

PPROM between 16 and 23 weeks' of pregnancy: when your waters break very early

A UK wide study of 364 women with early Preterm Prelabour Rupture of Membranes (PPROM)

Background

Babies grow and develop in a protective sac of fluid inside the mother's womb. Usually these "waters" break during labour, after 37 weeks of pregnancy, when they are no longer necessary. In a rare, but serious situation, these waters can break too early in pregnancy and before labour occurs. This condition is called Preterm Prelabour Rupture of the Membranes (PPROM).

This study focuses on when PPRM occurs exceptionally early in pregnancy, before 23 weeks. The baby is then at risk of infection, injury or dying. Additionally, there is a high chance of labour starting when the baby is too immature to survive, or at a stage of pregnancy where there is risk of long-term disability for survivors. Some mothers can also develop life-threatening complications, such as sepsis. For all these reasons, termination of the pregnancy for medical reasons (TFMR) is offered. However, some babies and mums have healthy outcomes.

Currently in the UK there are no national guidelines to tell doctors how best to care for women in this situation under 24 weeks' of pregnancy. Additionally, at present there is no accurate data to help guide the decision to continue with the pregnancy. This is because very early PPRM is such a rare condition that a single hospital may not even see a single case in a year.

The patient advocacy and support group, Little Heartbeats, contacted researchers at the University of Liverpool to try to improve information for doctors, women and families at the time of PPRM. They identified that some women were counselled with a focus on maternal and fetal risk, without providing data on babies with healthy outcomes. When several women and families reported their babies were born alive without any serious disability, despite being told there was no chance of a healthy outcome, it sparked distrust in the medical profession, and highlighted the urgent need for good quality and balanced data to inform care. Research teams from University of Liverpool and UKOSS (UK Obstetric Surveillance System) worked together to perform a national study of all women with PPRM from 16 weeks and 0 days to 22 weeks and 6 days of pregnancy over 18 months in 2019-2021.

The COVID-19 pandemic was declared six months after the study started collecting data. The study team collected data for six months more than initially planned and an extra analysis was performed about whether the pandemic affected the pregnancy outcomes.

Aims of our research

We wanted to be able to tell women, their families and doctors, at the time of PPROM, what the chances were of:

- The woman giving birth in the week after PPROM
- The baby being born alive
- The baby leaving hospital alive
- The baby leaving hospital alive without severe illness
- The mother developing sepsis
- The mother being admitted to intensive care
- The mother dying

In addition, we wanted to know survival rates of babies from twin pregnancies and how long surviving babies stayed in hospital. We also wanted to know whether there were differences in mother or baby outcomes in the periods September 2019-February 2020 (pre-pandemic) and March 2020-February 2021 (during the pandemic).

Progress of our work

Over the 18 months September 2019-February 2021 364 women were included in the study. 326 women had one baby and 38 women had twins or triplets.

Overall, 32% of women had a termination for medical reasons (TFMR). We have no information about why these women chose this course of action. To accurately report our data in the most useful way for future women and families facing PPROM under 23 weeks of pregnancy we have generated three figures for the outcomes for the baby:

- 1) We reported just the outcomes for the women that chose to continue with pregnancy. Women who had a TFMR were excluded.
- 2) We give the worst-case scenario. This assumes that all the women who had TFMR had clinical signs that would have led to a definite bad outcome for the baby e.g., they had signs of infection/sepsis.
- 3) We give the best-case scenario. This assumes that all the women who had TFMR would have had a baby that survived if they had continued with the pregnancy, despite medical concern.

The true value of these estimates of outcome is likely to lie somewhere between 2 and 3.

In this study when we say a baby has “severe illness” it meant that the baby needed oxygen after birth at 36 weeks (i.e. when the mother *would* have been 36 weeks in pregnancy) and/or a baby had a significant bleed on the brain, which in some babies leads to cerebral palsy. This definition of severe illness was used because previous research has shown that babies with these complications have higher rates of disability when they are toddlers. However, it is important to note that long term

disability is very hard to predict in babies, and in fact most babies (more than half) with severe illness do not have disabilities when they grow up.

