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Influence of polyhydramnios on perinatal outcomes in pregestational diabetic pregnancies

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Abstract

Objective:

This study was carried out to evaluate the perinatal outcomes of pregnancy with pregestational diabetes mellitus complicated by polyhydramnios.

Methods:

This was a retrospective study of singleton pregnancies, with an antepartum diagnosis of polyhydramnios, seen at Bint al-huda hospital. All pregnancies in women with pregestational diabetes with a singleton pregnancy beyond 24 weeks of gestation, were reviewed (n =100), and pregnancies complicated by polyhydramnios were identified (50). Pregnancy outcomes of women whose pregnancy was complicated with polyhydramnios were compared to those without this complication. Preterm delivery, macrosomia, congental anomalies, Respiratory distress syndrome, Neonatal death and stillbirth were studies.

Results:

100 patients were included in our study. Women with polyhydramnios had increased hemoglobin A1c (HbA1c) levels throughout the pregnancy. Significantly more mothers in the polyhydramnios group delivered preterm (40% vs. 29%). More pregnancies with polyhydramnios were delivered by Cesarean section (74% vs. 62%), with the majority being performed electively in both groups. Regardless, there were no significant differences in perinatal mortality rates, congenital abnormality rates, acidemia, hypoglycemia requiring intravenous therapy, phototherapy and ventilatory needs between the babies of the two groups.

Conclusion:

Pregnancies with polyhydramnios associated with many perinatal outcomes. Despite this, there is no significant increase in adverse perinatal outcome in these pregnancies, apart from a higher iatrogenic preterm birth rate. Prognosis depend on the cause.

Introduction

Polyhydramnios is the term used to describe an excess accumulation of amniotic fluid. This clinical condition is associated with a high risk of poor pregnancy outcomes [1–3]. The reported prevalence of polyhydramnios ranges from 0.2 to 1.6 %of all pregnancies [4–7].Under physiological conditions there is a dynamic equilibrium between the production and resorption of amniotic fluid. Fluid levels are influenced by fetal urination and fetal lung liquid production. Amniotic fluid is reabsorbed by fetal swallowing and intramembranous and intravascular absorption. The relative attribution of each of these mechanisms varies over the course of the pregnancy. A disturbed equilibrium can be the result of compromised swallowing function or increased urination and can lead to polyhydramnios [8–11].A fetus close to term will produce between 500–1200 ml urine and swallow between 210–760 ml of amniotic fluid per day. Even small changes in this equilibrium can result in significant changes in amniotic fluid volumes [9–11].

Etiology

An underlying disease is only found in 17 % of cases in mild polyhydramnios. In contrast, an underlying disease is detected in 91% of cases in moderate to severe polyhydramnios [5]. The literature lists the following potential etiologies [5, 7,12–19]:"fetal malformations and genetic anomalies (8–45 %)"maternal diabetes mellitus (5–26%)"multiple pregnancies (8–10%)"fetal anemia (1–11%)"other causes, e.g. viral infections, Bartter syndrome, neuromuscular disorders, maternal hypercalcemia. Viral infections which can lead to polyhydramnios include parvovirus B19, rubella, and cytomegalovirus. Other infections, e.g. toxoplasmosis and syphilis, can also cause polyhydramnios [80–82].Advances in detailed ultrasound scanning and the prevention of Rhesus isoimmunization in the last decades have changed the relative frequency of these etiologies and significantly reduced the number of idiopathic cases [12–19].Well-known malformations which impair the swallowing reflex include esophageal atresia, duodenal atresia [16,17] and neuromuscular disorders such as myotonic dystrophy. Increased urine

production, as occurs with increased cardiac output associated with fetal anemia, can also result in increased production of amniotic fluid [20, 21]. These changes can also occur in the con-text of chromosomal disorders such as trisomy 21 and different syndromes. Duodenal atresia is the most important etiology incases with trisomy 21 [79].Poorly managed gestational diabetes is associated with fetal macrosomia and polyhydramnios but the pathogenesis has not been elucidated yet [22]. One possible explanation is fetal hyperglycemia resulting in increased osmotic diuresis which subsequently leads to polyuria. This theory is supported by evidence of a strong association with high glycosylated hemoglobin values (HBA1c)incases with polyhydramnios [22, 23]. According to the AWMFS3-guideline, polyhydramnios can be an indication of diabetogenic fetopathy. However, due to the wide range in amniotic fluid volumes, polyhydramnios does not play an important role in monitoring gestational diabetes [68]. The prevalence of poly-hydramnios in maternal cases with diabetes mellitus is 18.8%[23]. As the cause could also be fetal metabolic syndrome, children born after pregnancy complicated by polyhydramnios should be followed up by a pediatrician [24, 25].

