Umbilical cord blood pTau217 and BD-tau are associated with markers of neonatal hypoxia: a prospective cohort study

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Word Count: 2903

Abstract

Objective: Current methods for early detection of hypoxic–ischemic encephalopathy (HIE) are limited by lack of specificity, cost, and time constraints. Blood tau protein concentrations reflect neuropathology in adults. This study examines tau as a potential HIE biomarker in neonates by relating cord blood levels to short-term fetomaternal outcomes. We aimed to examine 1) association of BD-tau with non-reassuring fetal status; 2) correlations between cord blood tau and other hypoxia biomarkers; 3) associations between tau levels and risk factors for fetomaternal morbidity; 4) associations between tau levels and short-term fetomaternal outcome.

Methods: 107 maternal participants were prospectively recruited at Royal Prince Alfred Hospital—a large Australian tertiary referral centre. Simoa analysis detected umbilical cord blood pTau217 and brain-derived (BD)-tau levels.

Results: Of 509 deliveries, cord blood was analysed in 107/110 recruited maternal participants. BD-tau correlated with non-reassuring fetal status (OR=3.0;95%CI=1.6–5.7;p=0.001), though not when adjusting for mode of delivery and gestational age. BD-tau was higher in vaginal deliveries, and positively associated with pTau217, NfL, and lactate ($p<0.001$), and negatively associated with pH and base excess. pTau217 was higher in preterm neonates and was associated with neurofilament light chain (Spearman's rho=0.44,$p<0.001$). BD-tau and pTau217 were associated with maternal hypertension and placental abnormalities.

Conclusions: Cord blood BD-tau correlates with surrogate markers of fetal hypoxia, whilst pTau217 may represent a marker of neurodevelopment. Further studies could explore whether these findings translate to clinical use of tau as an HIE biomarker.

64 **Funding:** US National Institutes of Health (grant:R01AG063849-01).

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66 **Keywords:** tau; asphyxia; hypoxic–ischemic encephalopathy; HIE.

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Introduction

Hypoxic–ischemic encephalopathy (HIE)—a subtype of neonatal encephalopathy—is a syndrome of central nervous system (CNS) dysfunction caused by abnormalities in cerebral blood flow and impaired gas exchange perinatally, resulting in multiple organ failure.[1] Approximately 40–60% of affected infants face mortality or severe neurodevelopmental disability by two years of age.[2]

Risk factors for HIE can broadly be categorised into antepartum (including fetal and maternal characteristics) and intrapartum factors. Understanding antepartum risk factors can complement intrapartum monitoring techniques used to detect 'non-reassuring fetal status' as defined by pathological fetal heart rate traces and fetal scalp blood sampling. Together, this information can identify fetuses at risk of hypoxic injury and guide decision-making regarding the urgency of delivery. However, intrapartum monitoring techniques are limited by a lack of specificity for pathological neurological damage, measurement difficulties, and poor inter-user reliability.[3,4]

The only proven neuroprotective treatment for HIE is therapeutic hypothermia (TH), which has only been validated in term or late preterm neonates.[2,5] Severity of HIE can be classified as mild, moderate, or severe based on clinical signs and grading systems such as the modified Sarnat score.[6] However, these scoring criteria are subjective, and grading may fail to identify neonates at risk of long-term adverse neurological sequelae; research has demonstrated abnormal neurological outcome in over 22% of cohorts of mild HIE.[5] At this

stage, TH is validated only in moderate to severe HIE, and there is insufficient evidence to recommend TH for mild HIE cohorts.[5] Cord blood biomarkers may be helpful in identifying subgroups of mild HIE who would benefit from TH. Further aids to establish aetiology and severity of HIE include electroencephalogram (EEG) monitoring, and neuroimaging studies including MRI and cranial ultrasound.[3,7] These tools are limited by time and cost constraints, require expert interpretation, and may be difficult to access in emergency situations.[7] This indicates an ongoing need for objective, cost-effective, and rapid measures of identifying HIE in order to appropriately identify subgroups of HIE patients that could benefit from early intervention.

Real-time physiological biomarkers could address this gap in diagnosis and prognostication by providing objective point-of-care testing. Current cord or whole blood markers such as pH, lactate, and base excess remain non-specific for neurological injury.[2] Tau is a promising biomarker of poor neurological outcome in adult cohorts with acute and chronic neurological disease.[8,9] Studies of tau in neonates has, to date, focused on correlation of total blood tau and cerebral injury-related outcome measures. However, compared to total blood tau, specific tau subtypes—in particular pTau217 and 'brain-derived tau' (BD-tau)—have demonstrated greater specificity for adult neurological injury.[10,11] This is the first study to examine tau subtypes in a neonatal cohort.

Given the paucity of evidence addressing tau subtypes and fetomaternal outcome, we conducted a prospective cohort study with the following aims:

1. Address feasibility of neonatal cord blood tau level measurement in an Australian cohort.

2. Assess the correlation between BD-tau and non-reassuring fetal status.
3. Assess correlations between cord blood tau—BD-tau, pTau217—and other cord blood biomarkers, maternal and neonatal risk factors for encephalopathy, and adverse outcome.

Materials and Methods

Study Population and Design

We performed a prospective cohort study of maternal and neonatal patients at the Royal Prince Alfred Hospital (RPAH), a tertiary referral centre in Sydney, Australia. Maternal participants of any age who were planned to birth at RPAH were eligible for study recruitment. Recruitment occurred prospectively from October 2022 at any time from 4 weeks prior to estimated date of delivery to the immediate post-partum period (with the option of retrospective consent). Trained recruiters obtained written, informed consent in English for all maternal participants in antenatal visits or on the birthing unit. Participants were excluded if they were non-English speaking, or had a history of psychological illness or other conditions that may interfere with capacity to provide informed consent after appropriate counselling in English.

