CDAPP Sweet Success Guidelines for Care

Chapter 5

Impact of Maternal Diabetes on Fetal Development and Neonatal Care

2015

California Diabetes and Pregnancy Program Sweet Success Guidelines for Care

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INTRODUCTION

Advances in the care of pregnant women who have diabetes have improved, but not eliminated, the risk of morbidity and mortality in their infants. Therefore, the newborn care provider must plan and assess for the specific problems frequently encountered by the infant of a woman with diabetes.

An infant of a woman with insulin dependent diabetes has as much as 7.9% higher risk of having congenital malformations than infants born to mothers without diabetes.[1-3] Complications vary based on the type of maternal diabetes, type 1 or type 2 diabetes versus Gestational Diabetes Mellitus (GDM) as well as the adequacy of maternal blood glucose control. A 1989 landmark study of 303 insulin-requiring pregnant diabetic women addressed the relationship of first-trimester hemoglobin A1c and spontaneous abortion or major malformations of fetus/infants that progressed beyond the first trimester. Table 1 provides the risk ratios associated with spontaneous abortion and infant major malformations in the presence of poor glycemic control.[4]

Table 1*: RISK RATIOS OF DELETERIOUS EFFECT OF POOR GLYCEMIC CONTROL OF TYPE 1 DIABETES[4]

hemoglobin A1c (%)	Spontaneous Abortions	Major Malformations for pregnancies beyond the first trimester
≤ 9.3	1.0	1.0
9.4 to 11.0	0.7	1.7
11.1 to 12.7	1.98	1.4
>12.8	>2.9	>12.8

* based on 303 insulin requiring diabetic women. 95% confidence interval.

Recent evidence suggests that women who have mild glucose intolerance [one abnormal value on a 100g Oral Glucose Tolerance Test (OGTT)] have infants with a higher incidence of neonatal obesity than the general population. For these infants, obesity frequently persists into adulthood.[5-7] Comorbidities associated with obesity during childhood and adulthood include an increased incidence of metabolic syndrome[8], hypertension, lipid abnormalities, renal disease[9], risk of type 2 diabetes[10], and psychomotor, memory and learning deficits.[11-13]

The fetus of a woman with impaired glucose control (e.g. pre-diabetes, type 1 diabetes, type 2 diabetes, and GDM) is at higher risk of morbidity and mortality during development and the neonatal period. Associated morbidity includes congenital anomalies, prematurity, perinatal depression, respiratory distress syndrome, and metabolic complications. Although insulin treatment and intensive prenatal and neonatal care have improved outcomes in the offspring of women with type 2 diabetes, this condition contributes to high perinatal mortality due to hyperglycemia-induced teratogenicity. Preconception care with strict glycemic control may significantly reduce hyperglycemia-related mortality and morbidity.[14] Maternal hyperglycemia is associated with an abnormal intrauterine environment. By the eighth week of gestation, diabetic embryopathy (birth defects and spontaneous abortions) may occur. Subsequently, diabetic fetopathy (macrosomia and fetal hyperinsulinemia) occurs during the second and third trimesters.

Table 2: PERINATAL MORTALITY AND NEONATAL MORBIDITY IN INFANTS OF DIABETIC MOTHERS[15-18]

Complications	Reported rates (%)
Perinatal mortality*	0.6 - 4.8
Cesarean delivery*	32 - 45
Premature deliveries	
<34 weeks gestation	14 - 16
<37 weeks gestation	24 - 33
Congenital anomalies*	1.7 - 9.4
Perinatal asphyxia (fetal distress, low 1-minute Apgar score or intrauterine death*	9 - 28
Macrosomia*	9 - 28
Intrauterine growth restriction	2 - 8
Respiratory distress syndrome	2 - 6
Metabolic complications	
Hypoglycemia**	5 - 25
Hypocalcemia	4
Polycythemia	5 - 33
Hyperbilirubinemia	11 - 29
Cardiomyopathy	
Symptomatic	2 - 10
Asymptomatic	30 - 50

*Lowest rates are associated with strict glycemic control
**Strong correlation with macrosomia

