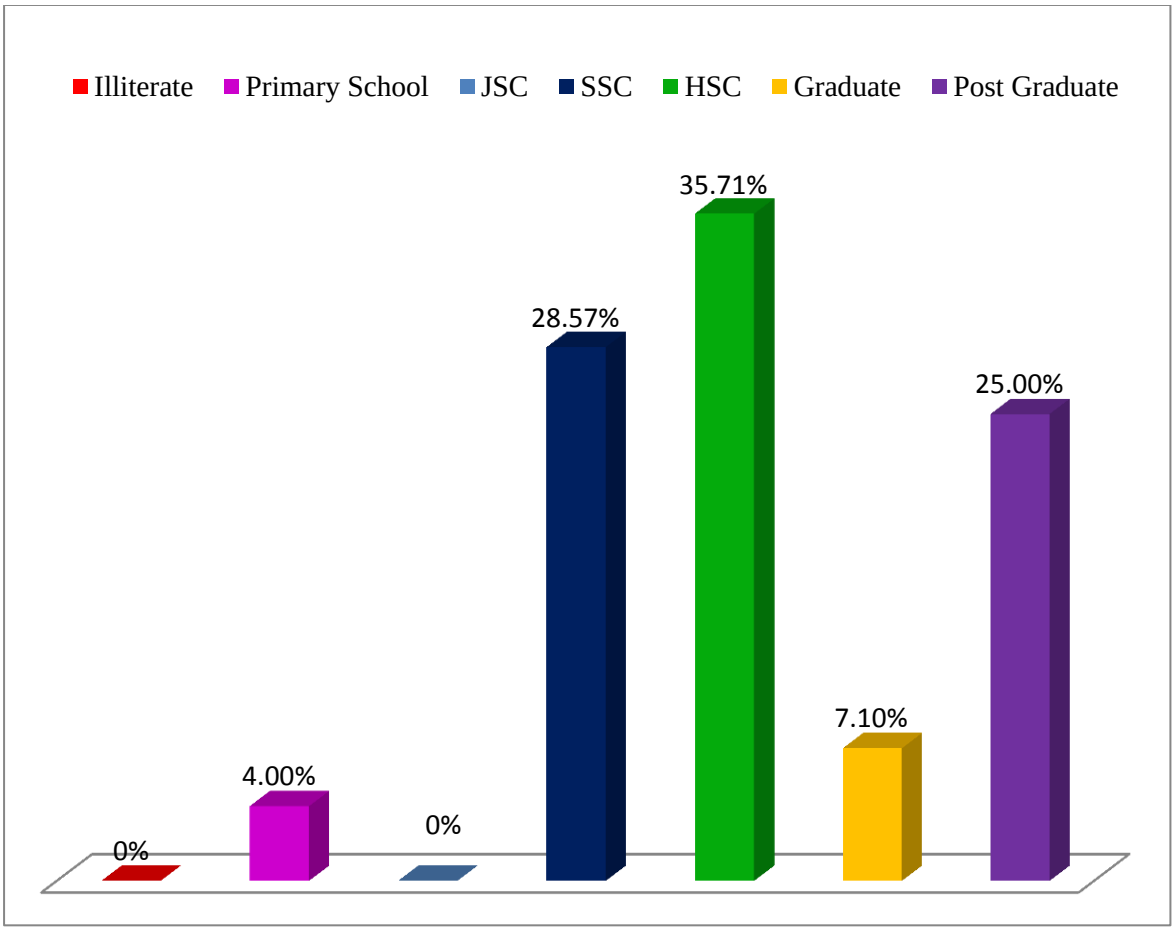

Figure 4.3: Educational qualification

The above figure shows that, among all the GDM patients, maximum respondents (35.71%) had a minimum qualification of HSC level. About 28.57% had minimum qualification of SSC level and 25% had completed their Post graduation. Very few of the respondents had educational background up to primary level (4%) and none of them (0%) were illiterate.

4.4 Occupational Status (n=28)

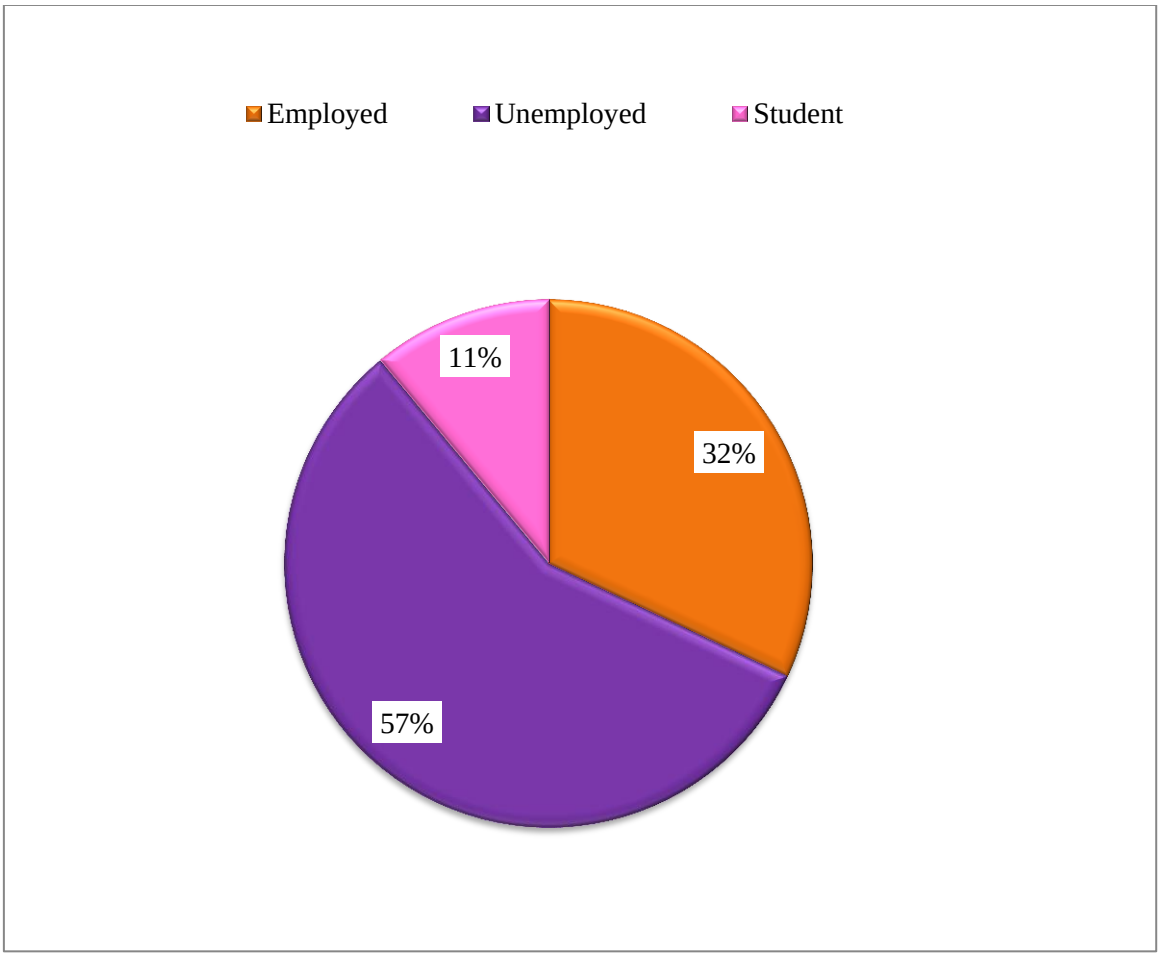

Figure 4.4: Occupational status

Among all the patients with GDM surveyed, about 57% respondents were unemployed, 32% women were employed and 11% were student.

4.5 Family History of Diabetes (n=28)

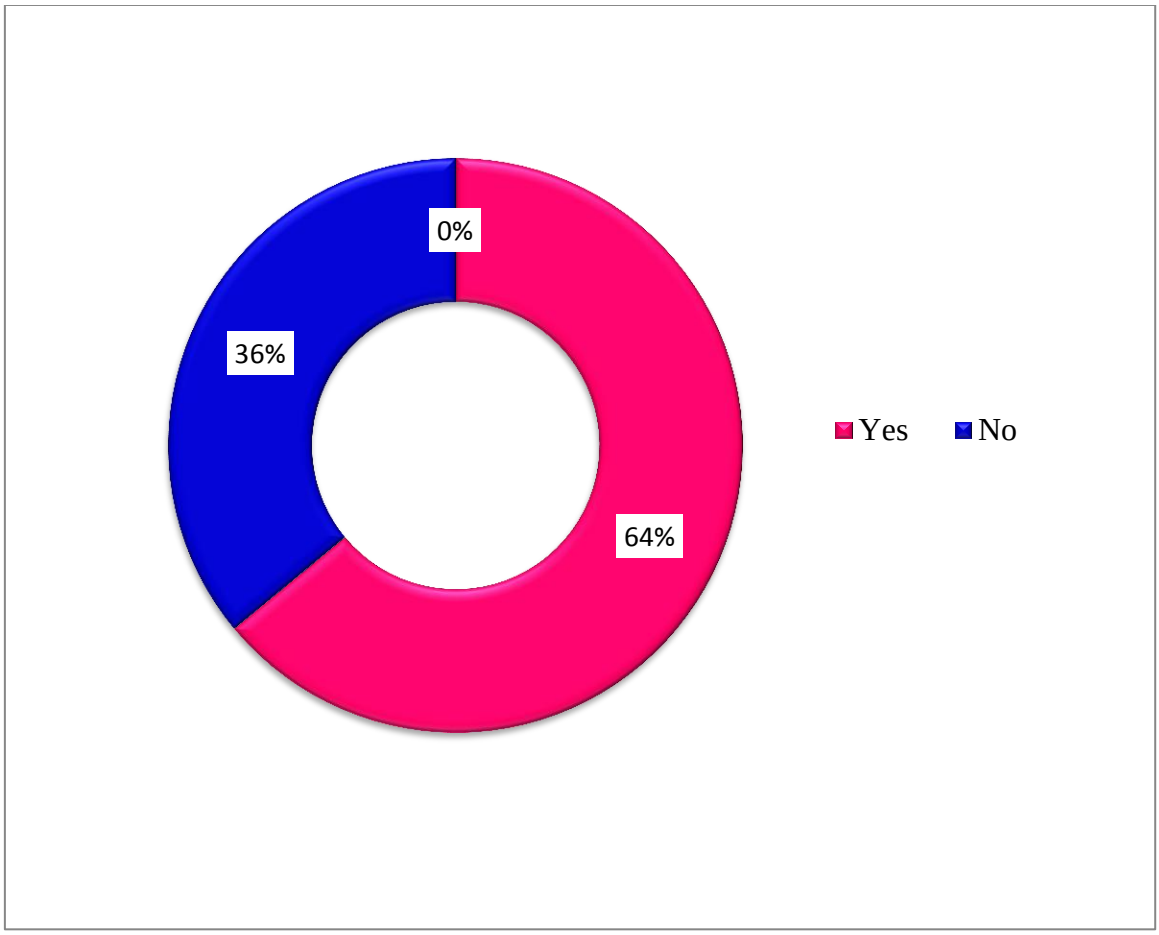

Figure 4.5: Family history of diabetes

The above figure shows that, most of the patients (64%) had a diabetes history in their family and rest of them (36%) responded negatively in this case.

4.6 Relation with the Patient in the Family Having Diabetes (n=18)

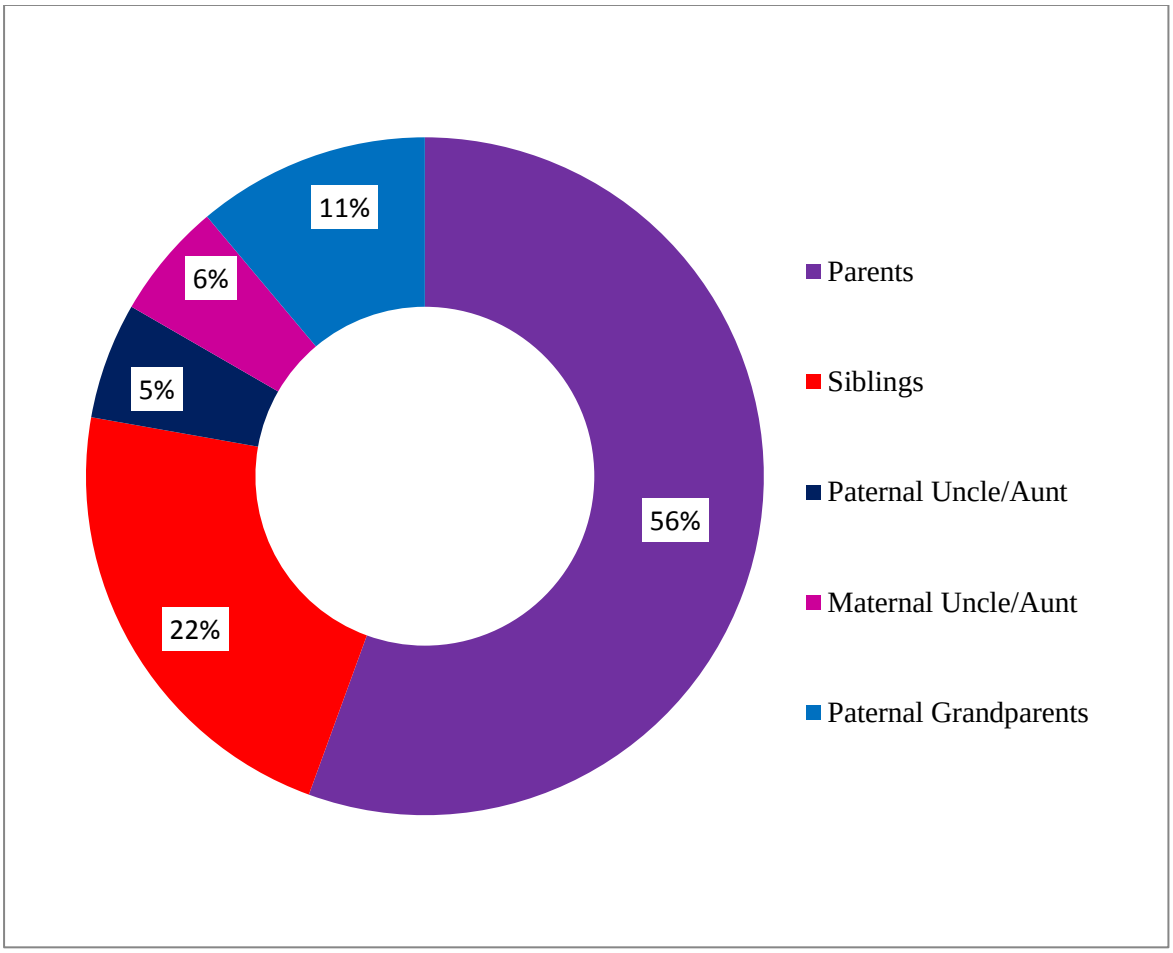

Figure 4.6: Relation with the patient in the family having diabetes

The figure above shows the percentage of people with Diabetes who were related as family member to the patients of this study. It is certain that most of the respondents' (56%) parents had Diabetes. Other family members also had Diabetes but the least were reported to be the patients' siblings & paternal relations (Uncle/Aunt).

