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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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MATERNAL AND CORD-BLOOD HOMOCYSTEINE AND NEONATAL S100B IN PRETERM BIRTH: ASSOCIATIONS WITH IN-HOSPITAL NEONATAL OUTCOMES IN A PROSPECTIVE COHORT

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Abstract.

Background/Objectives: Preterm birth is associated with substantial neonatal morbidity, while relationships between maternal and neonatal biochemical characteristics and neonatal outcomes remain incompletely understood. This study investigated mother–newborn homocysteine relationships and associations of homocysteine and neonatal S100B with in-hospital neonatal outcomes.

Methods: This prospective multicenter cohort included 280 mother–newborn pairs with singleton preterm births at 22+0–36+6 weeks. Maternal and umbilical cord blood homocysteine and neonatal S100B were assessed. A selected composite of IVH, invasive mechanical ventilation from birth, congenital or neonatal pneumonia, EOS, or LOS was analyzed post hoc. Separate adjusted logistic models evaluated maternal homocysteine, cord-blood homocysteine, and S100B, each with gestational age and birth weight; a combined five-variable model was retained as a sensitivity analysis.

Results: The selected composite occurred in 185/280 infants (66.1%). Maternal and umbilical cord blood homocysteine concentrations were strongly correlated ($\rho = 0.663$; $p < 0.001$). In separate adjusted models, maternal homocysteine (aOR 1.057, 95% CI 0.989–1.130; $p = 0.100$), cord-blood homocysteine (aOR 1.021, 95% CI 0.949–1.099; $p = 0.574$), and neonatal S100B (aOR 0.981 per 10-ng/L increase, 95% CI 0.947–1.016; $p = 0.278$) were not independently associated with the composite. Gestational age and birth weight were inversely associated with the composite in each model. The combined model and sensitivity analyses yielded consistent biomarker findings.

Conclusions: Maternal and umbilical cord blood homocysteine concentrations were strongly correlated, supporting a close maternal–fetal metabolic relationship; however, maternal homocysteine, cord-blood homocysteine, and neonatal S100B were not independently associated with the selected composite of in-hospital neonatal morbidity after adjustment for gestational age and birth weight.

Key words. Preterm birth, homocysteine, S100B, neonatal outcomes, prematurity.

Introduction.

Preterm birth, defined as delivery before 37 completed weeks of gestation, remains a major cause of neonatal morbidity and mortality worldwide [1,2]. Despite advances in perinatal and neonatal care, preterm infants remain at increased risk of respiratory, neurological, infectious, and other complications related to physiological immaturity [3]. Gestational age and birth weight are strongly associated with neonatal outcomes; however, infants born at similar gestational ages and with comparable birth weights may experience different clinical courses. This variability has stimulated interest in biological markers that may reflect maternal–newborn relationships and neonatal adaptation after preterm birth.

Homocysteine is a sulfur-containing amino acid involved in methionine and one-carbon metabolism. Elevated maternal homocysteine concentrations have been associated with endothelial dysfunction, oxidative stress, impaired placental function, and adverse pregnancy outcomes [4-6]. Maternal metabolism may also influence fetal homocysteine status, making paired maternal and umbilical cord blood measurements relevant for evaluating maternal–fetal metabolic relationships. However, evidence regarding the relationship between maternal and neonatal homocysteine concentrations and neonatal morbidity following preterm birth remains limited.

S100B is a calcium-binding protein predominantly expressed by astrocytes and is released in response to cellular stress and injury. Circulating S100B has been investigated as a biomarker of neonatal neurological injury, including hypoxic–ischemic brain injury and intraventricular hemorrhage (IVH) [7-11]. Preterm infants may be particularly relevant for S100B assessment because neurological vulnerability increases with decreasing gestational maturity. Nevertheless, the relationship between early neonatal S100B concentrations and subsequent complications among preterm infants remains incompletely characterized.

Despite increasing interest in biochemical characteristics of preterm newborns, data integrating paired maternal and umbilical cord blood homocysteine concentrations and neonatal S100B within the same prospective cohort remain limited. Examining these measures together may clarify maternal–newborn biochemical relationships and their associations with the neonatal clinical course.

Therefore, this study aimed to investigate the relationship between maternal and umbilical cord blood homocysteine concentrations and to examine the associations of maternal homocysteine, cord-blood homocysteine, and neonatal S100B with in-hospital neonatal outcomes among preterm infants.

