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Case Report

How Do Maternal Gestational Diabetes and Preterm Premature Rupture of Membrane (PROM) Contribute to Neonatal Jaundice and Sepsis? A Case Report and Narrative Review

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ABSTRACT

Gestational diabetes mellitus (GDM) and preterm premature rupture of membranes (PPROM) are significant obstetric conditions associated with heightened maternal and neonatal morbidity and mortality. Globally, complications of preterm birth, particularly due to PPROM, account for 35% of neonatal deaths. The coexistence of GDM and PPROM compounds risks, exacerbating adverse neonatal outcomes. This report about a 21 years old primigravida at 32-34 weeks of gestation with untreated GDM and PPROM for over 12 hours. The patient presented with decreased fetal movement and was managed conservatively with corticosteroids, antibiotics, and tocolytics. However, signs of fetal distress necessitated cesarean delivery, resulting in the birth of a male neonate 2370 g, APGAR 2/3, with asphyxia, respiratory distress, and hypoglycemia. Postnatal complications included jaundice and neonatal sepsis, which required 22 days of intensive NICU care with respiratory support, dextrose infusion, and antibiotics. The neonate showed gradual improvement. The coexistence of GDM and PPROM significantly increases the risk of adverse neonatal outcomes such as respiratory distress, hypoglycemia, jaundice, and sepsis. Early diagnosis, glycemic control, prophylactic antibiotics, and administration of corticosteroids are critical to improving maternal and neonatal outcomes. This case underscores the importance of a multidisciplinary approach and further research to refine best practices in managing GDM complicated by PPROM.

Keywords: Gestational; diabetes; premature; neonatal; sepsis; jaundice

1. INTRODUCTION

Gestational diabetes mellitus (GDM) and preterm premature rupture of membranes (PPROM) are significant obstetric conditions and major determinants of maternal and neonatal morbidity and mortality. Preterm birth complications account for approximately 35% of neonatal deaths, with a substantial proportion attributed to PPROM. (1) Uncontrolled GDM can also lead to adverse outcomes such as preterm labor, macrosomic fetuses, and neonatal

Hypoglycemia.⁽²⁾ Additionally, the coexistence of GDM and PPROM increases risks, posing challenges for both the mother and neonate. Analyzing global data indicates that neonatal mortality is high in cases of combined GDM and PPROM, underscoring the urgent need for effective management strategies.

The interaction between GDM and PPROM is believed to worsen neonatal sequelae through shared pathological mechanisms. Fetal hyperinsulinemia, induced by maternal hyperglycemia in GDM, may impair lung maturation and increase the risk of respiratory distress syndrome (RDS).(3) Furthermore, hyperglycemia predisposes newborns to hypoglycemia and weak immune responses, while PPROM heightens susceptibility to neonatal sepsis due to ascending infections.(4) This case report explores how the synergistic effects of GDM and PPROM significantly increase the risk of adverse neonatal outcomes. A narrative review of current literature suggests that GDM and PPROM are major contributors to neonatal morbidity. The relationship between GDM, PPROM, and adverse neonatal outcomes highlights the necessity of further research to refine best clinical practices.

Raising awareness about the importance of early identification and proactive management of GDM and PPROM is crucial to improving maternal and neonatal outcomes. Timely diagnosis, glycemic control, infection prevention, and evidence-based interventions such as corticosteroids to enhance fetal lung maturity and antibiotics to prevent infections or sepsis are essential. (5) This case emphasizes the need for multidisciplinary collaboration among obstetricians, neonatologists, and NICU teams. Since these conditions contribute to maternal and neonatal mortality, improving awareness, education, and access to healthcare can help reduce this burden.

2. CASE REPORT

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A 21-year-old female G0P0 (gravida 0 para 0) was referred from a regional hospital, complaining of clear fluid leaking from the birth canal for the past twelve hours before arriving at our hospital. Initially, the leakage was in a small amount, but over time, it increased. The patient denied mucus or bleeding, and contractions were mild and irregular. Since the onset of fluid leakage, she noted decreased fetal movement. She had a history of gestational diabetes mellitus in the first trimester, which was untreated. There was no history of

other diseases. Her mother had a previous history of diabetes mellitus.

