

The Impact of Maternal Ketonuria on Fetal Test Results in Patients with Post-term Pregnancy

Dr. Taif Jabbar Saleem ¹, Dr. Yasamin H. sharif Al-Shibany ²

Abstract

Background: Post-term pregnancy is currently defined as a pregnancy progressing to ≥ 42 weeks (294 days) of gestation. It is associated with increased risk of maternal and fetal complications. Ketonuria in the context of post-term pregnancy is associated with an increased risk of maternal and fetal outcomes.

Aim of the study: The objective of this study was to assess the effect of maternal ketonuria on fetal surveillance outcomes, specifically non-stress test (NST) and biophysical profile (BPP) results, in post-term pregnant women

Patients and methods: The current cross-sectional study was conducted in the Obstetrics and Gynecology Department at Al-Diwaniyah Maternity and Pediatric Teaching Hospital, Iraq, between February 2024 and September 2024. The study enrolled 50 pregnant women with post-term pregnancy, with an age range between 18 and 40 years old. Urine was collected (3-5ml) in a clean, dry container and transported to the laboratory within 30 minutes. The dipstick was dipped for 1–2 seconds in urine, and the color of the strip was then compared to the color chart on the strip container approximately 1 minute after immersion.

Results: Ketonuria was detected in 15 women (30.0%). Of these, 8 (16.0%) had mild (+), 3 (6.0%) moderate (++), and 4 (8.0%) severe (+++) ketonuria. Significant differences were observed in non-stress test (NST) reactivity (reactive, $p = 0.002$; non-reactive, $p = 0.001$), while equivocal results were not significant ($p = 1.000$). Intrapartum decelerations occurred more frequently in women with ketonuria compared to those without (40.0% vs. 11.4%). The relative risk (RR) of decelerations in ketonuric women was 3.51 (95% CI: 1.05–11.7, $p = 0.048$). No significant associations were found between ketonuria and liquor color (RR = 1.26, 95% CI: 0.57–2.77, $p = 0.558$) or Doppler findings (RR = 1.00, 95% CI: 0.29–3.44, $p = 1.000$).

Conclusion: Ketonuria was seen in 30% of post-term women and was associated with significantly worse non-stress test (NST) and biophysical profile (BPP) results, but not with liquor color or Doppler findings. Routine ketonuria screening may help identify high-risk fetuses in prolonged pregnancies..

Keywords: Maternal ketonuria, Post-term pregnancy, Non-stress test, Biophysical profile.

¹ M.B.Ch.B, Iraqi Board for Medical Specialties, Al-Diwaniyah Teaching Center for Obstetrics and Gynecology

² C.A.B.O.G, College of medicine Al Qadisiya University Maternity and Pediatric Teaching Hospital – AL Diwaniyah / Iraq

Introduction

Post-term pregnancy is currently defined as a pregnancy progressing to 42 weeks (294 days) of gestation or beyond(1). The most common reason for post-term gestation is the incorrect estimation of gestational age, and in most cases, the post-term pregnancy represents the upper extreme of the normal distribution of pregnancy duration(2). Some genetic disorders, such as fetal anencephaly, fetal adrenal hypoplasia, and placental sulfatase deficiency, are rare causes(3). Women with a history of previous post-term pregnancy or women who were the product of post-term pregnancy are significantly more likely to have post-term pregnancy(4). Low vaginal levels of fetal fibronectin at 39 weeks are predictive of an increased likelihood of post-term pregnancy(5). A defect or delay in the remodeling of the cervix that takes place before successful initiation of labour may cause post-term pregnancy(2). Post-term pregnancy could result from variations in the corticotropin-releasing hormone (CRH) system during pregnancy, such as variations in the corticotropin-releasing hormone (CRH) system during pregnancy—such as changes in receptor subtypes, altered signal transduction, or increased binding capacity of CRH-binding protein(6).

Ketonuria, defined as the presence of excess ketone bodies in urine, reflects a metabolic shift toward alternative energy sources(7,8). Numerous prior investigations have demonstrated that ketones induce modifications in the volume of amniotic fluid in human subjects(9). Given these effects, ketonuria may serve as a biochemical marker complementing traditional and revised biophysical profiles in assessing fetal well-being. Ketonuria in pregnancy is often transient and clinically insignificant, yet prolonged gestation may lead to sustained ketone exposure, potentially resulting in adverse maternal and fetal outcomes(9,10).