Materials and Methods.

Study design and Setting:

This prospective multicenter observational cohort study was conducted between January and December 2025 at two tertiary referral perinatal centers in Almaty, Kazakhstan: The Center of Perinatology and Pediatric Cardiac Surgery and Perinatal Center No. 3.

Consecutive women with singleton pregnancies who delivered preterm infants between 22+0 and 36+6 weeks of gestation were prospectively enrolled together with their newborns. A total of 280 mother–newborn pairs met the eligibility criteria and were included in the final analysis.

Ethical Considerations:

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Local Ethics Committee of the Center of Perinatology and Pediatric Cardiac Surgery, Almaty, Kazakhstan (Protocol No. 26, 31 October 2024). Written informed consent was obtained from all participating women before enrollment and collection of biological samples.

Study Population:

Women admitted for preterm delivery during the study period were consecutively screened for eligibility.

The inclusion criteria were singleton pregnancy, preterm delivery between 22+0 and 36+6 weeks of gestation, live birth, and written informed consent.

The exclusion criteria were major congenital fetal malformations, confirmed chromosomal or genetic abnormalities, severe maternal systemic disease in the stage of decompensation, and refusal to participate.

Only one mother–newborn pair per pregnancy was included.

Clinical Data Collection and Neonatal Outcomes:

Maternal demographic, obstetric, and clinical data were obtained from standardized electronic medical records and case report forms. Recorded maternal variables included age, height, pre-delivery weight, body mass index, gravidity, parity, gestational age at delivery, and mode of delivery.

Neonatal data included gestational age, birth weight, birth length, head circumference, Apgar scores at 1 and 5 min, respiratory support, neurological complications, infectious complications, other complications of prematurity, intensive care requirements, and survival.

Infants were followed from birth until hospital discharge, transfer to another healthcare facility, or death, whichever occurred first. Therefore, the outcomes evaluated in this study represent in-hospital neonatal outcomes.

IVH was assessed by cranial ultrasonography within the first 72 h of life and graded according to the Papile classification (grades I–IV): grade I, hemorrhage confined to the germinal matrix/subependymal region; grade II, intraventricular hemorrhage without ventricular dilatation; grade III, intraventricular hemorrhage with ventricular dilatation; and grade IV, hemorrhage with parenchymal involvement. When more than one cranial ultrasound examination was available during hospitalization, the highest documented IVH grade was used for analysis. Additional cranial ultrasonography was performed according to clinical indications.

Invasive mechanical ventilation was defined as the requirement for invasive mechanical ventilation from birth.

Congenital pneumonia was defined as pneumonia presenting at birth or during the immediate postnatal period and considered to have been acquired antenatally or intrapartum. Diagnosis was based on compatible respiratory clinical findings together with radiographic pulmonary abnormalities and supportive laboratory findings, where available.

Neonatal pneumonia was defined as pneumonia developing after birth during subsequent hospitalization, based on new or worsening respiratory signs together with new or progressive radiographic pulmonary abnormalities and supportive clinical and laboratory evidence of infection.

Early-onset sepsis (EOS) was defined as sepsis occurring within the first 72 h of life, whereas late-onset sepsis (LOS) was defined as sepsis occurring after 72 h. Culture-proven sepsis was defined by isolation of a pathogenic organism from blood or cerebrospinal fluid in an infant with compatible clinical features. Clinical sepsis was defined by compatible systemic clinical signs of infection supported by laboratory and/or inflammatory findings and treated according to the applicable clinical protocol in the absence of microbiological confirmation. Both culture-proven and clinically diagnosed cases were recorded.

The infectious components of the composite outcome were limited to congenital pneumonia, neonatal pneumonia, EOS, and LOS. Other site-specific infectious diagnoses were not included as separate components of the composite outcome.

Selected Composite Neonatal Outcome:

For the present analyses, a selected composite adverse neonatal outcome was defined post hoc as the occurrence of at least one of the following during the observation period:

- IVH of any grade;
- invasive mechanical ventilation from birth;
- congenital pneumonia;
- neonatal pneumonia;
- EOS;
- LOS.

The composite was used as an exploratory summary measure of in-hospital neonatal morbidity rather than as a single pathophysiological endpoint.