Recruitment was undertaken as part of the BABBies (Benefits of Analysing Brain Biomarkers in perinatal care) Study—a prospective observational cohort study exploring the biomarkers neurofilament light chain (NfL), BD-tau, and pTau217. Data were stored in Sydney Local

Health District (SLHD) REDCap electronic database. Ethics approval was obtained from SLHD Research and Ethics Committee (RPAH zone) (approval number: 2022/ETH01100). Our study was performed according to the National Statement on Ethical Conduct in Human Research (2007) and the CPMP/ICH Note for Guidance on Good Clinical Practice. Data reporting adhered to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Cord Blood Collection and Analysis

Umbilical venous cord blood was collected by the attending midwife in the immediate postpartum period. 1–3mL samples were collected and centrifuged in the RPAH Department of Anaesthetics laboratory, and plasma samples were then stored in deidentified cryovials.

Tau was measured on the Simoa HD-X platform with two-fold dilution factor in plasma. Plasma pTau217 and BD-tau were measured with previously validated assays.[12,13] Signal variations within and between analytical runs were assessed using three internal quality control samples at the beginning and the end of each run.

Outcome Data Collection

Demographic and outcome data were collected from RPAH electronic and paper medical records. Mode of delivery was classified categorically: vaginal delivery, emergency caesarean section, and elective caesarean section. Placental abnormalities were defined as any abnormality detected on placental ultrasound, on examination in the birth unit or in the operating theatre, or histopathology. The composite term 'histopathological placental abnormality' refers to only abnormalities detected on anatomical or histopathological

examination per the 2014 Amsterdam Working Group nosology for classification of placental clinicopathological disorders.[14] 'Non-reassuring fetal status' was defined as fetal blood sampling showing a pH ≤7.20 or lactate >4.7,[15,16] or intrapartum cardiotocography (CTG) changes identified as 'red zone' criteria according to NSW Health electronic fetal monitoring guidelines (Table S1).[17] 'Non-reassuring fetal status' did not include participants incidentally found to have abnormal umbilical cord blood values without meeting other criteria for non-reassuring fetal status.

Outcomes

Our primary outcome was the association of BD-tau with non-reassuring fetal status. We adjusted this analysis for gestational age and mode of delivery, given these variables have previously been associated with both non-reassuring fetal status and cord blood concentrations of other biomarkers of acidosis and anaerobic metabolism.[18] Secondary outcomes included the association of BD-tau and pTau217 with antenatal factors (gestational age, head circumference, birthweight), other cord blood biomarkers, maternal factors, delivery factors, and perinatal outcome. Resuscitation at birth was defined as cardiorespiratory support required following drying, warming, and mechanical stimulation.[19]

Power Analysis

Our power analysis was based on the association of NfL with non-reassuring fetal status, which is reported separately.[20] We used the previously reported baseline incidence of non-reassuring fetal status of 16%.[15] Based on a two-sided t-test with α=0.025, a sample size of 110 participants provides 80% power to detect a Cohen's d of 0.8 (i.e., a large effect size). The power analysis also applies to the primary outcome of this study, with a preserved type

1 error rate of α=0.05, as this value was halved a priori for the power calculation to account for additional analysis.

Statistical Methods

Primary outcome

Both BD-tau and pTau217 concentrations showed a strong positive skew, hence were $\log_{10}$-transformed for all analyses. To determine the association of BD-tau with non-reassuring fetal status after adjusting for other variables, we used logistic regression (binomial family with logit link) with maximum likelihood estimation of the model parameters. The parametric G-formula was used to compute the mean risk difference from logistic regression models.[21] We included a BD-tau*mode of delivery interaction in our model, as the relationship between neuronal biomarkers and fetal outcome would likely vary by birth route. To provide interpretable effect measures, we calculated the risk difference for the outcome per increase in BD-tau by its interquartile range (Q3 – Q1). The relative association of cord biomarkers with non-reassuring fetal status was quantified using the area under the receiver operator curve (AUROC). The 95% confidence interval for the AUROC was calculated using 2000 stratified bootstrap replicates.

Secondary outcomes

Bivariate biomarker correlations were assessed using rank-based nonparametric methods. The relative strength of biomarker correlations was tested using the method described by Meng, Rosenthal, and Rubin.[22] For continuous secondary outcomes, we used linear regression with the ordinary least squares estimator for the model parameters. Associations between biomarker concentrations and placental abnormalities were adjusted for low birth

weight (defined as birth weight <2.5kg, per World Health Organisation definition).[23] Binary secondary outcomes were tested for linearity, and analysed in the same fashion as our primary outcome.

We used a p-value <0.05 to denote statistical significance. No adjustments for multiple comparisons were made in this preliminary study. All analyses were conducted in R using RStudio (Version 2024.04.0; R Foundation for Statistical Computing, Vienna, Austria). The 'stats' package was used for linear and generalised linear models. The 'cocor' package was used to compare the strength of bivariate biomarker concentrations.[24] The 'plotROC' and 'pROC' packages were used for calculation and plotting of the AUROC.[25]

Results

Over the study period 24th October 2022 to 9th December 2022, 110 maternal study participants were recruited from a total of 509 deliveries at RPAH. Cord blood was collected for a total of 108 participants, of whom 107 had either BD-tau or pTau217 levels available; 105 had BD-tau values and 106 had pTau217 values (STROBE diagram: Figure S1). Cohort demographic information is summarised in Table S2.

