Chorioamnionitis and Neonatal Morbidity in Extremely Preterm Infants Born at 23–28 Weeks: A Single-Centre Retrospective Study

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Article

Chorioamnionitis and Neonatal Morbidity in Extremely Preterm Infants Born at 23–28 Weeks: A Single-Centre Retrospective Study

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Abstract

Background/Objectives: Chorioamnionitis, an inflammation, with or without infection, involving the amniotic fluid, placenta, fetal membranes or decidua, can significantly impact fetal and neonatal development. This study aimed to determine the incidence of chorioamnionitis and confirm its correlation with neonatal morbidity and mortality, in a single tertiary center. **Materials and Methods:** This observational, retrospective study was conducted over three years (2019-2021) in a tertiary neonatal intensive care unit, examining 80 preterm infants born at 23-28 weeks of gestation. Pearson correlation and χ^2 tests were used to assess associations between chorioamnionitis exposure and neonatal outcomes. **Results:** Among the 80 newborns analysed, clinical chorioamnionitis was identified in 12 preterm infants, while 46 presented histological chorioamnionitis. A weak but significant negative correlation ($r = -0.27$, $p = 0.0152$) between gestational age and chorioamnionitis stage indicated that preterm infants born at lower gestational ages are more frequently exposed to this intrauterine infection. Histological chorioamnionitis stage was significantly associated with early onset sepsis ($r=0.31$, $p=0.0048$), severity of respiratory distress syndrome ($r=0.25$, $p=0.0242$), bronchopulmonary dysplasia ($r=0.26$, $p=0.0212$), and retinopathy of prematurity ($r=0.26$, $p=0.0249$). **Conclusion:** Histological chorioamnionitis was significantly associated with early onset sepsis, respiratory distress syndrome, bronchopulmonary dysplasia, and retinopathy of prematurity. No significant association was found between chorioamnionitis and neonatal mortality. While clinical diagnostic criteria for chorioamnionitis demonstrated good specificity, their poor sensitivity underscores the urgent need for improved diagnostic tools.

Keywords: chorioamnionitis; prematurity; morbidity; mortality

1. Introduction

Chorioamnionitis is defined as an inflammation, with or without infection, of any combination of the amniotic fluid, placenta, fetal membranes or decidua [1]. The term "Triple I" (referring to intrauterine inflammation, or infection, or both) has been proposed to replace the traditional term "chorioamnionitis", distinguishing between "suspected" and "confirmed" intrauterine inflammation [2]. For clinical diagnosis, according to the ACOG Clinical Practice Update (July 2024), suspected intraamniotic infection is diagnosed when maternal temperature is ≥39.0°C, or when temperature is 38.0–38.9°C alongside at least one additional clinical risk factor, including fetal tachycardia >160bpm, maternal leukocytosis >15,000/mm^3 in the absence of corticosteroid therapy, or purulent cervical

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discharge [3]. It is now recognized that the syndrome encompasses three distinct etiologies: true intraamniotic infection, sterile intraamniotic inflammation in the absence of demonstrable microorganisms, and systemic maternal inflammation induced by epidural analgesia [4,5].

Despite these clinical criteria, a significant proportion of chorioamnionitis cases remain asymptomatic and are detectable only on histological examination of the placenta. Histological chorioamnionitis refers to acute placental inflammation characterized by neutrophilic infiltration across multiple sites within the organ [6]. Building on the framework established by the Perinatal Section of the Society of Pediatric Pathology [7], the Amsterdam Placental Workshop Group Consensus Statement introduced a structured staging system for maternal inflammatory responses, distinguishing three levels of escalating severity [8]. Stage I, termed acute subchorionitis or chorionitis, marks the earliest phase, with inflammatory changes confined to the chorion. As the process advances, stage II, or acute chorioamnionitis, develops when inflammation extends beyond the chorionic plate into the fibrous chorion and/or the amnion. In its most severe form, stage III, or necrotising chorioamnionitis, the inflammatory response produces frank cellular injury and tissue necrosis affecting both the amnion and chorion.

Fetal Inflammatory Response Syndrome (FIRS) represents the fetal counterpart of the systemic inflammatory response syndrome, first described in adults. In both the fetus and the adult, the primary diagnostic criterion is an elevation of blood IL-6 >11 pg/mL in fetal blood, with characteristic multisystem involvement. FIRS typically arises in the context of chorioamnionitis, and almost 50% of pregnancies complicated by histological and/or clinical chorioamnionitis result in premature delivery [4,9]. A study of 1,116 newborns demonstrated that FIRS is associated with a higher rate of neonatal complications (including early neonatal sepsis, bronchopulmonary dysplasia, intraventricular haemorrhage, periventricular leukomalacia, acute respiratory distress syndrome, and neonatal death) compared to those without FIRS [10].

