

Research Article

Correlation between Leukocyte Esterase and the Incidence of Preterm Birth and Maternal and Neonatal Outcomes

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Abstract

Objective: Leukocyte esterase (LE) is a diagnostic marker for urinary tract infections (UTIs), the management of which may mitigate the risk of preterm labor and neonatal complications. This study evaluates the correlation between positive LE, preterm labor, and subsequent infant outcomes.

Methods: This retrospective cohort study at Hasan Sadikin General Hospital analyzed medical records of singleton pregnancies in 2024. Using total sampling and multivariable logistic regression, the study evaluated the correlation between maternal urinalysis with positive leukocyte esterase, the incidence of preterm birth, and 5-minute APGAR scores.

Results: Of the 420 patients analyzed, preterm labor occurred in 60.5% of cases. Positive LE was identified in 42.1% of the cases. Multivariate analysis revealed that positive LE significantly increased the risk of preterm delivery (aOR = 1.57, $p = 0.042$). However, positive LE was not a significant determinant of neonatal asphyxia (OR = 0.97, $p > 0.999$), which demonstrated a stronger association with lower birth weight and infrequent antenatal care visits.

Conclusion: Maternal leukocyte esterase positivity is associated with approximately a 1.5-fold increase in the likelihood of preterm labor. Conversely, no significant association was observed between LE levels and neonatal asphyxia or 5-minute APGAR scores.

Keywords: Asphyxia; leukocyte esterase; preterm labor; urinary tract infections

Hubungan antara Leukosit Esterase dengan Kejadian Persalinan Prematur dan Luar Ibu dan Bayi

Abstrak

Tujuan: Leukosit esterase membantu mendiagnosis Infeksi Saluran Kemih (ISK), yang berpotensi mengurangi risiko persalinan prematur dan asfiksia kelahiran. Penelitian ini bertujuan menganalisis korelasi antara leukosit esterase, persalinan prematur, dan hasil bayi.

Metode: Studi kohort retrospektif yang dilakukan di Rumah Sakit Hasan Sadikin melalui data rekam medik, dilakukan *total sampling* pasien dengan kehamilan tunggal pada tahun 2024. Data dianalisis dengan uji Chi square, dilanjutkan dengan regresi logistik multivariat untuk mengevaluasi hubungan antara hasil urin leukosit esterase positif dengan persalinan prematur, dan skor APGAR 5 menit.

Hasil: Dari 420 pasien, persalinan prematur terjadi pada 60,5% kasus. Leukosit Esterase (LE) positif ditemukan pada 42,1% kasus persalinan prematur. Analisis multivariat menunjukkan bahwa LE positif secara signifikan meningkatkan risiko persalinan prematur (aOR = 1,57; $p = 0,042$). Namun, hal tersebut bukan merupakan penentu signifikan bagi asfiksia neonatal (OR = 0,97; $p > 0,999$), yang justru lebih kuat dikaitkan dengan berat badan lahir rendah dan kunjungan perawatan antenatal (*antenatal care*) yang lebih sedikit.

Kesimpulan: Leukosit esterase positif meningkatkan risiko persalinan prematur sekitar 1,5 kali lipat, namun tidak menunjukkan hubungan signifikan dengan asfiksia neonatal atau skor APGAR 5 menit.

Kata kunci: Asfiksia; infeksi saluran kemih; leukosit esterase; persalinan prematur.

Introduction

Preterm birth remains the leading contributor to neonatal morbidity and mortality worldwide,¹ accounting for an incidence rate of 5%–20% of all pregnancies.² Infection is its primary etiological factor, implicated in 30%–40% of cases.³ Defined as birth occurring between 20 and 37 weeks of gestation,⁴ preterm birth affected an estimated 152 million infants globally between 2010 and 2020. In 2020 alone, approximately 13.4 million infants were born prematurely, resulting in nearly 1 million deaths due to complications associated with prematurity.⁵