Ultrasound Assessment of Amniotic Fluid Volume

Ultrasound and subjective or semi-quantitative assessment is used to evaluate amniotic fluid volumes. With the subjective method, the examiner estimates the volume of amniotic fluid based on personal impressions of the amniotic fluid depot. The sonographer’s experience plays an important role here [26].When evaluating cases of oligo- or polyhydramnios, the use of biometric measurements and references is more accurate when examiners are less experienced, while evaluation based solely on subjective assessment is associated with good results if done by an experienced examiner [27].Various semi-quantitative methods to measure amniotic fluid volumes have been described. But these methods also have their limitations which must be taken into account [28].

The 4-quadrant method (AFI –Amniotic Fluid Index)

With this method, the deepest amniotic pocket in each of the four quadrants is measured vertically and the values added together. The uterus is divided vertically into two halves by an imaginary line along the linea nigra. An imaginary horizontal line through the umbilicus divides the uterus into an upper and a lower half. During measurement the transducer is held at right angles to the sagittal plane of the patient's abdomen. The transducer should not be tilted along the maternal abdomen, i.e. it must be kept at a right angle. The measured amniotic fluid pockets must be free of fetal extremities and the umbilical cord and must be at least 0.5 cm wide. The Amniotic Fluid Index (AFI) is the sum of measurements of all four quadrants. According to one study group, AFI values between 8.1 and 18 cm are normal, values be-tween 5.1 und 8.0 cm indicate oligohydramnios, an AFI value of less than 5.0 cm indicates severe oligohydramnios and a value above 18 cm is classified as polyhydramnios [31].Based on AFI values obtained during prenatal screening, some clinicians categorize polyhydramnios into three groups according to severity: mild polyhydramnios (AFI of 25–30 cm), moderate polyhydramnios (30.1–35 cm) and severe polyhydramnios(≥35.1 cm) [87].Moore und Cayle [32] investigated the distribution of AFI measurements in a population with normal pregnancies. In contrast to the definition of oligohydramnios proposed by Phelan et al.(AFI less than 5 cm [31]) they found that an AFI of 5 cm was only found in 1% of normal pregnancies. Intraobserver variation ranged between 0.5 and 1 cm, and interobserver variation was between 1 and 2 cm. Taking the calculated average of three measurements is recommended to achieve the greatest accuracy, particularly when the AFI is less than 10 cm [32]. The use of color flow Doppler has the advantage that umbilical cord loops are detected more easily. But, according to a retrospective study by Zlatnik et al. [34], AFI measured with color flow Doppler over-estimated oligohydramnios and underestimated polyhydramnios if standard AFI tables (obtained without color flow Doppler)were used [33,34].It should be noted that the pressure exerted by the transducer can change AFI and single deepest pocket measurements. If the pressure is minimal, AFI increases by 13%, while if strong pressure is exerted, AFI is underestimated by 21% [35–38].

Treatment Options to Reduce Amniotic Fluid Volume

Treatment consists of reducing the volume of amniotic fluid to improve maternal well-being and prolong the pregnancy. The following methods are used to reduce amniotic fluid volumes:

- amnioreduction (therapeutic amniocentesis) [53–55]
- pharmacological treatment [49–52]

Amnioreduction

To date, this method has not been evaluated in randomized or controlled studies, but it offers a clear clinical benefit if done after careful diagnostic evaluation. However, there is no consensus regarding the volume of aspirated amniotic fluid, the speed of aspiration and the use of tocolytics or antibiotics. The intervention is usually concluded when ultrasound examination shows an AFI of15 to 20 cm or if intra-amniotic pressure drops to < 20 mmHg[53,66]. In some cases, the intervention had to be terminated due to maternal discomfort or premature placental abruption. Tocolytics are routinely used as prophylaxis to prevent onset of preterm labor. Complications occur in 1–3% of cases and can include premature labor, placental abruption, premature rupture of membranes, hyperproteinemia and amniotic infection syndrome [52, 54]. After the procedure, regular monitoring of amniotic fluid volumes is recommended, with monitoring done every 1 to 3 weeks.