Primary outcome

Increased BD-tau was associated with a higher risk of non-reassuring fetal status; each IQR increase in BD-tau was associated with an increased odds of fetal distress (OR=3.0; 95% CI:

1.6, 5.7; p=0.001). However, this relationship was no longer observed when adjusting for mode of delivery and gestational age (OR=1.1; 95%CI=0.6, 1.2; p=0.667) (Table S3). BD-tau was not associated with non-reassuring fetal status when stratifying within each individual mode of delivery (Table S3). Comparative performances of BD-tau pH, lactate, and base excess in predicting non-reassuring fetal status are displayed in Figure 1. There was no association demonstrated between pTau217 and non-reassuring fetal status (Wilcoxon p=0.62).

Secondary outcomes

Antenatal Factors

Relationship between tau and fetal factors

pTau217 was negatively associated with gestational age (Spearman's rho=–0.25, p=0.0096). pTau217 was also negatively associated with birthweight (Spearman's rho=–0.23, p=0.019) and head circumference (Spearman's rho=–0.24, p=0.016), however, these associations were not significant when controlling for gestational age (Table S4). BD-tau did not demonstrate evidence of association with fetal parameters (Figure 2).

Relationship between tau and maternal factors

A total of 8 participants were classified as having maternal hypertension—either chronic hypertension, gestational hypertension, or pre-eclampsia. Both BD-tau and pTau217 were

positively associated with maternal hypertension (median BD-tau: 81.0 vs. 54.9pg/mL, Wilcoxon p=0.026; median pTau217: 10.3 vs. 7.7pg/mL, Wilcoxon p=0.029), but were not associated with other maternal health conditions (Figures S2 and S3).

Relationship between tau and intrapartum factors

BD-tau was associated with mode of delivery (Kruskal–Wallis p<0.001) (Figure 3), with BD-tau levels being higher with vaginal delivery compared to CS. On pairwise comparisons, no statistically significant difference was detected in BD-tau level between elective and emergency CS (median 48.4 vs. 53.6pg/mL, Wilcoxon p=0.22). pTau217 did not demonstrate a significant association with mode of delivery (Kruskal–Wallis p=.420). pTau217 was negatively associated with the duration of the second stage of labour (Spearman rho –0.4, p=0.042), whilst BD-tau and other biomarkers were not (Figure S4).

Correlation between tau and other biomarkers

Correlations between cord blood tau and other biomarkers are demonstrated in Figure 4. BD-tau demonstrated a positive association with pTau217 (Spearman's rho=0.66, p<0.001), NfL (Spearman's rho=0.58, p<0.001), and lactate (Spearman's rho=0.34, p<0.001), and a negative association with cord pH (Spearman's rho=–0.29, p=0.003) and base excess (Spearman's rho=–0.35, p<0.001). pTau217 demonstrated a positive correlation with NfL (Spearman's rho=0.44, p<0.001), but was not associated with other biomarkers. We did not observe evidence of a difference between pTau217 and BD-tau in the strength of the positive correlation with NfL (z=1.48, p=0.140) (Table S5).

Relationship between tau and fetoplacental outcome

A total of 11 participants had reported placental abnormalities, 6 of which were defined as histopathological placental abnormalities (Appendix 1). Adjusting for low birth weight, the presence of histopathological placental abnormalities was positively associated with BD-tau and pTau217 (Table S6).

pTau217 levels were associated with preterm birth (median 7.7 in term participants vs. 12.2pg/mL in preterm participants; Wilcoxon p=0.010). In addition, pTau217 levels were positively associated with respiratory complications (median 7.6 vs. 10.4pg/mL; Wilcoxon p=0.012) and resuscitation requirement at birth (median pTau217: 7.6 vs. 10.2pg/mL; Wilcoxon p=0.027), however these associations were not observed when adjusting for preterm birth (Table S7).

Discussion

Main findings

Our study adds credence to the use of cord blood tau as a biomarker of neurodevelopment, perinatal hypoxia, and CNS injury. It is the first to examine associations between fetomaternal outcomes and cord blood subtypes of tau—BD-tau and pTau217. We observed a correlation between BD-tau and surrogate markers of hypoxia, including serum biomarkers

of anaerobic metabolism and non-reassuring fetal status. Additionally, we found associations between tau and maternal and fetoplacental factors that could contribute to increased baseline risk of encephalopathy, including preterm birth, placental abnormalities, and maternal hypertension. Understanding the relationship between the pathogenesis of hypoxic brain injury, neuron-specific biomarkers, and clinically observed outcome could aid diagnosis, prognosis, and treatment of patients suffering from HIE.

Clinical implications and future research

By addressing surrogate markers of fetal and neonatal hypoxia, our study of predominantly 'healthy' participants aims to link blood tau levels with risk factors for HIE, and provide a foundation for future research into the clinical use of cord blood tau in HIE diagnosis. Our study demonstrated a strong correlation between tau levels and non-specific markers of acidosis and anaerobic metabolism, such as neonatal pH and lactate levels, extending previous research.[1,18,26–28] Importantly, our study is the first to examine BD-tau specifically, which offers an advantage over these traditional biomarkers due to its greater specificity for central nervous system (CNS) injury.[18,26–28] Previous studies have mainly involved case-control analyses of HIE cohorts, demonstrating a positive correlation between early serum tau levels, HIE diagnosis based on EEG and clinical criteria, as well as HIE severity.[26,28]