Neonatal complications associated with chorioamnionitis, and FIRS are classified as either short-term or long-term. Short-term complications include early neonatal sepsis, necrotising enterocolitis, retinopathy of prematurity, immunodeficiency, bronchopulmonary dysplasia, acute respiratory distress syndrome, white matter lesions, and intraventricular haemorrhage. Long-term complications include asthma, chronic obstructive respiratory diseases, cerebral palsy, developmental delay, hearing loss, and autism spectrum or schizophrenia disorders [4,11].

This study aimed to determine the incidence of chorioamnionitis in a cohort of extremely preterm infants and to assess its correlation with neonatal morbidity and mortality in a tertiary centre.

2. Materials and methods

2.1. Characteristics of the study

This observational, retrospective study was conducted over three years (2019–2021) in the Neonatology I Department of Cluj County Emergency Clinical Hospital. The study population consisted of preterm infants born at 23 to 28 weeks of gestational age who were admitted to the neonatal intensive care unit. Of the 109 subjects initially enrolled, 29 were excluded due to missing placental histopathological examination results, yielding a final sample of 80 subjects (40 male and 40 female). Participants were then divided into two subgroups: those exposed to stage I, II, or III chorioamnionitis (46 subjects) and those who were not (34). All data were extracted from patients' medical records and handled in strict accordance with confidentiality and anonymity regulations.

2.2. Clinical data

In the current study we analysed the correlation of chorioamnionitis exposure with in-hospital neonatal morbidities and mortalities. The neonatal morbidities analysed were: respiratory distress (RDS) and Silverman score for severity of the disease, intraventricular haemorrhage (IVH), gastrointestinal haemorrhage, pulmonary haemorrhage, pneumothorax, early onset sepsis (EOS), necrotising enterocolitis (NEC), bronchopulmonary dysplasia (BPD), and retinopathy of prematurity

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(ROP). All in-hospital complication diagnoses were extracted from the medical records of the enrolled patients.

Furthermore, the study also examined the association between maternal conditions and neonatal morbidities. Maternal and pregnancy variables studied were cervical cerclage, placenta previa, oligohydramnios, pre-eclampsia, pregnancy-induced hypertension, and urinary tract infection prior to delivery.

2.3. Statistical analysis

Data analysis was initially performed using univariate statistics (e.g., proportions, means). Subsequently, the search for a statistically significant association between the variables was conducted using Pearson's correlation test (for numerical and similar variables) and the χ^2 test (for categorical variables). For each test, relationships were considered significant if the $p \leq 0.05$. To improve the precision of our calculations, we decided to base them on histological chorioamnionitis values rather than clinically diagnosed values for the rest of the study. We therefore created a "pseudo-numeric" variable for histological chorioamnionitis by assigning the numbers 0, 1, 2, and 3 to the absence of histological chorioamnionitis and the three stages of histological chorioamnionitis severity. Given the approximate nature of this approach, we have also kept a variable of "binary chorioamnionitis" which therefore takes only two values (0 for absence and 1 for presence).

Throughout this paper, the term "histological CA stage I-II-III" is used to differentiate degrees of severity, and "with/without CA" to denote the presence or absence of histological chorioamnionitis.

2.4. Correlation analysis

A correlation heatmap was constructed using all numerical variables. Correlation coefficients and associated p-values were extracted for variable pairs meeting both thresholds: $|r| \geq 0.22$ and $p \leq 0.05$. The most clinically relevant findings are presented in Table 3.

3. Results

3.1. Study population and clinical vs histological chorioamnionitis prevalence

Clinical chorioamnionitis was identified in 12 of 80 (15%) preterm infants enrolled. In contrast, histological examination of the placenta revealed a significantly higher prevalence, with 57.5% (46 out of 80) of newborns showing signs of chorioamnionitis. Out of the 12 cases of clinical chorioamnionitis, 11 were confirmed by histopathological examination of the placenta retrospectively.

Table 1 presents an overview of the mean demographic data for the study group across several variables. We found no significant differences in demographic variables between the chorioamnionitis-exposed and non – exposed groups ($p>0.05$).

