E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.299

Research Article

Diagnostic Accuracy of Fetal Thymus Transverse Diameter on Ultrasound for Prediction of Chorioamnionitis in Preterm Prelabor Rupture Of Membranes (PPROM): Histopathology as the Gold Standard

Nimra Zulfiqar[1*], Najma Khurshid[2], Sadia Nasir Kiyani[3], Qamar Iqbal[4], Falak Khalil[5], Naseem Fatima[6], Attia Mustafa[7]

[1*]Department of Gynaecology and Obstetrics, Al Ahli Hospital, Doha, Qatar.
[2,3,4]MCH, Department of Gynaecology and Obstetrics, PIMS Hospital, Islamabad, Pakistan.
[5,6]MCH, Department of Gynaecology and Obstetrics, PIMS Hospital, SZABMU, Islamabad, Pakistan.
[7]Department of Obstetrics and Gynecology, Sir Gangaram Hospital, Lahore, Pakistan.

Corresponding Author: Nimra Zulfiqar
Department of Gynaecology and Obstetrics, Al Ahli Hospital, Doha, Qatar.
Email: lifecare.nr@gmail.com
Received: 14.04.2026, Revised: 02.07.2026, Accepted: 13.07.2026

ABSTRACT

Objectives: To determine the diagnostic accuracy of fetal thymus transverse diameter measured by ultrasound for predicting chorioamnionitis in women with preterm prelabor rupture of membranes (PPROM), using histopathology as the gold standard.

Study design: Cross-sectional validation study.

Place and duration of study: Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital, Lahore. From June-2024 to December-2024.

Methodology: A total of 105 women aged 18 to 40 years, gestational age ≥22 and <37 weeks, with singleton pregnancy, and diagnosed with PPROM were enrolled. Ultrasound was performed at the time of admission, and the fetal thymus was visualized in the transverse section of the fetal thorax at the three-vessel view. A small fetal thymus was considered when it was below the 5th percentile for gestational age. Placental and membrane tissues were examined histopathologically for chorioamnionitis after delivery. Diagnostic accuracy parameters, including sensitivity, specificity, and predictive values, were calculated.

Results: Histopathology diagnosed chorioamnionitis in 45 (42.86%), while a small fetal thymus was detected by ultrasound in 46 (43.81%) of women. There were 39 true positive, 7 false positive, 6 false negative, and 53 true negative cases. This assessment tool showed a sensitivity of 86.67%, specificity of 88.33%, positive predictive value of 84.78%, negative predictive value of 89.83%, and overall diagnostic accuracy of 87.62%.

Conclusion: Ultrasound assessment of fetal thymus transverse diameter demonstrated a good diagnostic accuracy for predicting chorioamnionitis in women with PPROM and therefore may serve as a useful non-invasive antenatal marker.

Keywords: Chorioamnionitis, Fetal Membranes, Fetal Thymus, Premature Rupture, Ultrasonography, Sensitivity and Specificity.

INTRODUCTION

Preterm prelabor rupture of membranes (PPROM) refers to rupture of the fetal membranes before the onset of labor and before 37 completed weeks of gestation. In obstetrics, PPROM is associated with preterm birth (PTB) which can lead to substantial maternal and neonatal morbidity. The condition contributes to a considerable proportion of preterm deliveries and may be complicated by ascending intra-amniotic infection.[1,2] In such pregnancies, chorioamnionitis is among the most significant complications, as the intrauterine inflammation can affect both maternal and fetal wellbeing and may contribute to adverse outcomes. Histological chorioamnionitis has been reported to occur in different proportions depending on gestational age (GA) and clinical factors, with higher rates reported in pregnancies complicated by preterm labor and ruptured membranes.[3,4]

Chorioamnionitis is not necessarily associated with maternal clinical signs. Inflammation may therefore remain undetected until delivery in cases of subclinical intra-amniotic infection, and it is only established through histological diagnosis of the placenta and membrane at delivery.[5] This important reference standard for identifying inflammatory lesions is, however, inherently a post-delivery diagnostic method and hence cannot provide timely antenatal information for making important decisions regarding fetal surveillance, antibiotic therapy, timing of delivery and counsel about possible neonatal risk. A simple, easily available, and reliable antenatal marker would therefore be clinically valuable in women presenting with PPROM.[6]

