Adverse Maternal and Fetal Outcomes in Pregnancies Complicated by Diabetes Mellitus: A Case Series

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Abstract

Pregnancy-related diabetes mellitus poses an increased risk of detrimental effects on the health of the mother and fetus. This case series aims to highlight the correlation between poorly managed diabetes and complications such as intrauterine fetal death (IUFD), preterm labor, macrosomia, and neonatal death. We analyzed cases of pregnant women with diabetes mellitus who experienced adverse outcomes within one year at our hospital. The cases were selected based on the seriousness of complications and gestational period at the time of occurrence. Three cases such cases were selected, IUFD was experienced by a 30-year-old woman with a gestational age of 36 weeks; a woman whose age was 29 years also experienced IUFD; whose gestational age was 37 weeks during the occurrence; and another case involved of a mother whose age was 34 and was at 3 months and 4 days of gestation, who underwent preterm delivery leading to neonatal death on the first postoperative day following the surgery. This critical nature of handling diabetes during pregnancy is emphasized in this case series to mitigate the adverse effects and the risks which include, IUFD, premature birth, macrosomia, and neonatal death. Along with continuous monitoring and glycaemic control, to avoid outcomes of complications caused by diabetes mellitus during pregnancy educating the patient is also very important.

Keywords: Fetal Wastage, Fetal Demise, Glycaemic Control, Maternal Mortality, Pre-existing Diabetes, Pregnancy Complications.

Introduction

Substantial advancements in insulin therapy and the meticulous management of blood glucose levels have significantly enhanced maternal and fetal health in pregnancies affected by pre-existing diabetes over the past century. It is reported that approximately one in four women in the South Asian region and around one in six women globally experience hyperglycemia during pregnancy, despite the improvements [1]. Risks of prenatal conditions and development of diabetes in both mother and baby are increased in individuals suffering from this condition [2, 3]. Our knowledge of this condition is expanding, revealing the heterogeneous nature of HIP [4, 5]. Previously, the terms "Hyperglycaemia In Pregnancy (HIP)" and "gestational diabetes mellitus (GDM)" were used interchangeably to describe any hyperglycaemic state initially detected during pregnancy [5]. Following a large-scale study across multiple centres examining perinatal outcomes. International the Association of Diabetes and Pregnancy Study Groups (IADPSG) implemented a new diagnostic criterion for GDM in 2010 [6, 7]. These criteria brought a significant advancement, by distinguishing "overt diabetes in pregnancies" from GDM as a much more severe form of hyperglycaemia. Organizations like the World Health Organization in 2013 made subsequent recommendations further emphasizing these distinctions, the International Federation of Gynaecology and Obstetrics (FIGO) in 2015 [4], and the American Diabetes Association (ADA) in 2020. These organizations highlighted the need for differentiating GDM from overt diabetes in pregnancy as distinct entities [8]. For the first time during pregnancy both the hyperglycaemic conditions GDM and overt diabetes were observed. Associated with poorer maternal and fetal outcomes overt diabetes is a much critical form of hyperglycaemia, necessitating intensive management and close monitoring [8, 9, 10, 11]. This case series aims to characterize fetal wastage in pregnancy associated with overt diabetes and explore the potential consequences for precise diagnosis and management of this condition.

Case Series

Case 1

A 30-year-old primigravida, married for 8 years, presented at 36 weeks of gestation with a body mass index (BMI) of 29.4. She had a

history of uncontrolled pregestational diabetes, with a high HbA1c level of 10.1, and was undergoing insulin therapy (injection HA) based on regular glycemic monitoring. The patient also had chronic hypertension but was not on regular medication. At 3 months of amenorrhea, she took Labetalol 100 mg tablets for a short duration. Additionally, she had hypothyroidism for 2 years, managed with Thyronorm 100 mcg tablets, and was prescribed Aspirin 75 mg tablets. In an emergency presentation, she arrived at the casualty complaining of reduced fetal movements and abdominal pain since the previous evening. Assessment revealed a capillary blood glucose (CBG) of 337 mg/dl, a pulse rate (PR) of 108 beats per minute, and a blood pressure (BP) of 130/80 mmHg. Abdominal examination showed a full-term uterus with cephalic presentation and contractions occurring every 3 minutes for 30 seconds. Unfortunately, fetal heart sounds were not easily localized, and an ultrasound confirmed IUFD. A vaginal examination indicated a fully dilated cervix with bulging membranes and the vertex at -1 station. For the management and delivery, a profile for pregnancy-induced hypertension (PIH) was sent, and 1 unit of packed red blood cells (PRBC) was reserved. Subsequently, the patient experienced the spontaneous rupture of membranes with brown-stained amniotic fluid drainage. She delivered the stillborn infant vaginally, with a birth weight of 3 kg, indicating no macrosomia. External examination and a previous antenatal scan confirmed appropriate fetal growth for gestational age. Postnatally, the patient's blood pressure remained within normal limits. Insulin therapy was adjusted to achieve glycemic control (injection HM 10-0-8). An ophthalmology evaluation showed no evidence of diabetic retinopathy.