The proposed role of tau as a surrogate marker of fetal hypoxia is further evidenced by the correlation between early cord blood BD-tau and non-reassuring fetal status observed in this study. This finding was not statistically significant when adjusting for mode of delivery and gestational age. However, operative delivery is commonly performed for fetal distress, and

adjusting for mode of delivery could therefore cause the association between BD-tau and fetal distress to be underestimated. Fetal distress, indicated by pathological fetal heart rate abnormalities, may signal early hypoxia compensation and correlate with neonatal acidosis, low APGAR scores, NICU admission, and resuscitation.[13,29] However, CTG interpretation is subjective, operator-dependent, and has low predictive value for long-term outcomes.[29] Biomarkers like BD-tau could improve diagnostic specificity and guide interventions such as therapeutic hypothermia. BD-tau may offer a more specific marker of neurological damage compared current blood biomarkers.[18,26–28]

Our study also explored potential correlations between neonatal tau levels and antenatal risk factors for adverse neurological outcomes. Macroscopic (e.g., cord knots, marginal cord insertion) and microscopic (e.g., avascular villi) abnormalities in the 'placenta–brain axis' can contribute to intrauterine growth restriction and increased susceptibility of the fetal brain to injury during acute stress.[30,31] We observed increased pTau217 levels in participants with histopathological placental abnormalities. Our findings should prompt further investigation into whether excessive tau phosphorylation may be related to aberrant placental function, indicating potential increased risk of neurological injury.

Microscopic placental changes may also occur as a consequence of pre-eclampsia (PET).[32] Non-PET hypertensive disorders may show some similar microvascular changes to a lesser unknown degree, manifesting in increased neonatal stroke risk.[32] Associations between increased tau and hypertension should be further explored to identify patients with microvascular placental changes who may be more vulnerable to physiologic stress and sentinel intrapartum events.

Phosphorylated tau (pTau217) showed a positive correlation with gestational age but not hypoxic markers. While tau phosphorylation is essential for neuronal function, excessive phosphorylation may contribute to neuronal dysfunction.[33,34] In adults, pTau217 elevation reflects blood-brain barrier disruption and protein aggregation rather than direct neuronal injury.[33,34] It remains unclear whether high neonatal pTau217 signals abnormal neuronal development or increased neuropathology risk. Further research is needed to clarify these mechanisms and define threshold levels for clinical significance.

Strengths and limitations

This study is the first to distinguish between specific tau subtypes—rather than relying solely on total tau levels—paving the way for more precise diagnosis and prognosis. Correlations between BD-tau and surrogate markers of hypoxia form a strong foundation for future research into the use of cord blood tau in birth asphyxia screening. The successful sample collection and analysis, using validated assays, highlights the potential for tau cord blood measurement to feasibly be incorporated into neonatal care in an Australian context.

Limitations of this study included the relatively small sample size, from a single centre. In addition, the largely 'healthy' maternal cohort and short-term follow-up limited adverse outcome data. Also, our study only included static biomarker measurement at time of delivery, missing serial neonatal samples. Late serum tau rises have been linked to neurodevelopmental issues at 1–2 years,[35] highlighting the need for further research on serial tau measurements.

Conclusions

This study establishes BD-tau and pTau217 as potential biomarkers for fetal hypoxia and neurological vulnerability. BD-tau correlated with fetal distress, cord lactate, and pH, while phosphorylated tau levels linked to maternal hypertension and placental abnormalities. Larger, longitudinal studies are needed to validate these findings and explore the integration of tau biomarkers into neonatal screening tools.

Acknowledgements

HZ is a Wallenberg Scholar and a Distinguished Professor at the Swedish Research Council supported by grants from the Swedish Research Council (#2023-00356; #2022-01018 and #2019-02397), the European Union's Horizon Europe research and innovation programme under grant agreement No 101053962, Swedish State Support for Clinical Research (#ALFGBG-71320), the Alzheimer Drug Discovery Foundation (ADDF), USA (#201809-2016862), the AD Strategic Fund and the Alzheimer's Association (#ADSF-21-831376-C, #ADSF-21-831381-C, #ADSF-21-831377-C, and #ADSF-24-1284328-C), the European Partnership on Metrology, co-financed from the European Union's Horizon Europe Research and Innovation Programme and by the Participating States (NEuroBioStand, #22HLT07), the Bluefield Project, Cure Alzheimer's Fund, the Olav Thon Foundation, the Erling-Persson Family Foundation, Familjen Rönströms Stiftelse, Stiftelsen för Gamla Tjänarinnor, Hjärnfonden, Sweden (#FO2022-0270), the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 860197 (MIRIADE), the European Union Joint Programme – Neurodegenerative Disease Research

(JPND2021-00694), the National Institute for Health and Care Research University College London Hospitals Biomedical Research Centre, and the UK Dementia Research Institute at UCL (UKDRI-1003).

Conflicts of interest

HZ has served at scientific advisory boards and/or as a consultant for Abbvie, Acumen, Alector, Alzinova, ALZPath, Amylyx, Annexon, Apellis, Artery Therapeutics, AZTherapies, Cognito Therapeutics, CogRx, Denali, Eisai, LabCorp, Merry Life, Nervgen, Novo Nordisk, Optoceutics, Passage Bio, Pinteon Therapeutics, Prothena, Red Abbey Labs, reMYND, Roche, Samumed, Siemens Healthineers, Triplet Therapeutics, and Wave, has given lectures sponsored by Alzecure, BioArctic, Biogen, Cellectricon, Fujirebio, Lilly, Novo Nordisk, Roche, and WebMD, and is a co-founder of Brain Biomarker Solutions in Gothenburg AB (BBS), which is a part of the GU Ventures Incubator Program (outside submitted work).