The fetal inflammatory response syndrome (FIRS) is a systemic fetal inflammatory state which is associated with intra-amniotic infection and inflammation. The fetal thymus (FT) is an important component of the developing immune system and may undergo involution in response to significant inflammatory stress.[7] This response can be observed through ultrasonography (USG) by a reduction in fetal thymic size (FTS). On USG, FT can be identified on the transverse view of the fetal thorax at the level of the great vessels. The fetal thymus transverse diameter (FTTD) increases with advancing GA; therefore, its interpretation according to gestational-age-specific reference values is important as TD less than 5th percentile has been used as a definition of a small FT.[8]

USG studies conducted previously have suggested a link between small FT size and histological chorioamnionitis in pregnancies complicated by PPROM. The reported diagnostic performance, however, varies considerably between studies, particularly for specificity and predictive values. These variations may reflect differences in study populations, GA, USG technique, diagnostic definitions and the reference standards. Despite these variations, measurement of the FT remains attractive because it is non-invasive, can be performed during the antenatal period and may provide useful information before histological confirmation is available.[9,10]

PPROM is a common condition in our local clinical settings and must be promptly evaluated for both maternal and fetal infection risk. Delayed recognition of intra-amniotic inflammation may contribute to the risk of poor perinatal outcomes, particularly in cases where the fetal inflammatory response is already initiated. Assessment of FT size may therefore provide an additional non-invasive approach for early identification of increased risk of chorioamnionitis. This study was initiated to determine the diagnostic accuracy of the TD of FT measured by USG for predicting chorioamnionitis in women with PPROM, using histological examination as the reference standard. These findings may help to assess the diagnostic utility of USG to support earlier identification of chorioamnionitis in pregnancies complicated by PPROM in our local obstetric units.

METHODOLOGY

This cross-sectional validation study was conducted at the Department of Obstetrics and Gynecology, Sir Ganga Ram Hospital, Lahore, from June-2024 to December-2024, after approval from the ethical committee of the hospital.

The sample size was calculated using a confidence level of 95%, an expected prevalence of chorioamnionitis of 48%, and the sensitivity and specificity of TD of the FT as 91% and 81%, respectively. With margins of error of 9% for sensitivity and 10% for specificity, the sample sizes were calculated for these two parameters, and the larger value of 105 participants was selected as the final sample size.[11]

A total of 105 women aged between 18 to 40 years with a singleton pregnancy, GA ≥ 22 and < 37 weeks, and diagnosed with PPROM were included in this study using consecutive sampling. Written informed consent was obtained from each participant prior to inclusion. The exclusion criteria consisted of women with fetal growth restriction, major fetal malformation, known chromosomal abnormality, vaginal bleeding, or signs of fetal hypoxia.

Baseline information was collected and recorded for each woman including maternal age, GA, parity and duration of membrane rupture. Each participant then underwent targeted USG assessment of the FT at the time of admission. The FT was assessed at the three-vessel view, identified as the transverse section of the fetal thorax lying between the sternum anteriorly and the great vessels posteriorly.[12]

The TD was defined as the maximum diameter of the FT measured perpendicular to the line joining the sternum and spine. The measurement was obtained 3 times and the mean value was used for analysis. A small FT

was defined as a TD below the 5th percentile for GA according to the reference nomogram.[13] Placental and membrane tissue was submitted for histopathological examination after delivery. Histological chorioamnionitis was diagnosed when neutrophilic infiltration was present in the chorion-decidua, chorionic plate, amnion or umbilical cord. USG assessment and histopathological results were compared to determine the true positive (TP), false positive (FP), false negative (FN) and true negative (TN) classifications. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated by using these findings.

Data were analyzed using SPSS version 26.0. Quantitative variables were summarized as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. A 2×2 contingency table was constructed to compare USG findings with the gold standard histopathology findings and the diagnostic accuracy measures were calculated. The chi-square test was used to assess the association between the USG classification and histopathological diagnosis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of USG findings were calculated. A p-value ≤0.05 was considered statistically significant.