The pathology associated with ketonuria encompasses a progressive decline in the supply of oxygen and nutritional resources, which can be sustained for a limited duration through the mitigation of metabolic demands and oxygen requirements, coupled with an elevation in hematocrit levels and catecholamine concentrations. Chronic hypoxemia, which is linked to placental insufficiency in post-term pregnancies, may manifest through discernible alterations in fetal heart rate or other biophysical parameters until such changes become substantial enough to precipitate acidemia. A decrease in the metabolic rate, which is concomitant with diminished oxygen delivery and a reduction in the storage of carbohydrates and fats, will precede the initiation of anaerobic metabolism, thereby heightening the likelihood of the development of acidemia(2).

The aim of the study:

This study was designed to assess the effect of maternal ketonuria on fetal well-being in post-term pregnant women.

Patients and methods

The current prospective observational analytic cohort study was conducted in the Obstetrics and Gynecology Department and the Emergency Department in Al-Diwaniyah Maternity and Pediatric Teaching Hospital, Iraq. The study period extended from February 2024 to September 2024. The study enrolled 50 pregnant women with post-term pregnancy with an age range between 18 and 40 years old.

This study was approved by the Iraqi Board for Medical Specialization and the Ethical Approval Committee of the Teaching Hospital. Written consent was obtained from all patients participating in the current study before being enrolled in the protocol.

Inclusion criteria:

- Age 18–40 years

- Singleton pregnancy at ≥ 42 weeks of gestation (post-term). Clarified distinction: late-term (41–41+6 weeks) vs. post-term (≥ 42 weeks)

Exclusion criteria:

- Chronic medical illness (e.g., hypertension, diabetes mellitus—chronic or gestational, renal or vascular disease)
- Unknown last menstrual period (LMP) or absence of early ultrasound dating
- Multiple pregnancy
- Intrauterine fetal demise
- Congenital fetal anomalies
- Smoking or drug abuse
- Obesity defined as BMI ≥ 30 kg/m²
- Vomiting due to urinary tract infection or gastroenteritis

Clinical assessment: All participants were admitted either in early latent labor or for induction of labor. A comprehensive history was obtained, including maternal age, parity, and gestational age. General, abdominal, and pelvic examinations were performed.

Urine sampling: A midstream urine sample (3–5 ml) was collected in a sterile container and analyzed within 30 minutes. The dipstick was dipped for 1–2 seconds in urine, and results were read exactly at 60 seconds, according to the manufacturer's instructions:

- No ketones = beige
- Mild ketonuria = 1.5 mmol/L (light pink)
- Moderate ketonuria = 4 mmol/L (dark pink)
- Severe ketonuria = 16 mmol/L (purplish).

Urine dipstick readings were performed by a single investigator who was aware of clinical status; lack of blinding is acknowledged as a limitation due to potential observer bias.

Fetal assessment:

- Non-stress test (NST): Conducted with two abdominal sensors (tocodynamometer and fetal heart rate monitor) for 20–40 minutes. Results were classified as:
 - ✓ Reactive: ≥ 2 accelerations of ≥ 15 bpm above baseline lasting ≥ 15 seconds
 - ✓ Non-reactive: No qualifying accelerations within 20–40 minutes
 - ✓ Equivocal: Indeterminate (equivocal) results were defined as inconclusive findings not meeting criteria for reactive or non-reactive
- Biophysical profile (BPP): Biophysical profile scoring was based on five components (fetal breathing, movement, tone, amniotic fluid volume, and NST), each scored 0–2, with a maximum score of 10.

NST and BPP interpretations were performed by a single investigator. Inter-observer reliability was therefore not assessed.

- Doppler study: Umbilical artery and middle cerebral artery indices assessed.
- Amniotic fluid assessment: Liquor color (clear or meconium-stained) was recorded following artificial rupture of membranes.

Statistical analysis

Data were entered into a Microsoft Excel 2010 and analyzed using SPSS (Statistical Package for Social Sciences) version 26. Quantitative variables were expressed as mean $\pm$ standard deviation (SD) and range. Qualitative variables were expressed as frequencies and percentages. Independent sample t-tests were used for continuous normally distributed variables; the Mann-Whitney U test was used for parity (non-normal distribution). Associations between categorical variables were tested using chi-square, Fisher's exact, or Yates's correction tests as appropriate. Statistical significance was set at $p \leq 0.05$.

Results:

The present study included 50 pregnant women with post-term pregnancy, aged between 18 and 40 years. Ketonuria was detected in 15 cases (30.0%). The distribution of ketonuria severity is shown in Table 1. Mild (+) ketonuria was present in 8 women (16.0%), moderate (++) ketonuria in 3 women (6.0%), and severe (+++) ketonuria in 4 women (8.0%).

