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Original Article

Accuracy of Raised Maternal Total Leukocyte Count for the Diagnosis of Chorioamnionitis in Patients Presenting with Preterm Prelabour Rupture of Membrane to a Tertiary Care Hospital

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ABSTRACT

Introduction: Scabies is a highly contagious parasitic infestation predominantly affecting children in resource-limited settings. Both topical permethrin 5% cream and benzyl benzoate 25% lotion are used in clinical practice, yet comparative data in the pediatric population from local tertiary care settings remain limited. **Objective**: To compare the efficacy and safety of topical permethrin 5% cream with topical benzyl benzoate 25% lotion in children with scabies presenting to a tertiary care dermatology centre. **Study Design**: Quasi-experimental study. **Setting**: Department of Dermatology, Mayo Hospital, Lahore. Duration: 1st January 2024 to 31st December 2024. **Subjects and Methods**: A total of 150 children aged 3–14 years with clinically diagnosed scabies were enrolled and allocated by alternate assignment to two groups of 75 each. Group A received topical permethrin 5% cream and Group B received topical benzyl benzoate 25% lotion. Clinical cure rates, time to pruritus resolution, and local adverse effects were assessed at 2 and 4 weeks following the first application. **Results**: At 2 weeks, clinical cure was achieved in 68 (90.7%) patients in Group A compared with 54 (72.0%) in Group B (p=0.006). At 4 weeks, cure rates were 96.0% and 84.0% respectively (p=0.023). Mean time to pruritus resolution was significantly shorter in Group A (8.1 ± 2.3 days vs 11.9 ± 3.4 days, p<0.001). Any adverse effect was recorded in 20.0% of Group A versus 50.7% of Group B (p<0.001). **Conclusion**: Topical permethrin 5% cream demonstrated superior efficacy and a more favorable safety profile compared with benzyl benzoate 25% lotion in children with scabies and is recommended as the preferred first-line scabicidal agent in this population. **Keywords**: Scabies, permethrin, benzyl benzoate, children, efficacy, safety, quasi-experimental.

INTRODUCTION

Preterm delivery is a worldwide public health problem and it occurs approximately in 6-12% of all pregnancies [1]. Preterm prelabour rupture of membranes (PPROM) is defined as amniotic fluid leakage before 37 weeks of gestation (confirmed by LMP or 1st Trimester Ultrasound) and it represents approximately 30-40% of all preterm deliveries. PPROM is responsible for substantial proportion of adverse maternal and neonatal complications associated with gestational age and risk of infection [2, 3]. Chorioamnionitis is an acute inflammation of membranes and chorion of the placenta, typically due to ascending bacterial infection in the setting of membrane rupture. It is frequently associated with preterm labor and delivery. At least 40% of all preterm births have been estimated to occur with mothers who have an intrauterine infection, which is largely subclinical [4]. The lower the gestational age at

delivery, the greater the frequency of intrauterine infection. Total leukocyte count (TLC) has been proposed as a marker of chorioamnionitis but studies regarding its diagnostic accuracy has shown not only scarcity but also considerable variation. An earlier study reported its sensitivity and specificity as 85.7% and 87.6% [5] respectively while later another study reported it the sensitivity, specificity, positive and negative predictive value as 66.7%, 94.4%, 57.14% and 92.13% [6] respectively. No local study is available in this context so far.

The rationale of this study is to determine the accuracy of TLC in the diagnosis of Chorioamnionitis in patients with PPROM presenting to a tertiary care hospital. As the literature available on this is limited and controversial with no such study done before in our population, this study will further provide evidence regarding the role of TLC in the diagnosis. In case of high level of accuracy of raised TLC for the diagnosis of Chorioamnionitis, the obstetrician will be able to predict and manage this condition timely and properly with a simple test done regularly and easily available to improve the maternal and neonatal outcome.

MATERIALS AND METHODS

Over a period of six months, from 1st March 2019 to 31st August 2019, this cross-sectional study was conducted in the Department of Obstetrics and Gynecology, Sheikh Zayed Medical College/Hospital, Rahim Yar Khan. A total of 120 women with preterm prelabour rupture of membrane were enrolled through non-probability consecutive sampling. Sample size was calculated using World Health Organization sample size software at 95% confidence level, taking expected prevalence of chorioamnionitis as 40%, expected sensitivity of raised total leukocyte count as 66.7% with 7% margin of error, and expected specificity as 94.4% with 5% margin of error, while placental histopathology was taken as the gold standard.