4.7 Diabetes Knowledge (n=28)

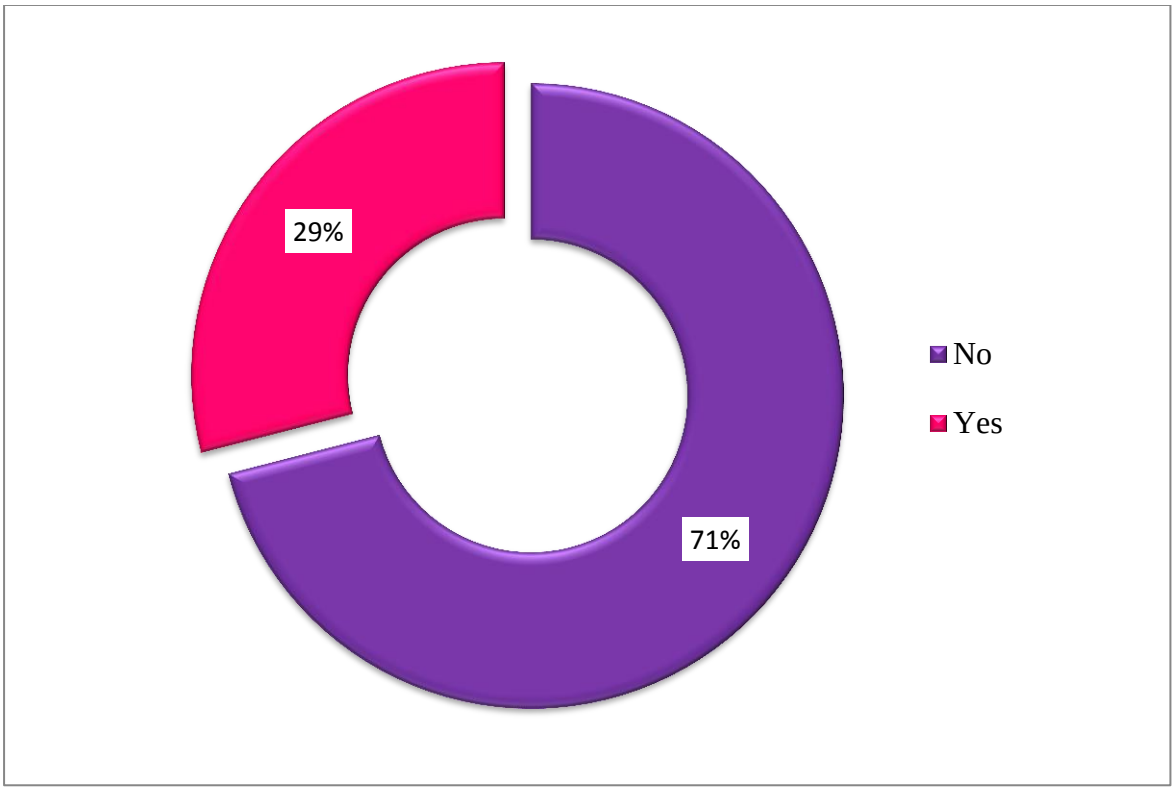

Figure 4.7: Knowledge about diabetes

Out of 28 patients were asked, whether they have had any knowledge about GDM or not, only 29% gave positive answer and rest of the patients (71%) had no diabetes education or knowledge in the past.

4.8 Other Medical Problem Apart from Gestational Diabetes Mellitus (n=28)

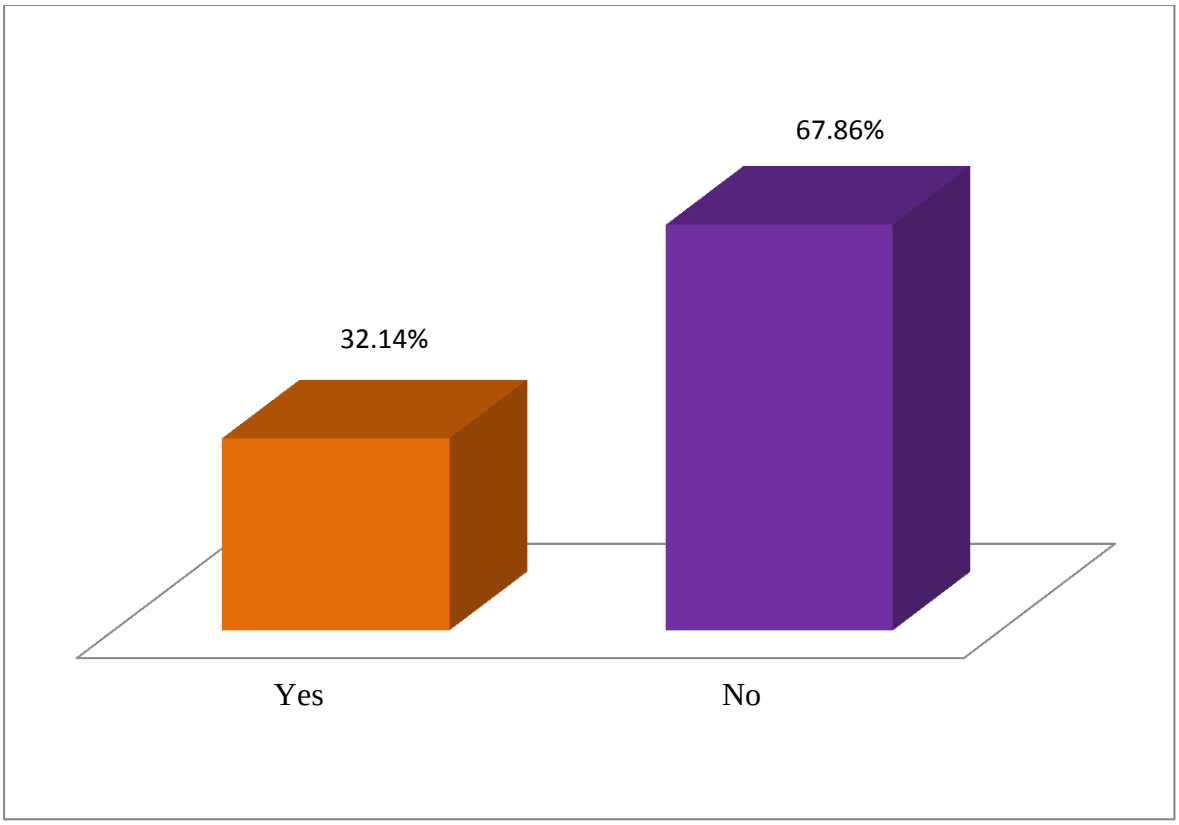

Figure 4.8: Other diseases apart from gestational diabetes

The study found that, 32.14% of the patients were suffering from other medical problem apart from GDM and 67.86% of the patients had no other medical problem.

4.9 Types of Other Diseases (n=9)

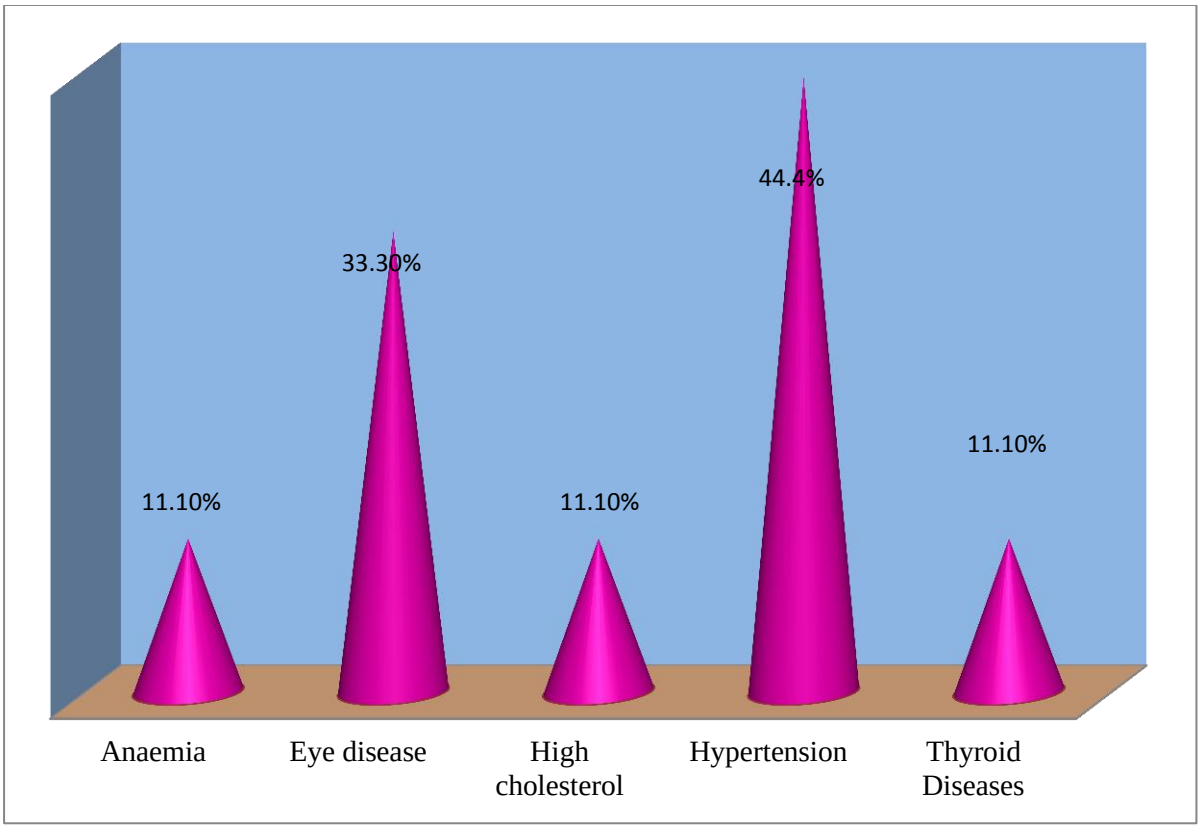

Figure 4.9: Types of other disease

Among 28 patients with GDM, 9 said that they were having some other medical problems apart from GDM. Among them 44.3% respondents were suffering from different types of eye disease, 11.10% had anaemia and 11.10% had high cholesterol. About 44.40% of the respondents were suffering from hypertension, and 11.10% had hypothyroidism.

4.10 Medication Intake (n=28)

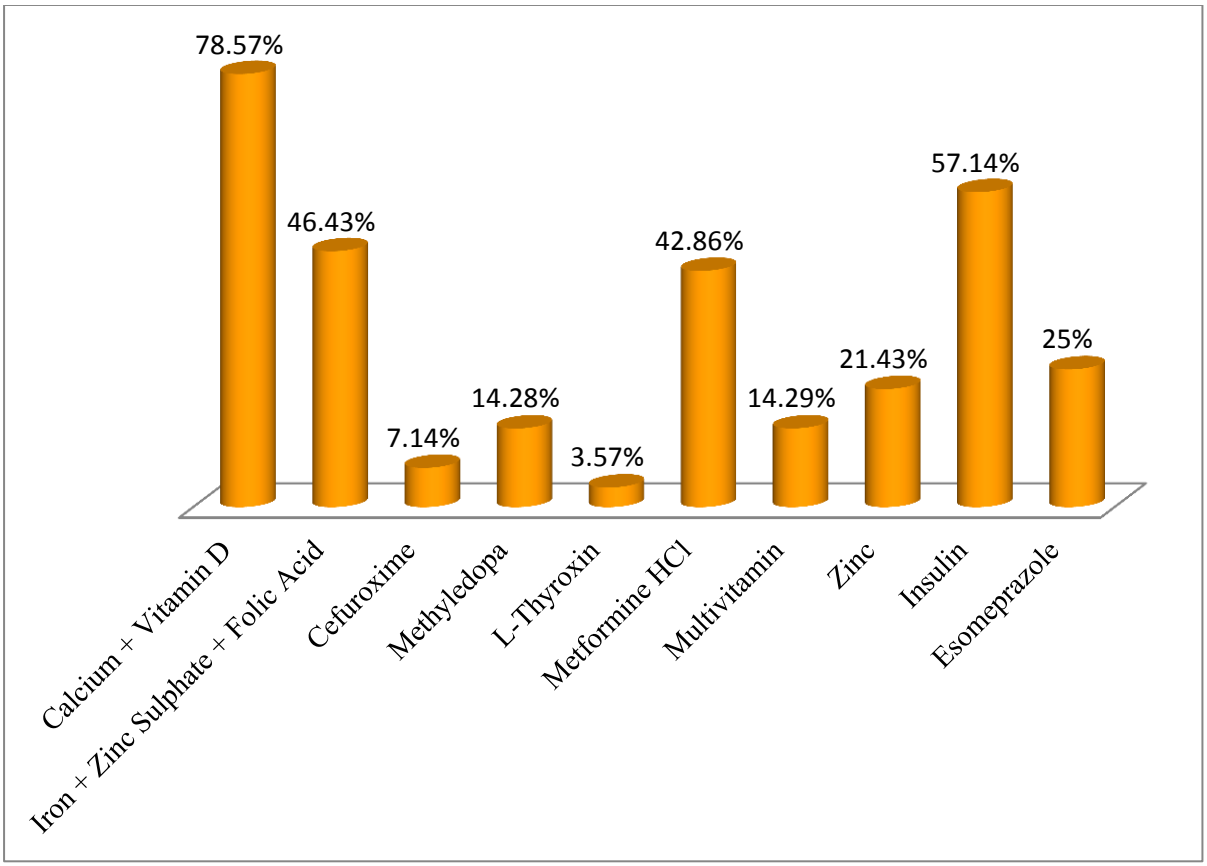

Figure 4.10: Medication intake

The study found that, the patients took mostly Insulin (57.14%) and Metformine HCl (42.86%) for the treatment of GDM. They also took Calcium + Vitamin D (78.57%), Iron + Sulphate +Folic acid (46.43%), Zinc (21.71%), Esomeprazole (25%), Multivitamin (14.29%), Methyldopa (14.28%), Cefuroxime (7.14%) and L-thyroxin (3.57%).