Prostaglandin synthetase inhibitor

Prostaglandin synthetase inhibitors stimulate fetal secretion of arginine vasopressin, resulting in vasopressin-induced antidiuresis [49, 57,58,62]. Reduced renal blood flow reduces fetal urine production. These substances can also inhibit fetal lung liquid production or increase reabsorption rates [56].However, prostaglandin synthetase inhibitors have not been approved for this indication in pregnancy in Germany. While these substances are used as an analgesic or in anti-inflammatory therapy in the 1st and 2nd trimesters of pregnancy, patients are advised against using these substances after the 28thweek of gestation [88]. It

should be noted that the use of these drugs is not generally approved in pregnancy.

Sulindac

Sulindac is a non-steroidal anti-inflammatory drug; use of sulindac can also lead to a reduction of amniotic fluid volume. There are some reports that sulindac decreases pulsatility in fetal ductus arteriosus less than indomethacin [58–61]. However, the efficacy of sulindac has not been confirmed by further studies yet.

Delivery

Fetal head presentation should be checked several times during labor, as fetal position change to breech presentation or trans-verse lie can occur intrapartum. Spontaneous rupture of membranes can lead to acute uterine de-compression with the risk of cord prolapse or placental abruption. Artificial rupture of membranes should therefore only be done under controlled conditions. Although polyhydramnios does not constitute a contraindication for the application of oxytocin or prostaglandins, these sub-stances should be administered with care. There is an increase drisk of atonic bleeding and amniotic-fluid embolism postpartum[57,67].

Methods

This was a retrospective study of singleton pregnancies, with an antepartum diagnosis of polyhydramnios, seen at Bint Al-huda hospital. The medical and ultrasound records of all pregnancies in women with pregestational diabetes and a singleton pregnancy beyond 24 weeks of gestation were reviewed (100) and pregnancies complicated by polyhydramnios were identified (50).

Inclusion criteria: Pregnancies with AFI>24cm

Exclusion criteria: pregnancies with normal AFI or oligohydramnios < 5cm.

Result

One hundred pregestational diabetic pregnancies were identified during the study period, after exclusion patients with oligohydramnios. Of these pregestational diabetic pregnancies, 50 were complicated by polyhydramnios. 50 pregestational diabetic pregnancies without polyhydramnios acted as a control group. There were no significant differences in maternal age (18_38 vs. 20_32 years), parity (2_5 vs.1_4), prepregnancy weight (65_86 vs. 63_82 Kg). The types of diabetes were not found to be significant in contributing to the development of polyhydramnios. There were deferent incidences of gestational hypertension and pre-eclampsia between the two groups. Significantly more mothers in the polyhydramnios group delivered preterm (40% vs. 29%). Despite the lower gestational age, higher incidences of macrosomia and large-for-gestational age were found in the polyhydramnios group, although these differences were not statistically significant. More pregnancies with polyhydramnios were delivered by Cesarean section (74% vs. 62%), with the majority being performed electively in both groups. The main indication for Cesarean section in the polyhydramnios group was macrosomia and for the control group was previous Cesarean section. There was no difference in the clinical outcome between the male and female infants. Two stillbirths were from the polyhydramnios group and zero were from the control group.

More babies from the polyhydramnios group were born with major congenital malformations (14% vs. 2 %).