Contribution of Authorship

RDS designed the study in consultation with BdV, KK, BM, FG, and HM. FG, HZ and KB supplied the assays and managed biofluid analysis. KK consulted hospital records for relevant cohort data. EP and TP conducted the statistical analysis. EP, FG, and TP drafted the manuscript. All authors provided critical feedback on the manuscript.

Ethics approval

Ethics approval was granted by the Sydney Local Health District Human Research and Ethics Committee (approval reference: 2022/ETH01100). Data were reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Funding

The work is supported by US National Institutes of Health (NIH) grant R01 AG063849-01 (RDS). NIH R01 grants are subject to external peer review for scientific quality, and priority score is based advisory council assessment. KB is supported by the Swedish Research Council (#2017-00915 and #2022-00732), the Swedish Alzheimer Foundation (#AF-930351, #AF-939721, #AF-968270, and #AF-994551), Hjärnfonden, Sweden (#FO2017-0243 and #ALZ2022-0006), the Swedish state under the agreement between the Swedish government and the County Councils, the ALF-agreement (#ALFGBG-715986 and #ALFGBG-965240), the European Union Joint Program for Neurodegenerative Disorders (JPND2019-466-236), the Alzheimer's Association 2021 Zenith Award (ZEN-21-848495), the Alzheimer's Association 2022-2025 Grant (SG-23-1038904 QC), La Fondation Recherche Alzheimer (FRA), Paris, France, and the Kirsten and Freddy Johansen Foundation, Copenhagen, Denmark. HZ is a Wallenberg Scholar and a Distinguished Professor at the Swedish Research Council supported by grants from the Swedish Research Council (#2023-00356; #2022-01018 and #2019-02397), the European Union's Horizon Europe research and innovation programme under grant agreement No 101053962, Swedish State Support for Clinical Research (#ALFGBG-71320), the Alzheimer Drug Discovery Foundation (ADDF), USA (#201809-2016862), the AD Strategic Fund and the Alzheimer's Association (#ADSF-21-831376-C, #ADSF-21-831381-C, #ADSF-21-831377-C, and #ADSF-24-1284328-C), the Bluefield Project, Cure Alzheimer's Fund, the Olav Thon Foundation, the Erling-Persson Family Foundation, Stiftelsen för Gamla Tjänarinnor, Hjärnfonden, Sweden (#FO2022-0270), the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement No 860197 (MIRIADE), the European Union Joint Programme –

448 Neurodegenerative Disease Research (JPND2021-00694), the National Institute for Health
449 and Care Research University College London Hospitals Biomedical Research Centre, and the
450 UK Dementia Research Institute at UCL (UKDRI-1003).

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Figure Captions

Figure 1:

Receiver–operator curve (ROC) analysis of BD-tau, pH, base excess, and lactate in predicting binary non-reassuring fetal status. (A) ROC for the generalised linear model predicting non-reassuring fetal status and including the regressors: biomarker, mode of delivery, and gestational age. (B) ROC for the generalised linear model predicting non-reassuring fetal status and including the regressors: biomarker and mode of delivery. ROC for the biomarkers only, including (C) all births, (D) excluding preterm births, (E) excluding elective caesarean section, and (F) excluding elective CS and preterm birth.

Figure 2:

Correlation between BD-tau and pTau217 and fetal factors—birthweight, head circumference, and gestational age. Spearman correlation coefficients are shown. Red dot: elective Caesarean section (CS); blue dot: emergency CS; green dot: vaginal delivery.

Figure 3:

Correlation between tau and mode of delivery. A: Correlation between Log_{10} BD-tau and mode of delivery. Wilcoxon p-values are shown for comparisons between individual modes of delivery. B: Correlation between Log_{10} pTau217 and mode of delivery. Red dot: elective caesarean section (CS); blue dot: emergency CS; green dot: vaginal delivery.