A range of demographic, behavioral, and clinical factors are associated with the risk of preterm birth, including maternal age, smoking, low pre-pregnancy body mass index (BMI), psychosocial stress, a history of preterm delivery, and infections, particularly urinary tract infections (UTIs).⁶ According to 2015 WHO data, the burden of preterm birth is disproportionately higher in low- and middle-income countries.⁷

Urinary tract infections are among the most prevalent bacterial infections during pregnancy, affecting approximately 2%–15% of pregnant women.⁸ If left untreated, asymptomatic bacteriuria (defined as the presence of a significant bacterial count ($\geq 10^5$ CFU/mL) from one or more species in a urine sample without clinical symptoms)⁸ may progress to acute pyelonephritis (APN) and is associated with an increased risk of preterm labor. However, recent clinical trials have yielded conflicting findings regarding this progression.⁹ Risk factors for gestational UTIs include multiparity,¹⁰ low educational attainment,¹¹ obesity,¹² maternal age, and gestational age;¹³ notably, employment status has not been shown to increase risk.¹⁴

Anatomical and physiological changes during pregnancy, such as ureteral dilation and decreased myogenic tone⁸ mediated by increased progesterone,⁶ alongside increased

bladder volume, contribute to urinary stasis and ureterovesical reflux. Furthermore, blood volume expansion and an increased glomerular filtration rate (GFR) reduce ureteral tone and increase urinary tract capacity,⁶ creating an environment conducive to bacterial proliferation.⁸

Early detection of UTIs via dipstick testing for nitrites and leukocyte esterase (LE) is a critical screening tool for identifying the risk of preterm labor. Although some studies suggest a correlation between elevated LE levels and preterm labor, data regarding its prognostic value for maternal and neonatal outcomes remain limited,⁸ necessitating further investigation. Effective management of UTIs during pregnancy is associated with a reduced risk of preterm birth;¹⁵ thus, early detection using LE testing offers a rapid and cost-effective screening method¹⁶ to mitigate neonatal mortality and complications. This study aims to evaluate the correlation between leukocyte esterase and the incidence of preterm birth, as well as the impact of leukocyte esterase on maternal and neonatal outcomes at Hasan Sadikin General Hospital (RSHS).

Method

This retrospective observational cohort study was conducted at Dr. Hasan Sadikin General Hospital (RSHS) in Bandung, Indonesia. The study analyzed medical records from January to December 2024 to evaluate the correlation between maternal leukocyte esterase (LE) levels, preterm birth incidence, and neonatal outcomes. Ethical approval was granted by the RSHS Ethics Committee (No. DP.04.03/D.XIV.6.5/208/2025).

A total sampling method was used, including all pregnant women who delivered at RSHS during the study period. Inclusion criteria were gestational ages of 20 to 37 weeks, maternal ages of 18 to 40 years, and singleton live intrauterine pregnancies.