Women aged 19 to 35 years presenting with preterm prelabour rupture of membrane were included. Preterm prelabour rupture of membrane was defined as painless vaginal leaking apparent in the fornices on per speculum examination between 24 and 37 completed weeks of gestation, determined by last menstrual period or ultrasound in patients with uncertain dates. Patients were excluded if they had any acute illness such as acute chest infection, human immunodeficiency virus infection, diabetes mellitus, lymphoma, leukemia, history of cervical incompetence, or refusal to participate in the study.

After informed consent, demographic and obstetric details including age, parity, and gestational week were recorded on a structured proforma. A 5 ml blood sample was collected under aseptic measures and sent to the laboratory for total leukocyte count estimation. Raised maternal total leukocyte count was defined as total leukocyte count >15000 cells/mm^3, while total leukocyte count <15000 cells/mm^3 was taken as normal. All patients were managed according to standard obstetric protocol until delivery. After the third stage of labour, placental tissue was collected by standard procedure and sent in a sterilized formalin container to the pathology laboratory. Chorioamnionitis on placental biopsy was defined by the presence of polymorphonuclear leukocyte infiltration of placental membranes and villi. Absence of polymorphonuclear leukocyte infiltration was considered negative for chorioamnionitis. Confidentiality of all patient data was maintained.

Statistical analysis: Data was entered and analyzed using Statistical Package for Social Sciences version 23.0. Quantitative variables such as age were presented as mean and standard deviation. Qualitative variables including raised total leukocyte count and histopathological diagnosis of chorioamnionitis were presented as frequency and percentage. A 2 × 2 table was constructed to calculate sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of raised maternal total leukocyte count for diagnosis of chorioamnionitis, while placental histopathology was taken as the gold standard. Chi-square test was used to assess the association between raised total leukocyte count and histopathological chorioamnionitis. Age-based stratification was also performed. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 120 women with preterm prelabour rupture of membrane were included. The age ranged from 19 to 35 years with a mean age of 27.950±2.95 years. Raised maternal total leukocyte count was observed in 46 patients, while 74 had normal total leukocyte count. Placental histopathology confirmed chorioamnionitis in 42 patients and was negative in 78 patients. These findings indicate that raised maternal total leukocyte count detected a slightly higher proportion of suspected cases than placental histopathology.

Table 1. Baseline age and overall frequency of raised maternal total leukocyte count and histopathological chorioamnionitis

Variable	Result
Total patients	120
Age range	19-35 years
Mean age	27.950±2.95 years
Raised maternal TLC positive	46 (38.3%)
Raised maternal TLC negative	74 (61.7%)
Histopathology positive for chorioamnionitis	42 (35.0%)
Histopathology negative for chorioamnionitis	78 (65.0%)

When raised maternal total leukocyte count was compared with placental histopathology, 33 cases were true positive and 65 were true negative. False positive results were observed in 13 patients, while false negative results were observed in 9 patients. The association between raised total leukocyte count and histopathological diagnosis of chorioamnionitis was statistically significant, with a chi-square value of 44.2 and $p<0.001$.

Table 2. Comparison of raised maternal total leukocyte count with placental histopathology

Raised maternal TLC	Histopathology positive	Histopathology negative	Total
Positive	33 (TP)	13 (FP)	46
Negative	9 (FN)	65 (TN)	74
Total	42	78	120

Chi-square = 44.2, $p<0.001$, TP: true positive, FP: false positive, FN: false negative, TN: true negative.

Raised maternal total leukocyte count showed a sensitivity of 78.5%, specificity of 83.3%, and diagnostic accuracy of 82.0% for diagnosis of chorioamnionitis using placental histopathology as the gold standard. Positive predictive value was 71.7%, while negative predictive value was 87.8%. The higher negative predictive value suggests that a normal total leukocyte count was comparatively more useful for excluding histopathological chorioamnionitis than a raised count was for confirming it.

Table 3. Diagnostic accuracy indices of raised maternal total leukocyte count

Diagnostic parameter	Value
Sensitivity	78.5%
Specificity	83.3%
Diagnostic accuracy	82.0%
Positive predictive value	71.7%
Negative predictive value	87.8%

Age-stratified results were reported for two age groups. In the 18-27 years group, the reported sensitivity, specificity, diagnostic accuracy, positive predictive value, and negative predictive value were 38.6%, 68.1%, 53.0%, 54.8%, and 52.6%, respectively. In the 28-35 years group, the corresponding values were 38.1%, 63.1%, 51.0%, 50.8%, and 50.5%. These stratified results showed no statistically significant association in either age group.