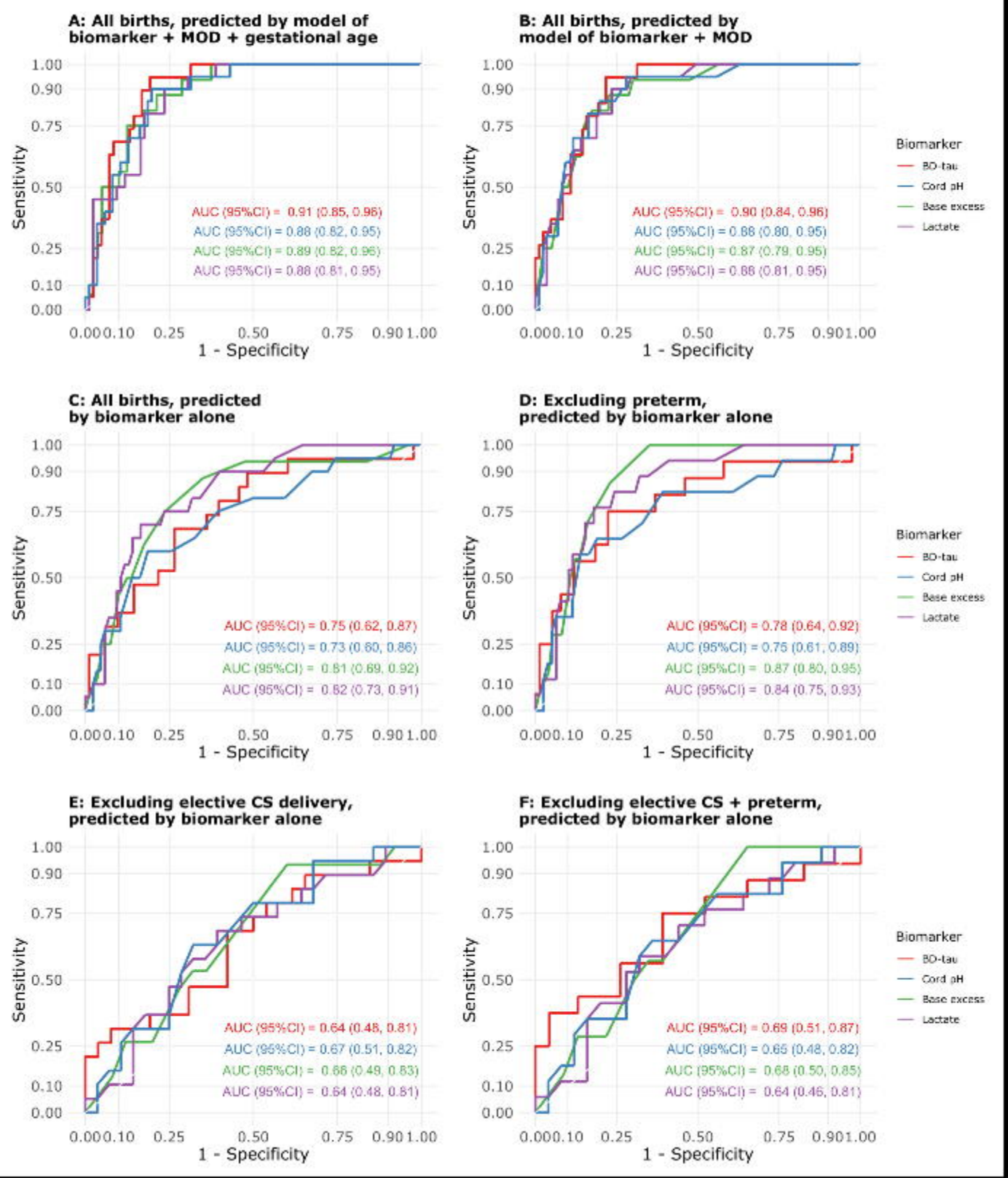
588 Figure 4:

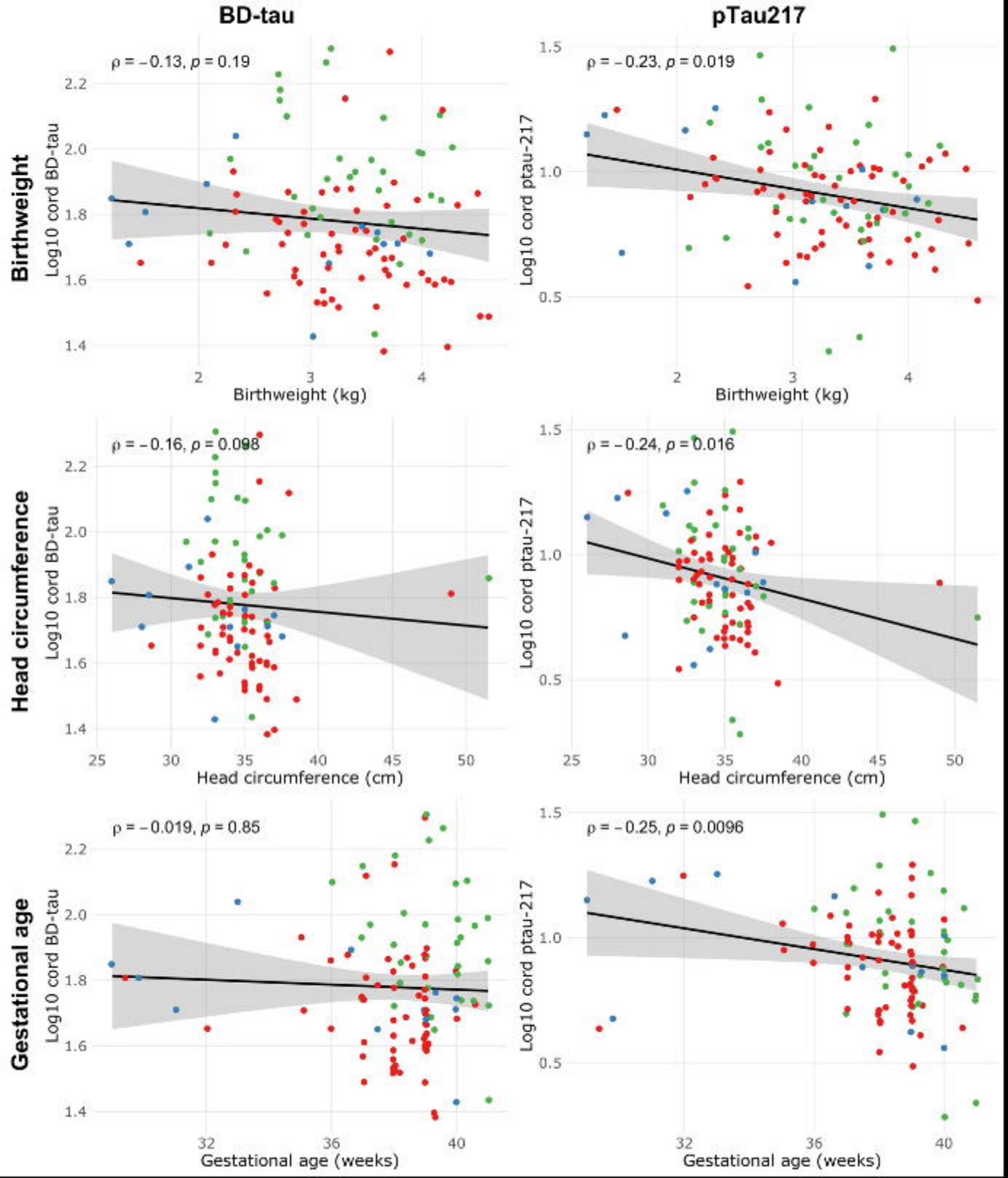
589 Correlation between cord blood biomarkers. Association of BD-tau with Neurofilament light