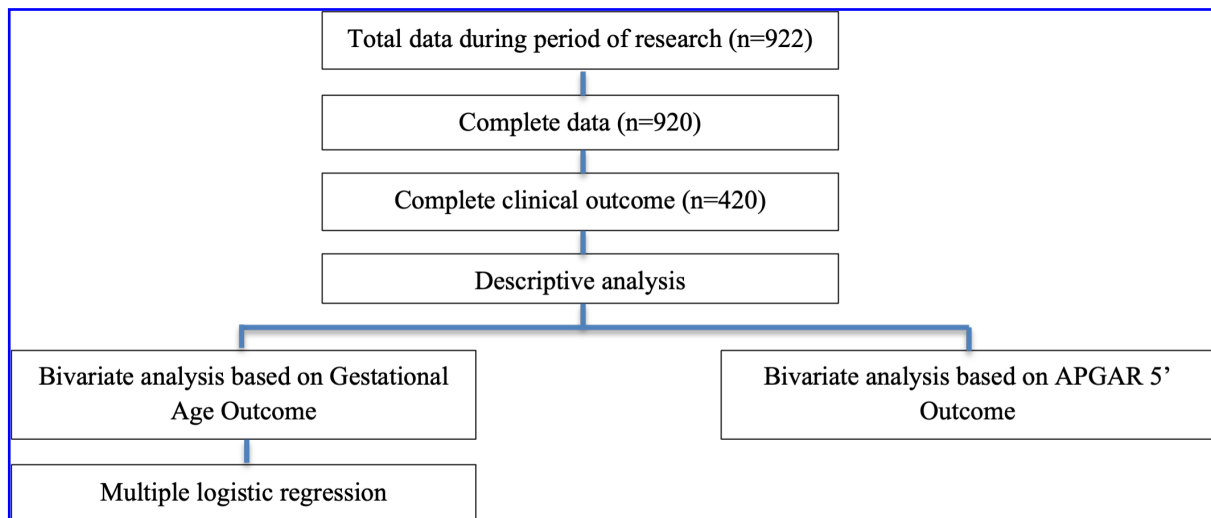


Figure 1 Data Selection and Analysis Flow

Meanwhile, exclusion criteria included incomplete medical records or confounding comorbidities, such as congenital uterine anomalies, amniotic fluid disorders (polyhydramnios or oligohydramnios), antepartum hemorrhage, and chronic conditions, specifically diabetes mellitus, chronic hypertension, or cardiac disease.

The independent variable was the leukocyte esterase level derived from maternal urinalysis, dichotomized into negative or positive. Positive results were defined by semi-quantitative values of +2, +3, or +4. The primary dependent variables were the incidence of preterm delivery and the 5-minute APGAR score. Preterm delivery was categorized nominally (yes/no), while the APGAR score was dichotomized into asphyxia (<7) or no asphyxia (≥ 7).

Statistical analyses were conducted in RStudio. Descriptive statistics were used to characterize the study population. For the primary analysis, clinical variables were initially screened with bivariate analyses. Variables showing statistical or borderline significance ($p \leq 0.05$) were subsequently included in a multivariable logistic regression model. This approach adjusted for potential confounders to estimate the adjusted odds ratios (aOR) with 95% confidence intervals (CI), reflecting the independent association

between leukocyte esterase levels and the specified outcomes (Figure 1).

Results

A total of 420 patients were included in the final analysis. Total sampling was used to minimize selection bias and ensure comprehensive representation of the patient population meeting the inclusion criteria.

Table 1 Demographic Data

Variable	n (%)
Maternal Age	
< 20 years	26 (6.2%)
20-30 years	183 (43.6%)
> 30 years	211 (50.2%)
Mean (SD)	29.44 (6.92)
BMI (kg/m²)	
Underweight	32 (7.6%)
Normal	210 (50.0%)
Overweight	107 (25.5%)
Obesity Grade 1	51 (12.1%)
Obesity Grade 2	20 (4.8%)
Mean (SD)	24.78 (5.33)
Gestational Age	
Preterm	254 (60.5%)
Aterm	165 (39.3%)
Postterm	1 (0.2%)

Parity	
Primipara	33 (7.9%)
Multipara	387 (92.1%)
Delivery Method	
Spontaneous	90 (21.4%)
Sectio Caesarean	223 (53.1%)
Misoprostol Induction	63 (15.0%)
Oxytocin Augmentation	34 (8.1%)
Forceps	6 (1.4%)
Vacuum	4 (1.0%)
Birth Weight (gr)	
ELBW (< 1000 gr)	24 (5.7%)
VLBW (1000-1499 gr)	49 (11.7%)
LBW (1500-2499 gr)	187 (44.5%)
Normal ($\geq$ 2500 gr)	160 (38.1%)

ELBW: Extremely Low Birth Weight; VLBW: Very Low Birth Weight; LBW: Low Birth Weight

Maternal age ranged from under 20 to over 30 years, with a mean of 29.44 ± 6.92 years; the majority of participants were over 30 years old (50.2%). Regarding nutritional status, 50.0% of participants had a normal BMI, while a significant portion was classified as overweight (25.5%) or obese (Grade 1: 12.1%; Grade 2: 4.8%). Preterm labor occurred in 254 cases (60.5%), and 92.1% ($n=387$) of the cohort were multiparous.