Table 1: Distribution of pregnant women according to the severity of ketonuria

Ketonuria	Frequency	Percent
Nil	35	70.0
+	8	16.0
++	3	6.0
+++	4	8.0
Total	50	100.0

There were no statistically significant differences between women with and without ketonuria regarding mean maternal age (26.67 ± 5.58 vs. 27.60 ± 6.75 years, $p = 0.640$), and mean gestational age (41.40 ± 0.36 vs. 41.36 ± 0.34 weeks, $p = 0.708$). Median parity was 1 (IQR 1) in the ketonuria group vs 2 (IQR 4) in the non-ketonuria group, reflecting skewed distribution due to small sample size (Table 2).

Table 2: Comparison of mean age, gestational age, and parity according to ketonuria status

Characteristics	Ketonuria present (n = 15)	Ketonuria absent (n = 35)	p-value
Age (years)			
Mean $\pm$ SD	26.67 ± 5.58	27.60 ± 6.75	0.640
Range	18–35	18–40	
Gestational age (weeks)			
Mean $\pm$ SD	41.40 ± 0.36	41.36 ± 0.34	0.708
Range	41–42	41–42	
Parity			
Median (IQR)	1 (1)	2 (4)	0.271
Range	0–3	0–5	

Note: Independent samples t-test (**I**) was used for age and gestational age; Mann-Whitney U test (**M**) for parity. **NS** = not significant.

Comparison of non-stress test (NST) results between the two groups is presented in Table 3. Reactive and non-reactive NST differences were analyzed using Fisher's exact test. Reactive NST was significantly less frequent in women with ketonuria compared to those without ketonuria (20.0% vs. 68.6%, $p = 0.002$). Conversely, non-reactive NST was significantly more common in the ketonuria group (73.3% vs. 22.9%, $p = 0.001$). Equivocal NST results showed no significant difference ($p = 1.000$). Intrapartum fetal heart rate decelerations (early, late, or variable if available) were also significantly more frequent in women with ketonuria (40.0% vs. 11.4%, $p = 0.048$).

Table 3: Comparison of non-stress test (NST) and intrapartum decelerations according to ketonuria status

Characteristics	Ketonuria present (n = 15)	Ketonuria absent (n = 35)	P-value
Non-stress test (NST)			
Reactive	3 (20.0%)	24 (68.6%)	0.002**
Non-reactive	11 (73.3%)	8 (22.9%)	0.001***
Equivocal	1 (6.7%)	3 (8.5%)	1.000
Intrapartum deceleration			
Yes	6 (40.0%)	4 (11.4%)	0.048*
No	9 (60.0%)	31 (88.6%)	

Note: Chi-square test (C) and Fisher's exact test (F) were used. * $p \leq 0.05$, ** $p < 0.01$, *** $p < 0.001$; NS = not significant.

Biophysical profile (BPP) results are shown in Table 4. Normal BPP is defined as ≥ 8 , abnormal ≤ 4 , and suspicious = 6. A normal BPP was significantly less common in the ketonuria group (20.0% vs. 54.3%, $p = 0.033$), whereas an abnormal BPP was significantly more frequent (53.3% vs. 20.0%, $p = 0.018$). Suspicious BPP results did not differ significantly between the groups ($p = 0.944$).

Table 4: Comparison of biophysical profile (BPP) results according to ketonuria status

BPP Category	Ketonuria present (n = 15)	Ketonuria absent (n = 35)	P-value
Normal	3 (20.0%)	19 (54.3%)	0.033*
Abnormal	8 (53.3%)	7 (20.0%)	0.018*
Suspicious	4 (26.7%)	9 (25.7%)	0.944

Note: Fisher's exact test (F) and Chi-square test (C) were used. * $p < 0.05$; NS = not significant

No significant association was found between the presence of ketonuria and the color of amniotic fluid ($p = 0.558$) (Table 5).

Table 5: Comparison of amniotic fluid color according to ketonuria status

Color of liquor	Ketonuria present (n = 15)	Ketonuria absent (n = 35)	P-value
Clear	6 (40.0%)	11 (31.4%)	0.558
Meconium-stained	9 (60.0%)	24 (68.6%)	

Note: Yates correction test (Y) was used. NS = not significant.

Similarly, there was no significant difference in Doppler study results between women with and without ketonuria ($p = 1.000$) (Table 6). Low statistical power due to the small number of abnormal Doppler findings, acknowledged in the Discussion

Table 6: Comparison of Doppler test results according to ketonuria status

Doppler Result	Ketonuria present (n = 15)	Ketonuria absent (n = 35)	P-value
Normal	13 (86.7%)	31 (88.6%)	1.000
Abnormal	2 (13.3%)	4 (11.4%)	

Note: Fisher's exact test (F) was used. NS = not significant.