Case 2

A patient, 29 years, gravida 3 para 1 living 1 abortion 1, with a previous lower segment cesarean section (LSCS), presented to the hospital due to decreased perception of fetal movements and for glycemic control. She was diagnosed with overt diabetes mellitus at 6 weeks of gestation (Oral Glucose Challenge Test-170) and initially started on Glycomet 500 mg tablets 1/2-0-1/2, later transitioning to insulin with regular glycemic monitoring. During the current pregnancy, she was also diagnosed with hypothyroidism and treated with Thyronorm 25 mcg tablets from 7 weeks of gestation. Upon admission, the patient reported perceiving fetal movements, but attempts to localize fetal heart sounds using fetal Doppler and NST machines were unsuccessful. A bedside ultrasound confirmed absent cardiac activity, mild pleural no subcutaneous edema. effusion, and Emergency Cesarean Section: The sudden intrauterine fetal demise necessitated immediate intervention. The patient underwent an emergency LSCS, delivering a nonviable fetus weighing 5.20 kg, which is considered large for gestational age. The postoperative period was uneventful, highlighting the success of timely and decisive action. Postoperative Management: Postoperative assessment included an ophthalmology consultation, which confirmed the absence of diabetic retinopathy. Blood sugar levels in the postpartum period were monitored, with FBS and PPBS recorded at 120 mg/dL and 190 mg/dL, respectively. The patient was advised to continue her oral hypoglycemic medication.

Case 3

A 34-year-old woman, gravida 2 para 1 living 1, with a previous normal delivery, presented at 33 weeks and 4 days of gestation. She had a history of overt diabetes for three years, managed with Metformin 500 mg tablets twice daily. At her initial visit, her fasting blood sugar (FBS), postprandial blood sugar (PPBS), and HbA1c levels were recorded as 179 mg/dL,

243 mg/dL, and 9.7%, respectively. At 24 weeks of gestation, she was advised to undergo a fetal echocardiogram, but she declined follow-up appointments. Subsequent prenatal check-ups, however, showed satisfactory fetal growth and well-being. During her current hospitalization, she presented with leaking per Examination revealed a uterus vagina. consistent with 34 weeks of gestation, cephalic effective contractions presentation, and (3/30/10). Fetal heart sounds were reassuring. Vaginal examination showed a soft, posterior cervix, 2 cm dilated, with the vertex at -3 station, indicating an adequate pelvis. Preterm consent was obtained, and the patient received an injection of dexamethasone 6 mg for fetal lung maturation. Due to persistent fetal bradycardia, an emergency cesarean section was performed. The neonate, admitted to the Neonatal Intensive Care Unit (NICU) due to respiratory distress, unfortunately passed away on the first postoperative day. An X-ray revealed cardiomegaly in the neonate. Postoperatively, the mother was prescribed Cabergoline 1 mg tablets orally. An ophthalmology consultation confirmed no evidence of diabetic retinopathy. Her postoperative FBS and PPBS levels were within acceptable limits at 93 mg/dL and 97 mg/dL, respectively. The patient was advised to continue Metformin 500 mg tablets twice daily for glycemic control.

Discussion

Cases 1 and 2 both involved the diagnosis of IUFD.

In Case 1, a 30-year-old primiparous woman presented with decreased fetal movements at 36 weeks gestation. A detailed history revealed a gradual reduction in fetal activity over the preceding evening. Physical examination demonstrated uterine contractions and the absence of audible fetal heart tones. Ultrasound findings confirmed the absence of fetal cardiac activity and movement, consistent with intrauterine fetal death. These combined clinical and ultrasound findings led to the diagnosis of IUFD.