Moreover, clinical outcomes revealed that Cesarean section was the most frequent delivery method, accounting for 53.1% of cases. There was a high incidence of Low Birth Weight (LBW), affecting 44.5% of newborns, with an overall mean birth weight of 2,212.54 grams (Table 1)

Table 2 shows that no significant differences were observed between the preterm and term groups in maternal age ($p=0.514$) or BMI ($p=0.649$). However, positive leukocyte esterase (LE) ($p=0.050$), frequency of antenatal care (ANC) visits, and fetal presentation were significantly associated with preterm birth. Women in the term group had a significantly higher mean number of ANC visits (7.08 ± 2.70) than those

in the preterm group (6.20 ± 3.05 ; $p=0.002$). Specifically, six or more ANC visits were associated with a higher likelihood of reaching full term ($p=0.015$; OR=1.71; 95% CI: 1.13–2.63). Fetal presentation also showed a strong association ($p=0.002$); cephalic presentation was more prevalent in the term group (91.5%) than in the preterm group (79.5%), with an odds ratio of 2.78 (95% CI: 1.48–5.20).

While delivery methods did not reach statistical significance ($p=0.309$), birth weight showed the most profound difference ($p<0.001$). The mean birth weight for the preterm group was significantly lower (1794.42 ± 529.92 g) than the term group (2867.85 ± 399.19 g). Furthermore, LBW was significantly associated with preterm delivery ($p<0.001$), with 64.2% of preterm infants classified as LBW compared to 14.5% of term infants (OR = 1.54; 95% CI: 1.02–2.32).

Although delivery methods did not reach statistical significance ($p=0.309$), birth weight variables showed the most pronounced differences ($p<0.001$). The mean birth weight for the preterm group was significantly lower (1794.42 ± 529.92 g) than that of the aterm group (2867.85 ± 399.19 g). Furthermore, Low Birth Weight (LBW) was significantly associated with preterm delivery ($p<0.001$). 64.2% of preterm infants fell into the LBW category, compared with only 14.5% of aterm infants (OR = 1.54; 95% CI: 1.02–2.32).

Multiple logistic regression was conducted to identify independent risk factors for preterm delivery (Table 3). Mothers with non-cephalic fetal presentation had 2.84 times higher odds of preterm delivery (aOR = 2.843; 95% CI: 1.479–5.465; $p=0.002$). LE positivity increased the odds by 1.57-fold (aOR = 1.572; 95% CI: 1.016–2.433; $p=0.042$). Conversely, frequent ANC visits were protective, with each additional visit reducing the odds of preterm birth (aOR = 0.907; 95% CI: 0.844–0.976; $p=0.009$)