Neonatal outcomes such as Apgar scores, NICU admission, and perinatal mortality were not collected in this study and therefore could not be analyzed

Discussion

Post-term pregnancies are associated with a severalfold increase in perinatal mortality and morbidity, particularly beyond 42 weeks of gestation. Consequently, optimal surveillance and timely management remain important clinical considerations.

In this study, maternal ketonuria was observed in 30% of the women with post-term delivery. Severity categories were mild (+) at 16%, moderate (++) at 6%, and severe (+++) at 8%. Maternal age, gestational age, and parity did not significantly correlate with ketonuria. This finding suggests that ketonuria during extended periods of gestation is more likely to indicate metabolic stress than be influenced by maternal characteristics. Previous studies have suggested that the increased risk may be more pronounced in nulliparous women (11); however, this was not demonstrated in our cohort.

The study demonstrated a clear negative impact of ketonuria on fetal well-being parameters. Reactive non-stress test (NST) results were significantly less frequent in women with ketonuria (20.0% vs. 68.6% in those without, $p = 0.002$), while non-reactive NST results were markedly more common (73.3% vs. 22.9%, $p = 0.001$).

Additionally, intrapartum fetal heart rate decelerations occurred more frequently in the ketonuria group (40.0% vs. 11.4%, $p = 0.048$). Regarding BPP scores, women with ketonuria had significantly fewer normal BPP scores than those without (20% vs 54.3%, $p=0.033$); conversely, they had significantly more abnormal BPP scores (53.3% vs 20%, $p=0.018$). Thus, it appears that there is a relationship between ketonuria and decreased fetal oxygenation and fetal reactivity, which may be related to substrate depletion, reduced amniotic fluid volume, and placental aging or insufficiency, as suggested by prior studies.

In contrast, no significant relationship was noted between the amniotic fluid colour and the presence of ketones in the urine of the participants. Meconium-stained amniotic fluid was seen in 60.0% of women with ketonuria compared to 68.6% of women without ketonuria, but no statistically significant difference was found (p -value = 0.558). Based on the results of the Doppler ultrasound assessments, there was also no significant difference in the rate of abnormal findings between the two groups, as 13.3% of the women in the ketonuria group had abnormal findings compared to 11.4% in the non-ketonuria group (p -value = 1.000). The lack of association between the colour of the amniotic fluid and the Doppler assessment results could be attributed to the limited sample size or to differences in the severity or timing of exposure to ketonuria between the two groups.

These results were consistent with prior studies, although the prevalence of ketonuria in the current study population was higher than in previous studies. For example, Abd-Alamieer and Farak (2013) found a rate of 10.8% of women in their study who had ketonuria at the time they gave birth, and found that 62.9% of the women with ketonuria who were included in their study had moderate to severe levels of ketonuria. Additionally, Abd-Alamieer and Farak found strong associations between oligohydramnios and non-stress testing that were available for those with and without ketonuria, with a prevalence of 85.1% of those with ketonuria and 45.7% of those without ketonuria having abnormal results. These results support the conclusion that there is a statistically significant relationship between the presence of ketonuria in pregnant women and adverse fetal test outcomes (7,8).

In a similar study, Hamdi et al. (2006) examined 360 women with gestational age >40 weeks and detected ketonuria in 9.44% of cases. Maternal ketonuria was significantly linked to oligohydramnios, abnormal fetal testing, and increased fetal heart rate decelerations (12). Onyeije and Divon (2001) conducted a major study with 3601 post-term pregnancies; they found that 10.9% of their patients had clinically detectable ketonuria. In addition, diabetic patients had more than double the incidence of oligohydramnios, more than triple the incidence of non-reactive non-stress testing, and much higher rates of fetal decelerations than patients without ketonuria (13). Similarly, research by Hamad (2011) with 100 subjects who were post-term found that 13.9% had ketonuria. Patients with ketonuria had increased

instances of oligohydramnios, non-reactive non-stress testing, and variable/late fetal heart rate decelerations versus those without ketonuria (14).

The higher prevalence of ketonuria in this study may be related to the characteristics of the local population or the diet of the population, or possibly the definitions and timing of post-term assessments differ from those used in the other studies.

Collectively, the evidence suggests that maternal ketonuria may serve as a helpful biochemical marker of fetal compromise in prolonged pregnancies, and may primarily affect non-stress tests (NST) and biophysical profile (BPP) parameters. Possible mechanisms may be attributed to chronic fetal hypoxia due to aging of the placenta, and decreased availability of carbohydrates, which would require the fetus to rely more heavily on fat metabolism and produce ketones.

