Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2023**; 50(5): 95
https://doi.org/10.31083/j.ceog5005095

Editorial

An Introduction to the Special Issue on Premature Rupture of Membranes in Pregnancy Including Its Etiology, Management, and Maternal and Neonatal Outcomes

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Academic Editor: Michael H. Dahan
Submitted: 5 January 2023 Accepted: 13 January 2023 Published: 6 May 2023

Premature rupture of membranes (PROM) is defined as the rupture of the chorioamniotic membranes prior to the onset of labor [1]. The occurrence of PROM ranges between 5–15% of all pregnancies depending on the demographic characteristics of the population studied [2]. The diagnosis is commonly confirmed by the visualization of amniotic fluid passing from the cervical canal and pooling in the vagina noted at speculum examination. There are several additional tests for amniotic proteins which have high sensitivity and specificity for diagnosing rupture of membranes such as the detection of placental alpha microglobulin-1 (PAMG-1) in the vaginal fluid in a sample obtained from the vaginal sidewall [3]. Approximately 8% of term pregnancies are complicated by PROM and subsequently, the early onset of spontaneous labor followed by delivery process commonly follows this complication [4]. The most substantial adverse outcome of the term PROM is intrauterine infection which increases with the length of time from the membrane rupture to delivery [5].

When the fetal membrane rupture occurs prior to labor and before 37 weeks of pregnancy, it is referred to as preterm PROM (PPROM). This obstetric condition complicates 3–5% of pregnancies and is the most identifiable cause of preterm birth, with one-third of preterm deliveries being the consequence of PPROM [6]. Obstetric outcomes of PPROM are associated with brief latency from membrane rupture to labor, complications secondary to infection, and adverse perinatal outcomes related to preterm birth [7]. The frequencies of neonatal morbidity and mortality are greater in cases complicated with PPROM than all the other causes of preterm delivery [8]. It is significant that surviving neonates generally suffer from long-term results, including numerous physiological effects (cardiovascular disorders, chronic lung disease, hearing or visual impairment), behavioral disorders, and neurodevelopmental delay [9]. These adverse outcomes represent a substantial burden for the healthcare system, families, and society [7]. Therefore, it is crucial to ascertain the mechanisms involved in PPROM and develop novel treatments and strategies to prevent or manage this entity.

Previable PPROM, which is the spontaneous rupture of membranes near or before the fetal viability limit at $24^{0/7}$ weeks of gestation, complicates less than 1% of all pregnancies with a reported incidence of 3.7/1000 pregnancies. This represents a devastating pregnancy complication with high maternal and fetal adverse outcomes [10]. Neonates are at high risk of perinatal morbidity and mortality, which is primarily because of extreme prematurity (bronchopulmonary dysplasia, necrotizing enterocolitis, cerebral damage, retinopathy, and cognitive impairment). The risks associated with the presence of prolonged oligohydramnios and expectant management of PPROM include limb deformities, pulmonary hypoplasia, umbilical cord compression, intraventricular hemorrhage, umbilical cord prolapse, perinatal infection, and in utero fetal demise. Maternal risks include retained placenta, placental abruption, chorioamnionitis, postpartum hemorrhage, and sepsis, which are mainly related to the prolonged latency period [11]. The challenge in cases experiencing previable PPROM is to maximize the latency period to delivery while minimizing adverse maternal and neonatal outcomes. Mothers are offered termination of pregnancy, known as active management, either immediately or in cases of oligohydramnios or chorioamnionitis, or expectant management with frequent evaluation for maternal and fetal well-being [10]. Recent case series have demonstrated that because of advances in maternal and neonatal intensive care, including the use of antenatal steroids, antibiotics, postnatal surfactant, probiotic, and nitric oxide administrations, along with optimizing respiratory support, outcomes for neonates delivered following PPROM at previable weeks or at the threshold of viability are superior to those previously reported [10,11]. However, there are limited and conflicting data concerning fetal and neonatal survival, short- and long-term outcomes of surviving neonates, and maternal complications making it difficult to correctly counsel pregnant women with previable PPROM. Moreover, there is no agreement among obstetricians regarding the management of this uncommon pregnancy complication. Case series have reported broadly varying maternal complication and neonatal survival rates. Thus, it is challenging to counsel the pregnant woman and her partner regarding maternal and neonatal prognoses and to elucidate the precise risk of expectant management [11].

Membrane rupture is noted to occur for a number of reasons. Although rupture of the membranes at term might arise from a physiologic weakening combined with shearing forces created by labor contractions, PPROM probably arises from a broad range of pathologic mechanisms that act singly or in combination [4]. PROM is considered an abnormality of fetal membranes. Membrane rupture may occur for a variety of reasons that induce accelerated membrane weakening through an imbalance between the pro-inflammatory and anti-inflammatory cytokine production. This imbalance results in the activation of different humoral and cellular immunologic components, including an increase in the production of prostaglandins and local cytokines, and the activation of matrix-degrading proteases that lyse collagen [12]. Histologic chorioamnionitis (HCA) is present in approximately 50–60% of pregnancies complicated by PPROM [13,14]. Prompt and accurate HCA diagnosis is crucial but placental pathology can only be evaluated after delivery. The inflammatory response may also be demonstrated in the maternal cervicovaginal fluid, fetal amniotic fluid, and fetal and maternal serum analyses in the presence of PPROM [15]. Thus, a less invasive and more straightforward procedure for examining these cytokines could be beneficial for the prediction of rupture of the membrane.

In conclusion, an accurate and timely diagnosis, a precise evaluation of gestational age, and awareness of the maternal, antenatal, and perinatal risks are crucial to relevant assessment, counseling, managing, and care of pregnancies complicated by PROM. An assessment of future findings might induce the dynamic evolution and development of various biomarkers to predict and follow up the intraamniotic inflammation in patients with PROM. As a Guest Editor of the Special Issue "Etiology, Management, and Maternal and Neonatal Outcomes of Pregnancies Complicated by Premature Rupture of Membranes", I am soliciting all experts in this field to contribute their current investigation results to this special issue that will potentially improve our knowledge regarding PROM.

Author Contributions

SCO designed and wrote the manuscript. SCO contributed to editorial changes in the manuscript. SCO read and approved the final manuscript.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The author declares no conflict of interest. Süleyman Cemil Oğlak is serving as one of the Guest editors of this journal. We declare that Süleyman Cemil Oğlak had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Michael H. Dahan.

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