Bivariate analysis (Table 4) indicated

Table 2 Bivariate Analysis based on Gestational Age Outcomes*

Variable	Preterm (n=254)	Aterm (n=165)	p-value	OR	95% CI
Maternal Age, mean (SD)	29.6 ±6.96	29.15 ±6.87	0.514		
<20 years, n (%)	16 (6.3)	10 (6.1)	0.994		
20 - 30 years, n (%)	128 (50.4)	83 (50.3)			
>30 years, n (%)	110 (43.3)	72 (43.6)			
BMI, mean (SD)	24.67 (SD 5.46)	24.91 ±5.14	0.649		
Underweight, n (%)	21 (8.3)	11 (6.7)	0.797		
Normal, n (%)	128 (50.4)	82 (49.7)			
Overweight, n (%)	63 (24.8)	44 (26.7)			
Obesity grade 1, n (%)	28 (11.0)	22 (13.3)			
Obesity grade 2, n (%)	14 (5.5)	6 (3.6)			
Leucocyte Esterase (Positive), n (%)	107 (42.1)	53 (32.1)	0.050	1.54	1.02 – 2.32
Nitrite positive, n (%)					
ANC**, mean (SD)	6.20 ±3.05	7.08 ±2.70	0.002		
<6, n (%)	105 (41.3)	48 (29.1)	Ref		
≥6, n (%)	149 (58.7)	117 (70.9)	0.015	1.71	1.13 – 2.63
Fetal Presentation					
Cephalic, n (%)	202 (79.5)	151 (91.5)	0.002	2.78	1.48 – 5.20
Transverse, n (%)	17 (6.7)	8 (4.8)	Ref		
Oblique, n (%)	1 (0.4)	0 (0.0)	Ref		
Breech, n (%)	34 (13.4)	6 (3.6)	Ref		
Delivery Method					
Section Caesarean, n (%)	129 (58.1)	93 (41.9)	0.309	0.80	0.54 – 1.18
Spontaneous, n (%)	71 (28.0)	19 (11.5)	Ref		
Misoprostol Induction, n (%)	39 (15.4)	24(14.5)	Ref		
Oxytocin Augmentation, n (%)	14 (5.5)	20 (12.1)	Ref		
Forceps, n (%)	1 (0.4)	5 (3.0)	Ref		
Vacuum, n (%)	0 (0.0)	4 (2.4)	Ref		
Parity					
Primipara, n (%)	229 (90.2)	157 (95.2)	0.095	1.81	0.82 – 4.00
Multipara, n (%)	25 (9.8)	8 (4.8)	Ref		
Birth Weight, mean (SD)	1794.42 ±529.92	2867.85 ±399.19	<0.001		
ELBW (<1000g), n (%)	24 (9.4)	0 (0.0)			
VLBW (1000-1499g), n (%)	48 (18.9)	1 (0.6)			
LBW (1500-2499g), n (%)	163 (64.2)	24 (14.5)	<0.001	1.54	1.02 – 2.32
Normal (≥ 2500g), n (%)	19 (7.5)	140 (84.8)	Ref		

ELBW: Extremely Low Birth Weight; VLBW: Very Low Birth Weight; LBW: Low Birth Weight

*Bivariate analysis using the chi-square test

**Antenatal Care is divided into two categories: less than 6 times visits, and equal to or more than 6 times

Table 3 Multiple Logistic Regression of Predictors of Preterm Birth

Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval	p-value
Abnormal Fetal Position	2.843	1.479 – 5.465	0.002
Prenatal Care	0.907	0.844 – 0.976	0.009
Leukocyte Esterase (Positive)	1.572	1.016 – 2.433	0.042

Table 4 Bivariate Analysis based on APGAR 5' Outcomes*

Variable	Normal (n=330)	Asphyxia (n=90)	p-value	OR	95% CI
Maternal Age, mean (SD)	29.24 (6.94)	30.20 (6.80)	0.238		
<20 years, n (%)	23 (7.0)	3 (3.3)	0.302		
20 - 30 years, n (%)	168 (50.9)	43 (47.8)			
>30 years, n (%)	139 (42.1)	44 (48.9)			
BMI, mean (SD)	24.59 (5.16)	25.45 (5.90)	0.214		
Underweight, n (%)	29 (8.8)	3 (3.3)	0.172		
Normal, n (%)	161 (48.8)	49 (54.4)			
Overweight, n (%)	88 (26.7)	19 (21.1)			
Obesity grade 1, n (%)	39 (11.8)	12 (13.3)			
Obesity grade 2, n (%)	13 (3.9)	7 (7.8)			
Leucocyte Esterase (Positive), n (%)	127 (38.5)	34 (37.8)	>0.999	0.97	0.60 – 1.57
Nitrite positive, n (%)	16 (4.8)	1 (1.1)	0.196	0.22	0.03 – 1.69
ANC*, mean (SD)	6.74 (3.01)	5.93 (2.72)	0.016		
<6, n (%)	114 (34.5)	39 (43.3)	Ref		
>=6, n (%)	216 (65.5)	51 (56.7)	0.158	0.69	0.43 – 1.11
Fetal Presentation					
Cephalic, n (%)	285 (86.4)	69 (76.7)	0.026	1.93	1.08 – 3.45
Transverse, n (%)	20 (6.1)	5 (5.6)	Ref		
Oblique, n (%)	1 (0.3)	0 (0.0)	Ref		
Breech, n (%)	24 (7.3)	16 (17.8)	Ref		
Delivery Method					
Sectio Caesarean, n (%)	176 (53.3)	47 (52.2)	<0,001	3,81	2,16 - 6,71
Spontaneous, n (%)	81 (24.5)	9 (10.0)	Ref		
Misoprostol induction, n (%)	35 (10.6)	28 (31.1)	Ref		
Oxytocin Augmentation, n (%)	29 (8.8)	5 (5.6)	Ref		
Forceps, n (%)	5 (1.5)	1 (1.1)	Ref		
Vacuum, n (%)	4 (1.2)	0 (0.0)	Ref		
Parity					
Primipara, n (%)	303 (91,8)	84 (93,3)	0,801	1,25	0,50 - 3,12
Multipara, n (%)	27 (8.2)	6 (6.7)	Ref		