Table 1. Demographic data of study group.

	Without chorioamnionitis		**With chorioamnionitis (CA)**	
Variable	Mean	Standard Deviation	Mean	Standard Deviation
Gestational age (weeks)	25.713	1.250	25.714	1.490
Weight (g)	772.181	130.364	748.571	174.085
Length (cm)	34.359	3.165	34.714	4.497
Head circumference (HC) (cm)	24.012	2.318	23.857	1.844
Ponderal index (PI)	2.080	0.487	2.017	0.280

 doi:10.20944/preprints202605.0022.v1

3.2. Maternal and pregnancy characteristics by chorioamnionitis exposure

Cervical cerclage, placenta praevia, and oligohydramnios were observed exclusively in the CA-exposed group (17.0%, 2.1%, and 4.3% respectively), with none recorded in the non-exposed group, though these differences should be interpreted cautiously given the small sample size. Pre-eclampsia, pregnancy-associated hypertension, and urinary tract infection were all more frequent in the non-exposed group (12.1% vs. 4.3%; 12.1% vs. 6.4%; 15.2% vs. 6.4% respectively). A significant positive correlation was found between cervical cerclage and histological CA stage ($r = 0.28$, $p = 0.0121$), and a significant negative correlation between pre-eclampsia and histological CA presence ($r = –0.22$, $p = 0.0479$), however, both these findings need to be interpreted cautiously given the small sample size.

3.3. Chorioamnionitis stage and gestational age

A weak but significant negative correlation was observed between histological chorioamnionitis stage and gestational age at birth ($r=–0.27$, $p=0.0152$). While cases at the most extreme prematurity (23-24 weeks) were predominantly found in higher CA stages, the relationship was not uniform across all stages, with stages II and III both showing cases extending to 28 weeks, inclusive (Figure 1).

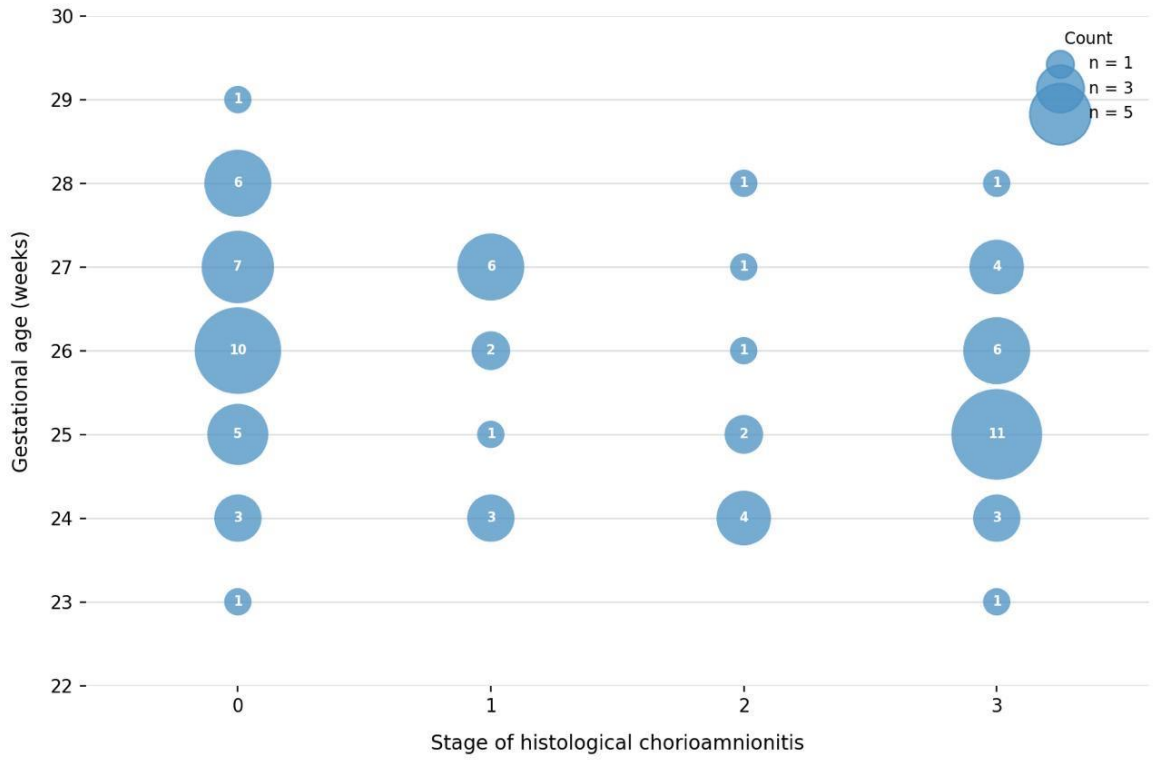

Figure 1. Relationships between chorioamnionitis stages and gestational age (stage 0 = absence of chorioamnionitis, stage 1,2,3 -stages of histological chorioamnionitis).