Because grade I–II IVH accounted for most IVH events, a sensitivity analysis used a modified composite that excluded grade I–II IVH while retaining grade III–IV IVH and all other components. A second sensitivity analysis added in-hospital death to the selected composite.

Biological Sample Collection and Processing:

Maternal venous blood was collected during the first stage of labor or immediately before cesarean delivery using sterile vacuum tubes containing clot activator and separation gel.

Umbilical cord blood was collected immediately after delivery following cord clamping and before placental separation. Approximately 5 mL of blood was aseptically collected from the umbilical vein.

Peripheral venous blood for neonatal S100B measurement was collected within the first 12–24 h of life.

Blood samples were transported to the laboratory immediately after collection and centrifuged at 3000 rpm for 10 min within 1 h. Serum aliquots were separated and stored at −80 °C until analysis. Aliquoting was used to minimize repeated freeze–thaw cycles. Specimen-level storage duration and the exact number of freeze–thaw cycles were not retained in the final analytical dataset and therefore could not be reconstructed reliably.

Laboratory Measurements:

Maternal serum and umbilical cord blood serum total homocysteine concentrations were measured using the Axis®

Homocysteine EIA (Axis-Shield Diagnostics Ltd., Dundee, UK; FHCY100/AX51301) according to the manufacturer's instructions. The manufacturer protocol uses 25 µL of pretreated serum/plasma and six calibrators (2, 4, 8, 15, 30, and 50 µmol/L), with absorbance read at 450 nm and concentrations calculated using a four-parameter logistic calibration curve. The stated calibrator range is 2–50 µmol/L, and the manufacturer-reported limit of quantification is 1.0 µmol/L at CV <20%. The AX51301 manufacturer instructions report within-run precision of 7–8% and total precision of 9–10% across control means of 6.1–20.6 µmol/L, recommend duplicate calibrators, and recommend a new calibration curve for each run. Batch identifiers, patient-sample replicate data, and study-specific coefficients of variation were not retained in the clinical analytical dataset; therefore, duplicate testing of individual study samples could not be verified retrospectively.

Neonatal serum S100B concentrations were measured using the CanAg® S100 EIA (Fujirebio Diagnostics AB, Gothenburg, Sweden; product no. 708-10) according to the manufacturer's instructions. The assay is a solid-phase non-competitive sandwich EIA using 50 µL serum. The manufacturer protocol specifies duplicate determinations for calibrators and unknown samples and a calibration series of approximately 0, 50, 100, 500, 1500, and 3500 ng/L; absorbance is read at 620 nm or at 405 nm after stop solution. The manufacturer-reported detection limit is <10 ng/L, with within-run CVs of 1.3–2.5% and between-day CVs of 1.5–2.5% across concentrations of approximately 70–2260 ng/L. The study dataset contains final S100B concentrations but not replicate absorbances or plate/batch identifiers; therefore, specimen-level duplicate testing could not be independently verified from the retained analytical data. Formal blinding of laboratory personnel to subsequent clinical outcome status was not documented.

Statistical Analysis:

Statistical analyses were performed using Statistica version 13.0 (TIBCO Software Inc., Palo Alto, CA, USA) and Python statistical libraries (Pandas, SciPy, and Statsmodels).

Normality of continuous variables was assessed using the Shapiro–Wilk test. Non-normally distributed continuous variables are presented as median and interquartile range (IQR), and between-group comparisons were performed using the Mann–Whitney U test.

Categorical variables are presented as frequencies and percentages and were compared using the χ^2 test or Fisher's exact test, as appropriate. The maternal–cord homocysteine relationship was evaluated using Spearman's rank correlation coefficient (ρ).

The exact composition of the selected morbidity composite and the five-variable combined regression model were not documented in a time-stamped statistical analysis plan before examination of the outcome data. Accordingly, the composite-outcome regression analyses are reported as post hoc/exploratory analyses.

Because maternal and cord-blood homocysteine were strongly correlated and represent related points in the same metabolic pathway, the main adjusted analyses used three separate binary logistic regression models: maternal homocysteine + gestational age + birth weight; cord-blood homocysteine + gestational age + birth weight; and neonatal S100B + gestational age + birth weight. All 280 participants had complete data for these variables. Gestational age was modeled per 1-week increase, birth weight per 100-g increase, and S100B per 10-ng/L increase. Results are reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs).