FETAL EFFECTS OF MATERNAL DIABETES

Diabetic Embryopathy

Diabetic embryopathy is related to the severity of hyperglycemia.[19,20] A program of preconception care, strict glycemic control prior to conception and during pregnancy in women with type 1 diabetes may reduce the rate of congenital malformations.[2,16]

However, Leguizamón et al points out that "Hyperglycemia alone does not offer a complete explanation to the teratogenic process."[21] This study looks into "Other factors such as myoinositol and arachidonic acid deficiency, hyperketonemia, and excess of free oxygen radicals." These indicators were associated with birth defects in diabetic pregnancies.[21]

Diabetic Fetopathy

Diabetic fetopathy, a disease of the fetus after the mother's third month of pregnancy, results from intermittent maternal hyperglycemia. This results in premature maturation of fetal pancreatic islets, with hypertrophy of the beta cells and resultant hyperinsulinemia (Pedersen hypothesis).[22] Macrosomic neonates display significantly more hyperinsulinemia than appropriate for gestational age (AGA) infants.[23]

Fetal Growth Patterns

Fetal growth is similar in diabetic and nondiabetic pregnancies during the first and early second trimesters. After 24 weeks' gestation, maternal hyperglycemia results in disproportionate fat deposition and visceromegaly, while head growth remains normal.[24] Insulin can affect certain hormones (e.g. leptin), placental vasculature, and the transport and storage of glucagon in the placenta. The human placenta undergoes change partly due to hyperglycemic insults resulting in altered transport of nutrients such as glucose, amino acids and cytokines, thereby affecting fetal growth.[25] Increased growth velocity in the third trimester has been identified in the large for gestational age (LGA) infant of a diabetic mother.

Fetal Hypoxemia

Fetal hypoxemia is a significant contributor to fetopathy in infants of diabetic mothers. Elevated metabolic rate may lead to:

- Increased oxygen consumption: fetal hypoxemia has been demonstrated in fetal animal models.[26] Hypoxemia stimulates erythropoietin synthesis resulting in polycythemia.[27] Polycythemia is associated with an increased rate of neonatal jaundice.

- Nold and Georgieff reported that "Chronic fetal hyperglycemia and hyperinsulinemia can result in glycogen loading of the intraventricular septum," which leads to fetal cardiomyopathy.[28]

Macrosomia and Large for Gestational Age

Two terms are used to quantify excessive fetal growth: macrosomia and large for gestational (LGA). A term infant with a birth weight greater than 4,000 grams is considered to have macrosomia. An infant whose birth weight is greater than the birth weight of 90% of infants born at the same gestational age is considered LGA. Excessive fetal growth is documented in the literature as occurring in 20% to 30% of infants of women with diabetes.[28]

Macrosomia is caused by excessive nutrient supply, which causes increased fetal growth, particularly of insulin-sensitive tissues (liver, muscle, cardiac muscle, and subcutaneous fat).[28] Excessive growth is associated with poor maternal glucose control, especially during the third trimester and can be minimized by optimal maternal glycemic control).

Macrosomia is associated with an increased risk of[29,30]:

- Cesarean delivery
- Newborn hyperglycemia
- Hypoglycemia
- Birth injury
- Long-term risk of obesity and diabetes

BIRTH DEFECTS

Congenital Anomalies

As discussed above, infants of diabetic mothers are at significant risk for major congenital anomalies (refer to Table 2 and Table 3). Congenital anomalies occur in the infant of an insulin-dependent woman with diabetes at rates of two to four times higher than in the general population.[17] A diabetic woman who adheres to a rigid blood glucose control program during the preconception and early pregnancy periods reduces the incidence of congenital anomalies to normal nondiabetic levels.[21] The systems most commonly affected in the infant of a diabetic mother are cardiovascular, central nervous and neural tube, skeletal, gastrointestinal and genitourinary.[14] Leguizamón et al give guidelines for preconception care that consists of blood glucose control before conception and throughout pregnancy as well as examination into a patient's history and physical health. They also suggest analyzing potential laboratory determinants due to complications related to diabetes.[21]