3.4. Neonatal transition and Apgar scores

The neonatal transition quantified by the Apgar score over the first twenty minutes after birth (Figure 2) highlights a different dynamic in newborns exposed to chorioamnionitis compared to those born without the exposure to the inflammatory environment. From the first minute of life, a significant difference is observed: the average Apgar score of newborns with CA is around 3, while that of newborns without CA is around 5. This disparity persisted over the next few minutes, with the curve of newborns exposed to CA remaining consistently below that of unexposed newborns. Nevertheless, we note a narrowing of this gap around twenty minutes, though CA-exposed infants remained below their non-exposed counterparts.

 doi:10.20944/preprints202605.0022.v1

These observations are supported statistically by significant negative correlations between histological CA presence and Apgar scores at 10 minutes (r=–0.35, p=0.0094) and 20 minutes (r=–0.39, p=0.0106), indicating that CA-exposed neonates had a more difficult transition to extrauterine life and a prolonged resuscitation requirement (Table 2).

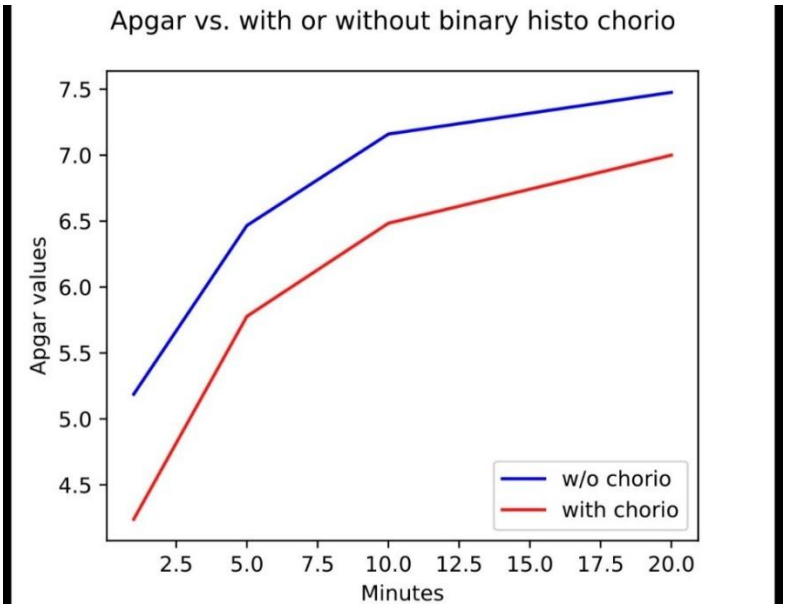

Figure 2. Apgar score evolution according chorioamnionitis exposure.

Table 2. Correlations of chorioamnionitis and Apgar score.

Correlated variables	Correlation coefficient (r)	p-value (p)
Histological CA (binary) and Apgar score	*10 min* : –0.35 *20 min* : –0.39	*10 min* : 0.0094 *20 min* : 0.0106
Histological CA (stages) and Apgar score	*1 min* : –0.24 *10 min* : –0.19	*1 min* : 0.0309 *10 min* : 0.0067

