How safely can post-term pregnancies with uncertain gestational age be followed up using amniotic fluid index measurements?

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Objective. To review whether 2 weeks' follow-up is safe for women at 42 weeks with an uncertain gestational age (GA) and amniotic fluid index (AFI) of \geq 10 cm, as well as reassuring cardiotocography (CTG).

Methods. A retrospective descriptive study of women with an uncertain GA of 42 weeks was done at Tygerberg Hospital. The women had weekly CTG and AFI determinations. Induction of labour followed non-reassuring CTG or an AFI of <5.

Results. A total of 135 women were studied. The time interval between first evaluation at uncertain 42 weeks and delivery ranged between 0 and 46 days (median 10 days). Of the women, 104 had normal vaginal deliveries and 31 (23.0%) caesarean sections. Eleven women (8.1%) with an AFI \geq 10 had CS for fetal distress within 2 weeks of the visit at 42 weeks. No neonatal morbidity or mortality was noted.

Conclusion. Weekly monitoring with CTG and AFI at 42 weeks with unsure GA is safe. A follow-up visit after 2 weeks cannot be recommended, as 8% of women required CS within less than 2 weeks because of fetal distress.

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Post-term pregnancy refers to a pregnancy that has continued to or beyond 42.0 weeks' gestation from the first day of the last menstrual period.^[1-3] About 5 - 10% of all pregnancies reach a gestational age (GA) that could be considered as post term.^[4,5] The

perinatal mortality rate at 40 weeks is about 2 - 3 deaths per 1 000 deliveries, doubling at 42 weeks.^[67]

In normal pregnancies amniotic fluid volume (AFV) increases gradually till 36 weeks, then starts to reduce as pregnancy progresses.^[8] At 42 weeks the range of AFV between the 3rd and the 97th centile is wide and cannot be used to predict post-term pregnancies.^[8] A decline in the amniotic fluid index (AFI) to <5 cm in uncomplicated post-term pregnancies is associated with a raised incidence of fetal heart rate abnormalities during labour and a significantly increased caesarean section (CS) rate due to fetal distress.^[9,10]

A biophysical profile (BPP) is a method of antenatal assessment of fetal wellbeing performed to identify babies that may be at risk of poor pregnancy outcome. A BPP includes ultrasound monitoring of fetal movements, fetal tone and fetal breathing, ultrasound assessment of liquor volume and assessment of the fetal heart rate using non-stress cardiotocography (CTG).^[11] The presence of these biophysical variables implies absence of significant central nervous system hypoxaemia and acidaemia at the time of testing.

A modified BPP was developed to shorten the time necessary for testing and simplify the examination by concentrating on those components of the profile that are most predictive of outcome.^[12] Assessment of AFV and non-stress testing appears to be as reliable a predictor of short-term fetal wellbeing as a complete BPP. The rate of stillbirth of about 0.8/1 000 women within 1 week of a normal modified BPP is the same as with the complete BPP.^[13]

Two meta-analyses $^{\rm [14,15]}$ support induction of labour (IOL) in the 41st week but not later than 41 completed weeks rather than

expectant management, as a significantly lower perinatal mortality rate was found with no significant increase in the rate of CS in the induction group. However, expectant management could also be considered acceptable to deal with post-term pregnancies, using regular antenatal fetal surveillance to monitor fetal wellbeing. A modified BPP including non-stress CTG and AFI measurement is regarded an acceptable method to monitor the fetus.^[1,14]

Most of the studies regarding the management of prolonged pregnancy dealt with pregnancies of certain GA, where women had had early ultrasound scans.^[1-7,14] A study done at Tygerberg Hospital (TBH) two decades ago evaluated pregnant women with uncertain GA using fundal height or the last menstrual period (LMP) to determine GA.^[16] Weekly monitoring of Doppler velocimetry of the umbilical artery, CTG and assessment of the AFV were done. The authors concluded that in this group of patients expectant management is recommended, provided that CTG is reactive and the AFV remains normal. Doppler velocimetry measurement was not predictive of pregnancy outcome. The current TBH protocol from 42 weeks of uncertain gestation is weekly follow-up of patients with a modified BPP. If the AFI is \geq 5 cm and CTG reactive, expectant management continues; otherwise IOL is required.