Type 1 Diabetes

One study of approximately 8,000 infants found that the relative risk for major malformations in infants of mothers with type 1 diabetes was 7.9 times that of infants of nondiabetic mothers.[3] Congenital malformations account for a significant proportion of the perinatal deaths in newborns born to women with type 1 diabetes. Two-thirds of the anomalies in infants of women with type 1 diabetes involve cardiovascular (8.5 per 100 live births) or central nervous system (5.3 per 100 live births). Anencephaly and spina bifida occur 13 and 20 times more frequently in infants of women with type 1 diabetes than in infants of nondiabetic mothers.[3]

Type 2 Diabetes

Birth defects due to hyperglycemia are also seen in the infants of women with type 2 diabetes. Since birth defects are associated with obesity, women with type 2 diabetes who are also obese may have an increased risk above that based only on hyperglycemia.[15] Watkins et al found that compared with average-weight women, obese women have a higher likelihood to deliver a neonate with heart defects, spina bifida, omphalocele or multiple anomalies.[31] Table 3 summarizes congenital anomalies associated with infants of diabetic mothers.

Table 3: CONGENITAL ANOMALIES ASSOCIATED WITH INFANTS OF DIABETIC MOTHERS[3,14,21]

Systems	Anomalies
Skeletal	Caudal regression syndrome (sacral agenesis) Hemivertebrae
Cardiovascular	Ventricular septal defect (VSD), patent ductus arteriosus, or atrial septal defect Transposition of the great vessels with or without VSD Coarctation of the aorta with or without VSD Single ventricle, hypoplastic left ventricle Pulmonic stenosis, pulmonary valve atresia, double outlet right ventricle, truncus arteriosus
Gastrointestinal	Duodenal atresia Imperforate anus Anorectal atresia Small left colon syndrome Situs inversus
Genitourinary	Ureteral duplication Renal agenesis Hydronephrosis
Neurologic	Anencephaly, arrhinencephaly Microencephaly, holoprosencephaly Neural tube defects (meningomyelocele and other variants)
Other	Single umbilical artery

PERINATAL COMPLICATIONS

Premature Delivery

Spontaneous premature labor occurs more frequently in diabetic women than in nondiabetic women. Preterm birth rates among women with diabetes vary, depending on the type of maternal diabetes, maternal age, and whether other factors, such as congenital anomalies, are present.[32,33]

A literature review on premature delivery among diabetic mothers shows the following:

- Spontaneous Premature labor occurred in 31% of 181 pregnancies among women with type 1 diabetes compared to 7 to 10% in the general population.[33]
- A similar preterm delivery rate of 31% was noted in a study of women with type 2 diabetes.[15]

Perinatal Asphyxia

Type 1 diabetes is associated with an increased risk for intrauterine or perinatal asphyxia, which often is defined broadly to include fetal heart rate abnormalities during labor, low Apgar scores, and intrauterine death. In a study of 160 diabetic women, 26% of fetuses had perinatal asphyxia.[33] Perinatal asphyxia was correlated with maternal hyperglycemia during labor[33], prematurity, and nephropathy. Maternal vascular disease, manifested by nephropathy, may contribute to the development of fetal hypoxia, oxidative stress, and subsequent perinatal asphyxia and potential stillbirth.[34]

Birth Injury

Macrosomia occurs among all classes of diabetic pregnancies, except those with vasculopathy that results in intrauterine growth restriction (IUGR). Macrosomia predisposes the neonate to birth injury, especially shoulder dystocia, and can result in brachial plexus injury, clavicular or humeral fractures, perinatal asphyxia, and less often, cephalohematoma, subdural hemorrhage, or facial palsy.[35,36] Cesarean delivery without labor often is recommended in diabetic pregnancies if the fetal weight is estimated to be greater than 4300 - 4500g, contributing to the high rate of operative delivery for women with diabetes.[35] Ultrasound parameters are not always accurate in predicting macrosomia.[35]

Intrauterine Growth Restriction

Intrauterine Growth Restriction (IUGR) can occur in poorly controlled diabetes, especially when diabetes is complicated by vasculopathy. Preeclampsia, a frequent complication of diabetic pregnancies, can impair growth by impeding flow of blood and nutrients to the fetus.