Variable	Normal (n=330)	Asphyxia (n=90)	p-value	OR	95% CI
Birth weight, mean (SD)	2365.33 (642.73)	1685.79 (711.40)	<0,001		
ELBW (<1000g), n (%)	6 (1.8)	18 (20.0)			
VLBW (1000-1499g), n (%)	28 (8.5)	21 (23.3)			
LBW (1500-2499g), n (%)	151 (45.8)	36 (40.0)	<0,001	2,3	1,21 - 4,39
Normal ($\geq$ 2500g), n (%)	145 (43.9)	15 (16.7)	Ref		

ELBW: Extremely Low Birth Weight; VLBW: Very Low Birth Weight; LBW: Low Birth Weight

*Bivariate analysis using the chi-square test

**Antenatal Care is divided into two categories: less than 6 times visits, and equal to or more than 6 times

that neonatal asphyxia was significantly associated with fewer ANC visits, non-cephalic fetal presentations, specific delivery methods, and lower birth weights. The normal APGAR group had a significantly higher mean number of ANC visits (6.74 ± 3.01 vs. 5.93 ± 2.72 ; $p=0.016$). Meanwhile, cephalic presentation was associated with a higher likelihood of a normal outcome ($p=0.026$; $OR=1.93$). Delivery method ($p<0.001$) and birth weight ($p<0.001$) showed the strongest associations. Neonates in the asphyxia group had a lower mean birth weight (1685.79 ± 711.40 g) and a higher prevalence of Extremely Low Birth Weight (20.0%) than the normal group.

Importantly, LE positivity was not significantly associated with 5-minute APGAR scores ($p>0.999$). This indicates that while LE is a significant predictor of preterm birth, it does not determine neonatal asphyxia in this cohort.

Discussion

This study analyzed demographic and clinical data from 420 mothers who delivered at Hasan Sadikin General Hospital. The cohort was characterized by a predominance of mothers aged 20–30 years (50.9%), a high rate of multiparity (92.1%), and a high frequency of Cesarean sections (53.1%). Notably, a significant proportion of neonates were born with low birth weight (1500–2499 g), reflecting the high incidence of preterm

birth at this referral center. This study aimed to evaluate the association between urinary leukocyte esterase (LE) results and clinical outcomes, specifically gestational age, neonatal asphyxia, and birth weight.

The analysis demonstrated a significant association between positive urinary LE and both preterm birth ($p=0.05$) and lower birth weight ($p<0.001$). However, no significant association was found with neonatal asphyxia ($p>0.99$). Elevated LE levels are a reliable indicator of inflammation or infection typically associated with UTIs. The data suggest that LE is a significant predictor of delivery timing but not a primary determinant of the neonate's immediate physical status (APGAR scores). This implies that neonatal outcomes may be more heavily influenced by other factors, such as maternal comorbidities, antenatal care frequency, and acute intrapartum complications. These findings are consistent with previous studies that also failed to find a significant correlation between LE and these events.