RESULTS

The final analysis included a total of 105 women, with mean age of 28.30 ± 6.17 years (an age range of 18–40 years). Histopathological examination diagnosed chorioamnionitis in 45 (42.86%) of participants, whereas USG assessment identified a small FT in 46 (43.81%) of the study participants. The details of demographics and clinical findings are shown in Table-I.

Table-I: Demographics, Clinical Characteristics and Diagnostic Findings (N = 105)

Demographic and clinical variables	Mean ± SD / n (%)
Maternal age (years)	28.30 ± 6.17
Gestational age (weeks)	32.36 ± 2.82
Parity	2.36 ± 1.25
Chorioamnionitis as per histological findings	45 (42.86)
Chorioamnionitis as per USG findings	46 (43.81)

There were 39 TP cases and 53 TN cases with USG assessment, keeping histological findings as reference standard. Seven participants were classified as FP and six as FN, as shown in Table-II.

Table-II. Comparison of USG Assessment of Fetal Thymus with Histology as the Gold Standard (N = 105)

USG of small FT	Histology positive	Histology negative	Total
Positive	39 (True positive)	7 (False positive)	46
Negative	6 (False negative)	53 (True negative)	59
Total	45	60	105

Based on these findings, USG assessment of the FT demonstrated a high sensitivity (86.67%), specificity (88.33%), PPV (84.78%), and NPV (89.83%) and overall diagnostic accuracy (87.62%) for predicting chorioamnionitis in women with PPROM. The association between USG classification and histological diagnosis was found to be significant ($p < 0.001$).

Table-III: Diagnostic Accuracy of TD of the FT on USG Keeping Histology as the Gold Standard

Diagnostic parameter	Results
Sensitivity (%)	86.67
Specificity (%)	88.33
PPV (%)	84.78
NPV (%)	89.83
Diagnostic accuracy	87.62

DISCUSSION

This study included 105 women with PPROM, and USG of FTTD demonstrated good diagnostic performance for predicting histological chorioamnionitis. Histopathological examination confirmed chorioamnionitis in 45 (42.86%) women, while small FT was detected by ultrasound in 46 (43.81%). The USG assessment correctly identified 39 TP and 53 TN cases, with 7 FP and 6 FN cases. This assessment demonstrated a high sensitivity of 86.67%, specificity of 88.33%, PPV of 84.78%, NPV of 89.83%, and diagnostic accuracy of 87.62%. The significant association between USG classification and histopathological diagnosis further supported the potential value of FT size as a non-invasive marker of fetal inflammatory response.

Similar findings have also been reported in previous studies that evaluated FT size as a reliable antenatal marker for the prediction of chorioamnionitis in pregnancies complicated by PPROM.

Zych-Krekora K et al. established GA-specific reference ranges for FT size, noting that thymus size is proposed as a marker for conditions including intrauterine growth restriction, preterm birth, and chorioamnionitis. In this large study involving 410 fetuses, TD, circumference, and area were reliably measured across GA (14–40 weeks). The results yielded statistically significant growth models ($p<0.0005$), supporting the use of thymus nomograms for identifying at-risk fetuses.[14]

Aksakal SE et al. evaluated transverse, anteroposterior (AP), and areal diameters of FT to predict histological chorioamnionitis in 50 patients with PPROM. Histological chorioamnionitis occurred in 48% of cases. TDFT was a better predictor than other assessments and showed 91% sensitivity, 81% specificity, 82% PPV, and 91% NPV, supporting its utility in early antenatal infection screening.[11]

Similarly, Musilova I et al. evaluated FTTD to predict histologic chorioamnionitis and funisitis in 216 PPROM pregnancies. A small FT, defined as TD <5th percentile, predicted chorioamnionitis with 79% sensitivity, 47% specificity, 71% PPV, 59% NPV ($p<0.0001$), and funisitis with 88% sensitivity, 35% specificity ($p=0.004$). Small FT was therefore found sensitive but not specific enough for clinical management.[15]