Congenital anomalies associated with diabetic pregnancies also may lead to IUGR. Although close control of maternal glucose limits the development of macrosomia, excessively aggressive glucose control may lead to growth restriction.[20]

NEONATAL DIABETES ASSESSMENT, COMPLICATIONS, AND MANAGEMENT

Neonatal Assessment

Prior to delivery, the health care provider should obtain a maternal-fetal history through chart review and communication with the obstetric care provider and the patient. Review the chart for the following:

- Outcomes of previous pregnancies
- Gestational age and estimation of fetal size
- Control of diabetes preconceptionally and prenatally
- Results of screening, diagnosis, and treatment of gestational diabetes and genetic evaluations
- Antenatal fetal surveillance results
- Monitoring during labor

Optimal management of the infant of a diabetic mother involves the following components:

- A general neonatal assessment
- Evaluation for and, if present, treatment of hypoglycemia
- Assessment and management of diabetes-related neonatal problems
- Facilitation of family communication and support

Neonatal Complications

Hypoglycemia

Hypoglycemia, defined as blood glucose levels below 40 mg/dL, occurs frequently in infants of diabetic women.[28] The onset typically occurs in the first few hours after birth and requires close monitoring. Hypoglycemia is most common in macrosomic infants; this incidence is related to persistent hyperinsulinemia in the newborn after interruption of the intrauterine glucose supply from the mother.[28] Strict glycemic control during pregnancy decreases, but does not eradicate, the risk of neonatal hypoglycemia. Preterm infants and infants of women with type 1 diabetes who are SGA are at increased risk of hypoglycemia because glycogen stores are reduced and hyperinsulinemia decreases the ability to mobilize hepatic glycogen.[37-39]

Blood glucose values in the first 2 to 3 hours after birth may drop to low levels and then rapidly and spontaneously improve.[37,40] Transient low blood glucose levels during this time should be monitored every 15 minutes until recovery is evident. Transient hypoglycemia implies low levels during the 2-3 hours after birth confined to the newborn period. Persistent and recurrent hypoglycemia implies that long-term management is indicated with glucose infusion and/or pharmacological intervention.[37]

Signs and Symptoms of Infant Hypoglycemia

Symptoms of hypoglycemia are highly variable and can either be present or not. Infants of diabetic mothers encounter hypoglycemia up to 50% of the time, in the early neonatal period.[28] A large proportion of hypoglycemic infants will be asymptomatic. Consequently, routine screening is recommended for all infants of women with diabetes. Common symptoms of hypoglycemia in the neonate include[28,40]:

- Abnormal cry
- Apnea
- Feeding difficulty
- Lethargy, stupor
- Hypothermia
- Respiratory distress
- Tachycardia
- Grunting, tachypnea
- Irritability
- Hypotonia, limpness
- Unexplained cyanosis
- Seizures
- Jitteriness, tremors
- Sweating

Recommended Feeding Practices for Asymptomatic Infants

As discussed below, while treatment is needed for the symptomatic neonate, the following feeding practices are recommended for asymptomatic infants who, nevertheless, have blood glucose levels in the hypoglycemic range:

- Promote early feeding by breast by one hour of age[41], hourly for three or four feedings until the blood glucose is stable (> 40 mg/dL) and then every two to three hours until 12 hours of age.
- The first colostrum has the highest level of glucose and may be given by spoon when pumped or hand-expressed.
- Breastfeeding is not contraindicated for hypoglycemic infants. It may require the support of a lactation consultant and supplementation.[37] Due to lethargy, feeding difficulties and need for optimal intake, it may be necessary to alternate feeding methods (cup, syringe, gavage) while the mother uses a breast pump to establish and maintain a milk supply.
- Glucose water is not recommended. It is rapidly absorbed by the gastrointestinal tract and can stimulate the release of insulin, which may further worsen hypoglycemia in the infant of a woman with diabetes.
- If oral or gavage infant feedings are not tolerated, or the infant blood glucose level drops to 30-40 mg/dL and/or the infant is symptomatic, parenteral treatment may be indicated.[42]

Treatment for Symptomatic Infants

Facilities should have specific protocols for treatment of infant hypoglycemia. The protocol described below provides recommendations for infants who have hypoglycemia despite feeding, have low birth weight, or are preterm.