In this study, women with prolonged pregnancy with an uncertain GA and an AFI of ≥ 10 cm and reassuring CTG were assessed to determine whether follow-up over 1 week or 2 weeks is required.

Method

A retrospective descriptive study included all patients with possible prolonged pregnancies and with uncertain GA referred to the fetal evaluation clinic (FEC).

Patients included in the study had an uncertain GA (no ultrasound before 24 weeks), AFI ≥ 10 cm, reactive CTG, singleton pregnancy, cephalic presentation, intact membranes and an

uncomplicated pregnancy. Pregnancy complications that excluded patients from the study were pre-eclampsia, diabetes, pregnancy-induced hypertension, suspected intrauterine growth restriction, and umbilical artery Doppler resistance index \geq 95th centile. The outcomes of all patients included in the study are described.

In the context of this study, reactive CTG and reassuring CTG had the same meaning; likewise non-reactive and non-reassuring CTG were the same. Pathological CTG had poor variability with regular decelerations or late decelerations. Pathological CTG was an indication for immediate delivery.

The patients were followed up with weekly AFI assessments and CTG until either the AFI decreased to <5 cm or CTG was non-reassuring. With either of these, IOL or CS was offered depending on the patient's obstetric history and the fetal condition. Patients were identified by searching the FEC database and the outcome of pregnancies determined by retrieving information on maternal and neonatal medical records. The outcome criteria of interest were: mode of delivery, fetal distress, meconium in liquor, Apgar score at 1 and 5 minutes, neonatal mortality, neonatal intensive care unit (ICU) or high-care admission and meconium aspiration.

The sample size calculation was based on determining whether weekly or 2-weekly follow-up is required in patients with an uncertain GA of 42 weeks and with an AFI ≥ 10 cm, as well as reactive CTG. The justification of the follow-up period was based on an analysis of the complications associated with labour. The proportion of patients experiencing complications associated with labour occurring during the first week following referral was compared with the proportion who experienced complications associated with labour during the second week following referral. If these two proportions were not significantly different (within clinically meaningful limits), a follow-up period of 2 weeks instead of weekly intervals could be motivated for the patient population. A description of the complications that occurred following referral are included. Medians or means were used as the measures of central location for ordinal and continuous responses. With this framework the proportions were seen as (clinically) significantly different if they differed by 0.2 (20%) or more. A sample size of 135

with an 80% power will detect a noninferiority margin difference between the group proportions of 0.2000. The reference group proportion was 0.3000. The test statistic used was the one-sided *t*-test. The significance level of the test was targeted at 0.05. MS Excel was used to capture the data and Statistica version 9 (StatSoft Inc. 2009 Statistica www.statsoft.com) was used to analyse the data.

This study was ethically approved by the Human Research Ethics Committee of the Faculty of Medicine and Health Sciences, Stellenbosch University. The Institutional Review Board number is IRB0005239.

Results

A total of 135 pregnant women were studied. The average age of subjects was 25 years. Gravidity ranged from 1 to 7 (median 2) and the median parity was 1 (range 0 - 5). Thirty-seven patients (27.4%) were infected with HIV. All were on treatment either with highly active antiretroviral therapy (HAART) or zudovidine for prevention of mother-to-child transmission of HIV. Syphilis was diagnosed in three patients, all of whom were fully treated. One patient's blood group was rhesus-negative.

Most of the patients included in this study booked late with an uncertain LMP, so booking fundal height (BFH) plotted on a centile chart for fundal height was used to determine their GA.^[17] The median GA at booking was 25 weeks (range 16 - 44). BFH was used in 132 patients (97.8%) to determine GA, while certain LMP was used in one patient. The other two patients had a BFH that was equal to their LMP. Some patients were judged to be \geq 44 weeks at booking by BFH measurement. One hundred and fourteen patients (84.4%) were seen at the FEC at 42 weeks of uncertain gestation, 18 (13.3%) at >42 weeks at first visit, two patients at 44 weeks, and one at 45 weeks.