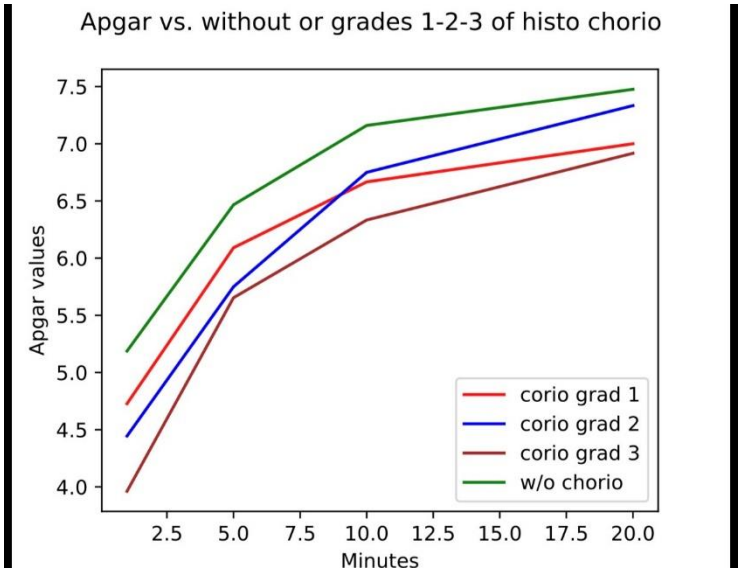

Figure 3. Apgar score and severity of histological chorioamnionitis (stages I, II or III).

This pattern is also visible when we consider the severity of histological chorioamnionitis: higher CA stages were associated with a lower Apgar score, suggesting a more difficult neonatal transition

 doi:10.20944/preprints202605.0022.v1

and a greater resuscitation need (Figure 3), a finding supported by significant negative correlations between histological CA stage and Apgar scores at 1 minute (r=–0.24, p=0.0309) and 10 minutes (r=–0.19, p=0.067) (Table 2).

3.5. Mortality and morbidities of study group

Of the total newborns included in the study, 25/80 (31.25%) died after birth. Mortality was higher in the group that had not been in contact with chorioamnionitis13/34 (38.23%) than in the CA-exposed group 11/46(23.91%), a counterintuitive finding that was not statistically relevant for either binary (r=–0.16, p=0.1608) or staged histological CA (r=–0.17, p=0.1327). A trend towards significance was observed for clinical CA and mortality (r=–0.22, p=0.0567), though this did not reach the threshold for statistical significance (Table 3). The absence of a significant association between chorioamnionitis and mortality is discussed further in section 4.

Table 3. Correlations of chorioamnionitis and neonatal mortality.

Correlation with mortality	Correlation coefficient (r)	p-value (p)
Clinical CA	–0.22	0.0567
Histological CA (binary)	–0.16	0.1608
Histological CA (stages)	–0.17	0.1327

The most frequent neonatal complication in both populations was intraventricular haemorrhage (71.25%), followed by early onset sepsis (42.50%), pulmonary haemorrhage (31.65%) and gastrointestinal haemorrhage (30.38%). Exposure to chorioamnionitis was associated with a higher incidence of most neonatal morbidities across all categories examined (Table 4).

Table 4. Chorioamnionitis correlation with main morbidities.

Correlated variables	Correlation coefficient (r)	p-value (p)
Histological CA (stages) and GA	–0.27	0.0152
Histological CA (stages) and RDS (severity)	0.25	0.0242
Histological CA (stages) and Silverman score	0.26	0.0218
Histological CA (binary) and Silverman score	0.35	0.0015
Histological CA (stages) and EOS	0.31	0.0048
Histological CA (stages) and BPD	0.26	0.0212
Histological (binary) CA and ROP	0.26	0.0249
Histological CA (stages) and CRP (DOL1)	0.25	0.0338
Histological (binary) CA and cervical cerclage	0.28	0.0121
Histological CA (stages) and pre-eclampsia	–0.22	0.0479

CA: Chorioamnionitis; GA: gestational age; RDS: respiratory distress syndrome; EOS:early onset sepsis; BPD:bronchopulmonary dysplasia; ROP:retinopathy of prematurity; CRP: C-reactive protein.

Early onset sepsis occurred more than twice as frequently in CA-exposed neonates (55.32% vs 24.24%), consistent with a significant positive correlation between histological CA stage and EOS (r=0.31, p=0.0048). Similarly, IVH was more frequent in the CA-exposed group (76.6% vs 63.64%), as were pulmonary haemorrhage (36.17% vs. 25.0%), NEC (17.39% vs. 9.09%), and BPD (21.74% vs 3.12%), the latter showing a significant correlation with histological CA stage (r=0.26; p=0.0212). A significant positive correlation was also observed between histological CA stage and ROP (r=0.26; p=0.0249), indicating that higher CA stages correspond to greater retinopathy of prematurity risk.