4.11 Pregnancy Duration (n=28)

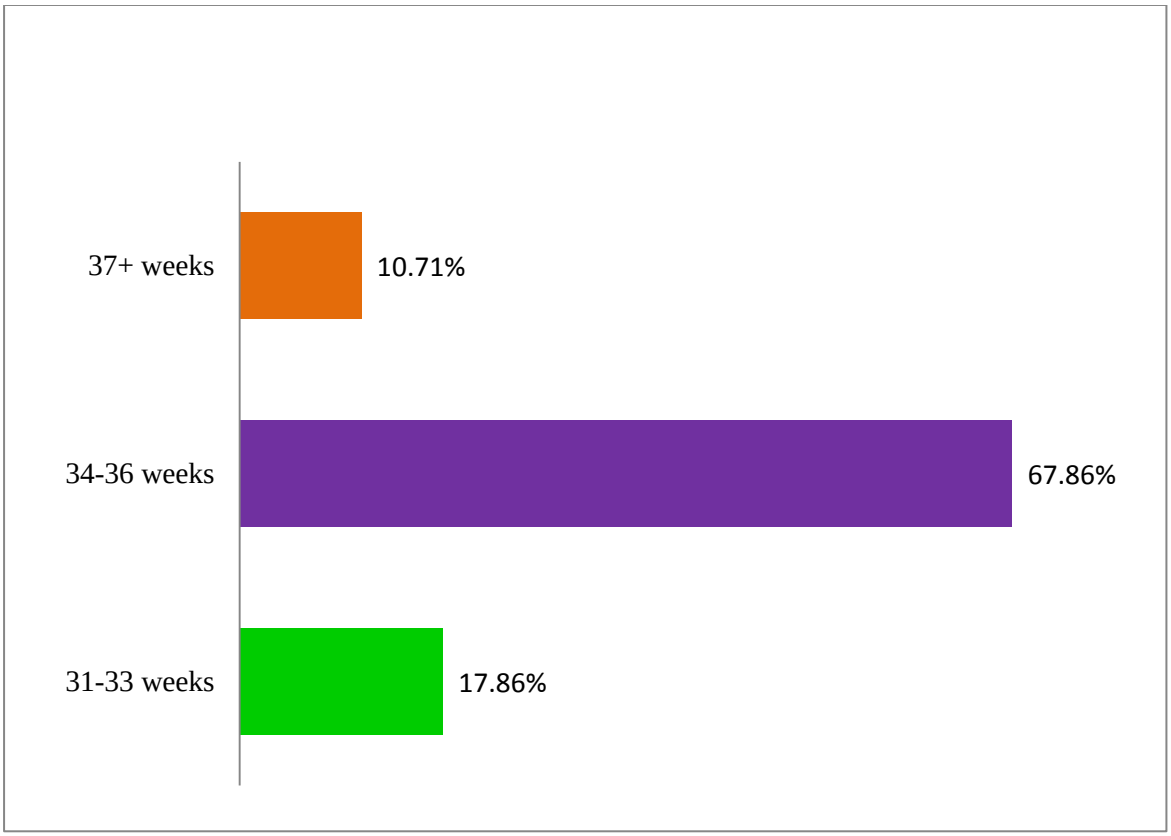

Figure 4.11: Pregnancy duration

In this study most of the respondents were from the group of 34-36 weeks (67.86%), of gestational period. Only 17.86% were in the group of 31-33 weeks and 10.71% women were found in the group of 37 weeks & above.

4.12 Current Numbers of Children (n=28)

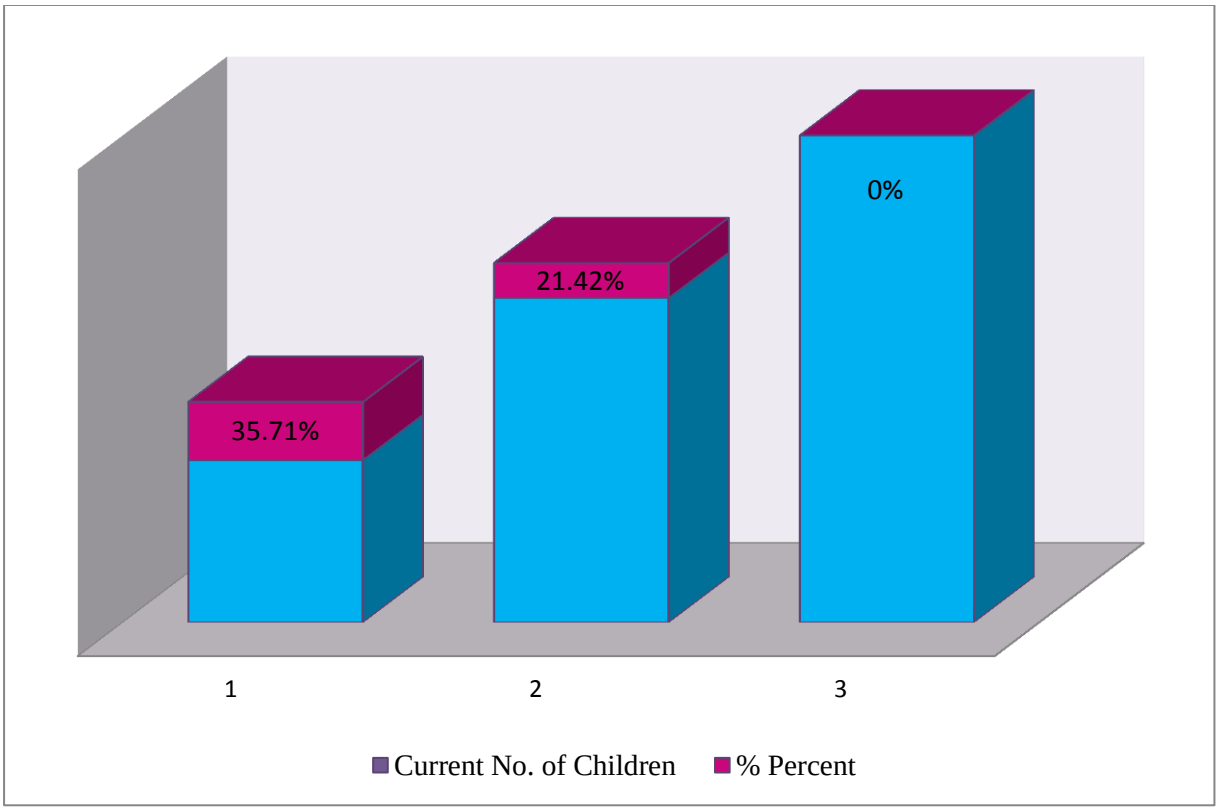

Figure 4.12: Current numbers of children

Among 28 patients, 35.71% said that they had already one child and 21.42% said that they had 2 children. For rest of them, this was the first pregnancy.

4.13 Baby's Term Condition (n=28)

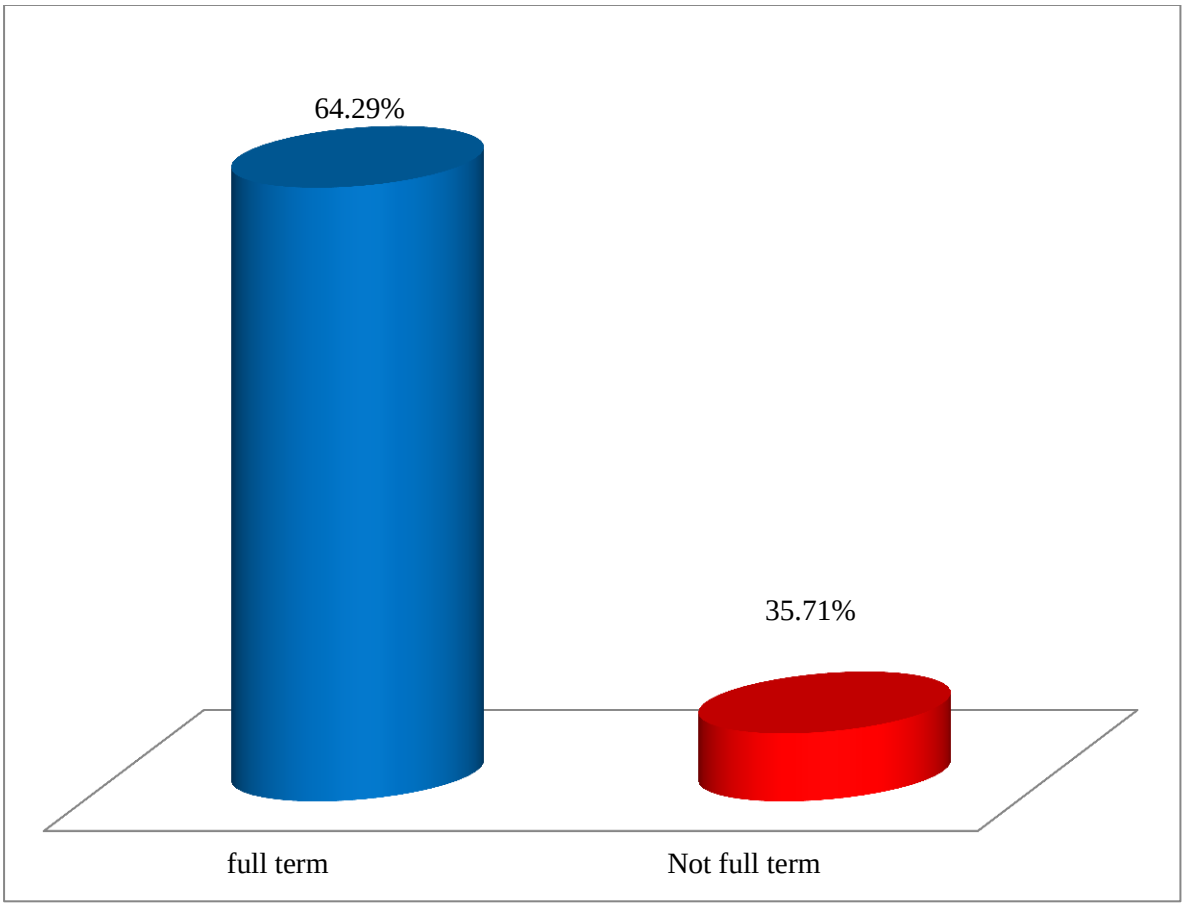

Figure 4.13: Baby's term condition

Almost 64.29% of the babies were full term delivered and 35.71% were either premature or post mature.

4.14 Percentages of Premature Babies (n=10)

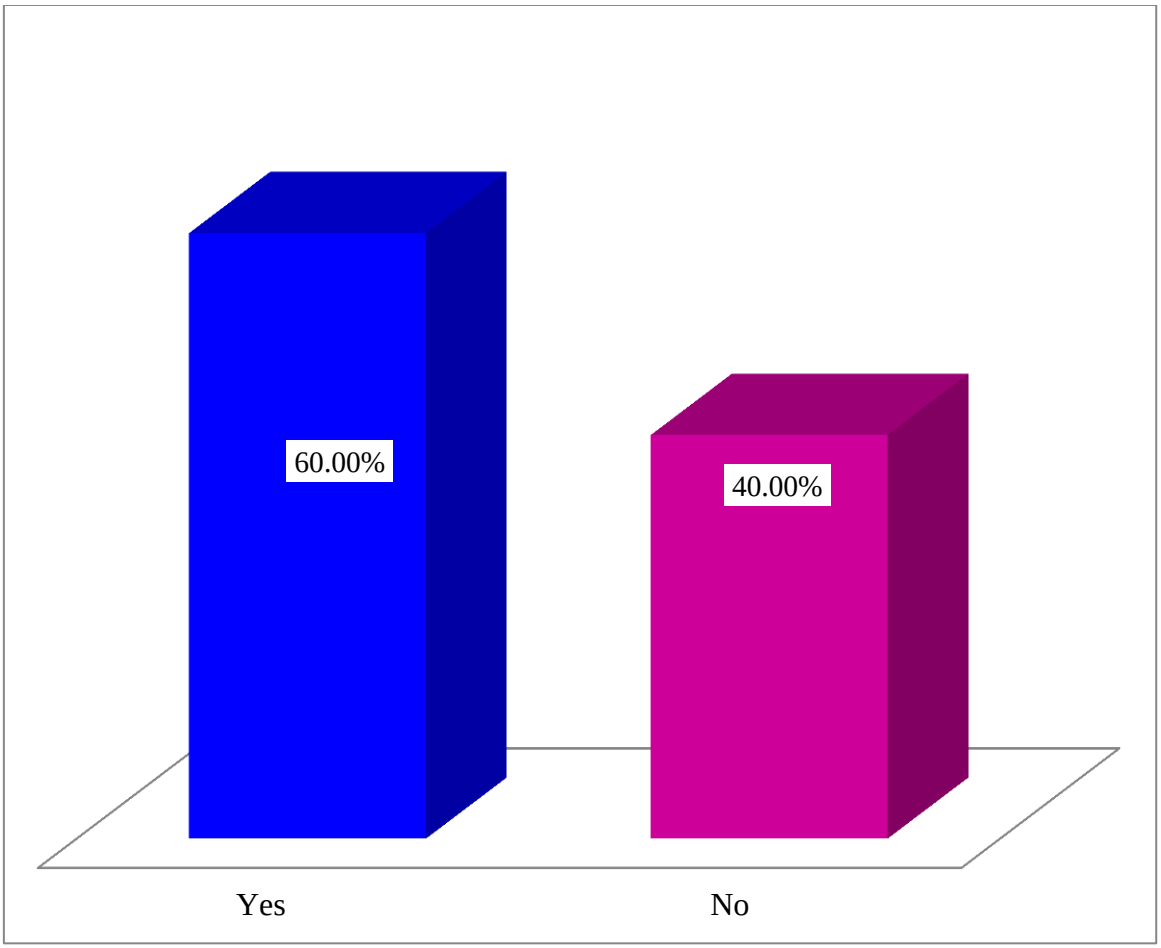

Figure 4.14: Percentages of premature babies

Among 28 women with GDM served in this study, total numbers of 10 (35.71%) babies were not full term. Among them 60% were born as premature and rest of them were post mature.