Previous antenatal examinations had been conducted twice at a regional hospital by a midwife and an obstetrician-gynecologist. On physical examination, the patient was generally in good condition, with a blood pressure of 129/97 mmHg, heart rate of 88 beats per minute, body temperature of 36.6°C, weight of 88 kg, height of 155 cm, and upper arm circumference of 28 cm. General examination revealed no edema abnormalities. Obstetric examination found a fundal height of 26 cm, a fetal heart rate of 140 beats per minute, and a cephalic fetal position. There were no uterine contractions, and cervical dilation was 2 cm with ruptured membranes.

Random blood glucose was 192 mg/dL, and HbA1C was 8.1%, confirming the diagnosis of uncontrolled gestational diabetes mellitus. The patient was diagnosed with a G1P0A0 pregnancy at 32 to 34 weeks of gestation, with premature membrane rupture lasting more than 12 hours and gestational diabetes mellitus. She was conservatively managed with total bed rest, dexamethasone injection for fetal lung maturation, ceftriaxone injection for infection prevention, ketoprofen suppositories for pain control, and nifedipine for tocolysis.

While undergoing conservative management, signs of fetal distress emerged, including a maternal temperature of 37.8°C, a fetal heart rate of 168 bpm with inadequate contractions, a category II non-stress test (NST), and a random blood glucose level of 197 mg/dL. Due to the worsening condition, an emergency cesarean section was performed. The patient underwent a section under spinal cesarean anesthesia. transperitoneal profunda cesarean was performed via a 10 cm Pfannenstiel incision. A male infant was delivered 20 minutes later, weighing 2,370 g, measuring 46 cm in length, with an APGAR score of 2/3. The amniotic fluid was clear. Gentle traction was used to remove the placenta 10 minutes later, with an estimated blood loss of 200 cc.

The newborn's condition at birth was critical, presenting with asphyxia, cold extremities, respiratory distress, cyanosis, retractions, weak sucking and swallowing reflexes, and penile edema. In the neonatal intensive care unit (NICU), treatment for severe asphyxia was initiated. On the sixth day of treatment, neonatal jaundice appeared, and by the seventh day, the condition worsened due to signs of neonatal sepsis.

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However, after twenty-two days of intensive care including respiratory support, administration of dextrose fluids, and antibiotic therapy the infant's condition gradually improved. Jaundice and hypoglycemia were more controlled and continuously monitored, though further observation remained necessary.

3. DISCUSSION

This case underscores the complexity of managing GDM complicated by PPROM at 32-34 weeks of gestation. The coexistence of these conditions can lead to compounded complications affecting both maternal and neonatal outcomes. We suspect that the patient's poorly controlled GDM (HbA1c 8.1%) was a significant factor contributing to this case. Uncontrolled increases hyperglycemia during pregnancy predisposition to infections, inflammation, and poor wound healing. Premature rupture of membranes (≥12 hours) also increases the risk of ascending infections such as chorioamnionitis, even with the use of prophylactic antibiotics. Current guidelines recommend conservative management with corticosteroids to promote fetal lung maturity and tocolytics to delay delivery. However, due to worsening maternal and fetal conditions, cesarean delivery was performed. The postoperative course was uneventful, except for transient hyperglycemia, which was managed with insulin and a low sugar diet. This highlights the importance of glycemic control in improving maternal recovery and reducing complications. Combined with neonatal GDM, PPROM can lead to very poor neonatal outcomes. The newborn presented asphyxia APGAR 2/3, respiratory distress hypoglycemia and manifestations, features characteristic of maternal hyperglycemia and prematurity. The NICU team treated these complications with supportive care that included intensive monitoring, respiratory support, and dextrose fluids. Postnatal course was further complicated by the development of neonatal jaundice and sepsis. Bacteria may ascend from the maternal genital tract, and as such, neonatal sepsis is a recognized risk in prolonged cases of rupture of membranes. Timely intervention and proper antimicrobial coverage played a significant role in stabilizing the newborn, supported by clinical improvement after 22 days in the NICU.

3.1 Comparisons to Literature

This case aligns with previous studies emphasizing the increased maternal and neonatal morbidity associated with GDM and PPROM. Poorly controlled GDM and PPROM have been shown to elevate the risk of cesarean delivery and neonatal complications, such as hypoglycemia, RDS, neonatal jaundice, and sepsis. In this case, the administration of corticosteroids and antibiotics contributed to improved neonatal survival, particularly in the context of preterm birth.