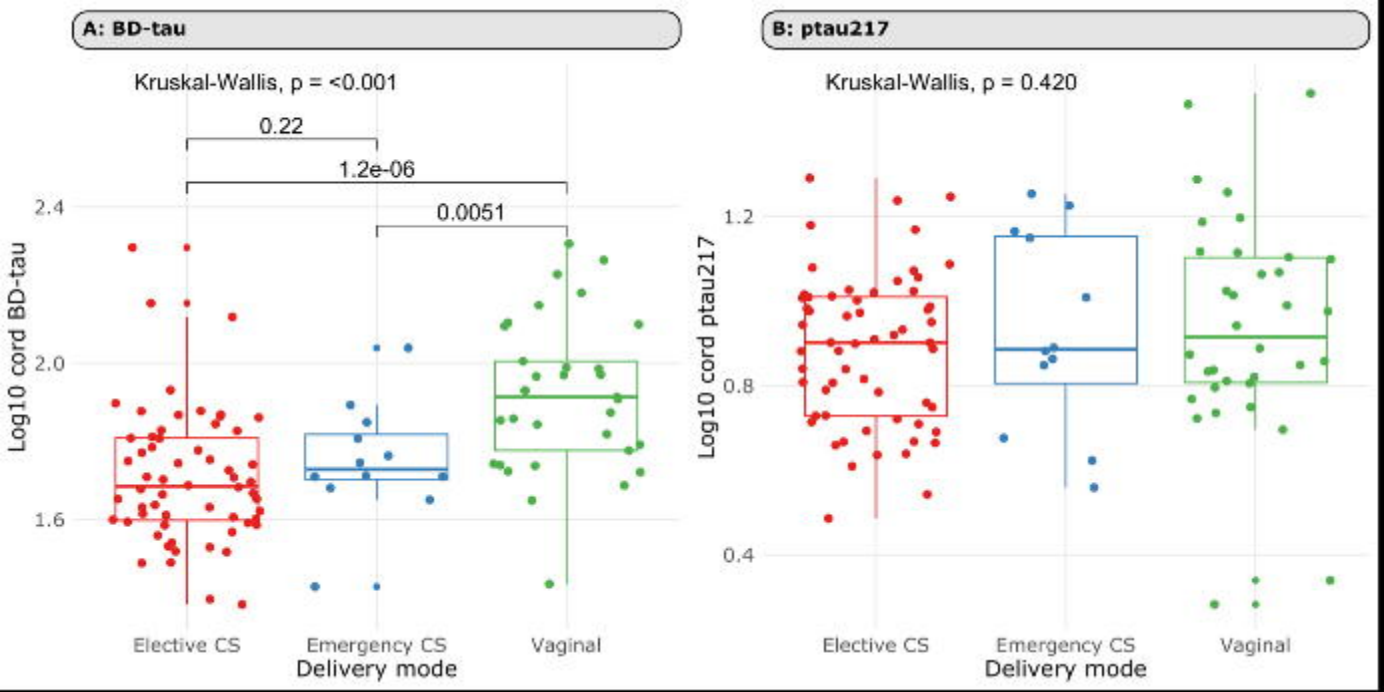
590 chain (NfL) (n=105), pH (n=104), base excess (n=94), and lactate (n=103); association of