4.15 Percentages of Miscarriages (n=28)

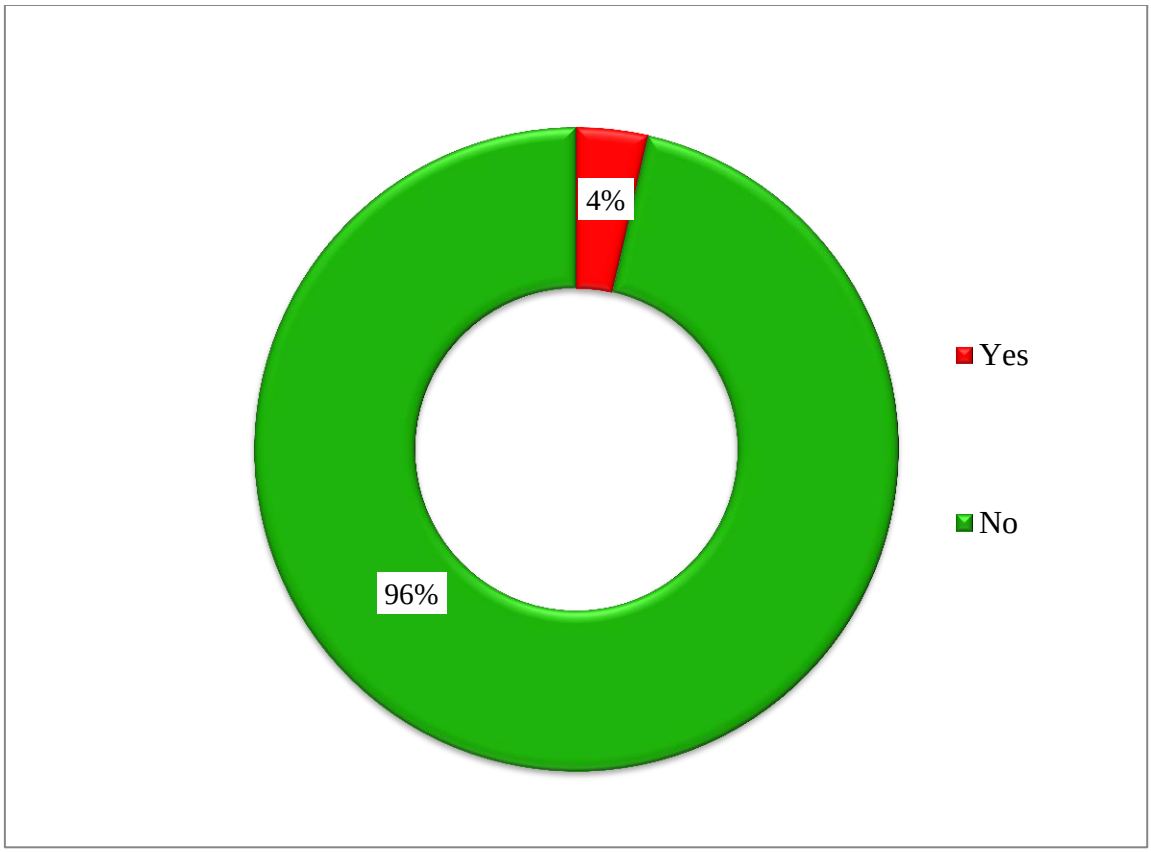

Figure 4.15: Percentages of miscarriages

In this study it was found that, about 4% of the subjects had miscarriages.

4.16 Complication During Pregnancy (n=28)

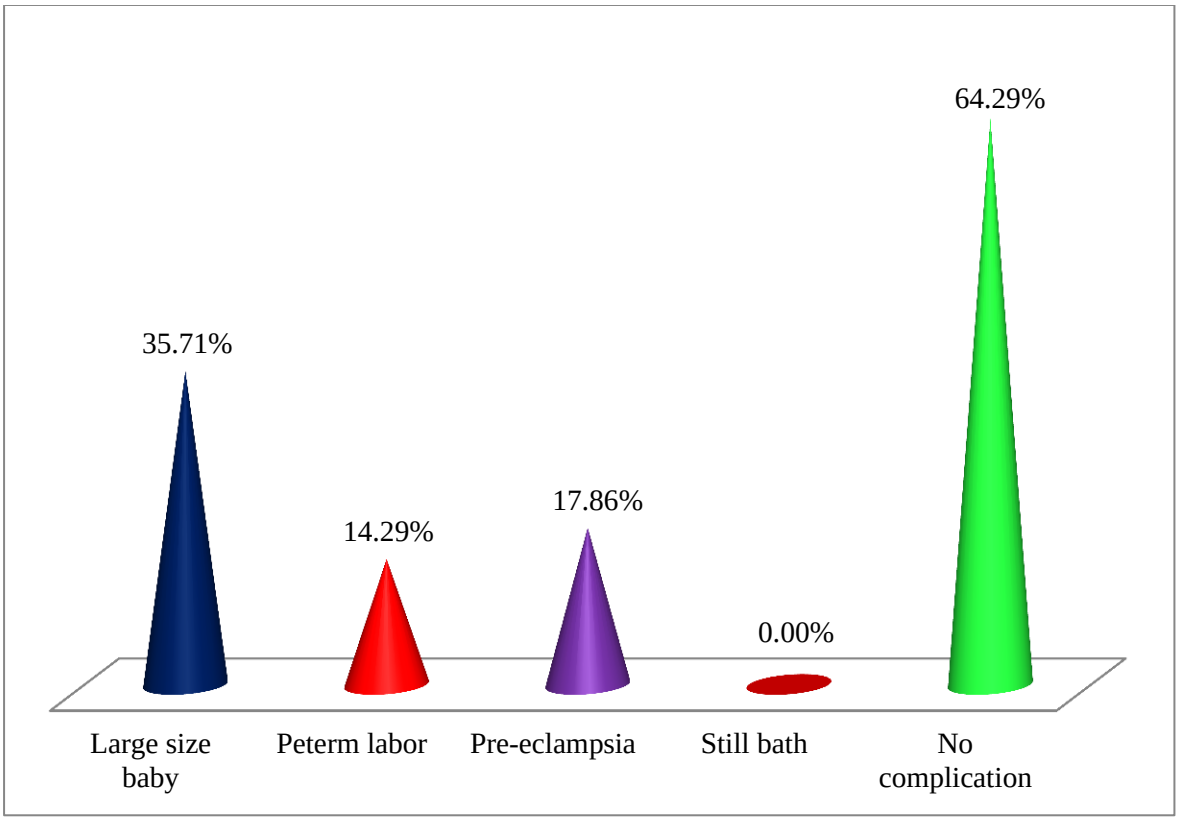

Figure 4.16: Complication during pregnancy

From the study, 64.29% of respondents were found to have no complication in prior to pregnancy, 17.86% had pre-eclampsia, 14.29% had preterm labor and 35.71% had large size baby (macrosomia).

4.17 Weight Distribution (n=28)

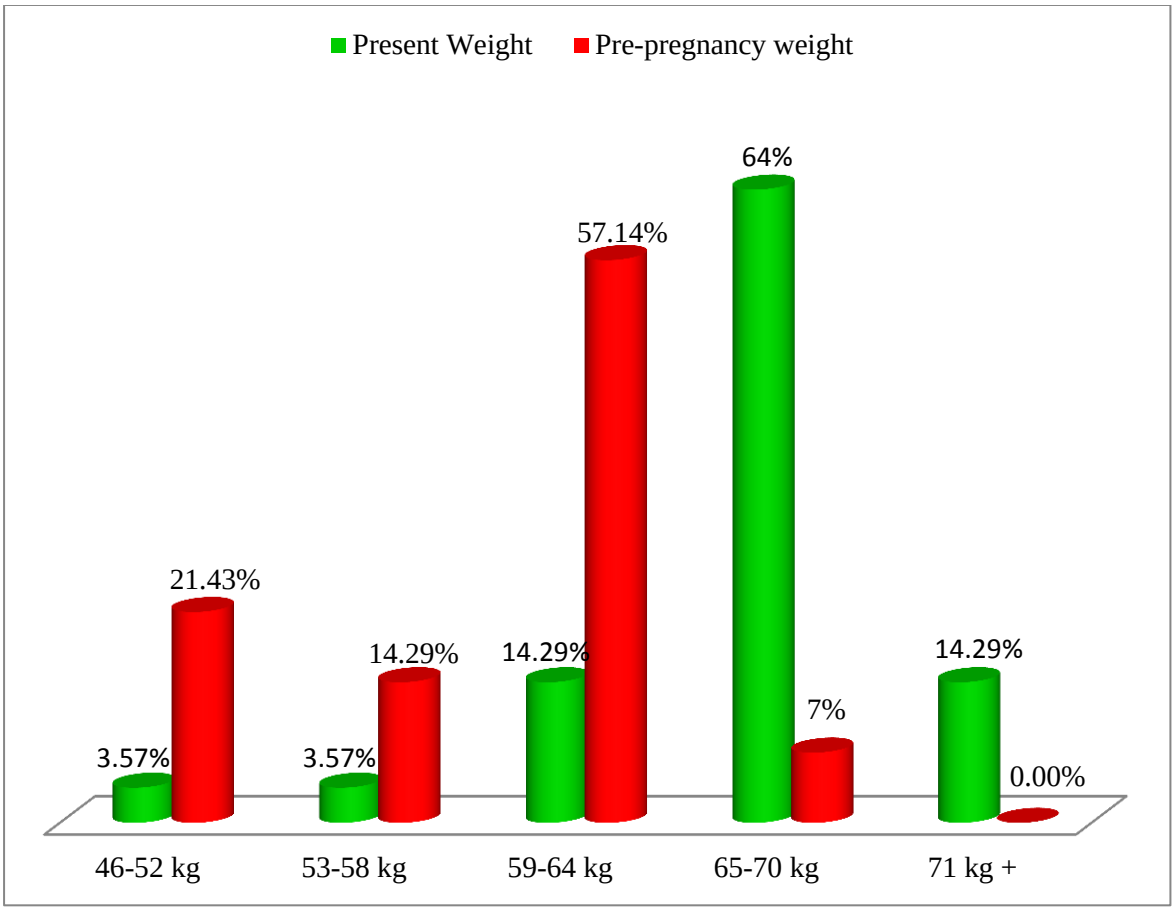

Figure 4.17: Weight distribution

In pre-pregnancy weight most of the respondents were between 59-64kg. About 57.14% were between this range and no respondents were found in the group of 71kg or above.

In pregnancy, most of the responder's weights were between 65-70kg. About 64% were between this range and the lowest (3.57%) respondents were found between the ranges of 53-58kg.

4.18 Snacks Intake (n=28)

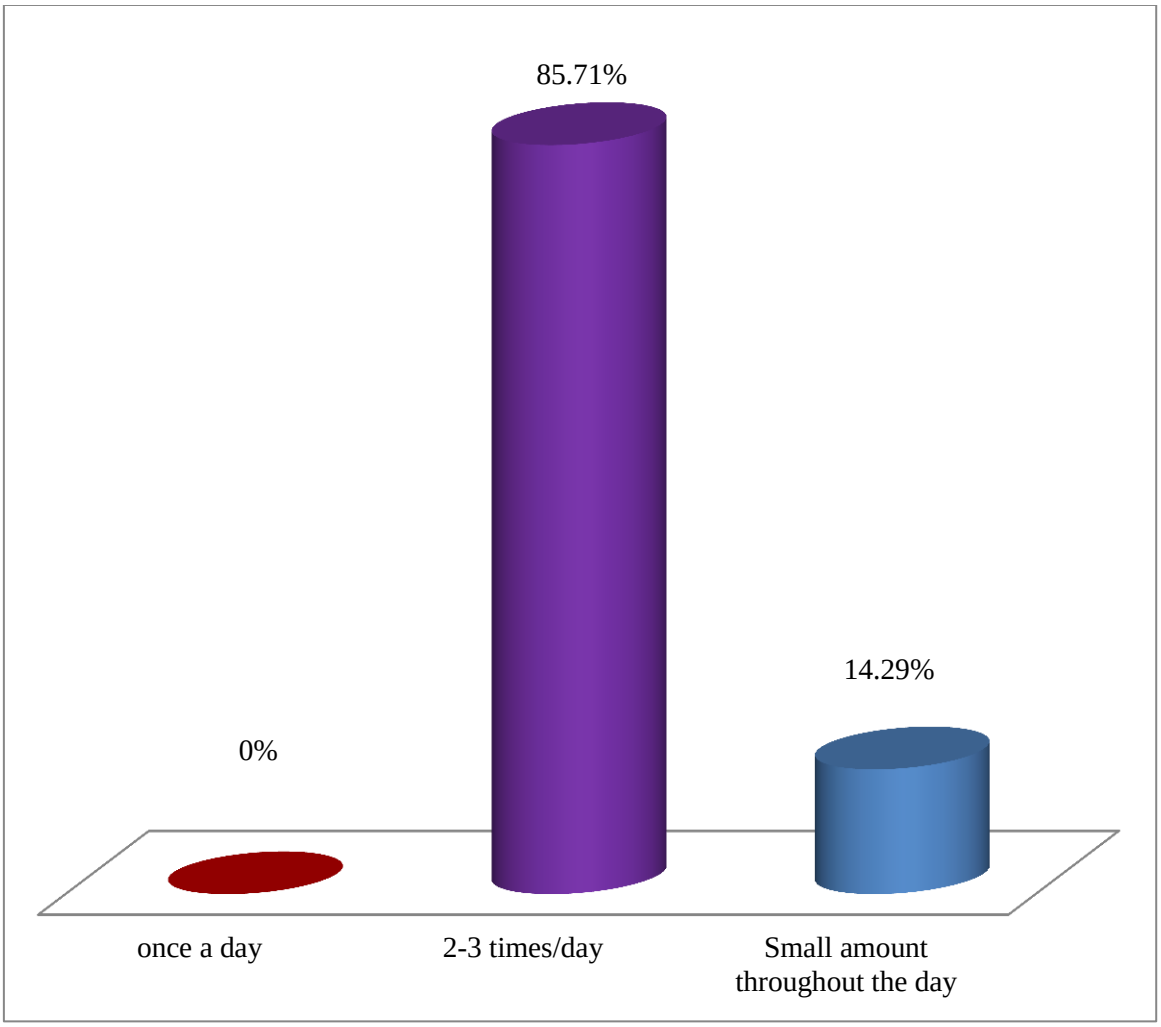

Figure 4.18: Snacks intake

From the above figure, 85.71% responders were found taking their snacks 2-3 times per day, 14.29% were taking snacks at a small amount throughout the day and no one was found who take snack once a day.