3.2 Risk Factor

A study analyzing data from 18,174 pregnant women across 21 studies confirmed that multiple factors are strongly associated with PROM, including low body mass index (BMI), short interpregnancy interval (IPI), preterm birth, history of PROM, cesarean section, previous abortion, GDM, gestational hypertension, infections, abnormal fetal position, and increased abdominal pressure. (6) Notably, GDM and a history of abortion were significant risk factors for PPROM, with GDM increasing the odds of PPROM sixfold compared to non-GDM women, while a previous abortion history increased the risk fivefold. (7)

Advanced maternal age, a pre-conceptional BMI over 25, and a history of preterm birth are all factors linked to an increased risk of preterm delivery in women with GDM. In line with these findings, a study also confirmed that mothers with GDM are more likely to have large-for-gestational-age (LGA) preterm infants, often due to insulin resistance. Managing weight and controlling GDM can help mitigate these risks. Additionally, while newborn sex, birth weight, and Apgar scores showed no significant differences between groups, male infants were more prevalent in the GDM group. Importantly, GDM was associated with a higher risk of RDS in preterm infants, likely due to impaired lung development. Infants of diabetic mothers are also at a higher risk of hypoglycemia due to the effects of maternal hyperglycemia on fetal insulin production.⁽⁸⁾

3.3 Pregnancy Outcome

Another study of 1,076 advanced primiparous women, divided into GDM (434) and non-GDM (642) groups, found significant differences in prepregnancy BMI, gestational age, and gestational weight gain (GWG). The GDM group had lower gestational age, lower GWG, and a higher proportion of inadequate

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GWG compared to the non-GDM group. Additionally, the GDM group had higher rates of macrosomia, polyhydramnios, low birth weight, preterm birth, and NICU admissions.⁽⁹⁾ Preterm birth can result in significant health challenges for newborns, including respiratory complications, cardiovascular issues, and long-term conditions such as cerebral palsy. As the prevalence of GDM continues to rise, largely due to obesity and sedentary lifestyles, affected women face an elevated risk of perinatal complications.

Neonates born to mothers with GDM also have an increased risk of hyperbilirubinemia, which can be attributed to immature liver enzyme function leading to impaired bilirubin conjugation and increased hemolysis. A birth weight over 4,000 g has a protective effect, whereas normal birth weight is associated with an increased risk. Hyperbilirubinemia is more common in full-term infants than in preterm infants, as chronic maternal hyperglycemia results in fetal hyperinsulinemia and polycythemia, leading to elevated bilirubin levels. This risk is further exacerbated by the presence of sepsis, which disrupts bilirubin metabolism. Early meconium clearance has been suggested as a strategy to reduce hyperbilirubinemia since bilirubin reabsorption in the gut is minimized. Hypoglycemia remains an independent risk factor associated with both maternal diabetes status and neonatal health.(10) Among 640 observed preterm infants, 33.9% were born to mothers with GDM, while 66.1% were born to mothers without diabetes. Infants from GDM mothers had significantly higher rates of RDS and sepsis. GDM is a known risk factor for RDS, fetal hyperglycemia, and hyperinsulinemia, which, in turn, disrupt cortisol and surfactant production, particularly in neonates born between 32 and 34 weeks of gestation. These infants are also at higher risk for hypoglycemia, sepsis, necrotizing enterocolitis (NEC), and bronchopulmonary dysplasia (BPD). Maternal hyperglycemia in GDM impairs neonatal immune responses, increasing the likelihood of infection. Additionally, fetal hypoglycemia in very low birth weight infants (VLBWIs) arises from the abrupt interruption of glucose supply during delivery, leading to a higher risk of brain injury.(11)

3.4 Management of GDM Pregnancies

Studies on women with GDM show that those requiring insulin treatment have significantly higher odds of cesarean section, preterm delivery, low Apgar scores, macrosomia, and LGA infants. Most guidelines recommend that pregnant women with GDM receive counseling on diet and exercise, with medical therapy started if lifestyle changes fail to maintain normal blood sugar levels. Insulin, metformin, or glyburide can be used as first line treatments in the second and third trimesters. Metformin is preferred over glyburide. Insulin is recommended for diagnosis before 20 weeks, the need for medication after 30 weeks, fasting glucose over 110 mg/dL, post-meal glucose over 140 mg/dL, or weight gain over 12 kg during pregnancy. (12) Insulintreated women also had an increased likelihood of requiring neonatal intensive care, developing RDS, and experiencing neonatal jaundice. Further analysis of insulin use revealed that women requiring insulin due to inadequate glycemic control had higher odds of cesarean section and preterm delivery, suggesting that elevated maternal glucose levels contribute to poorer pregnancy outcomes.(7)

4. CONCLUSION

Managing GDM complicated by PPROM requires early recognition, individualized treatment, and a multidisciplinary approach. Strict glycemic control, antenatal corticosteroids (24-34 weeks), and antibiotic Hospitalization prophylaxis essential. are recommended for membrane rupture >12 hours to enable fetal monitoring and timely intervention. Delivery should be based on gestational age, fetal wellbeing, and signs of infection, with urgent intervention for fetal distress or chorioamnionitis. Postnatal care includes NICU monitoring, respiratory support if needed, and early management of hypoglycemia, jaundice, and sepsis. Long-term follow-up is crucial, and further research is needed to refine management protocols and optimize outcomes.