Results

- We had fewer pregnancies reported per month during the period of the COVID-19 pandemic than before the COVID-19 pandemic.
 - We did not find a significant difference in mother or baby outcomes according to whether the PPROM occurred before or during the pandemic.
- Amongst women who chose to continue their pregnancy 39% gave birth in the week after PPROM
 - This means that a lot of babies were born too early to survive or very premature.
- Amongst women who chose to continue their pregnancy 44% had a baby that was born alive.
 - If we include the women who had TFMR within the results the worst-case scenario is that 30% of babies may be born alive, and the best-case scenario is 62%.
- The chance of the baby being born alive was better when the waters broke slightly later in pregnancy.
 - When the waters broke at 16-17 weeks of pregnancy 33% of women who chose to continue with pregnancy had a baby that was born alive.
 - The worst-case scenario for women whose waters broke at 16-17 weeks is 17% and the best-case is 65%. This range is so wide because 45% of women with PPROM at this stage of pregnancy had TFMR.
 - When the waters broke in the 22nd week of pregnancy 67% of women had a baby born alive.
 - The worst-case scenario for all women with PPROM at 22 weeks was 54% and the best-case scenario was 73%.
- The chance of the baby leaving hospital alive was 26% amongst women who chose to continue with pregnancy.
 - If we include the women who had TFMR; the worst-case scenario is 17% and the best case is 53% of babies leave hospital alive.
 - The chance of the baby leaving hospital alive was better if the pregnancy was more advanced when the baby was born.

- The chance of the baby leaving hospital alive without severe illness was 18% amongst women who chose to continue with pregnancy.
 - If we include the women who had TFMR; the worst-case scenario is 12% and the best-case scenario is 48% of women, who may have left the hospital with a surviving baby, without serious illness.
 - The chance of the baby leaving hospital alive without severe illness was better if the pregnancy was more advanced when the baby was born.
- Of the babies born alive; 39% left hospital without severe illness, 16% left hospital with severe illness, 29% died, and 16% did not have follow up data.
- There was a lot of variation in how long surviving babies stayed in hospital. The average length of hospital stay was 2 months, but 1 in 4 babies stayed in hospital less than 17 days and 1 in 4 babies stayed more than 3 months.
- Twins had similar outcomes to the pregnancies with just one baby, especially if each twin had its own placenta and own sac (these are called dichorionic diamniotic pregnancies, DCDA).
- The chance of sepsis was 14% in women overall. This was 12% in women with one baby and 29% in women with twins or triplets.
- The chance of admission to the intensive care was 1.1% in mothers
- There were two women with early PPRM in this study who died, both due to sepsis. This gives a chance of maternal death of 0.5%.

Implications for future prevention, treatment or cure and future work

The key outcomes are now being used to develop resources for women, families and doctors to use at the time of PPRM. These will help all those involved to make informed decisions about the pregnancy after PPRM.

These findings highlight the complexity of pregnancies with very early PPRM. We now have figures showing clearly that some babies and mothers have very good outcomes, but also some babies and mothers get very ill or even lose their lives to this condition.

In order to improve outcomes for future women with very early PPRM the research team suggests that two strategies are needed, in parallel. One strategy is to work out how best to organise care for women after PPRM with current available treatments, and ensure that appropriate support, counselling and education are offered. The other strategy is to develop new interventions. Now that we know the baseline outcomes for mums and babies these studies can be planned.

This study shows that there is a lot of uncertainty about outcomes of pregnancies with PPRM and understanding the optimal time to deliver the baby, balancing both mother's and baby's health. The patient support and advocacy group, Little Heartbeats, has worked closely with the study team

throughout this project. Little Heartbeats highlight that behind the uncertainty about physical health after very early PPROM, many women and their partners will be struggling with their psychological health. Future work should also focus on how best to psychologically support families through these difficult pregnancies.