- IV glucose administration is best accomplished with a peripheral IV catheter. However, due to the likelihood and danger of infiltration into the tissues, central access is required if glucose concentrations greater than 12.5% are necessary.
- Initial treatment includes 2 ml/kg D10W (200 mg/kg/dose) bolus; follow with 4-8 mg glucose/kg/minute (D10W at 80-120 ml/kg/day) infusion.[43]
- Do not wait for lab results to verify hypoglycemia and therefore postpone treatment.[40]
- Measure blood glucose levels every 15 to 30 minutes until glucose is stable and above 40 mg/dL.
- Observe IV site frequently and treat loss of IV access as an emergency. Reactive hypoglycemia may follow a sudden interruption of glucose infusion.
- Begin oral feedings if not contraindicated; monitor plasma blood glucose and decrease glucose infusion concentration and rate as tolerated oral feeding volume increases.
- An infant who requires a high glucose infusion, whose plasma blood glucose drops to less than 20 mg/dL, is unresponsive to treatment, or has sustained hypoglycemia may require a neonatology consult.

Hypocalcemia

Hypocalcemia, defined as a total serum calcium concentration of less than 7 mg/dL, or an ionized calcium value of less than 4 mg/dL, or less than 3.2 mg/dL in infants with birth weight less than 1500 g, occurs in at least 10% to 20% of infants of women with diabetes. The lowest serum calcium concentration typically occurs between 24 and 72 hours after birth and often is associated with hypomagnesemia. The extent of hypocalcemia is related to the severity and duration of maternal diabetes.[28]

Hypocalcemia is thought to be caused by the lower concentration of parathyroid hormone (PTH) after birth that is observed in neonates of diabetic mothers.[44] Higher serum ionized calcium concentrations in utero may suppress the fetal parathyroid glands. The development of hypomagnesemia, prematurity, and birth asphyxia may be contributing factors.[44] Hypocalcemia usually is asymptomatic and resolves without treatment in term infants of diabetic mothers. As a result, routine screening is not recommended. However, the serum calcium concentration should be measured in infants with:

- Jitteriness
- Lethargy
- Apnea
- Tachypnea
- Seizures

and in infants who have the following complications:

- Prematurity
- Asphyxia
- Respiratory distress
- Suspected infection

Hypomagnesemia

When serum magnesium concentration is less than or equal to 1.5 mg/dL hypomagnesemia occurs. Hypomagnesemia appears within the first three days after birth in up to half of pregnancies complicated by diabetes.[28,45] The mechanism is thought to be maternal hypomagnesemia, caused by increased urinary loss secondary to diabetes.[28,45] Prematurity may also be a contributing factor. Hypomagnesemia usually is transient and asymptomatic, and thus usually is not treated. However, hypomagnesemia can reduce both parathyroid hormone (PTH) secretion.[46] As a result, in some neonates with hypocalcemia and hypomagnesemia, the hypocalcemia may not respond to treatment until the hypomagnesemia is corrected.

Respiratory Distress Syndrome

Respiratory distress syndrome (RDS) occurs more frequently in infants of diabetic women in comparison to infants of nondiabetic mothers. This is especially significant in infants born before 38 weeks with suboptimal glycemic control or poor gestational dating.[47,48] The mechanism may be delayed maturation of surfactant synthesis caused by hyperinsulinemia, possibly by interference with the induction of lung maturation by glucocorticoids.[47,49] In contrast, fetal lung maturation may occur early in diabetic pregnancies stressed by vasculopathy.

Respiratory distress may also be due to hypertrophic cardiomyopathy[50], other cardiac or pulmonary anomalies, or transient tachypnea of the newborn (TTN).[51,52] Respiratory distress increases the work of breathing and glucose utilization, and warrants diagnostic evaluation and early treatment.