4.19 Snacks Types (n=28)

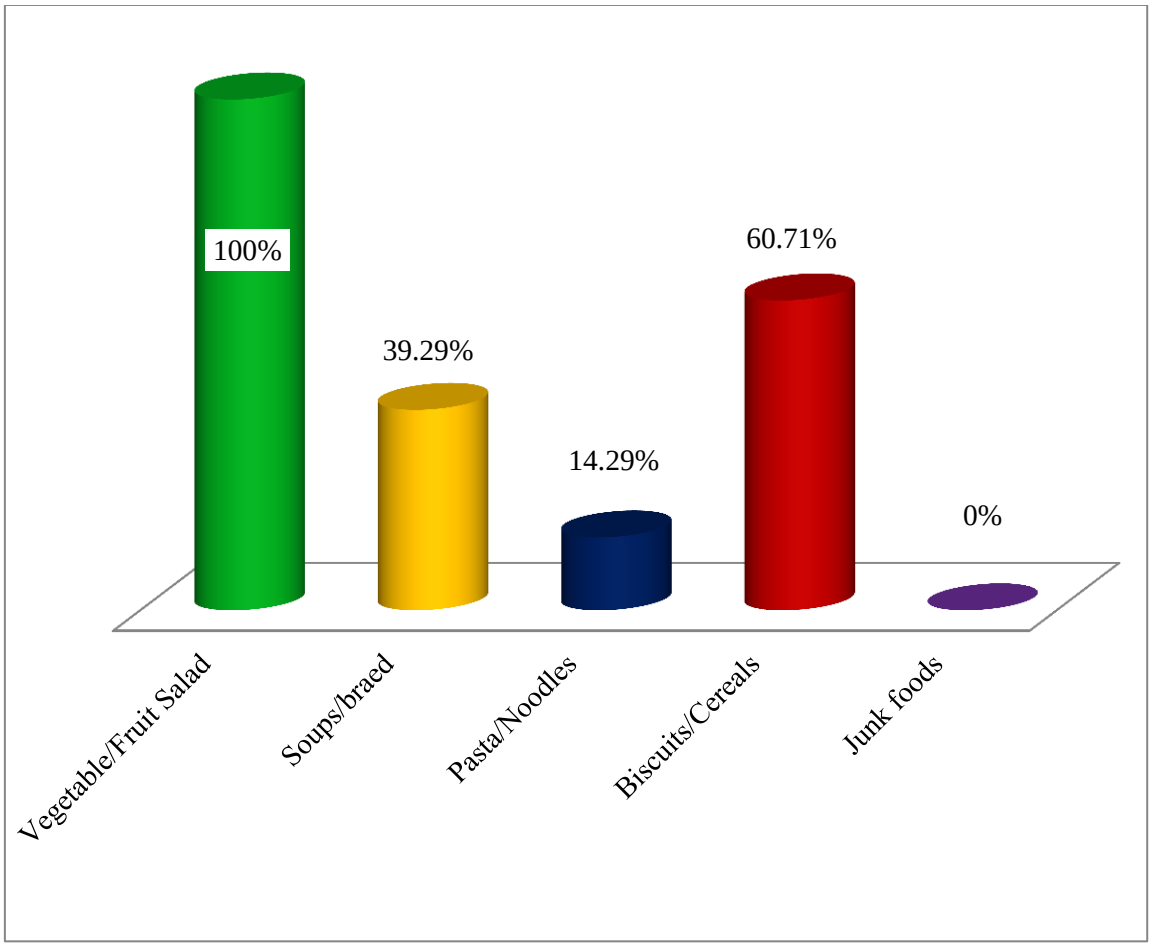

Figure 4.19: Snacks types

From the above figure, 100% of the patients were found who said that they take vegetable/fruit salad, 60.71% were found taking biscuits/cereals, 39.29% were taking soups/bread and no one was found taking junk foods.

4.20 Physical Exercise (n=28)

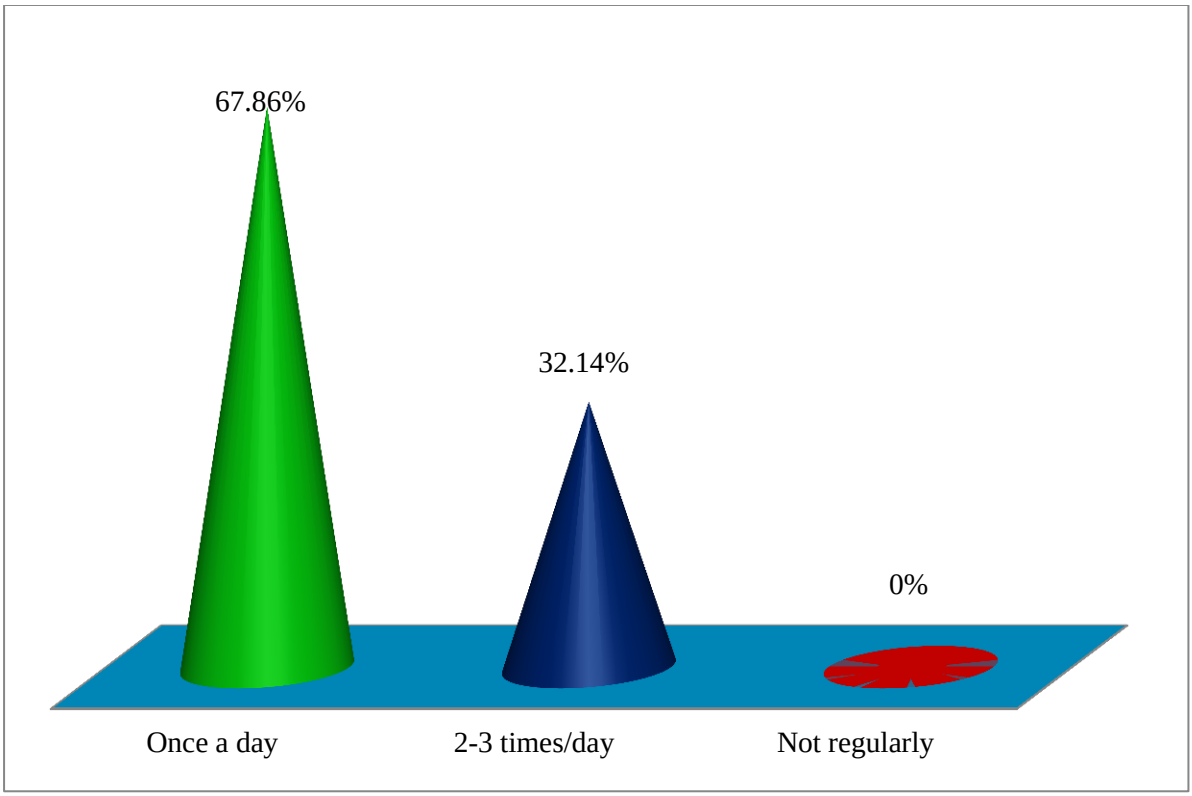

Figure 4.20: Physical exercise

From the above figure, it can be clearly said that, all of the patients (100%) did physical exercise. Among them, 67.86% of the respondents were found doing exercise once a day and 32.14% did it 2-3 times per day. There was no one found who did not take exercise regularly.

4.21 Level of Mental Stress (n=28)

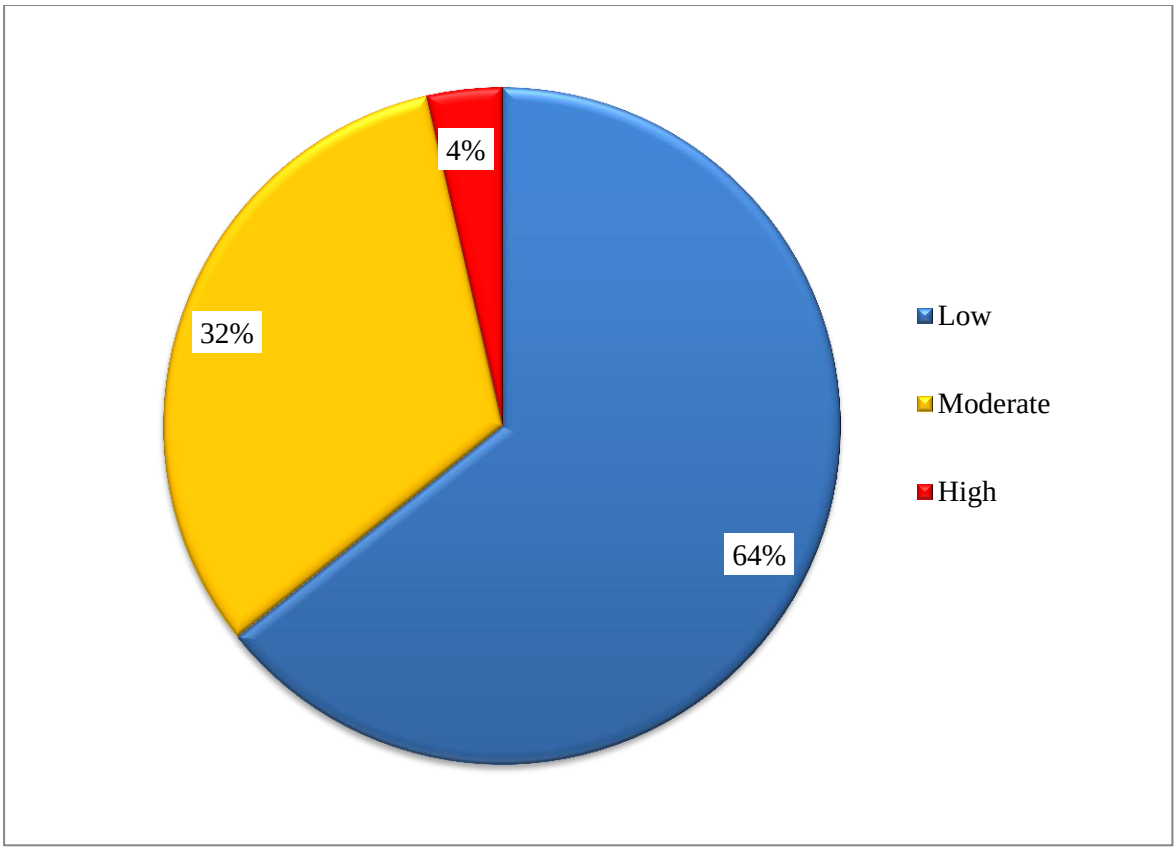

Figure 4.21: Level mental of stress.

The above figure points out that, about 64% of the patients had low stress level and 32% of patients were having moderate stress level and only 4% of the patients said that, they had high stress during gestational period.

4.22 Stress Handling (n=28)

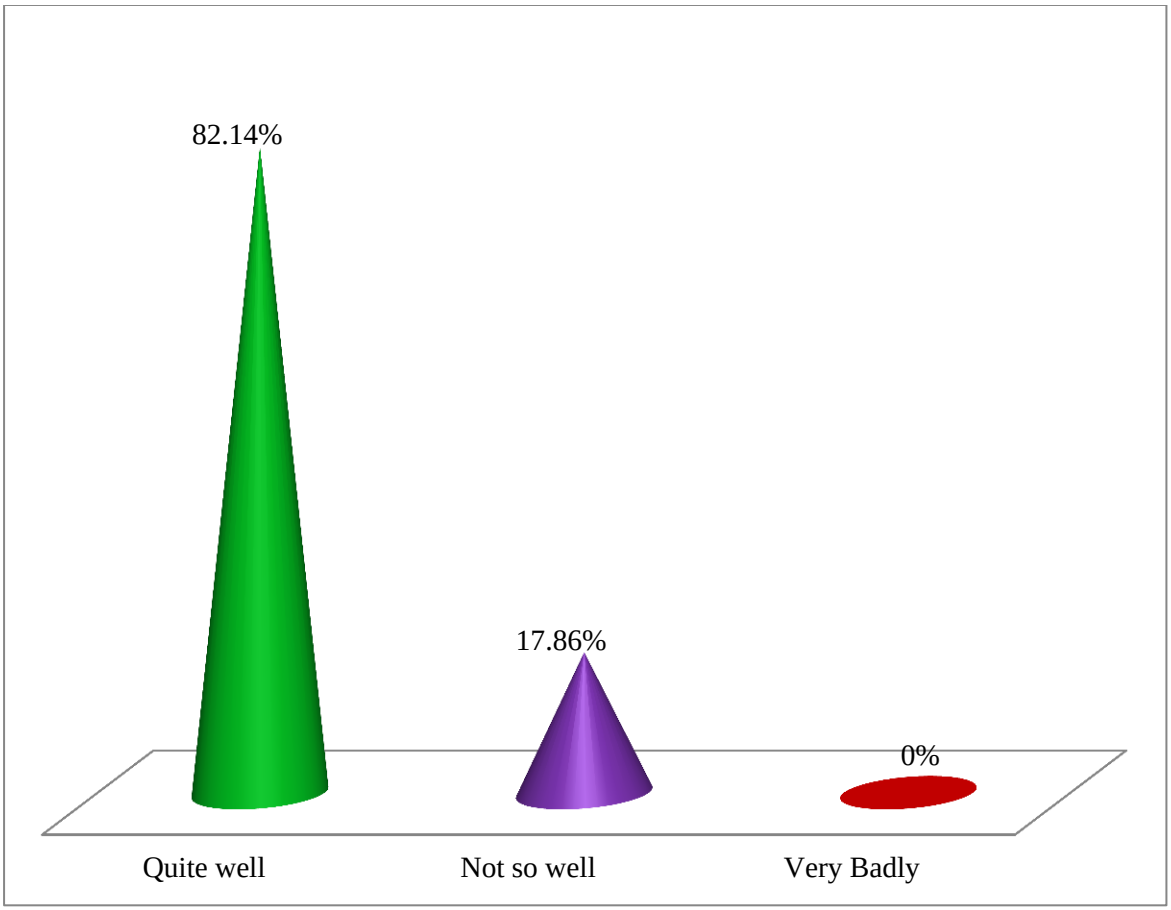

Figure 4.22: Handling stress by the patient

Most of the respondents (82.14%) were found to have handling their stress quite well and 17.86% said that they are not so well in handling their stress.