Conclusion

Maternal ketonuria was detected in 30% of women with post-term pregnancy and ranged from mild to severe. It was not significantly associated with maternal age or parity ($p > 0.05$), although the study was underpowered to detect small differences. Ketonuria was significantly associated with adverse fetal surveillance outcomes, including fewer reactive non-stress test (NST) results, more non-reactive NST results, increased intrapartum fetal heart rate decelerations, and poorer biophysical profile (BPP) scores. No significant associations were found with amniotic fluid color or Doppler findings. These results indicate that maternal ketonuria may serve as a simple, useful biochemical marker of fetal compromise in post-term pregnancies, complementing conventional NST and BPP monitoring. Routine ketonuria screening is recommended for women with prolonged gestation to identify those at higher risk of abnormal fetal test results.

Authorship and Financial Disclosure Statement

The author certifies that there are no actual or potential conflicts of interest related to this work. No financial, professional, or personal competing interests influenced the research or its outcomes. This study was conducted independently without external funding or institutional support. The author assumes full responsibility for all aspects of the work.

Authors' Contributions

The authors were collectively responsible for the conception, study design, data collection, analysis, and writing of this manuscript. Each author contributed substantially to the work, reviewed the final draft, and approved the manuscript for submission. All authors agree to be accountable for the integrity and accuracy of the study.

References

1. Mitao M, Mwita WC, Antony C, Adinan H, Shayo B, Amour C, et al. Recurrence of post-term pregnancy and associated factors among women who delivered at Kilimanjaro Christian Medical Centre in northern Tanzania: A retrospective cohort study. *PLoS One*. 2023;18(4):e0282078. doi:10.1371/journal.pone.0282078.
2. Edmonds DK. Assessment of fetal well-being in late pregnancy. In: Lees C, Condon C, Drife J, editors. *Dewhurst's textbook of obstetrics and gynaecology for postgraduates*. 6th ed. UK: Blackwell Publishing; 2018. p. 122-5.
3. Galal M, Symonds I, Murray H, Petraglia F, Smith R. Post-term pregnancy. *Facts Views Vis ObGyn*. 2012;4(3):175-87. PMID: 24753906.
4. Naidu K, Fredlund KL. Gestational Age Assessment. [Updated 2023 Jul 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK526000/>.

5. Kenny LC, Myers JE, editors. *Obstetrics by ten teachers*. 20th ed. Boca Raton: CRC Press; 2017. doi:10.1201/9781315382401.
6. Cunningham F, Leveno KJ, Dashe JS, Hoffman BL, Spong CY, Casey BM, editors. *Williams Obstetrics*. 26th ed. New York: McGraw-Hill; 2022. Available from: <https://accessmedicine.mhmedical.com/content.aspx?bookid=2977§ionid=263812626>.
7. Abd-Alamieer WS, Farak IN. Maternal ketonuria and results of fetal testing in the impending post-term pregnancy. *Iraqi J Med Sci*. 2013;11(4):393-8.
8. Singh S, Rai S, Prajwal S, Rao PS. Role of modified biophysical profile in the management of post-term pregnancy. *Int J Reprod Contracept Obstet Gynecol*. 2018;7(2):456-61.
9. Qian M, Wu N, Li L, Yu W, Ouyang H, Liu X, et al. Effect of elevated ketone body on maternal and infant outcome of pregnant women with abnormal glucose metabolism during pregnancy. *Diabetes Metab Syndr Obes*. 2020;13:4581-8. doi:10.2147/DMSO.S280851.
10. Tang J, Gou W, Fu Y, Li K, Guo X, Huang T, et al. Association between post-term pregnancy and adverse growth outcomes in preschool-age children. *Am J Clin Nutr*. 2022;116(2):482-90. doi:10.1093/ajcn/nqac123.
11. Edmonds K, editor. *Dewhurst's textbook of obstetrics and gynaecology*. 9th ed. Hoboken: John Wiley & Sons; 2018. doi:10.1002/9781119211457.
12. Hamdi K, Bastani P, Gafarieh R, Mozafari H, Hashemi SH, Ghotbi MH. The influence of maternal ketonuria on fetal well-being tests in post-term pregnancy. *Arch Iran Med*. 2006;9(2):144-7. PMID: 16649357.
13. Onyeije CI, Divon MY. The impact of maternal ketonuria on fetal test results in the setting of post-term pregnancy. *Am J Obstet Gynecol*. 2001;184(4):713-8. doi:10.1067/mob.2001.111247.
14. Hamad LH. The influence of maternal ketonuria on biophysical fetal test results in the evaluation of post-term pregnancy. *Iraqi Journal of Medical Sciences*. 2011;9(4).