Transient Tachypnea of the Newborn

Transient tachypnea of the newborn (TTN) is the most common cause of respiratory distress in the term infant of a woman with diabetes. TTN occurs two to three times more commonly in these infants compared with infants of nondiabetic mothers.[53] The newborn will exhibit tachypnea within the first two hours of birth.[54] This condition develops as a result of residual fetal lung fluid following delivery, is mostly benign, and will usually resolve within a few hours or within two days following delivery.[54] Cesarean delivery for fetal macrosomia increases the risk of developing TTN.[55]

Polycythemia and Hyperviscosity Syndrome

Polycythemia is characterized as a central venous hematocrit of more than 65%.[28,51,56] Symptoms include:

- Poor feeding
- Tachypnea
- Plethora
- Lethargy
- Cyanosis
- Irritability
- Respiratory distress

- Hyperbilirubinemia
- Hypoglycemia
- Thrombocytopenia

The mechanism for polycythemia is uncertain, but is related to increased erythropoietin concentrations caused by chronic fetal hypoxemia.[57]

Polycythemia may lead to hyperviscosity syndrome, which can include ischemia, and infarction of vital organs. Hyperviscosity is thought to contribute to renal vein thrombosis seen in infants of diabetic mothers. Polycythemia may also contribute to rare occurrence of stroke, seizures, necrotizing enterocolitis, and renal failure.[28,56] The hematocrit should be measured within 12 hours of birth to detect polycythemia. Treatment recommendations for infants with polycythemia depend on whether the infant is symptomatic.[28]

Hyperbilirubinemia

Hyperbilirubinemia occurs in 25 to 50% of infants of diabetic women.[46] It is associated with poor maternal glycemic control, and macrosomic infants are at highest risk.[58] Increased red blood cell production secondary to increased erythropoietin results in increased breakdown of red blood cells and an increase in bilirubin production. The relative immaturity of hepatic bilirubin conjugation and excretion contributes to this process. In addition, the excess hemolysis may result from glycosylation of erythrocyte membranes. Polycythemia and prematurity are contributing factors.

Large for gestational age infants of diabetic mothers may be at a greater risk for hyperbilirubinemia.[18] In a study conducted by Peevy et al, "Peak serum bilirubin concentrations were also significantly higher in LGA IDM [large for gestational age infants of diabetic mothers] than in AGA IDM [appropriate for gestational age infants of diabetic mothers] or control infants."[18]

Diagnosis and treatment depend not only on measured bilirubin levels, but also on the age and condition of the infant. Infants born to mothers with well-controlled diabetes appear to have fewer problems with hyperbilirubinemia.

Hypertrophic Cardiomyopathy

Hypertrophic Cardiomyopathy is one of the most commonly reported cardiac malformations and is characterized as a thickening of the heart muscle. It is thought to be caused by fetal hyperinsulinemia leading to an accelerated growth of cardiac cells.[59,60] It is most likely to occur in mothers with poor glycemic control during pregnancy although it has still been found in infants of diabetic mothers who have great glycemic control. These changes have been reported to occur in up to 30% of all infants of diabetic mothers.[60-62] In the fetus of women with pre-existing diabetes, cardiac function changes are evident in the first trimester and cardiac enlargement in the third trimester.[63]

Diagnosis is best made by echocardiogram. This condition is transient and rapidly resolves as insulin concentrations normalize.[28,60] The newborn is often asymptomatic. However, some infants will exhibit congestive cardiac failure and there have been a few fetal deaths reported in the literature.[62-64]

Signs and symptoms of hypertrophic cardiomyopathy and congestive heart failure include:

- Tachycardia
- Tachypnea
- Decreased heart rate with poor variability
- Poor peripheral perfusion
- Systolic ejection murmur
- Lethargy
- Fast, heavy breathing and sweating during feedings

Symptomatic infants typically recover after two to three weeks of supportive care and echocardiogram findings resolve within 6 to 12 months.[64,65] Supportive care includes intravenous fluid administration, ventilatory support, correction of any metabolic conditions, and beta-blockers.[28]

Small Left Colon Syndrome

Small left colon syndrome presents with abdominal distention, failure to pass meconium, and bile-stained vomiting.[28] The problem is transient and usually resolves after the evacuation of the colon.[66] Diagnosis is made with water-soluble contrast enema radiographic studies[66], which often results in the passage of meconium and is thus therapeutic. However, glycerin suppositories may be needed for the first few weeks of life.