Respiratory involvement was prominent across both groups. Severe respiratory distress syndrome was more common in CA-exposed infants (24/46; 52.17%) than in non-exposed ones (8/34; 23.52%). This is further reflected in the Silverman scores, where the majority of CA-exposed cases

 doi:10.20944/preprints202605.0022.v1

recorded a score of 8 (16/46; 34.78%), while non-exposed cases had a predominant score of 6 (9/34; 26.47%), as shown in Figure 4. A significant positive correlation was found between histological CA stage and RDS severity (r=0.25; p=0.0242), and between histological CA presence and Silverman score, both as a staged variable (r=0.26; p=0.0218) and as a binary one (r=0.35; p=0.0015), indicating that chorioamnionitis exposure is associated with more severe respiratory compromise at birth (Figure 4).

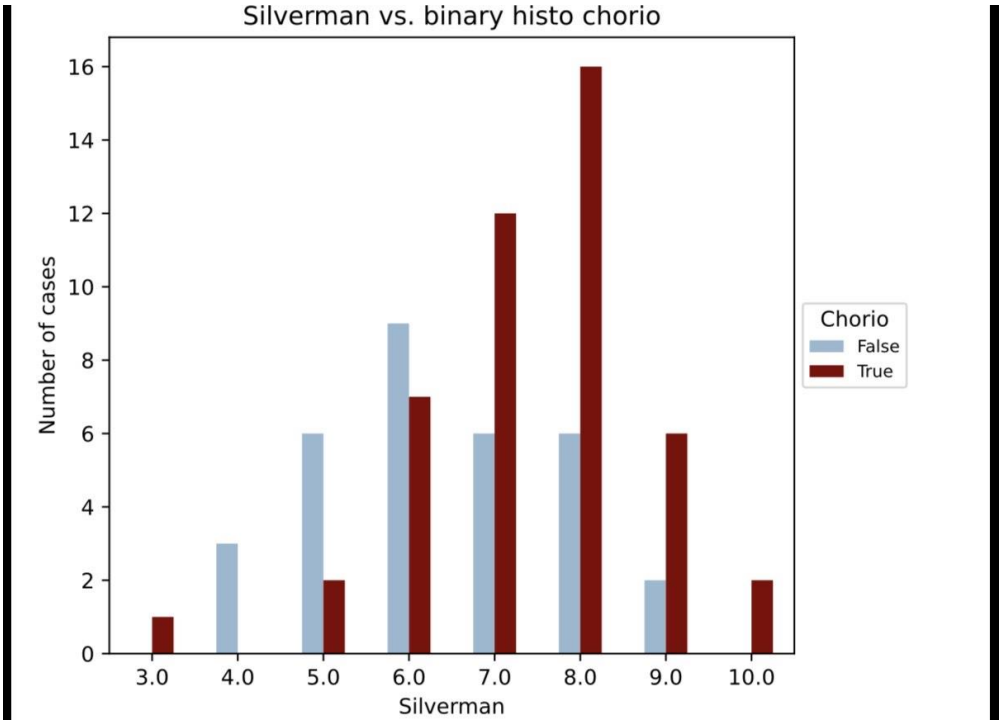

Figure 4. Silverman scores vs chorioamnionitis.

Consistent with the systemic inflammatory response observed across these morbidities, C-reactive protein (CRP) measured on the first day of life showed a significant positive correlation with histological CA stage (r= 0.25, p=0.0338), supporting its potential utility as an early indicator of chorioamnionitis exposure.

4. Discussion

This study demonstrated that the risk of neonatal complications is higher in preterm infants exposed to histological chorioamnionitis than in non-exposed ones. Notably, the mortality of patients exposed to histological chorioamnionitis was not significantly correlated with CA exposure. Despite comparable gestational ages between the two groups (Table 1), the mortality rate was lower in the CA-expose group (25.53%) than in the cohort overall (31.25%), a counterintuitive finding for which the most likely explanation is limited statistical power given the small sample size. The incidence and severity of acute complications such as RDS or IVH were higher in CA-exposed infants than in non-exposed ones.

Olguin et al. reported an early death incidence of 3.5% and stillbirth rate of 14%, though their cohort has a significantly higher gestational age (30.2 ± 5.4 weeks and 32.5 ± 5.1 weeks) than our study population of ≤ 28 weeks, limiting direct comparability [12]. Yu et al., in a Chinese cohort of pregnancies before 34 weeks, reported a clinically diagnosed chorioamnionitis incidence of 17.8% and a neonatal mortality rate of 7.4%, with major neonatal complications occurring in 40% of cases [13]. The higher mortality rates in our cohort likely reflect the more extreme prematurity of our study population rather than a specific effect of chorioamnionitis exposure. Histological chorioamnionitis was significantly associated with several neonatal complications in this cohort, including respiratory

 doi:10.20944/preprints202605.0022.v1

distress, early onset sepsis, bronchopulmonary dysplasia, retinopathy of prematurity, and poorer transition to extrauterine life.