4.23 Knowledge about Gestational Diabetes Mellitus (GDM) (n=28)

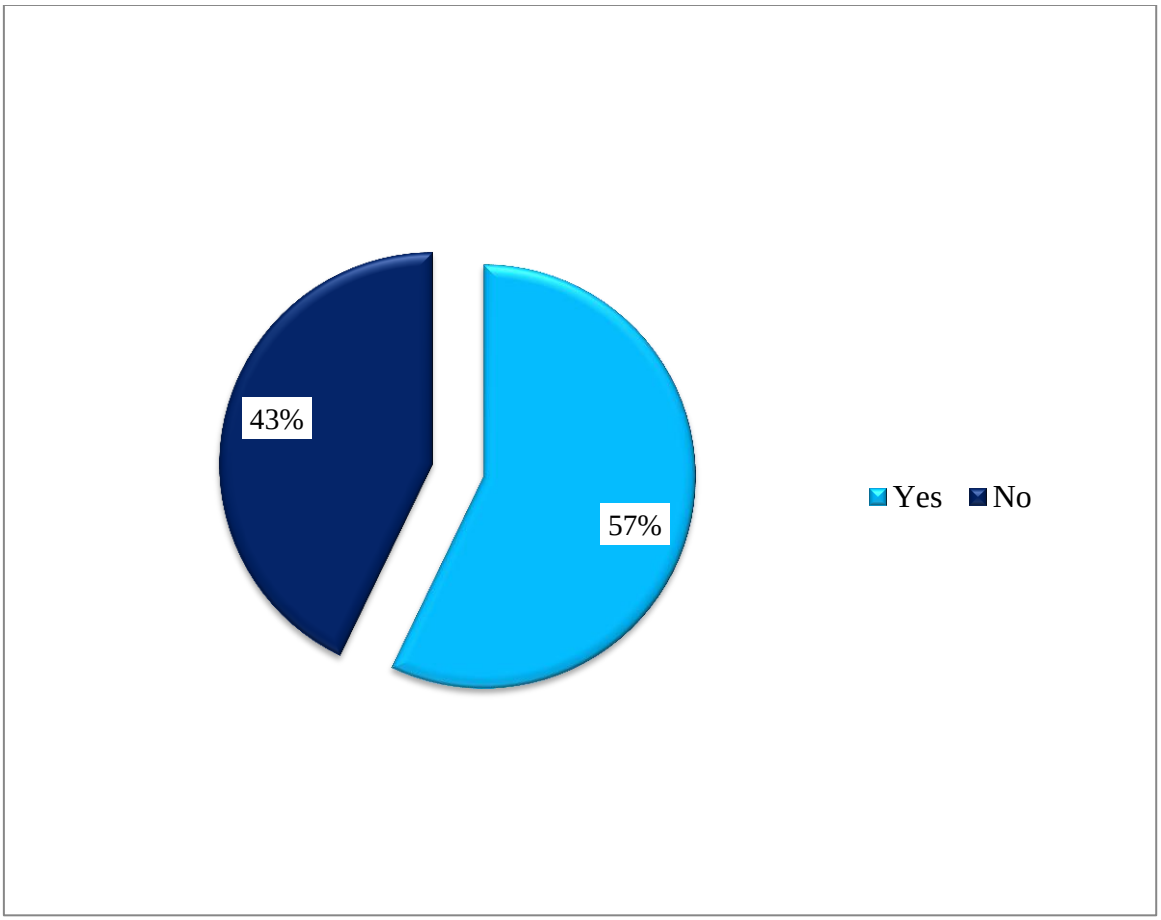

Figure 4.23: Knowledge about Gestational Diabetes Mellitus (GDM)

The above figure shows the percentages of patients being surveyed about knowledge of GDM. It was found that 57% of the patients had knowledge about GDM and 43% were not aware.

4.24 Sources of Knowledge about GDM (n=16)

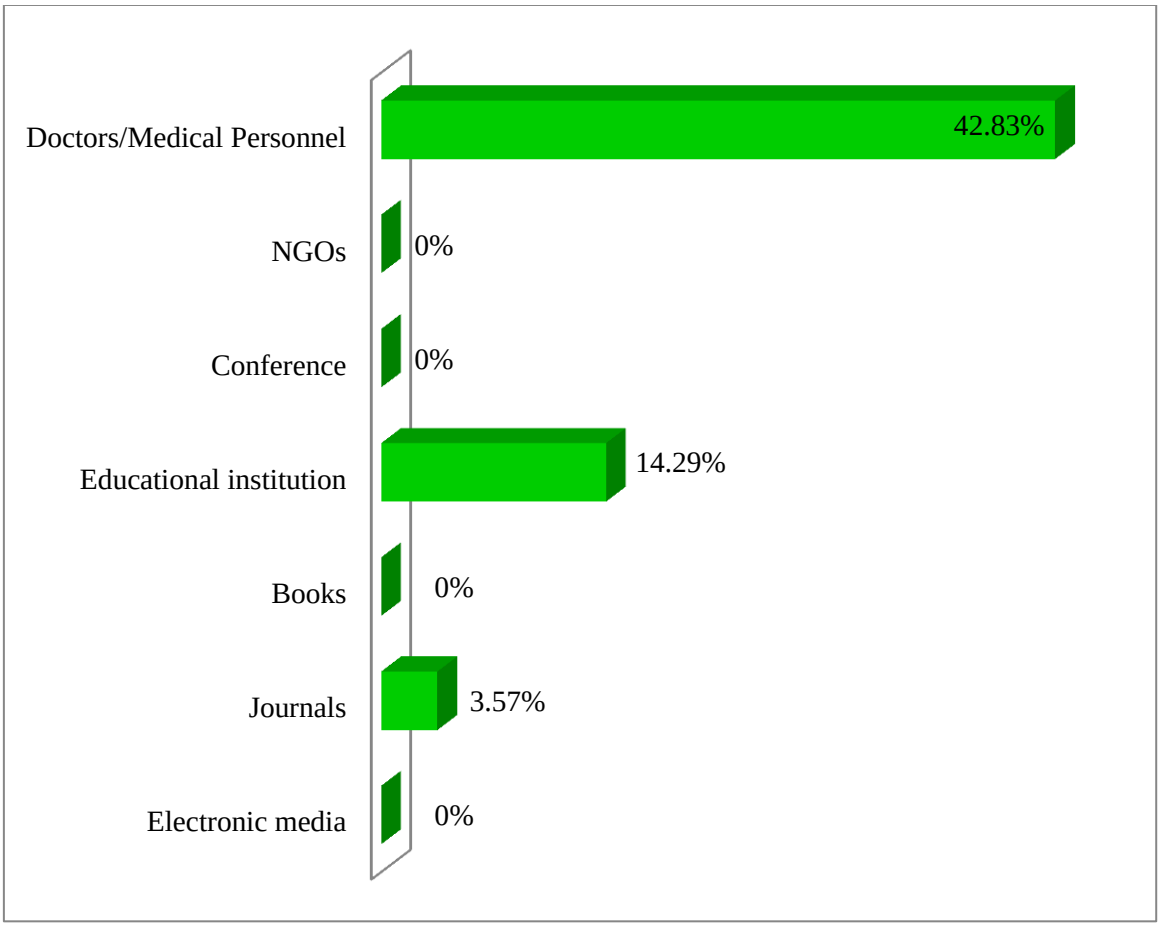

Figure 4.24: Source of knowledge

Most of the respondents (42.83%) were found to gain knowledge of GDM from different doctors/medical personnel. And others got to know about it from their educational institution (14.29%) and different journals (3.57%).

4.25 Reasons Behind GDM (n=16)

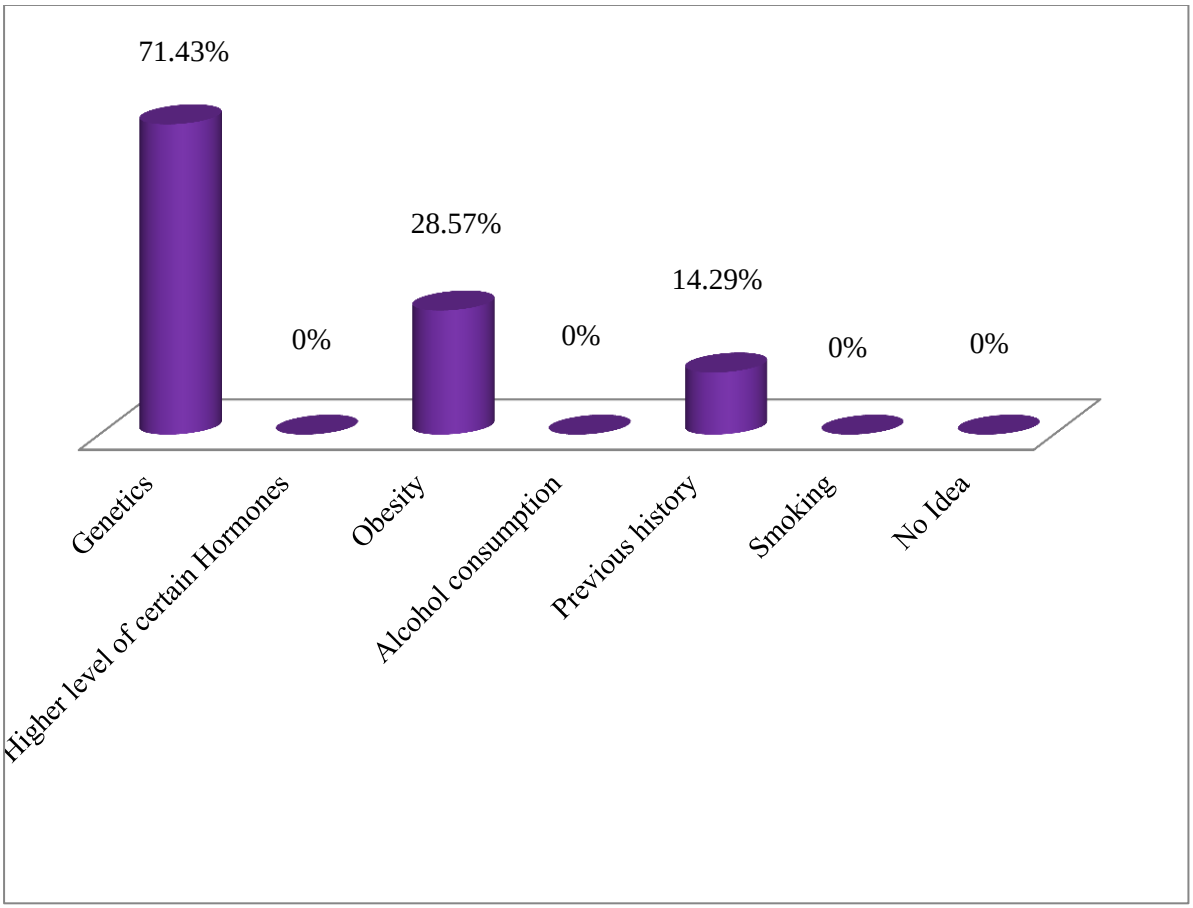

Figure 4.25: Reason behind gestational diabetes

From the above figure, the reasons behind gestational diabetes according to the patients' knowledge were found to have genetics (71.43%), obesity (28.57%) and previous history of diabetes (14.29%). None of them thought that high level of certain hormones, alcohol consumption or smoking as any of the reason behind GDM.

4.26 Knowledge of treatment about GDM (n=16)

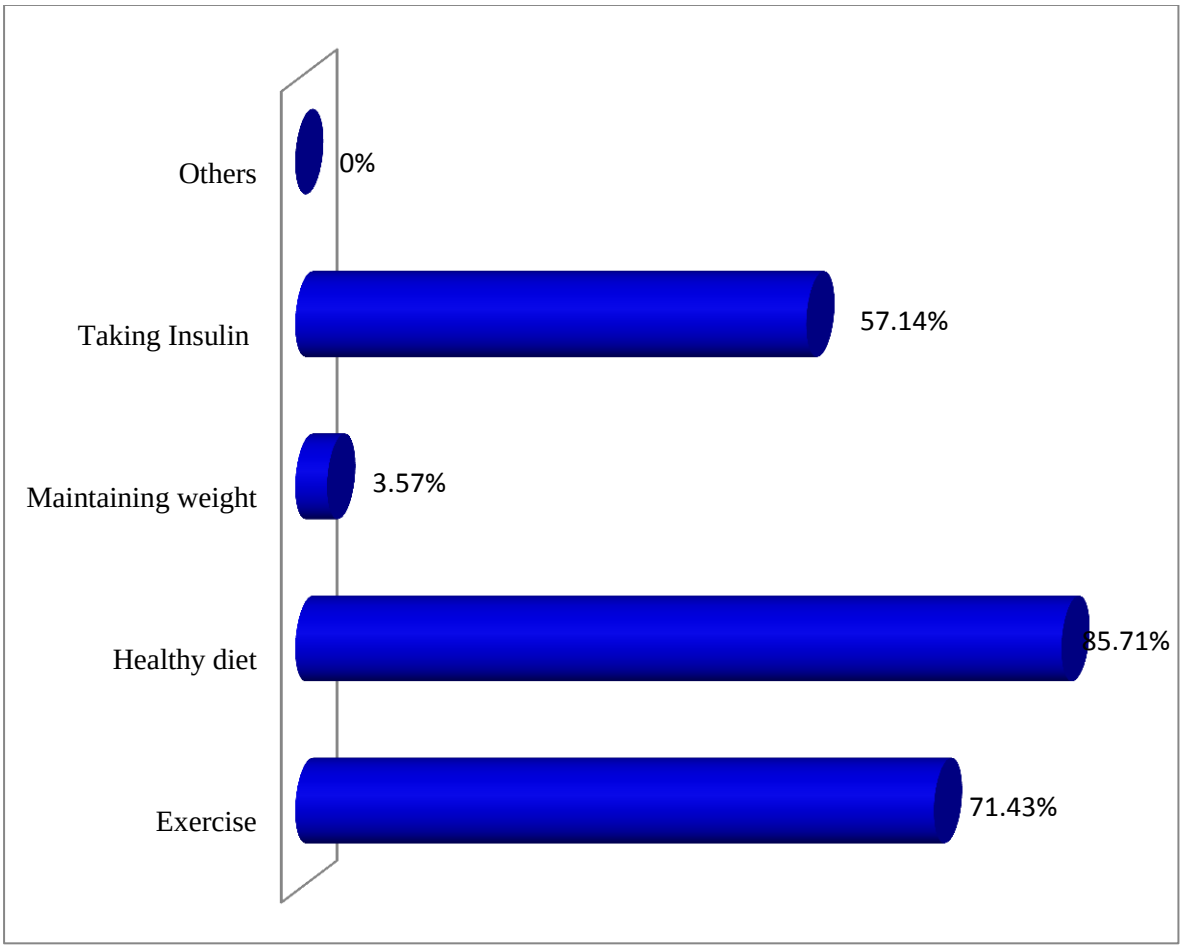

Figure 4.26: Knowledge of treatment about gestational diabetes

The above figure shows the percentage of patients' knowledge regarding the treatment of GDM. 57.14% of the respondents thought taking insulin is the treatment. 3.57% thought maintaining weight, 85.71% thought healthy diet and 71.43% thought doing exercise were the treatment of GDM.