Urinary tract infections during pregnancy are often triggered by anatomical and physiological changes. Increased progesterone levels relax smooth muscle in the urinary tract, slowing urine flow and facilitating the retrograde ascent of bacteria to the kidneys. These infections trigger inflammatory cascades that can lead to uterine contractions and damage to amniotic membranes, thereby increasing the risk of preterm labor.^{15,17} Previous literature suggests

complications of UTIs during pregnancy include PPRM (6.3%), preterm labor (11%), and low birth weight (8.2%).¹⁸

Research findings at Dr. Kariadi General Hospital in Semarang indicate a link between nitrite levels and the incidence of UTIs in pregnant women.¹⁹ A meta-analysis indicates a significant association between UTIs during pregnancy and preterm birth.²⁰ Women with UTIs have a higher risk of preterm birth, with an adjusted risk ratio (aRR) of 1.1–1.4. Among women diagnosed with infections caused by various bacterial species, 28.8% experienced preterm birth. The risk of PTB remains high even with antibiotic treatment (aRR 1.4 for those treated, aRR 1.5 for those untreated).

Based on the research data, 420 patients met the inclusion criteria, and 107 had positive leukocyte esterase test results associated with preterm birth. This study found a correlation between leukocyte esterase and the incidence of preterm delivery at Dr. Hasan Sadikin General Hospital (p -value = 0.05). These findings align with Wibawa,²¹ which found that leukocyturia has a significant correlation with preterm birth and premature membrane rupture. These results contradict a study by Pratiwi,²² which indicated no significant correlation between leukocyte esterase and the latent period of premature membrane rupture or preterm birth. These differing results may be due to studies that did not specify inclusion and exclusion criteria or failed to control for bias and confounding factors. According to the WHO, preterm birth can be caused by maternal factors such as multiple pregnancies, infections during pregnancy, chronic conditions in the mother, and genetic factors. Preterm birth can also be caused by the mother's lifestyle, such as dietary habits or smoking.²³

Untreated UTIs can lead to complications such as premature rupture of membranes, chorioamnionitis, anemia, preterm birth, low birth weight, and intrauterine growth

restriction (IUGR). Therefore, early screening and treatment of UTIs in pregnant women are important to reduce the risk of infection.²⁴

Regarding neonatal outcomes, this study found no significant correlation between LE and 5-minute APGAR scores. This contradicts findings by Chiabi et al., who suggested that UTIs could increase the risk of neonatal asphyxia by up to fifteen-fold. The proposed mechanism involves activation of the monocyte–macrophage system and the subsequent release of cytokines that stimulate prostaglandin biosynthesis, potentially compromising fetal oxygenation. The lack of association in our study suggests that at Dr. Hasan Sadikin General Hospital, labor management or other physiological factors may mitigate the direct impact of maternal inflammation on neonatal respiratory status.

²⁵

This study has several limitations, including a potentially small sample size and unmeasured confounding factors, which may influence the results. While this research identifies LE as a significant marker, it examines only a subset of the multifactorial causes of preterm birth. At Dr. Hasan Sadikin General Hospital, the findings indicate that urinary tract infection is the primary cause of preterm birth. Other contributing factors should still be considered. Future prospective studies should incorporate urine cultures (the gold standard) alongside dipstick testing to further refine the prognostic value of LE.¹⁵ Despite these limitations, LE remains a critical diagnostic adjunct in resource-limited settings where rapid clinical decision-making is essential.

Conclusion

A positive leukocyte esterase (LE) test is a statistically significant risk factor for preterm birth, increasing the likelihood by about 1.5-fold. However, LE positivity is not associated with neonatal asphyxia or low 5-minute

APGAR scores. While LE screening is an effective and rapid tool for identifying mothers at risk of preterm delivery, it does not predict the newborn's immediate respiratory or neurological status.

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