The disparity between clinical and histological chorioamnionitis (15% vs 57.5%) prevalence in our cohort suggests that clinical diagnostic criteria, such as the presence of fever, tachycardia, and purulent cervical discharge, have good specificity, but poor sensitivity. This likely reflects, on the one hand, the large proportion of cases that remain asymptomatic, despite harbouring histological evidence of chorioamnionitis, a subclinical course that most likely reflects detection at an early, pre-symptomatic stage of the underlying process; and the limited ability to make a histological diagnosis antenatally, on the other. These results highlight the need for improved chorioamnionitis diagnostic tools, including highly sensitive maternal biomarkers, or the combined use of clinical, biological, and ultrasound criteria, which would extend detection to subclinical cases that are missed or underdiagnosed. Notably, histological chorioamnionitis is not exclusively of infectious origin: in the absence of any microbiological evidence, the condition can arise through sterile intra-amniotic inflammation, driven by danger signals released during cellular stress, injury, or death [14–17].

Placental histopathological examination carries significant diagnostic value in pregnancies complicated by premature rupture of membranes (PROM), prolonged PROM, preterm delivery, maternal fever, maternal leucocytosis, fetal tachycardia, or purulent cervical discharge, and should be considered standard practice in this clinical context.

Our study identified a weak but significant negative correlation between histological chorioamnionitis stage and gestational age at birth ($r = –0.27$, $p = 0.0152$), consistent with the high prevalence of histological chorioamnionitis (57.5%) observed in this extremely preterm cohort. While higher CA stages showed greater concentrations at 23-26 weeks, the relationship was not monotonic across all stages, with stages II and III both including cases at 27-28 weeks, reflecting the weak and non-uniform nature of this association (Figure 1). Fahmi et al. described a significant correlation between high-grade histologic chorioamnionitis and spontaneous preterm birth in a Swedish cohort [18], consistent with our observations. Overall, intrauterine inflammatory exposure is a widely described risk factor for preterm birth and subsequent perinatal complications [19]; in a previous study from our group, a significant correlation was found between early inflammatory markers and the incidence of NEC [20].

CA-exposed newborns were at increased risk of most neonatal complications examined, with significant positive correlation confirmed between histological chorioamnionitis stage and early onset sepsis, respiratory distress syndrome, bronchopulmonary dysplasia, and retinopathy of prematurity, with correlations ranging from 0.25 to 0.31. EOS occurred more than twice as frequently in CA-exposed neonates (55.32% vs 24.24%). The meta-analysis by Beck et al. found that both histological and clinical chorioamnionitis were associated with significantly increased odds of confirmed and early-onset neonatal sepsis, and with higher odds of late-onset sepsis in preterm neonates [14], supporting our findings. Our study examined only early onset sepsis; the association with late-onset sepsis warrants consideration in future studies of this population. IVH was also more frequent in the CA-exposed group (76.6% vs 63.64%), as was NEC (17.39% vs 9.09%), though neither reached statistical significance in the correlation analysis; these are findings that merit investigation in larger cohorts.

BPD was substantially more common in CA-exposed infants in our cohort (21.74% vs 3.12%), with a significant correlation with histological CA stage ($r=0.26$; $p=0.0212$). This is consistent with Villamor-Martinez et al., whose meta-analysis of 244,000 infants concluded that chorioamnionitis increased the risk of BPD [21], though reports from the Canadian Neonatal Network and Laughon et al. found no such association [22]. A plausible reconciliation is the two-hit model: chorioamnionitis provides the first inflammatory hit, with subsequent postnatal mechanical ventilation and oxygen exposure constituting the second hit. Evidence supports this, with BPD risk decreased overall in ventilated CA-exposed infants but increased in those infants ventilated for more than seven days or with postnatal sepsis [23–25].

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These findings collectively highlight the importance of increased surveillance of extremely preterm infants, regardless of whether chorioamnionitis was clinically suspected, given the poor sensitivity of clinical diagnostic criteria and the significant morbidity burden associated with histological exposure. Early detection and appropriate management of chorioamnionitis in pregnant women may reduce the risk of preterm birth and its associated complications. The significant association between cervical cerclage and higher histological chorioamnionitis stage (r= 0.28, p=0.0121) suggests that women who have undergone this procedure warrant enhanced antenatal surveillance for chorioamnionitis, though this finding should be interpreted cautiously given the small number of affected cases in this cohort.