Renal Vein Thrombosis

The incidence of renal vein thrombosis is increased in the infant of a woman with diabetes, but remains rare. If it is not identified on a prenatal ultrasound, the presence of newborn hematuria, hypertension and/or a flank mass requires further investigation.[28] This complication usually resolves with conservative and supportive management that includes careful fluid and electrolyte management to treat any hypertension.[28] Subspecialty consultation is recommended.

POSTNEONATAL COMPLICATIONS/ LONG-TERM SEQUELAE

Risk of Developing Diabetes

Children of mothers with diabetes have an increased risk of developing diabetes that is, in part, genetically determined.[30,67] The lifelong risk of developing diabetes is difficult to quantify and multifactorial. Rates may be up to 6% in singleton offspring of diabetics, and 33% in their identical twins (versus 0.4% in subjects with no family history).[68]

The abnormal metabolic environment of a diabetic pregnancy affects the development of type 2 diabetes and predisposing risk factors such as obesity.[8,30,67,69] The prevalence of both type 2 diabetes and obesity has increased via a "vicious cycle" - a greater likelihood of diabetes in the mother increases the likelihood of diabetes in the offspring.[30,70,71] Intrauterine exposure to hyperglycemia and hyperinsulinemia affects the development of adipose tissue and pancreatic beta cells, leading to future obesity and altered glucose metabolism.[30] Macrosomia at birth resolves by one year of age, but obesity recurs in childhood, resulting in a greater body mass index in offspring of diabetic mothers than controls. Impaired glucose tolerance has been documented in 36% of offspring of diabetic mothers, an abnormality associated with elevated amniotic fluid insulin concentrations.[72] An increased incidence of high body mass index at 4 - 7 years of age has been noted in macrosomic offspring of mothers with gestational diabetes.[73]

Several studies have shown that metabolic syndrome, which consists of insulin resistance, hypertension, obesity, and dyslipidemia, has increased in the offspring of women with diabetes. In one study, the incidence of metabolic syndrome seen at 11 years of age in the LGA offspring of women with GDM was 50%, however it was only 21% in the average weight offspring of women with GDM, and 4.8% in the average weight offspring of nondiabetic mothers.[8]

The studies mentioned in this section raise the issue of working with women to control their blood glucose levels and their infants' birth weights. Healthcare practitioners should encourage women to provide an environment and lifestyle that will prevent or reduce obesity, diabetes, and metabolic syndrome in their families. Lifestyle modifications that are encouraged for women after a GDM pregnancy include exclusive breastfeeding, physical activity, and healthy nutrition.[74,75]

Neurodevelopmental Outcomes

Studies on long-term neurodevelopmental outcomes have appeared in the literature since 1960, but research has been sporadic and has often used animal models. The neurodevelopmental outcomes of infants of women with well-controlled diabetes are similar to those of normal infants.[11,13,76,77] In contrast, poorly controlled diabetes may result in neurodevelopmental abnormalities in the offspring.[13,78]

In one study, for example, head circumference at three years of age was negatively correlated with A1c levels during pregnancy.[13,77,78] In another study of 196 offspring of women with type 1 diabetes, psychomotor development at 6 - 9 years of age correlated with maternal ketone concentrations during the second and third trimesters.[11] IUGR and central nervous system damage and malformations also contribute to developmental delays.

FACILITATION OF FAMILY COMMUNICATION AND SUPPORT

Psychological Impact of Abnormal Fetal Imaging and Parental Response

Conveying abnormal prenatal ultrasound findings to concerned parents is a difficult task and requires provider skill. Abnormal test results confront parents with life-altering decisions about anomalies that are either incompatible with life or will irrevocably alter their child's and their family's future.