Ethical Approval

Not required.

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Competing Interests

All the authors declare that there are no conflicts of interest.



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Underlying Data

Derived data supporting the findings of this study are available from the corresponding author on request.

REFERENCES

- Zahroh RI, Hazfiarini A, Eddy KE, Vogel JP, Tunçalp Özge, Minckas N, et al. Correction: Factors influencing appropriate use of interventions for management of women experiencing preterm birth: A mixed-methods systematic review and narrative synthesis. PLOS Medicine. 2022;19(9):e1004105. http://dx.doi.org/10.1371/journal.pmed.1004105
- Buchanan TA, Xiang AH, Page KA. Gestational diabetes mellitus: risks and management during and after pregnancy. Nature Reviews Endocrinology. 2012;8(11):639–649. http://dx.doi.org/10.1038/nrendo.2012.96
- 3. Crowther CA, Middleton PF, Voysey M, Askie L, Zhang S, Martlow TK, et al. Effects of repeat prenatal corticosteroids given to women at risk of preterm birth: An individual participant data meta-analysis. Myers JE, editor. PLOS Medicine. 2019;16(4):e1002771. http://dx.doi.org/10.1371/journal.pmed.1002771
- Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The Lancet. 2008;371(9606):75–84. http://dx.doi.org/10.1016/s0140-6736(08)60074-4
- 5. Sweeting A, Wong J, Murphy HR, Ross GP. A Clinical Update on Gestational Diabetes Mellitus. Endocrine Reviews. 2022;43(5):763–793. http://dx.doi.org/10.1210/endrev/bnac003

- Lin D, Hu B, Xiu Y, Ji R, Zeng H, Chen H, et al. Risk factors for premature rupture of membranes in pregnant women: a systematic review and meta-analysis. BMJ Open. 2024;14(3):e077727. http://dx.doi.org/10.1136/bmjopen-2023-077727
- Argaw M, Mesfin Y, Geze S, Nuriye K, Tefera B, Embiale A, et al. Preterm Premature Ruptures of Membrane and Factors Associated among Pregnant Women Admitted in Wolkite Comprehensive Specialized Hospital, Gurage Zone, Southern Ethiopia. Baig AA, editor. Infectious Diseases in Obstetrics and Gynecology. 2021;2021:1–6. http://dx.doi.org/10.1155/2021/6598944
- 8. Dewangan M, Mithlesh SD. Retrospective analysis of the risk factors for preterm delivery in gestational diabetes mellitus and their adverse neonatal outcomes [Internet]. Obstetrics and Gynaecology Forum. 2024;34(3s):3116-3119.
 - https://www.obstetricsandgynaecologyforum.com/index .php/ogf/article/view/925 (Accessed on 25 Jan 2025)
- Yang H, Xiao C, Tu J. The effect of gestational diabetes mellitus on pregnancy outcomes in advanced primiparous women: A retrospective study. Medicine. 2024;103(13):e37570. http://dx.doi.org/10.1097/md.0000000000037570
- 10. Biade D, Wibowo T, Wandita S, Haksari EL, Julia M. Faktor Risiko Hiperbilirubinemia pada Bayi Lahir dari Ibu Diabetes Melitus. Sari Pediatri. 2016;18(1):6. http://dx.doi.org/10.14238/sp18.1.2016.6-11
- 11. Zhang CH, Zhang PL. Adverse perinatal outcomes complicated with gestational diabetes mellitus in preterm mothers and preterm infants. Experimental and Therapeutic Medicine. 2023;26(3). http://dx.doi.org/10.3892/etm.2023.12124
- 12. Oskovi-Kaplan ZA, Ozgu-Erdinc AS. Management of Gestational Diabetes Mellitus. Diabetes: from Research to Clinical Practice. 2020;257–272. http://dx.doi.org/10.1007/5584_2020_552