Case 3 involved a 29-year-old woman with a history of one previous cesarean delivery and overt diabetes managed with insulin who presented with decreased fetal movements and also experienced intrauterine fetal demise.

By the WHO and The American College of Obstetricians and Gynecologists (ACOG) definitions, intrauterine fetal death is characterized by fetal demise in utero at or beyond 20 weeks' gestation and with a fetal weight of 350 grams or more [12].

The diagnosis of IUFD is often challenging to definitively establish based solely on medical history and physical examination due to inherent limitations in these assessment methods [13]. Research indicates a strong correlation between reduced fetal movements and adverse pregnancy outcomes, including stillbirth. Studies have shown that а conspicuous proportion of women reporting decreased fetal movement within a week subsequently experience stillbirth, underscoring the importance of maternal perception in fetal well-being surveillance [14]. While the absence of fetal heart rate on physical examination suggests IUFD, definitive diagnosis requires ultrasound confirmation to exclude fetal cardiac activity [13]. A multitude of factors, including maternal, fetal, and underlying pathological conditions, can contribute to fetal demise. DM is one such maternal condition associated with an increased risk of fetal loss [15]. There is a fivefold risk of IUFD in pregnant women suffering from diabetes mellitus than in the general population [13].

Case 3 involved a 34-year-old woman with a prior history of a standard vaginal delivery who presented at 33 weeks and four days of gestation with premature rupture of membranes (PROM). Distinguishing PROM from preterm premature rupture of membranes (PPROM) is cardinal, which happens before 37 weeks of gestation [16]. DM during pregnancy is associated with an increased risk of preterm birth and premature rupture of membranes [17, 18-21]. Recent studies suggest a link between PPROM and sterile inflammation of the amniotic membranes. This inflammatory process may underlie the association between GDM and PPROM. The formation of advanced glycation end products (AGEs) can be induced by DM, which binds to receptors for advanced glycation end products (RAGE), contributing to this inflammatory pathway [18, 21].

In Case 3, the neonate was born preterm with a low birth weight, exhibiting respiratory distress and a low initial Apgar score. These complications necessitated admission to the NICU. Increased risk of respiratory distress syndrome and poor neonatal outcomes are observed in infants born to mothers with DM, as reflected by lower Apgar scores [19, 20-23]. The increased morbidity in these infants is primarily attributed to their preterm birth.

Conclusion

Diabetes mellitus in pregnancy is associated with a significant risk of adverse maternal and fetal outcomes. This case series highlights the severe consequences of uncontrolled diabetes, including intrauterine fetal demise, preterm birth, and neonatal complications. Early diagnosis, intensive glycemic control, and comprehensive management are essential for mitigating these risks. A multidisciplinary approach, including patient education and support, is crucial for optimizing maternal and fetal health. Further research is needed to elucidate the underlying pathophysiology of diabetes-related pregnancy complications and to develop targeted interventions.

Conflict of Interest

Authors declare no conflict of interest to this work

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References

[1]. Home R., 2024. Gestational Diabetes Mellitus, *IDF Diabetes Atlas*, 11, 2024.

[2]. Coustan, D. R., 2013. Gestational Diabetes Mellitus, *Clin. Chem.*, 59, 1310–1321.

[3]. McIntyre, H. D., Catalano, P., Zhang, C., Desoye, G., Mathiesen, E. R., and Damm, P., 2019. Gestational diabetes mellitus, *Nat. Rev. Dis. Primer*, 5, 1–19.

[4]. Hod. M *et al.*, 2015. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on gestational diabetes mellitus: A pragmatic guide for diagnosis, management, and care, *Int. J. Gynaecol. Obstet. Off. Organ Int. Fed. Gynaecol. Obstet.*, 131, 173-211.

[5]. Gupta, Y., Goyal, A., Kalra, S., and Tandon, N., 2020. Variation in the classification of hyperglycaemia in pregnancy and its implication, *Lancet Diabetes Endocrinol.*, 8, 264–266.

[6]. Metzger, B. E., Gabbe, S. G., Persson, B., Buchanan, T. A., Catalano, P. A., Damm, P., Dyer, A. R., Leiva, Ad., Hod, M., Kitzmiler, J. L., Lowe, L. P., McIntyre, H. D., Oats, J. J., Omori, Y., Schmidt, M. I., 2010. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy, *Diabetes Care*, 33, 676–682.