Cetin O et al. evaluated TDFT in 40 PPROM pregnancies for predicting early neonatal sepsis, comparing it with cord blood TNF-α and IL-6. Decreased TD showed 100% sensitivity, 73% specificity, 55% PPV, and 100% NPV, outperforming TNF-α (80% sensitivity, 90% specificity) and IL-6 (90% sensitivity, 63.3% specificity) in predicting early sepsis, underscoring its utility as a promising prenatal sepsis predictor.[16]

Akgün Aktaş B et al. compared thymic measurements in 50 women with PPROM and 60 women as controls (24–37 weeks). TD was significantly lower in PPROM cases (26±7.06 mm vs 35.1±11.9 mm; $p<0.001$), and thymic-thoracic ratio was also reduced (0.30±0.06 vs 0.39±0.08; $p<0.001$). There was also a significant negative correlation between fetal thymic-thoracic ratio and maternal WBC count ($r=-0.318$, $p=0.010$), supporting a link between thymic involution and maternal inflammatory response as discussed in above studies.[17]

The role of small FT for predicting chorioamnionitis was supported in a recent study by Awaad MM et al. This research compared 30 PPROM cases with 30 controls (GA 24–36 weeks) and showed that small FT size was significantly more frequent in PPROM cases ($p=0.013$), alongside higher puerperal endomyometritis (30% vs 0%) and lower Apgar scores at 5 and 10 minutes ($p<0.001$, $p=0.042$). The authors concluded that small FT may indicate subclinical chorioamnionitis and adverse neonatal outcomes.[18]

These findings across multiple studies consistently support the diagnostic accuracy of FTTD on USG for prediction of chorioamnionitis in PPROM, supporting its potential as a non-invasive marker of intrauterine inflammation. Incorporating FT assessment into routine antenatal USG protocols may therefore enhance early risk stratification and guide timely clinical decisions in this high-risk population.

This research was conducted at a single center and with a modest sample size, which may limit the generalizability of these findings to larger populations. Moreover, USG of FT size may also be influenced by fetal position, image quality and operator expertise. Another important limitation of this study is that the histopathology was available only after delivery and therefore could not provide real-time antenatal confirmation.

CONCLUSION

These findings suggest that reduction in FT size is associated with underlying histological inflammation and may provide useful antenatal

information before the availability of post-delivery histopathological confirmation. USG assessment of TD of the FT therefore appears to be a useful non-invasive approach for identifying risk of chorioamnionitis in women with PPROM. This assessment is simple and can be incorporated into routine USG evaluation of women with PPROM and may assist clinicians in identifying pregnancies requiring closer maternal and fetal surveillance and earlier consideration of management decisions. Validation of these results through further studies involving larger and diverse populations is warranted to determine the clinical usefulness of FT assessment in routine obstetric practice.