When confronted with the discovery of a fetal abnormality, expectant parents are faced with acute emotional trauma that can threaten their own functioning ability at the time, their developing role as parents, and their attachment to their future child. Prenatal diagnosis of malformations is the most ethical medical practice although it does cause parents more psychological distress than postnatal diagnosis despite having more time to adjust.[79,80] Research has found that prenatal diagnosis was a significant predictor of acute psychological distress in parents, especially among mothers who were being admitted to a tertiary care center.[79,81] As a result, the remainder of the pregnancy can be fraught with underlying anxiety and uncertainty for parents as they struggle with perceived loss of control.

When parents decide to continue with the pregnancy, they will seek ongoing support from health care professionals who respect their choice and help them maintain both a sense of hopefulness and normalcy. Fear of healthcare professionals rejecting their choice is common. Parents experience much relief when their decisions are met with acceptance and respect.[81]

When women are faced with results showing fetal abnormalities in an intended pregnancy and decide to terminate their pregnancy, their bereavement is very similar to women who experience spontaneous pregnancy loss.[82] Bereavement is often confounded by the choice involved, ambivalent feelings about screening, abortion, and disability.

Guidelines for Counseling Parents Facing Abnormal Prenatal Ultrasound Findings

- Provide the critical information of the ultrasound results with empathy and understanding for the parents' stress response and grief process.
- Coordinate timely visits with the tertiary care center team (perinatologist, social worker, etc.) to ensure continuity of care for parents.
- Respect the parents' decision and offer nonjudgmental support if termination of pregnancy is an option.[81]
- Attend to and validate the complexity of parents' reactions and emotional responses.
- Assess available social support services and offer resources appropriate to the family's needs.
- Provide appropriate referral to a mental health professional as needed.

Guidelines for Counseling Parents of Infants with Abnormalities During the Postnatal Period

While caring for the infant with abnormalities, keep these maternal and family-related issues in mind:

- Anticipatory guidance pertaining to a known problem may decrease maternal and familial anxiety. This can include a visit to a NICU, if the mother expresses an interest.
- The woman who has a newborn with medical problems has an increased need for psychosocial support. If the baby is in the NICU, she may be frustrated about barriers between her and the baby and experience depression associated with her perceived helplessness and limited or lack of opportunity to bond with the baby. All of these feelings may occur in the father as well as in extended family members. The stress of having an infant in the NICU can exacerbate already strained relationships, which can magnify the mother's anxiety, depression and hopelessness.
- Even if the newborn is relatively well, the mother will need additional reassurance and support to resolve the stress associated with her pregnancy.
- A mother with diabetes is particularly vulnerable during the postpartum period. She has just experienced a high risk pregnancy, is coping with a chronic illness, and has a newborn who requires special medical attention.
- Women and families from other cultures may have different beliefs about the causes of diabetes, the implications of the mother having diabetes, and the impact of this illness on her baby. The woman and her family may require special counseling from a staff person who understands and can relate to diverse cultural beliefs. Refer to *Chapter 10: Cultural Competency* for additional information.

- Support for breastfeeding, if the infant's condition permits, should be provided. Refer to *Chapter 8: Breastfeeding* of this manual for more information.

Refer to *Chapter 9: Behavioral and Psychosocial Components of Care* of this manual for more complete information on psychosocial evaluation and intervention.

Counseling Parents about the Newborn's Diabetes Risk

Diabetes is a unique chronic illness where the majority of care and responsibility occurs in the home. The family as a whole, rather than healthcare professionals, is the "management team" of the disease. Adhering to a philosophy of diabetes as a family disease is often useful when counseling parents about an increased risk for diabetes in their newborn.[83] It is important to increase the family's overall understanding about lifestyle changes that benefit both the children and adults. The family is seen as the focus of intervention with comprehensive education about behavioral changes that positively influence glycemic control.[83] Care coordination with the family's pediatrician is another preventive measure with long-term positive implications for disease management.

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