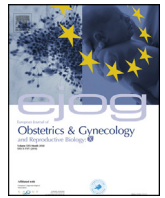




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## Prediction of recurrent preterm delivery in asymptomatic women- an anxiety reducing measure?



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### ABSTRACT

**Objectives:** The QUIPP application is used to predict the risk of recurrent preterm birth (PTB) in asymptomatic high risk women with a previous PTB. Our study aims to evaluate the impact of the use of the QUIPP app on maternal anxiety levels.

**Study design:** A retrospective cohort study on asymptomatic pregnant women attending the Prevention of Preterm Birth Clinic in a busy tertiary unit. Women included in the study had a history of previous PTB. The study assessment occurred at approximately 4 weeks prior to the gestation of the earliest previous PTB and included measurement of cervical length and vaginal fetal fibronectin. Data was inputted into the QUIPP application, which in turn estimated risk of preterm delivery at specific intervals. Measured outcomes were gestation at delivery, time from risk assessment to delivery, infant birth weight, NICU admission and length of stay. In addition, maternal anxiety levels were retrospectively assessed using a questionnaire with a Likert scale.

**Results:** Seventy six women were included in the study. All women were asymptomatic for preterm labour at assessment. The mean gestation at the time of risk assessment was 27 weeks, the mean time from risk assessment to delivery was 72 days. Average gestation at time of delivery was 37 weeks (range 22–42 weeks). The preterm birth rate was 29% (n = 22). Seventy seven percent of women who delivered <37 weeks, and 80% who delivered <34 weeks were given QUIPP scores predicting a  $\geq 5\%$  chance of PTB within four weeks of their actual delivery date. Sixteen percent of infants were admitted to NICU (n = 12) with a mean length of stay of 21 days. All infants went home well with their parents.

Eighty four percent of respondents to our questionnaire reported feeling anxious about their pregnancy prior to attending the clinic. After receiving a QUIPP score 90% said they felt reassured and 79% reported that they felt less anxious.

**Conclusion:** In asymptomatic women, the use of the QUIPP app helps to predict, prevent, and optimise PTB. This surveillance has a beneficial role for maternal mental well-being in that it reduces anxiety at a key time during a pregnancy.

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### 1. Introduction

More than one in ten babies worldwide are born prematurely [1]. Preterm birth (PTB), defined as birth before 37 weeks gestation, is a major cause of infant morbidity and mortality, as well as maternal mental health morbidity [2]. In Ireland the rate of PTB for singleton pregnancies is 4.6% [3]. The risk of recurrence of PTB is reported to be between 15% and 30% [4–6].

Anxiety is prevalent in pregnancy, with between 15 and 23% of pregnant women reporting anxiety symptoms [7]. The prevalence of anxiety in subsequent pregnancies, amongst mothers who have had a previous PTB, is understandably higher at approximately 38% [8].

This is problematic, as anxiety increases the risk of PTB [9–11]. One systematic review and meta-analysis found that maternal anxiety during pregnancy was associated with a significantly increased risk of PTB with a pooled RR of 1.50 (95% CI = 1.33–1.70) [9].

The QUIPP application was developed to accurately identify women at high risk for preterm labour [12]. The app uses an algorithm that combines maternal history (number of fetuses, history of cervical surgery and previous PTB, preterm prelabour rupture of membranes or late miscarriage) and quantitative measurements of fetal fibronectin (fFN) and cervical length (CL) to predict the percentage risk of PTB at various time intervals. It is designed for use in two clinical settings:

- 1) Asymptomatic women at risk for PTB attending surveillance clinics.
- 2) Women with symptoms suggestive preterm labour.

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Prediction of PTB allows for targeted intervention for high risk women, such as cervical cerclage, antenatal corticosteroids, magnesium sulphate and tocolysis, that may prevent or optimise preterm delivery [13]. In addition, low predictive scores may provide reassurance for women and reduce maternal anxiety about the risk of recurrent PTB in subsequent pregnancies [13].

## 2. Materials and methods

The purpose of our study was to assess the impact of risk assessment using the QUIPP application on maternal mental health well-being and anxiety levels during pregnancy in women at risk of recurrent PTB.

This was a retrospective cohort study on asymptomatic pregnant women attending the Prevention of Preterm Birth Clinic in a busy tertiary unit over a two year period (December 2015 to December 2017). Women included in the study had a history of at least one previous preterm delivery (<37 weeks gestation) or late miscarriage (between 16<sup>+0</sup> to 23<sup>+6</sup> weeks gestation). Women were seen in the clinic for a first visit shortly after their booking visit. The study assessment included the woman's history, and quantitative measurement of CL and vaginal fFN. This assessment occurred at approximately four weeks prior to gestation of the earliest previous preterm delivery. For example, if a woman had a history of previous delivery at 34 weeks gestation, the assessment was carried out at approximately 30 weeks gestation in her subsequent pregnancy.