The significant positive correlation observed between day-of-life C-reactive protein (CRP) and histological CA stage (r=0.25; p=0.0338) reflects the systemic inflammatory response associated with chorioamnionitis exposure in the neonatal period. CRP and more specific biomarkers such as interleukins support the concept of chorioamnionitis as a first inflammatory hit that contributes to preterm birth and subsequent neonatal morbidity [11,26]. At the maternal level, both procalcitonin (PCT) and CRP are appropriate biomarkers in predicting subclinical intrauterine infection in women with PROM before 34 weeks of gestation, with PCT particularly applicable between 28 and 33 + 6 weeks [27]. A retrospective Swedish cohort study of 500 term singleton deliveries found that elevated inflammatory markers were associated with both neonatal infection and asphyxia-related complications, supporting the inclusion of maternal CRP into the clinical management of chorioamnionitis [14].

A significant negative correlation was observed between pre-eclampsia and histological chorioamnionitis presence ($r = -0.22$, $p = 0.0479$), suggesting that women with pre-eclampsia may be less likely to develop histological chorioamnionitis. One possible explanation is that the distinct pathophysiological mechanisms underlying these two conditions differ, so that the inflammatory response specific to pre-eclampsia could inhibit or modulate the development of chorioamnionitis. This finding should not be generalised given the small sample size and retrospective character of the study. Future research should investigate this inverse relationship in larger cohorts.

Our results are broadly consistent with those reported in a study conducted at a provincial perinatal centre in China, in 2014-2015 [19]. Although their sample size was substantially larger, with 14,166 cases compared to 80 in our study, the findings converge on several key points. Both studies demonstrated that histological chorioamnionitis was significantly associated with various neonatal complications, and that histological assessment had greater diagnostic value in predicting complications than clinical assessment alone. Both also support the importance of routine histological examination of the placenta. However, unlike our study, the Chinese study observed a significantly higher neonatal mortality rate in histologically CA-exposed newborns compared to non-exposed ones, a discrepancy that may reflect differences in sample size, gestational age distribution, or local clinical management practices, and that warrants further investigation.

This study has several limitations. First, the study population was restricted to infants born at 23-28 weeks of gestation, and no comparison was made with less preterm or term infants. This limits the ability to disentangle complications attributable to extreme prematurity from those specifically related to chorioamnionitis exposure and should be considered when interpreting the findings.

Second, data on the temporality of events were not assessed, including the onset of early vs. late neonatal sepsis, and the precise timing of death. Early neonatal sepsis is more directly related to chorioamnionitis, while late sepsis is more commonly a consequence of prematurity itself. Similarly, early death is more likely to reflect the direct impact of chorioamnionitis, whereas death at an older gestational age may be more attributable to the consequences of premature birth. The absence of this temporal data limits the interpretation of the mortality findings.

Third, maternal antibiotic treatment for chorioamnionitis was not accounted for in the analysis. Antenatal antibiotics may potentially influence neonatal outcomes, representing a confounding variable that could not be controlled for in this study.

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Finally, the small overall sample size limits statistical power and the generalisability of several findings. This is particularly relevant for the cervical cerclage, pre-eclampsia, and mortality correlations, where the number of affected cases within subgroups is very small; these findings should be interpreted accordingly.

5. Conclusion

Histological chorioamnionitis was significantly associated with several neonatal complications, including early onset sepsis, respiratory distress syndrome, bronchopulmonary dysplasia, and retinopathy of prematurity. No significant association was found between the presence or severity of histological chorioamnionitis and neonatal mortality. The clinical diagnostic criteria for chorioamnionitis demonstrated good specificity but poor sensitivity, highlighting the need for improved diagnostic tools.

A weak but significant negative correlation was observed between histological CA stages and gestational age at birth, though this relationship was not uniform across all stages.

Significant correlations between chorioamnionitis exposure and neonatal C-reactive protein support the potential utility of inflammatory biomarkers in the early identification of chorioamnionitis-exposed neonates.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Ethics Committee of County Emergency Hospital, Cluj-Napoca approved the study protocol code 53874 and date of approval 23 December 2020.

Informed Consent Statement: Informed consent was obtained from participants in the study.

Data Availability Statement: All data generated or analysed during this study are included in this published article.

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Conflicts of Interest: The authors report no conflict of interest.

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