All patients included in this series had reactive CTG and AFIs ≥ 10 cm at their first presentation to the FEC. One patient was included in this study with non-reactive CTG at entry; this was discovered while reviewing the data. The median first AFI was 14.8 cm (range 10 - 30) (Fig. 1). After the FEC first visit, 36 patients had an AFI value determined in the second week, 21 in the third week, and 6 in the fourth week. No clear trend was found in AFI measurements in subsequent weeks. The median second-week AFI was 12.6 cm (1.8 - 26.5), the median third-week AFI 12 cm (2 - 24) and the median fourth-week AFI 10 cm (6 - 20).

There was no obvious trend in the values of the second AFI measurements among the 36 women. The values increased in some women and decreased in others, and some

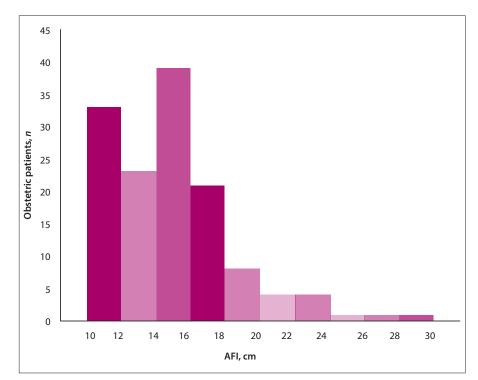


Fig. 1. *AFI measurements at the first visit to the FEC. (AFI = amniotic fluid index; FEC = fetal evaluation clinic.)*

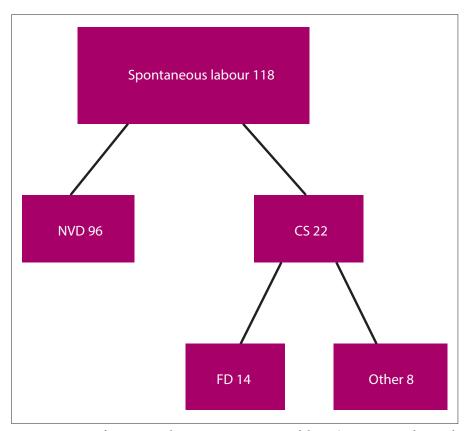


Fig. 2. Outcomes for patients who went into spontaneous labour. (NVD = normal vaginal delivery; CS = caesarean section; FD = fetal distress.)

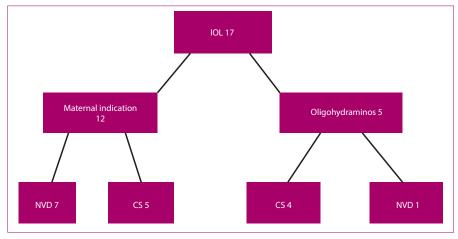


Fig. 3. Outcomes of patients with IOL. (IOL = induction of labour; NVD = normal vaginal delivery; CS = caesarean section.)

women's AFI was the same. Of those with a decrease in AFI, 5 out of 26 women had a significant drop from >10 cm to <4 cm in the second week. All of them were delivered by CS because of fetal distress, 3 after IOL and 2 after spontaneous onset of labour before induction could be commenced. Subsequent to referral, 6 (4.4%) patients had gestational hypertension and another 6 (4.4%) developed pre-eclampsia. All of them had inductions at the time of diagnosis.

The patients delivered at different levels of care facilities. The majority (62, 45.9%) gave birth at midwife obstetric units, while 50 (37.0%) gave birth at district hospitals and the remaining 23 (17.0%) at the referral hospital (TBH). A total of 118 women (87.4%) went into spontaneous labour, 22 (18.6%) of whom had a CS. Of the 22 women, 14 patients had pathological CTG, 7 within the first 14 days of first presentation to the FEC. Two of the 14 had a CS because of fetal distress after 23 and 41 days of first entry, respectively (Fig. 2). Both of them missed their follow-up after the second AFI measurements, which were 10.2 cm and 10 cm, respectively. Seven women had CS due to cephalopelvic disproportion (CPD) or poor progress during labour.