[7]. Metzger, B. E., Lowe, L. P., Dyer, A. R., Trimble, E. R., Chaovarindr, U., Coustan, D. R., Hadden, D. R., McCance, D. R., Hod, M., McIntyre, H. D., Oats, J. J., Persson, B., Rogers, M. S., Sacks, D. A., 2008. Hyperglycemia and Adverse Pregnancy Outcomes | *New England Journal of Medicine*. 16,115-144.

[8]. Goyal, A., Gupta, Y., and Tandon, N., 2022. Overt Diabetes in Pregnancy, *Diabetes Ther.*, 13, 589–600.

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[9]. Wong, T., Ross, G. P., Jalaludin, B. B., and Flack, J. R., 2013. The clinical significance of overt diabetes in pregnancy, *Diabet. Med. J. Br. Diabet. Assoc.*, 30, 468–474.

[10]. Corrado, F., Pintaudi, B., D'Anna, R., Santamaria, A., Giunta, L., and Di Benedetto, A., 2016. Perinatal outcome in a Caucasian population with gestational diabetes and preexisting diabetes first diagnosed in pregnancy, *Diabetes Metab.*, 42, 122–125.

[11]. Egan, A. M., Dow, M. L., and Vella, A., 2020. A Review of the Pathophysiology and Management of Diabetes in Pregnancy, *Mayo Clin. Proc.*, 95, 2734–2746.

[12]. Metz, T. D., Berry, R. S., Fretts, R. C., Reddy,
U. M., and Turrentine, M. A., 2020, Obstetric Care
Consensus Management of Stillbirth: (Replaces
Practice Bulletin Number 102, March 2009), *Am. J. Obstet. Gynecol.*, 222, B2–B20.

[13]. Maslovich, M. M., and Burke. L. M., 2024. Intrauterine Fetal Demise, in *StatPearls*, 35, 2091–2098.

[14]. Bekiou, A., and Gourounti. K., 2020. Reduced Fetal Movements and Perinatal Mortality, *Mater. Socio-Medica*, 32, 227–234.

[15]. Lynch, T. A., Westen, E., Li, D., Katzman, P. J., Malshe, A., and Drennan, K., 2022. Stillbirth in women with diabetes: a retrospective analysis of fetal autopsy reports, *J. Matern. Fetal Neonatal Med.*, 35, 2091–2098.

[16]. Dayal, S., and Hong, P. L., 2024. Premature Rupture of Membranes, in *StatPearls*, Treasure Island (FL): StatPearls Publishing. Accessed: Aug. 11, 2024.

[17]. Muche, A. A., Olayemi, O. O., and Gete, Y. K., 2020. Effects of gestational diabetes mellitus on risk of adverse maternal outcomes: a prospective cohort study in Northwest Ethiopia, *BMC Pregnancy Childbirth*, 20, 73.

[18]. Bouvier, D *et al.*, 2019. Risk Factors and Outcomes of Preterm Premature Rupture of Membranes in a Cohort of 6968 Pregnant Women Prospectively Recruited, *J. Clin. Med.*, 8, 1987.

[19]. Yildiz Atar, H., Baatz, J. E., and Ryan, R. M.,2021. Molecular Mechanisms of Maternal DiabetesEffects on Fetal and Neonatal Surfactant, *Children*,8, 281.

[20]. Li, Y., Wang, W., and Zhang, D., 2019. Maternal diabetes mellitus and risk of neonatal respiratory distress syndrome: A meta-analysis, *Acta Diabetol.*, 56, 729–740.

[21]. Shanmugam, R., Tharani, M., Abullais, S.S.,2024. Black seed assisted synthesis,characterization, free radical scavenging,

antimicrobial and anti-inflammatory activity of iron oxide nanoparticles. *BMC Complement Med Ther* 24(24), 241.

[22]. Habeeb Rahuman HB., Dhandapani R., Narayanan S., Palanivel V., Paramasivam R., Subbarayalu R., Thangavelu S., Muthupandian S., 2022. Medicinal plants mediated the green synthesis of silver nanoparticles and their biomedical applications. *IET Nanobiotechnol.* 16,115-144.

[23]. Wadhwa R., Paudel KR., Chin LH., Hon CM., Madheswaran T., Gupta G., Panneerselvam J., Lakshmi T., 2021. Anti-inflammatory and anticancer activities of Naringenin-loaded liquid crystalline nanoparticles in vitro. *J Food Biochem.* 45, 13572.