Table 1 Maternal and pregnancy characteristics of the study population

Characteristics	Polyhydramnios	Normal amniotic fluid
Maternal age	**18 _ 38 Year**	**20_32 Year**
Gravidity	**3_5**	**2_6**
Parity	**2_5**	**1_4**
Prepregnancy weight	**65_86 Kg**	**63_82 Kg**
Diabetes mellitus	**50 (100%)**	**50 (100%)**
Gestational HTN	**14 %**	**3 %**
Pre-eclampsia	**18 %**	**5 %**
Cesarean section	**74 %**	**62 %**
Induction of labour	**26 %**	**34 %**

DISCUSSION

The prevalence of polyhydramnios in our study population was significantly higher than that in the general population, of around 1%. This study assessed the significance of polyhydramnios in pregnancies complicated with pre-existing diabetes. We excluded pregnancies with oligohydramnios and fetal growth restriction to avoid the confounding effect of abnormal fetal growth on adverse perinatal outcome. In this study, we found that polyhydramnios is associated with poor diabetic control. Women with raised levels of HbA1c were more likely to have polyhydramnios. Pregestational diabetes mellitus is a known human teratogen. As such, the rate of congenital abnormality in infants of pregestational diabetic mothers is higher than in the general population. Several population based studies have reported a range of congenital abnormality. Similarly, polyhydramnios alone has been shown to be associated with an increased risk of congenital abnormality19. Pregestational diabetic pregnancies with polyhydramnios, with raised periconceptional HbA1c, reflecting poor glycemic control, would therefore

be expected to be associated with a higher risk of congenital abnormalities in affected pregnancies. Of these, pregnancies with polyhydramnios recorded a higher rate of abnormality at 14 % when compared with the control group; however, the difference was not statistically significant because of the small sample size. The types of abnormalities were consistent with those of diabetic embryopathy, the majority being cardiovascular and musculoskeletal abnormalities. While pregestational diabetes mellitus alone has been shown to be associated with preterm delivery, we found that polyhydramnios further confounded it, with 40 % of the affected pregnancies delivered before 37 weeks, compared with 29 % of pregnancies in the control group.

Outcomes	Polyhydramnios	Normal amniotic fluid
Preterm delivery	**20 (40%)**	**29 %**
Macrosomia	**4 (8%)**	**3 %**
Congenital anomalies	**7 (14%)**	**2 %**
Respiratory distress	**2 (4%)**	**12 %**
Neonatal death	**6 (12%)**	**0**
Stillbirth	**2 (4%)**	**0**

The tendency to deliver pregestational diabetic pregnancies with polyhydramnios earlier is partly a result of the difficulty in fetal monitoring as current fetal surveillance is unsatisfactory for women whose pregnancies are complicated with pre-existing diabetes. Umbilical artery Doppler, which is the best fetal monitoring technique currently available, is less effective in these pregnancies as the majority have normal placental function, and thus normal umbilical artery Doppler results. The Cesarean section rate in our study population was 74 % in the polyhydramnios group and 62% in the control group, with a similar rate of elective and emergency Cesarean sections between the two groups. Similarly, in our group, the commonest indication for elective Cesarean section in the polyhydramnios group

was suspected macrosomia. Perinatal mortality is higher in diabetic pregnancies than in the general population. Women with polyhydramnios are more likely to deliver prior to term. The other possible explanation is that not all poorly controlled diabetes resulted in an adverse perinatal outcome. The sample size may be too small to show a significant difference in rare perinatal outcomes. One of the limitations of this study was the small sample size and therefore it might not have sufficient power to show differences in rare perinatal outcome. There were great variations in the management, indication for induction of labor or elective Cesarean section. However, the adverse outcomes did not differ significantly between the two groups. Diabetic women are particularly at risk of iatrogenic delivery, particularly because of the lack of an effective fetal monitoring modality for them. As such, there is an urgent need to identify a better fetal monitoring technique for these women. Further studies need to be carried out to form a consensus on antenatal testing for this particular patient population in order to help obstetricians decide when to deliver these patients.

Conclusion

Pre-gestational pregnancies with polyhydramnios have increased risk of Fetomaternal complications and perinatal outcomes. Most of them carry bad prognosis to neonates and morbidities to mothers. Despite this, there is no significant increase in adverse perinatal outcome in these pregnancies, apart from a higher iatrogenic preterm birth rate. However there is no significant variation between both groups because the study based on small sample size.

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