Table 4. Age-stratified diagnostic performance of raised maternal total leukocyte count

Age group	Reported n	Sensitivity	Specificity	Diagnostic accuracy	PPV	NPV	p-value
18-27 years	44	38.6%	68.1%	53.0%	54.8%	52.6%	0.503
28-35 years	76	38.1%	63.1%	51.0%	50.8%	50.5%	0.867

Important data note: The age-stratified cross-tabulated counts in the dissertation show internal inconsistency between stated subgroup size and row/column totals. The above table includes the reported stratified diagnostic indices, but the original SPSS output should be checked before journal submission.

DISCUSSION

The present study evaluated the diagnostic accuracy of raised maternal total leukocyte count for detection of chorioamnionitis among women presenting with preterm prelabour rupture of membrane. The main finding was that total leukocyte count >15000 cells/mm³ showed moderate diagnostic performance, with sensitivity of 78.5%, specificity of 83.3%, diagnostic accuracy of 82.0%, positive predictive value of 71.7%, and negative predictive value of 87.8%. These findings indicate that total leukocyte count may provide useful initial information at admission, particularly where advanced inflammatory markers or amniotic fluid testing are not readily available.

Maternal leukocyte assessment has practical value because it is inexpensive, rapid, widely available, and routinely performed in obstetric units. However, interpretation during pregnancy requires caution because physiological leukocytosis and trimester-related variation reduce the discriminatory value of isolated white blood cell count [7]. In this study, a count >15000 cells/mm³ was associated with histopathological chorioamnionitis, as shown by the significant comparison with placental biopsy findings. The comparatively higher negative predictive value suggests that normal leukocyte count may be more helpful for ruling out chorioamnionitis than a raised count is for confirming it.

The diagnostic indices observed in the present study are broadly comparable with earlier work, although variation exists between published reports. Pandey et al. reported sensitivity and specificity of 85.7% and 87.6%, respectively, for leukocyte count at admission in women managed expectantly for preterm prelabour rupture of membrane [5]. In contrast, Deo et al. reported sensitivity, specificity, positive predictive value, and negative predictive value of 66.7%, 94.4%, 57.14%, and 92.13%, respectively [6]. The present results fall between these estimates, with a stronger negative predictive value than positive predictive value. Such variation may be explained by differences in diagnostic threshold, timing of blood sampling, patient selection, gestational age, latency period, and whether clinical or histological chorioamnionitis was used as the reference outcome.

Previous studies have shown that intra-amniotic inflammation and fetal inflammatory response are common in preterm prelabour rupture of membrane and are associated with adverse maternal and neonatal outcomes [8-12]. Yoon et al. reported that women with preterm premature rupture of membranes and chorioamnionitis had higher maternal white blood cell count at hospital admission, supporting the biological basis for using leukocyte count as a marker of inflammatory activity [9]. However, leukocyte count alone cannot fully represent the intra-amniotic inflammatory environment. Chorioamnionitis is biologically heterogeneous, with different microbial agents, microbial loads, and host inflammatory responses. Oh et al. reported a more intense inflammatory response in cases with genital mycoplasmas, while other studies showed that the inflammatory response may be related to microbial load rather than organism presence alone [13-16].

Different leukocyte thresholds have been used in previous studies, commonly ranging from 10×10^9/L to 16×10^9/L [9, 17, 18]. The threshold of >15000 cells/mm³ used in this study lies within this reported range. Although the overall diagnostic accuracy was acceptable, the positive predictive value was modest, indicating that raised leukocyte count should not be used as an independent confirmatory test. Romero et al. emphasized that preterm prelabour rupture of membrane can be classified into subgroups based on microbial and sterile intra-amniotic inflammation, allowing more precise interpretation of inflammatory markers [19]. Similarly, cervical fluid interleukin-6 and maternal serum C-reactive protein have been studied as adjunctive markers of intra-amniotic complications [20, 21].

The findings support the use of raised maternal total leukocyte count as a screening adjunct rather than a definitive diagnostic test. Placental histopathology remains more reliable for confirmation, but it is available only after delivery and therefore cannot guide early clinical decision-making. In routine clinical practice, total leukocyte count may be interpreted together with maternal fever, uterine tenderness, fetal tachycardia, foul-smelling liquor, C-reactive protein, and clinical progression. Further

studies with complete subgroup data, standardized sampling time, and comparison with additional biomarkers may improve risk prediction in women with preterm prelabour rupture of membrane.

CONCLUSION

Leukocyte count of >15000 cells/mm^3, at the time of admission has shown sensitivity of 78.5%, specificity 83.3%, diagnostic accuracy by 82%, PPV 71.7% and NPV 87.8% for diagnosis of Chorioamnionitis. Whereas the individual components of differential leukocyte counts were found to be not of much help in this regard.

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