This data was inputted into the QUIPP application, which in turn estimated a percentage risk of preterm delivery at specific intervals. The measured outcomes were gestation at delivery, time from risk assessment to delivery, infant birth weight, NICU admission, and length of stay in NICU.

In addition to this, maternal anxiety levels were assessed retrospectively using a survey with a Likert scale. No validated tool exists to retrospectively assess anxiety. Therefore we decided to create our own questionnaire, as this was a retrospective assessment of anxiety. We attempted to contact all women by telephone to ask if they would be willing to participate in the survey. Those women who were contacted were asked to provide their email address. We sent a Survey Monkey link to a Questionnaire to these women by email, followed by a reminder email two weeks later to improve response rate. This was an anonymous survey and therefore a blinded evaluation, thus the investigators did not know the neonatal outcomes corresponding to the respondents.

## 3. Results

Seventy six women were included in the study (n = 76), all were asymptomatic for preterm labour at the time of assessment.

Maternal demographics are presented in Table 1. The mean age was 33 years (range 18–45 years), 76% were Irish, 11% smoked during their pregnancy and 14% had had previous cervical surgery.

Perinatal outcomes are presented in Table 2. The mean gestation at risk assessment was 27 weeks (range 18–32 weeks). The mean time from risk assessment to delivery was 72 days. Average gestation at time of delivery was 37 weeks (range 22–42 weeks). 22 women (29%) delivered between 24<sup>+0</sup> and 36<sup>+6</sup> weeks. Of these, the majority (55%, n = 12) of preterm deliveries occurred after 34 weeks gestation. Nine births (41%) occurred between 28 and 34 weeks, and one birth occurred before 28 weeks. One baby was born at a pre-viable gestation (22 weeks) and unfortunately did not survive. This woman had a history of a previous late miscarriage at 21 weeks. Her risk assessment was carried out at 18 weeks after which she had a cerclage placed for a short cervix (11 mm). fFN was 192 at the time of risk assessment and the QUIPP

**Table 1**  
Maternal demographics.

Maternal demographics n = 76	
<b>Age in years, mean (range)</b>	33 (18–45)
<b>Ethnicity, n (%)</b>	
White Irish	58 (76.32)
White non-Irish	9 (11.84)
Non- White	9 (11.84)
Parity, mean (range)	2 (1–7)
<b>Smoking status, n (%)</b>	
Never smoker	48 (63.16)
Ex- smoker	19 (25)
Smoked during pregnancy	9 (11.84)
<b>Cervical surgery, n (%)</b>	11 (14.4)
<b>History of previous PTB</b>	
2nd trimester miscarriage 16+0-23+6, n (%)	4 (5.26)
PTB 24+0-27+6, n (%)	19 (25)
PTB 28+0-33+6, n (%)	40 (52.63)
PTB 34+0-36+6, n (%)	13 (17.11)

**Table 2**  
Perinatal outcomes.

Gestation in weeks at risk assessment, mean (range)	27 (18–32)
Time (in days) from risk assessment to delivery, mean (SD)	72 (25)
Gestation in weeks at delivery, mean (range)	37 (22–42)
Preterm Delivery 24+0-36+6 weeks, n (%)	22 (29)
24+0-27+6 weeks	1 (4.55)
28+0-33+6 weeks	9 (40.91)
34+0-36+6 weeks	12 (54.54)
Birthweight (in grammes), mean (range)	2948 (440–4220)
Mode of delivery	
Vaginal, n (%)	62 (81.58)
Caesarean Section, n (%)	14 (18.42)
Elective CS, n (%)	12 (85.71)
Emergency CS, n (%)	2 (14.29)
Onset of Labour	
Induction of labour, n (%)	18 (29.03)
Spontaneous labour, n (%)	44 (70.97)
NICU admission, n (%)	12 (16%)
Length of stay in days in NICU, mean (range)	21 (3–49)

application predicted an 11% chance of PTB within four weeks of assessment and a 49% chance of PTB before 30 weeks.

The QUIPP scores received by women in our study ranged from 0% to 84.4%. Seventy seven percent (17/22) of those women who delivered <37 weeks, and 80% (8/10) of those who delivered <34 weeks were given QUIPP scores predicting a ≥5% chance of PTB within four weeks of their actual delivery date.

Eighty two percent of women (n = 62) had vaginal deliveries and 18% were delivered by Caesarean section (n = 14). The majority (86%) of Caesarean sections were elective repeat Caesarean sections, 14% were emergency Caesarean sections (n = 2). Of those women who delivered vaginally, 29% (n = 18) were induced, the remaining 71% (n = 44) had a spontaneous onset of labour.

Seventy three percent of preterm deliveries were optimised with steroids and 80% (4/5) of those who delivered at <32 weeks (n = 5) received magnesium sulphate. Sixteen percent of infants were admitted to NICU (n = 12) with a mean length of stay of 21 days (range 3–49 days). All infants went home well with their parents.