IOL was offered to 17 women (12.6%), of whom 12 had pregnancy-related complications and 5 an AFI <5 (Fig. 3). Of the 5 who had IOL because of diminished AFI, 4 patients had CSs because of nonreactive CTG within 2 weeks of entry. The remaining patient with a diminished AFI had a successful IOL.

Of the 135 women, 104 (77.0%) had normal vaginal deliveries, 8 following successful IOL. The remaining 31 (23.0%) were delivered by CS. The indications were 18 (13.3%) for fetal distress, 5 for failed IOL, 4 for CPD, 3 for poor progress, and 1 elective delivery for fetal macrosomia. Time intervals between the first visit to the FEC and delivery varied between 0 and 46 days (median 10). The woman delivered at first presentation to the FEC who had a CS for non-reactive CTG was included in the study. Meconium was found in 11 patients, of whom 8 had CSs for different indications. Fetal distress was reported in 4 of them.

Within the first 2 weeks of presentation to the FEC at TBH, 11 patients (8.1%) had a CS because of fetal distress. Four of the women had AFIs that decreased to <5 cm, with CTG indicating fetal distress following IOL. The remaining 7 women went into spontaneous labour 3 - 5 days after the last AFI measurement; of these, 3 had meconium in the liquor.

The mean birth weight of the babies was 3 366 g (range 2 320 - 4 730). The biggest baby was delivered by CS for CPD after 46 days after the first visit to the FEC. This mother had postpartum haemorrhage and a massive blood transfusion. Mean Apgar scores for all babies were 9 at 1 minute and 10 at 5 minutes. No neonatal ICU or high-care admissions were noted, and no neonatal morbidity or mortality was reported. There were no differences on comparing the neonatal outcome of being delivered during the first and second weeks after the first visit to the FEC.

Discussion

Most studies of post-term pregnancy management have dealt only with certain GA pregnancies. This study is one of very few studies reporting on the management of patients reaching an uncertain GA of 42 weeks. The scientifically based policy of IOL in or on completion of the 41st week does not apply to this group. In the study population BFH was used to determine GA in most cases; the majority of patients would therefore have had a true GA of less than 41 weeks, as BFH tends to overestimate GA.^[17,18] IOL at or before 41 completed weeks will result in more failed inductions and an increase in CS rate.

The management of patients with uncertain GA of 42 weeks at TBH depends on the results of weekly follow-up with a modified BPP. A non-reactive CTG and/or an AFI <5 cm are indications for delivery. Phelan *et al.*^[19] also used an AFI \leq 5 cm to define oligohydramnios, which was associated with adverse neonatal outcome in a review of retrospective studies.

A prospective study that examined serial changes in AFI in a population of women with prolonged pregnancy reported a large variation.^[20] Neither a decrease nor an increase in AFI is significant unless values declined to <5 cm. No information is available about the AFI at the time when a pathological CTG occurred in this study. A review of more than 10 000 women with longitudinal AFIs done at a single institution reported that AFIs >8 cm at a confirmed GA of 41 weeks were related to a 0.5% chance of developing oligohydramnios within 4 days.^[21]

The lower than expected complication rate in this study population, with 13.3% developing fetal distress, ruled out the possibility of a meaningful comparison between the first and second week following referral. Within the first 2 weeks of presentation, however, 11 patients (8.1%) had a CS because of fetal distress. The other common finding with reduced AFV is the presence of meconium, which is associated with more frequent variable decelerations.^[22,23] The current study found meconium in the liquor of 8% of patients. Weekly evaluation may fail to detect prolonged pregnancies resulting in a rapid decrease of AFV.^[24,25] Future studies need to assess twice-weekly modified BPPs to refine the management of patients reaching 42 weeks with an uncertain GA.

Conclusion

Follow-up after 2 weeks of women with an uncertain GA of 42 weeks, an AFI of ≥ 10 cm and reassuring CTG may fail to detect prolonged pregnancies at risk for fetal distress.

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