4.27 Problem to Manage GDM (n=28)

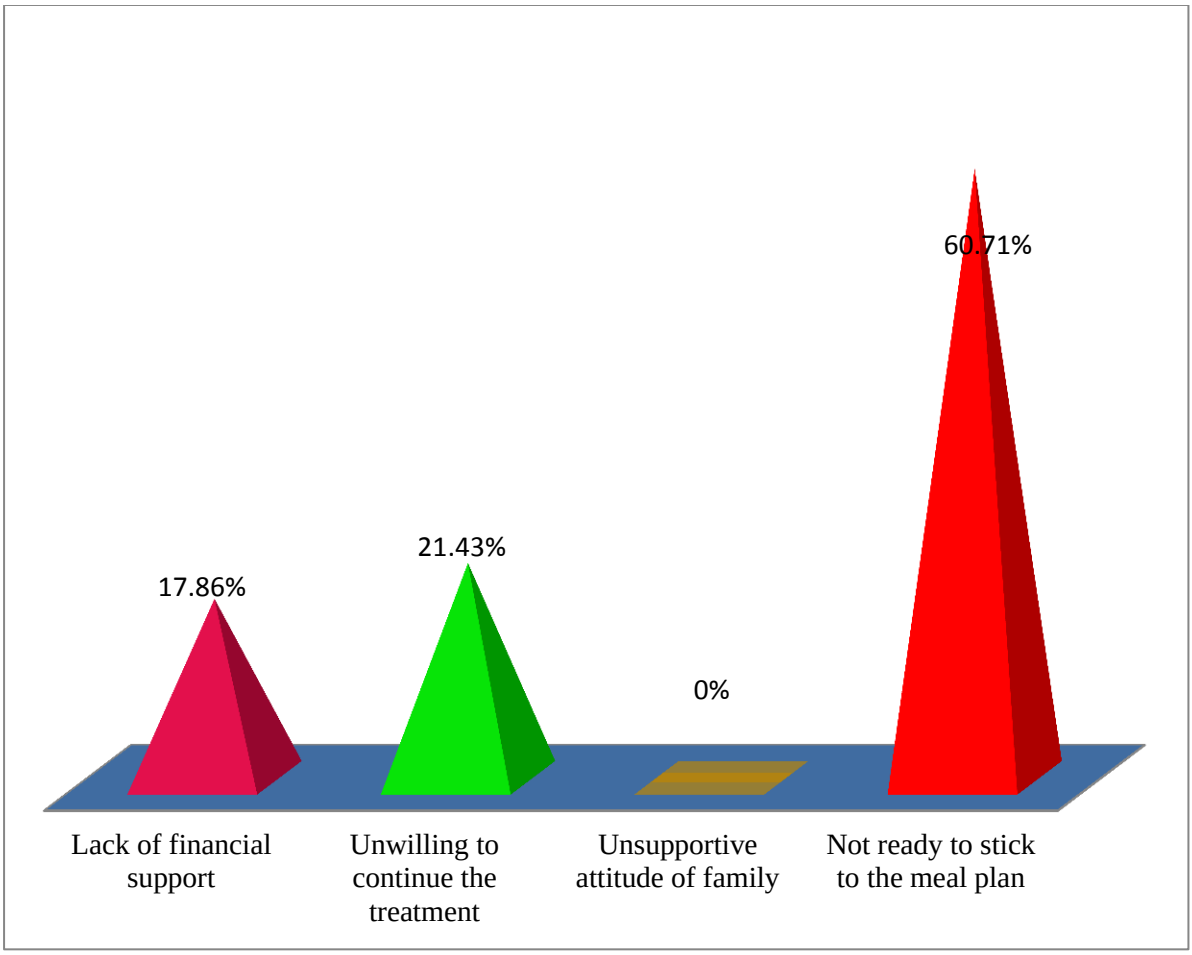

Figure 4.27: Problem to manage GDM

The above figure shows that, 17.86% of the patients were faces problem to managing GDM due to lack of financial support, 21.43% due to unwilling to continue the treatment and 60.71% faces problem to managing GDM due to not ready to stick to the meal plan.

4.28 Support to Manage GDM (n=28)

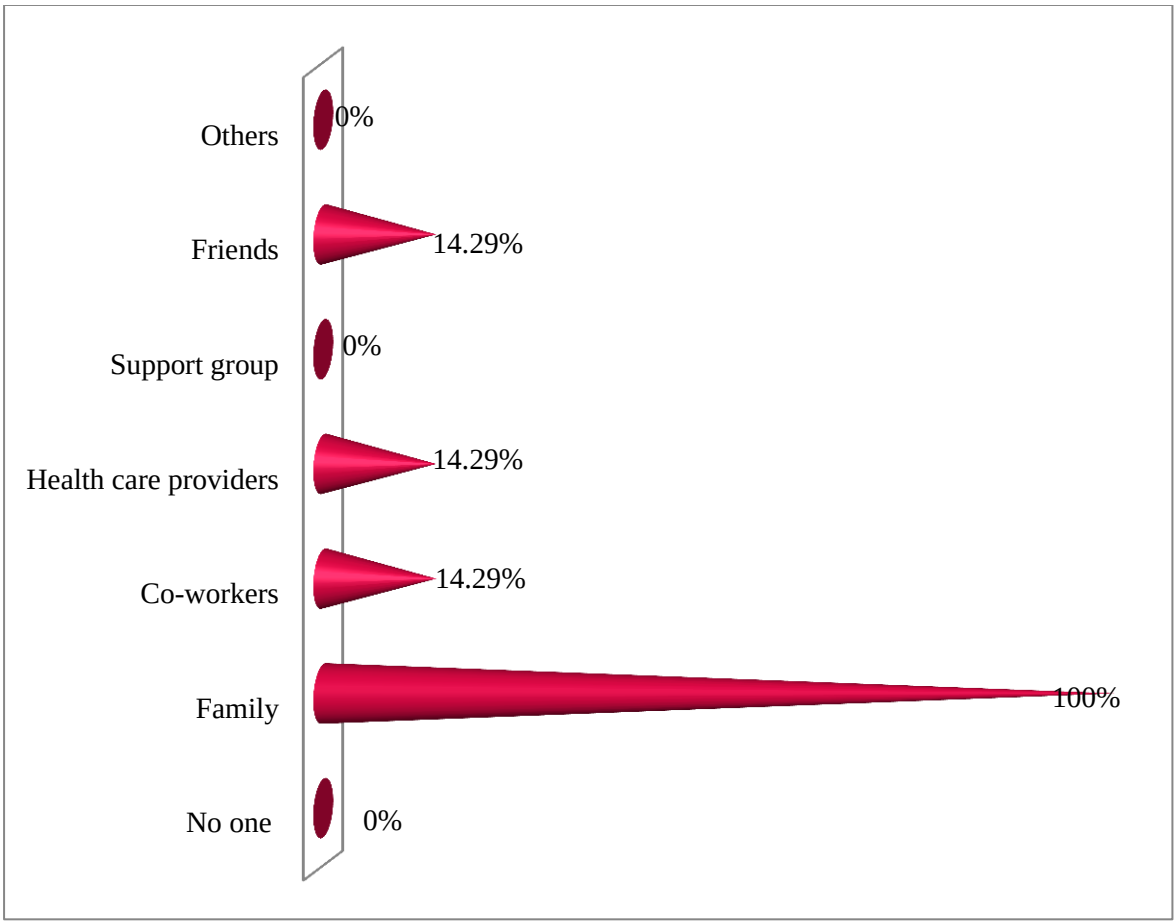

Figure 4.28: Support to manage GDM

Study shows that, the patients were found to be supported 100% by their family members. 14.29% from co-workers, health care providers & friends individually and no one get any support from the support groups & others.

4.29 Weight of Neonate (n=28)

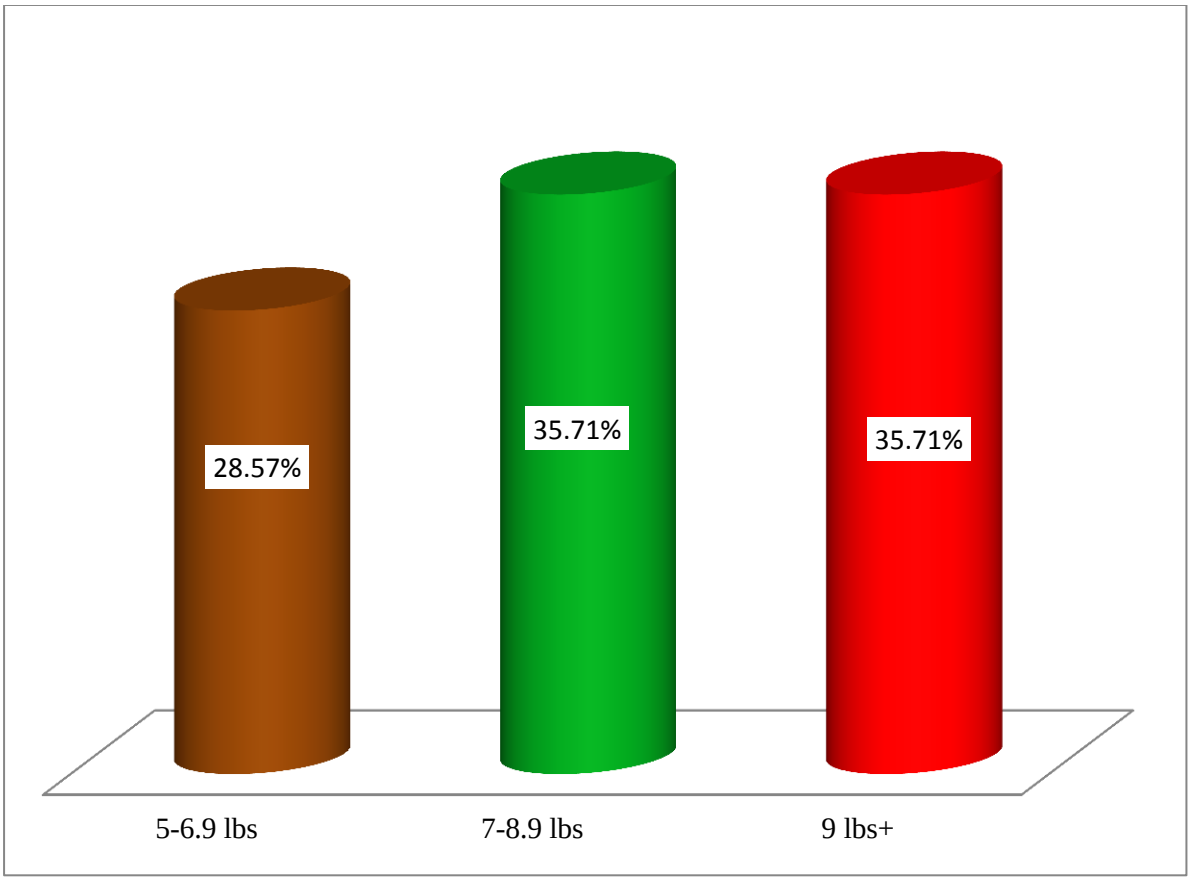

Figure 4.29: Weight of neonate

Above figure shows that, 35.71% of the babies weight were found in the groups of 7-8.9 pounds, 28.57% of the babies weight were found in the groups of 5-6.9 pounds and 35.71% were found in the group of 9 pounds & above. That means 35.71% babies were born as macrosomic.