## 4. Survey results

Sixty patients (79%) were successfully contacted by phone, and 59 patients (78%) agreed to complete the survey and provided their email addresses. Forty four patients (57%) responded to our survey. The questions and responses to the questionnaire are presented in Table 3.

84% of women reported that they felt anxious about their pregnancy prior to attending the Prevention of Preterm Birth Clinic. 80% said they felt reassured attending the PTB clinic, 50% of these stated that they felt very reassured. 93% said that they found the screening test (measurement of ffN and CL) to be an acceptable test. After attending the clinic and receiving a QUIPP score 90% said they felt reassured and 79% reported that they felt less anxious.

## 5. Comment

In asymptomatic women, the use of the QUIPP app screening tool helps to predict, prevent, and optimise preterm delivery. In addition, this surveillance seems to have a beneficial impact on maternal mental wellbeing in that it reduces anxiety at a key time during a pregnancy.

The QUIPP app generates a percentage score for the risk of preterm birth at various time intervals from the date of testing (within 1 week, 2 weeks, 4 weeks, <30 weeks, <34 weeks and <37 weeks). In our study the scores ranged from 0% to 84.4%. We used a score >5% when presenting our results as this is the suggested threshold for intervention in a study performed by the developers of the QUIPP app in symptomatic women [14].

This is the first study that we are aware of that assesses anxiety reduction, following risk assessment using the QUIPP app, in this high risk group for recurrent PTB. Thus, this is a novel area of study. However, our study has some limitations in that it involved a retrospective assessment of anxiety, does not use a validated tool to measure anxiety, and the survey results were blinded.

Of course, a retrospective assessment of anxiety is not as informative as a prospective one and there is an inherent bias it involves asking women to recall how anxious she felt in the past, rather than assessing anxiety symptoms in real time. The mother's recollection of her past anxiety will almost certainly

be influenced by the perinatal outcomes and the health of her baby at the time she completed the survey. However, we decided to assess anxiety levels after initial data collection of neonatal outcomes, thus we had no choice but to retrospectively assess anxiety. This was an anonymous survey and thus it was not possible to match the survey responses to the perinatal outcomes. Validated anxiety tools, such as the Hospital Anxiety and Depression Scale- Anxiety subscale (HADS-A) [15], are not suitable for retrospectively assessing anxiety, thus we devised our own questionnaire.

We made several attempts to contact all of the patients by telephone. Some of the telephone numbers listed for patients were incorrect or no longer in service, thus it was not possible to contact every patient. Only one of the women we contacted by phone did not provide her email address, and this was because she did not have an email address and due to language difficulties she did not wish to complete the survey over the phone. Forty four women responded to our survey, which gave an overall response rate of 57%. However, only 59 women (78%) actually received the survey. Thus the response rate of those who received the survey was 75% (44/59) which is higher than the 60% response rate which should be the target for researchers [16].

The survey was a blinded evaluation, and responses were anonymous, so it was not possible to see whether those women who reported feeling reassured and less anxious had low risk QUIPP scores or what the neonatal outcomes were for these women. The reported reduction in anxiety is likely not solely to do with reassuring QUIPP scores, but also attendance at a specialised Prevention of Preterm Birth Clinic, where the women had increased surveillance and were seen by a senior obstetrician at each visit.

This was a preliminary study. We plan to expand this work by prospectively assessing pregnancy related anxiety in women prior

**Table 3**

Survey questions and responses.

Q1. I felt anxious about my pregnancy prior to attending the pre term birth clinic
Strongly agree 50.00% (22)
Agree 34.09% (15)
Neither agree nor disagree 11.36% (5)
Disagree 2.27% (1)
Strongly disagree 2.27% (1)
Q2. I felt reassured attending the pre term birth clinic
Strongly agree 50.00% (22)
Agree 29.55% (13)
Neither agree nor disagree 13.64% (6)
Disagree 4.55% (2)
Strongly disagree 27% (1)
Q3. I found the screening test (measurement of cervical length and fetal fibronectin) to be an acceptable test.
Strongly agree 59.09% (26)
Agree 34.09% (15)
Neither agree nor disagree 2.27% (1)
Disagree 4.55% (2)
Strongly disagree 0% (0)
Q4. Was it reassuring to be given a percentage risk of pre term labour after attending the pre term birth clinic?
Extremely reassuring 43.18% (19)
Very reassuring 36.36% (16)
Somewhat reassuring 11.36% (5)
Not so reassuring 9.09% (4)
Not at all reassuring 0% (0)
Q5. Did you feel more or less anxious after receiving a percentage risk score of pre term labour?
Much more anxious 0% (0)
Somewhat more anxious 9.09% (4)
No change 11.36% (5)
Somewhat less anxious 43.18% (19)
Much less anxious 36.36% (16)

to and after receiving a QUIPP score in our clinic using a validated anxiety tool. Our hope would be that by using the QUIPP app, we could not only predict, prevent and optimise PTB, but also reassure women with low risk scores, reduce maternal anxiety and in turn reduce the risk of recurrent PTB.

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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