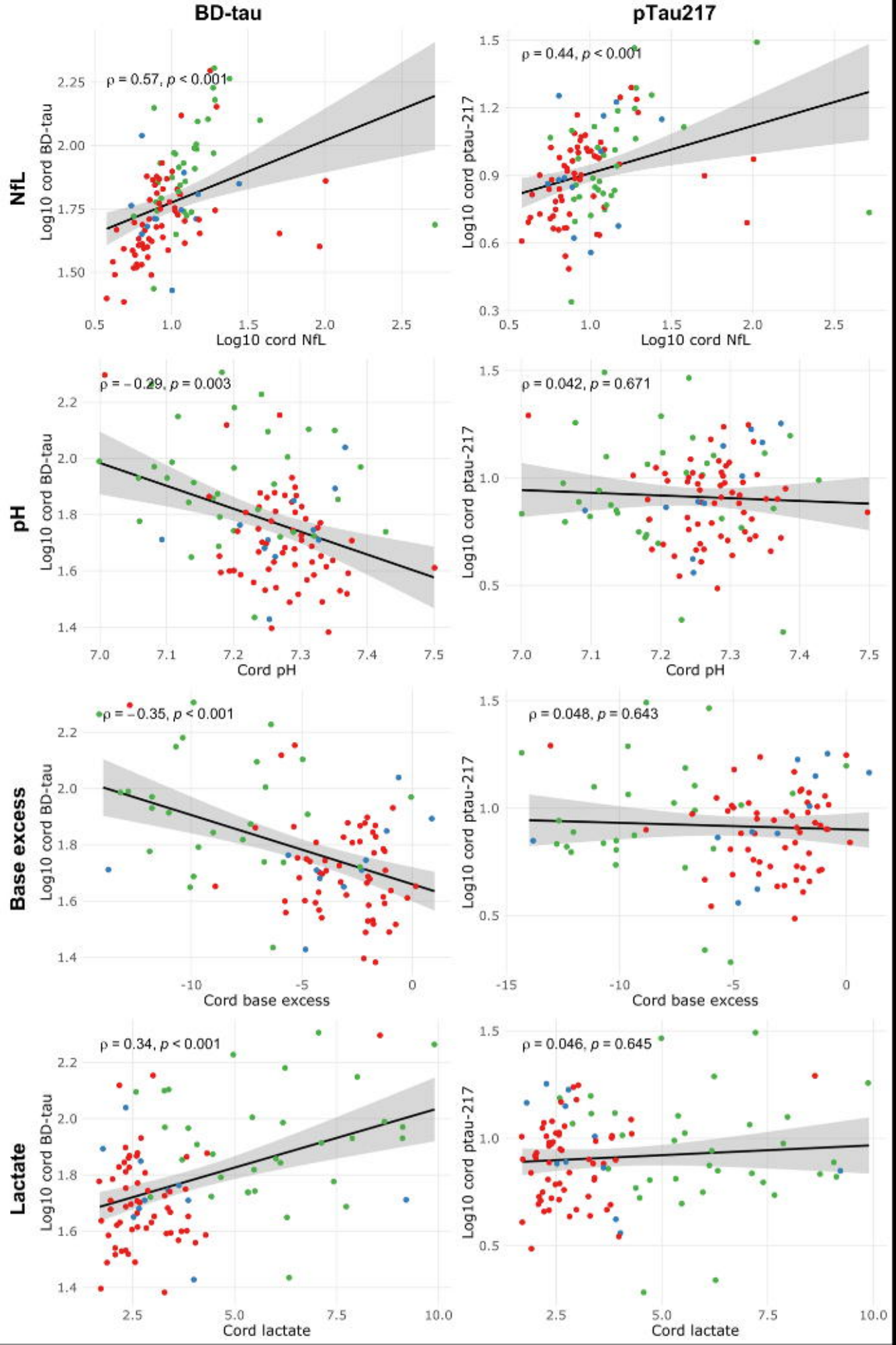
591 pTau217 and NfL (n=106), pH (n=105), base excess (n=95), and lactate (n=104). Red dot:

592 elective caesarean section (CS); blue dot: emergency CS; green dot: vaginal delivery.


A: All births, predicted by model of biomarker + MOD + gestational age
AUC (95%CI) = 0.91 (0.85, 0.96)
AUC (95%CI) = 0.88 (0.82, 0.95)
AUC (95%CI) = 0.89 (0.82, 0.96)
AUC (95%CI) = 0.88 (0.81, 0.95)
B: All births, predicted by model of biomarker + MOD
AUC (95%CI) = 0.90 (0.84, 0.96)
AUC (95%CI) = 0.88 (0.80, 0.95)
AUC (95%CI) = 0.87 (0.79, 0.95)
AUC (95%CI) = 0.88 (0.81, 0.95)
C: All births, predicted by biomarker alone
AUC (95%CI) = 0.75 (0.62, 0.87)
AUC (95%CI) = 0.73 (0.60, 0.86)
AUC (95%CI) = 0.81 (0.69, 0.92)
AUC (95%CI) = 0.82 (0.73, 0.91)
D: Excluding preterm, predicted by biomarker alone
AUC (95%CI) = 0.78 (0.64, 0.92)
AUC (95%CI) = 0.75 (0.61, 0.89)
AUC (95%CI) = 0.87 (0.80, 0.95)
AUC (95%CI) = 0.84 (0.75, 0.93)
E: Excluding elective CS delivery, predicted by biomarker alone
AUC (95%CI) = 0.64 (0.48, 0.81)
AUC (95%CI) = 0.67 (0.51, 0.82)
AUC (95%CI) = 0.66 (0.49, 0.83)
AUC (95%CI) = 0.64 (0.48, 0.81)
F: Excluding elective CS + preterm, predicted by biomarker alone
AUC (95%CI) = 0.69 (0.51, 0.87)
AUC (95%CI) = 0.65 (0.48, 0.82)
AUC (95%CI) = 0.68 (0.50, 0.85)
AUC (95%CI) = 0.64 (0.46, 0.81)
Sensitivity
1 - Specificity
0.00 0.10 0.25 0.50 0.75 0.90 1.00
Biomarker
BD-tau
Cord pH
Base excess
Lactate


BD-tau
pTau217
Birthweight
Head circumference
Gestational age
ρ = −0.13, p = 0.19
ρ = −0.23, p = 0.019
ρ = −0.16, p = 0.098
ρ = −0.24, p = 0.016
ρ = −0.019, p = 0.85
ρ = −0.25, p = 0.0096
Log10 cord BD-tau
Log10 cord ptau-217
Birthweight (kg)
Head circumference (cm)
Gestational age (weeks)


A: BD-tau
Kruskal-Wallis, p = <0.001
0.22
1.2e-06
0.0051
2.4
2.0
1.6
Log10 cord BD-tau
Elective CS
Emergency CS
Vaginal
Delivery mode
B: ptau217
Kruskal-Wallis, p = 0.420
1.2
0.8
0.4
Log10 cord ptau217
Elective CS
Emergency CS
Vaginal
Delivery mode


BD-tau
pTau217
NfL
pH
Base excess
Lactate
ρ = 0.57, p < 0.001
ρ = 0.44, p < 0.001
ρ = −0.29, p = 0.003
ρ = 0.042, p = 0.671
ρ = −0.35, p < 0.001
ρ = 0.048, p = 0.643
ρ = 0.34, p < 0.001
ρ = 0.046, p = 0.645
Log10 cord BD-tau
Log10 cord ptau-217
Log10 cord NfL
Cord pH
Cord base excess
Cord lactate