4.30 Disease Condition of the Neonate (n=28)

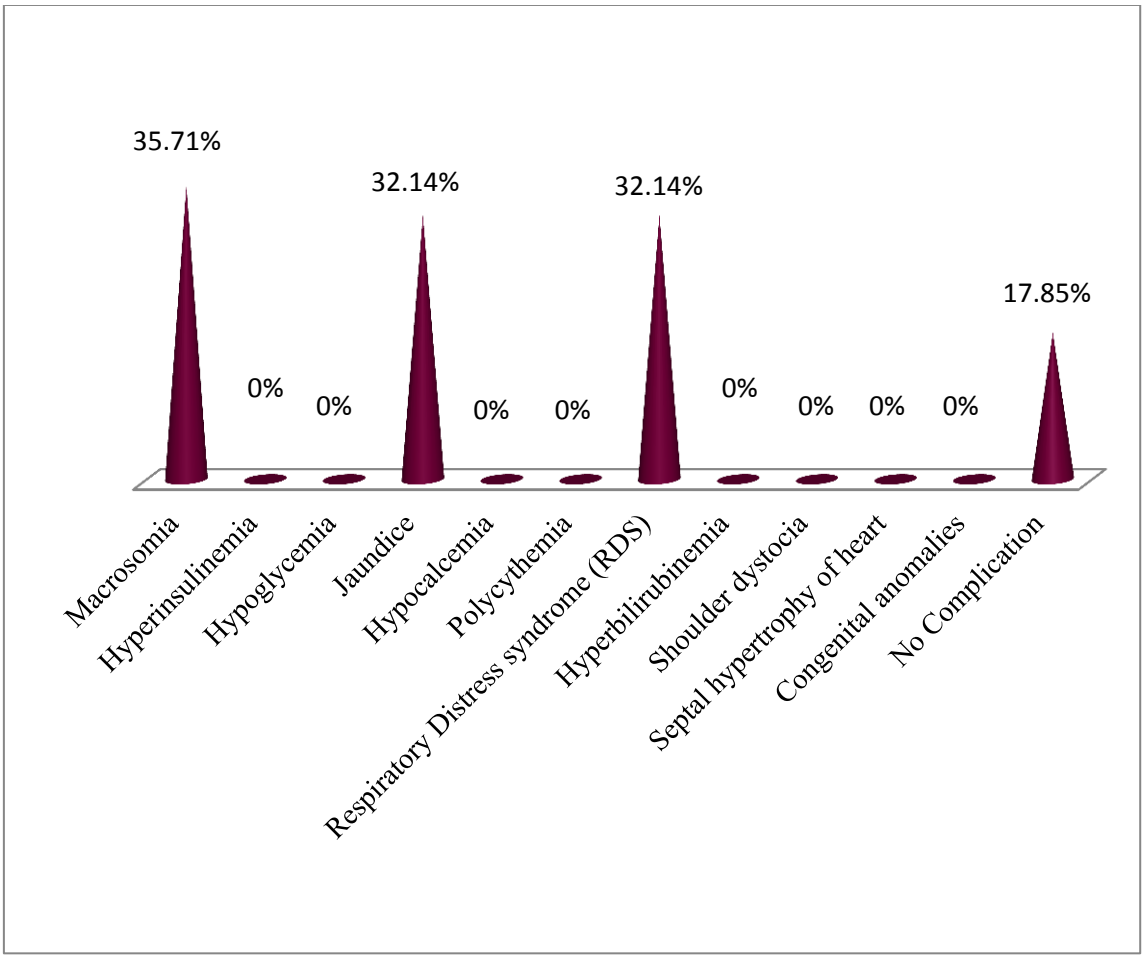

Figure 4.30: Disease condition of the neonate

From the above figure, 35.71% of the respondent gave birth to a macrosomic baby. About 32.14% babies were suffering from jaundice after birth, 32.14% suffering from respiratory distress syndrome (RDS) and 17.85% were found who have no problems.

4.31 Mother Condition (n=28)

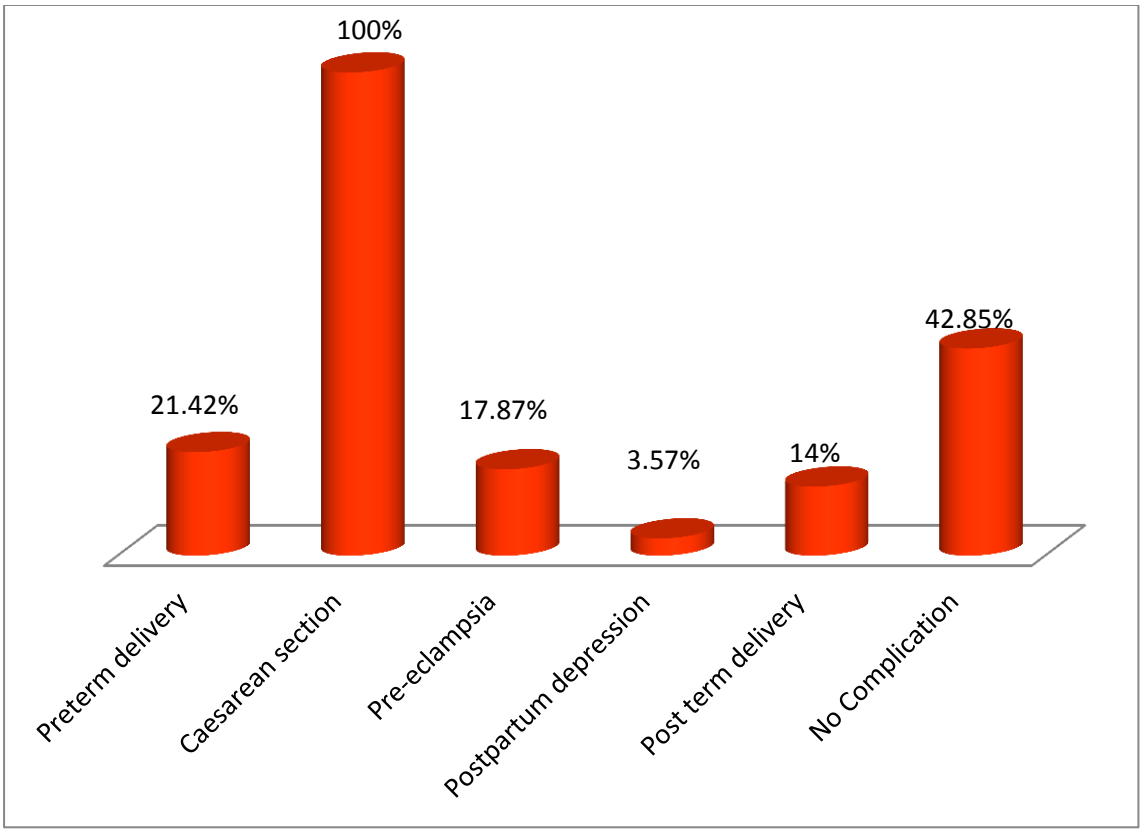

Figure 4.31: Condition of mother

From the above figure, it can be clearly said that all of the women (100%) delivered by caesarean section, 17.87% suffered from pre-eclampsia, 21.42% had preterm delivery & 3.57% had postpartum depression. About 42.85% of the women had no complication after delivery.

3.32 Future Risk for the Baby (n=28)

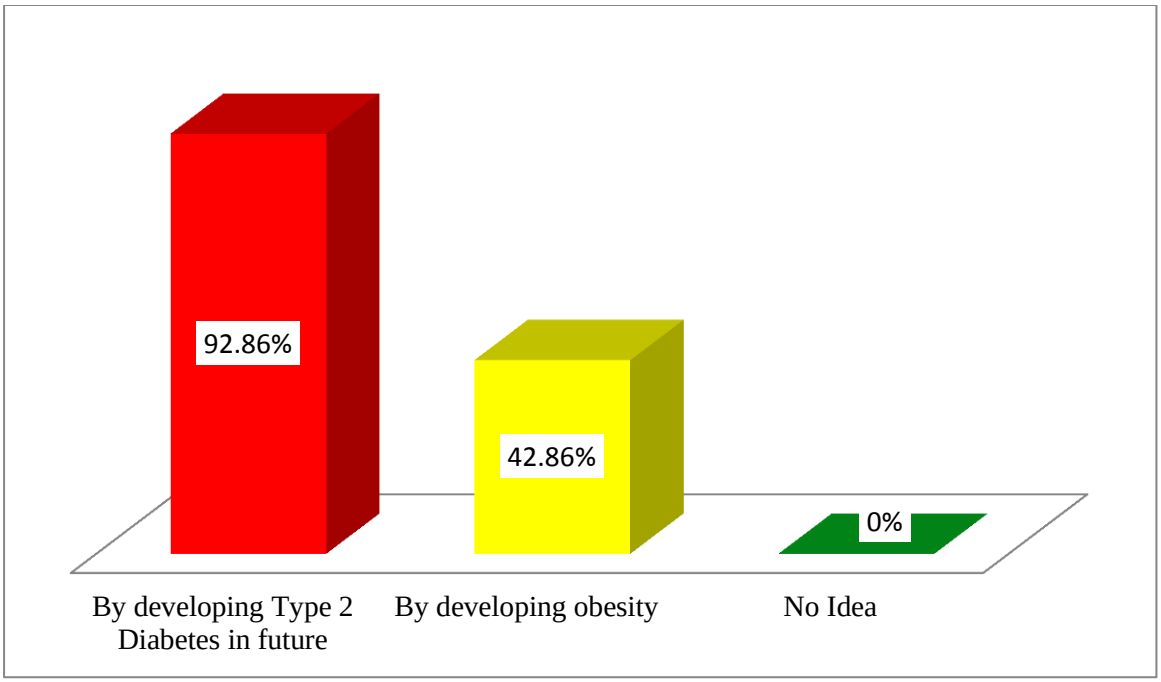

Figure 3.32: Future risk for the baby

The study result shows that, 92.86% of the respondents were found who think that the baby can become affected by developing Type 2 diabetes in future and 42.86% thought that, their baby may obese in future.

Discussion

Gestational diabetes mellitus (GDM), a condition characterized by glucose intolerance during pregnancy, is associated with a variety of adverse birth outcomes, including excessive fetal weight gain and related increases in the rate of cesarean delivery and prenatal injury. GDM increases the risk for a number of longer term adverse outcomes, including progression to type2 diabetes (T2D) in the mother as well as increased risk of obesity, diabetes, and possibly adult cardiovascular disease in the infant (Reece *et al.*, 2010).

The present study was carried out on pregnant women to see the prevalence of Gestational Diabetes Mellitus (GDM). Out of 150 pregnant women surveyed, 28 (18.67%) were found to be patients of GDM. Seshiah *et al* performed a study in various cities in India on 2004, they found that the prevalence of GDM was 16.2% in Chennai, 15% in Thiruvananthapuram, 21% in Alwaye, 12% in Bangalore, 18.8% in Erode and 17.5% in Ludhiana. An overall GDM prevalence of 16.55% was observed. So it was showed that, prevalence of gestational diabetes mellitus varies widely. 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 GDM in this present study was similar to that reported by Seshiah *et al* in India.

The present study found that, approximately 57.24% of the patients were taking Insulin and 42.29% were taking Metformin HCl for managing their GDM. Insulin is the first line treatment in GDM and the insulin regimen should be individualized to meet glycemic targets. There is growing interest in the use of oral anti diabetic agents including glyburide and metformin, because of increased convenience and potential cost savings (Serlin *et al.,* 2009).

This study also shows that, all of the patients had a meal plan and they followed that meal plan. Almost all of them were taking balance diet, which include carbohydrates, meat, fat, vegetables and fruits. All of patients were also doing physical exercise in which, 68% were doing this once a day and 32% were 2-3times per day. The results of two large randomized controlled trials conducted in Australia and the United States by Crowther & Landon *et al* shows that, the vast majority of women (80% to 90%) in these trials were managed solely with meal planning and lifestyle changes. They recommend moderate physical activity, including brisk walking or arm exercises while seated in a chair, as part

of the treatment program for women with GDM. These recommendations are suggesting that exercise lowers fasting and postprandial glucose concentrations and may reduce the number of women with GDM requiring insulin therapy (Crowther & Landon *et al*., 2005).

In the present study, 17.87% of the women with GDM were found to be pre-eclampsic, 21.42% had preterm labor and 35.71% gave birth to large sized baby (macrosomia). All the patients (100%) had to undergo caesarean section to avoid the risk of different complications during delivery period. The result also shows that, 35.71% newborn babies were suffering from macrosomia, 32.14% were suffering from jaundice and 32.14% were from respiratory distress syndrome (RDS). Mannan *et al* conducted a survey on 2012 and observed that, there was no maternal mortality but morbidities like pre-eclampsia, preterm labor and surgical interventions were more prevalent in GDM compared to non GDM groups. There was one perinatal mortality (due to respiratory distress syndrome) and one congenital anomaly observed in neonates of GDM mothers. More pre-term, post-term, low birth weight and macrosomic babies were found among the babies of GDM mothers than non GDM mothers. More babies also suffered from neonatal jaundice and respiratory distress syndrome in GDM groups than non GDM groups (Mannan *et al., 2012*).

Family history of diabetes mellitus has been reported to be associated with higher chances of developing GDM. In our study, a significantly higher percent (64%) of women with GDM had positive family history of diabetes mellitus. Seshiah *et al* observed a significant association between the family history of diabetes mellitus and the occurrence of GDM among pregnant women (Seshiah *et al.*, 2004).

Obesity is an important risk factor for the development of GDM. In the present study, GDM was found to be significantly high in women with higher weight (64%) in conception. Kim *et al* observed that approximately 30% of women with GDM are normal weight at conception, and 70% are overweight or obese (Kim *et al.,* 2010).

In this present study, approximately 35.71% respondent gave birth to macrosomic babies and another 35.71% were not macrosimoc but healthy. Kuti *et al* conducted a study on 2011 and found that the incidence of fetal macrosomia was higher (66.7%) amongst women with GDM (Kuti *et al.*, 2011).

GDM is increasingly recognized as a general risk factor for the development of type2 diabetes. The present study result shows that, 92.86% of the responses were found who think that the baby can become affected by developing Type 2 diabetes in future and 42.86% of the responses were found who think the baby can become affected by developing obesity. Kim *et al* observed that, up to 60% of babies were at high risk level to develop T2D. Their studies suggest that 11% to 33% will display evidence of impaired glucose tolerance, and 1% to 8% will have obesity (Kim *et al.*, 2002).

Conclusion

Gestational Diabetes Mellitus is one of the major health problems throughout the world. It is emerging as a serious health problem in Bangladesh and other developing countries. GDM may occur due to genetics, improper diet, unwillingness towards exercise and obesity. The consequences include macrosomia, congenital anomalies, still birth, pre-eclapmsia, jaundice, respiratory distress syndrome, hyperinsulinemia, polycythemia, shoulder dystocia etc. Our negligence and unawareness may lead to these life threatening diseases. Not only the mother but their babies are also at a high risk of developing type2 diabetes and obesity in future. In a third world country like Bangladesh, it puts a great pressure on the economy to treat high cost diseases such as diabetes or gestational diabetes mellitus. Diabetes prevention initiatives should be given high priority to avoid high rates of GDM in the future. But the gigantic problem of GDM cannot be solved by Government alone, so creating awareness among average people has become essential.

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