REFERENCES

1. Dayal S, Jenkins SM, Hong PL. Preterm and Term Prelabor Rupture of Membranes (PPROM and PROM) [Updated 2024 Oct 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532888/.
2. Nambiar S. Preterm birth: a syndrome with unsolved issues. In: Coomarasamy A, Di Renzo GC, Fonseca E, editors. Pregnancy shortening: etiology, prediction and prevention. The Continuous Textbook of Women's Medicine Series, Obstetrics Module, Vol 19. Glob Libr Women's Med; 2024. Available from: https://doi.org/10.3843/GLOWM.419053.
3. Menon R, Richardson LS. Preterm prelabor rupture of the membranes: A disease of the fetal membranes. Semin Perinatol. 2017;41(7):409-419. doi: 10.1053/j.semperi.2017.07.012.
4. Wahabi H, Elmorshedy H, Bakhsh H, Ahmed S, AlSubki RE, Aburasyin AS, et al. Predictors and outcomes of premature rupture of membranes among pregnant women admitted to a teaching Hospital in Saudi Arabia: a cohort study. BMC Pregnancy Childbirth. 2024;24(1):850. doi: 10.1186/s12884-024-07020-x.
5. Jain VG, Willis KA, Jobe A, Ambalavanan N. Chorioamnionitis and neonatal outcomes. Pediatr Res. 2022;91(2):289-96. doi: 10.1038/s41390-021-01633-0.
6. Goldstein JA, Gallagher K, Beck C, Kumar R, Gernand AD. Maternal-Fetal Inflammation in the Placenta and the Developmental Origins of Health and Disease. Front Immunol. 2020; 11:531543. doi: 10.3389/fimmu.2020.531543.
7. Giovannini E, Bonasoni MP, Pascali JP, Giorgetti A, Pelletti G, Gargano G, et al. Infection Induced Fetal Inflammatory Response Syndrome (FIRS): State-of-the-Art and Medico-Legal Implications-A Narrative Review. Microorganisms. 2023;11(4):1010. doi: 10.3390/microorganisms11041010.
8. Gök K, Özden S. Finding the best method for screening for gestational diabetes mellitus: fetal thymic-thoracic ratio or fetal thymus transverse diameter. Rev Assoc Med Bras (1992). 2023;69(2):303-307. doi: 10.1590/1806-9282.20221012.
9. Lanzarone V, Polkinghorne A, Eslick G, Branley J. Diagnostic tests for the prediction of histological chorioamnionitis and funisitis in pregnant women with preterm premature rupture of membranes: A systematic review. Aust N Z J Obstet Gynaecol. 2025;65(1):13-24. doi: 10.1111/ajo.13864.
10. Carter SWD, Neubronner S, Su LL, Dashraath P, Mattar C, Illanes SE, et al. Chorioamnionitis: an update on diagnostic evaluation. Biomedicines. 2023;11(11):2922. doi:10.3390/biomedicines11112922.
11. Aksakal SE, Kandemir O, Altınbas S, Esin S, Muftuoglu KH. Fetal tyhmus size as a predictor of histological chorioamnionitis in preterm premature rupture of membranes. J Matern Fetal Neonatal Med. 2014;27(11):1118-22. doi: 10.3109/14767058.2013.850666.
12. Hamamoto TENK, Hatanaka AR, França MS, Sarmento SGP, Helfer TM, Nomura RMY, et al. An enlarged fetal thymus may be the initial response to intrauterine inflammation in pregnant women at risk for preterm birth. Rev Assoc Med Bras (1992). 2023;69(5):e20221678. doi: 10.1590/1806-9282.20221678.
13. Pittyanont S, Luewan S, Tongsong T. Cardio-STIC based reference ranges of fetal thymus size in singleton pregnancies. J Ultrasound Med.

2017;36(6):1181-8. doi:10.7863/ultra.16.07041.

14. Zych-Krekora K, Krekora M, Słodki M, Grzesiak M, Kaczmarek P, Zeman K et al. Nomograms of the fetal thymus for clinical practice. Archives of Medical Science. 2021;17(6):1657–62. doi:10.5114/aoms.2019.86189.
15. Musilova I, Hornychova H, Kostal M, Jacobsson B, Kacerovsky M. Ultrasound measurement of the transverse diameter of the fetal thymus in pregnancies complicated by the preterm prelabor rupture of membranes. J Clin Ultrasound. 2013;41(5):283-9. doi: 10.1002/jcu.22027.
16. Cetin O, Dokurel Cetin I, Uludag S, Sen C, Verit FF, Guralp O. Serial ultrasonographic examination of the fetal thymus in the prediction of early neonatal sepsis in preterm premature rupture of membranes. Gynecol Obstet Invest. 2014;78(3):201-7. doi: 10.1159/000364871.
17. Akgün Aktaş B, Agaoglu Z, Atalay A, Öcal FD, Tanacan A, Şahin D. Fetal thymus size in pregnancies complicated by preterm premature rupture of the membranes: a case-control study. East J Med. 2025;30(3):397-402. doi:10.5505/ejm.2025.60343.
18. Awaad MM, Elnamoury MM, Aldorf AA, Abozeid EH. Diagnostic value of ultrasonographic assessment of fetal thymus gland size in pregnancies associated with the preterm prelabor rupture of membranes. Int J Clin Obstet Gynaecol. 2023;7(1):41-5. doi: 10.33545/gynae.2023.v7.i1a.1253.