The linearity-in-the-logit assumption for continuous predictors was assessed using the Box–Tidwell approach. No, statistically significant evidence of non-linearity was identified for maternal homocysteine, umbilical cord blood homocysteine, neonatal S100B, gestational age, or birth weight (all $p > 0.05$).

A combined five-variable model containing maternal homocysteine, cord-blood homocysteine, neonatal S100B, gestational age, and birth weight was retained as a sensitivity analysis to estimate mutually adjusted associations. Multicollinearity in this combined model was assessed using variance inflation factors (VIFs), and model calibration was evaluated using the Hosmer–Lemeshow goodness-of-fit test.

Additional sensitivity analyses used (1) the modified composite excluding grade I–II IVH and (2) a death-inclusive composite adding in-hospital death to the selected morbidity composite. The same five covariates and scaling as in the combined sensitivity model were used.

Duration of in-hospital observation was approximated by the sum of recorded bed-days across neonatal inpatient units. Because some ward-level fields were incomplete or contained non-numeric status/time entries, this summary was restricted to infants with complete numeric bed-day entries across all recorded units (n = 259). Observation duration was summarized overall and by selected composite-outcome status and compared using the Mann–Whitney U test.

A two-sided $p < 0.05$ was considered statistically significant. No imputation was performed for missing observation-duration fields.

Results.

Baseline Characteristics of the Study Population:

A total of 280 mother–newborn pairs with preterm birth were included in the final analysis. Maternal baseline characteristics are presented in Table 1.

The median maternal age was 32.0 years (IQR, 27.0–36.0), and the median body mass index (BMI) was 27.0 kg/m² (IQR, 24.0–30.0). Overall, 65.7% of women were classified as overweight or obese (BMI ≥ 25 kg/m²). The median gravidity and parity were 2.0 (IQR, 1.0–4.0) and 2.0 (IQR, 1.0–3.0), respectively, indicating that most participants were multiparous women (Table 1).

Additional maternal and antenatal characteristics were recorded. Hypertensive disorders of pregnancy were present in 88 women (31.4%), anemia in 74 (26.4%), cervical insufficiency in 41 (14.6%), thyroid dysfunction in 34 (12.1%), diabetes mellitus in 18 (6.4%), and sexually transmitted infections in 21 (7.5%). Twenty-four pregnancies (8.6%) were conceived through in vitro fertilization, and fetal growth restriction was recorded in 40 cases (14.3%). Antenatal corticosteroid prophylaxis was complete in 77 pregnancies (27.5%), incomplete in 13 (4.6%), and not administered in 190 (67.9%).

The neonatal characteristics are summarized in Table 2. The median gestational age at delivery was 34.0 weeks (IQR, 32.0–35.0), and the median birth weight was 2170 g (IQR, 1660–2490). The median birth length and head circumference were 44.5 cm (IQR, 42.0–46.0) and 32.0 cm (IQR, 30.0–34.0), respectively. Median Apgar scores were 6 (IQR, 5–6) at 1 minute and 7 (IQR, 7–7) at 5 minutes. Male newborns accounted for 51.3% of the study population, while 63.2% of deliveries were performed by cesarean section.

The distributions of gestational age and birth weight are shown in Figure 1. More than half of the neonates were born at 34–36 weeks of gestation (52.1%), while 22.9% were born before 32 weeks. Regarding birth weight, 23.2% of neonates weighed <1500 g at birth.

In-Hospital Neonatal Outcomes:

Neonatal complications were frequently observed during hospitalization (Table 3). The most common complication was intraventricular hemorrhage (IVH), diagnosed in 149 infants (53.2%). Most IVH cases were low grade: grade I IVH occurred in 89 infants (31.8% of the total cohort) and grade II in 48 (17.1%), whereas grade III and grade IV IVH occurred in 5 (1.8%) and 7 (2.5%) infants, respectively. Thus, grade III–IV IVH was observed in 12 infants (4.3%).

Congenital pneumonia occurred in 93 newborns (33.2%), whereas 74 infants (26.4%) required invasive mechanical ventilation from birth. Neonatal pneumonia developed in 45 infants (16.1%), while early- and late-onset neonatal sepsis occurred in 4 (1.4%) and 2 (0.7%) newborns, respectively.

The selected composite adverse neonatal outcome occurred in 185 of 280 infants (66.1%), whereas 95 infants (33.9%) experienced none of its selected components. Overall, 128 infants (45.7%) experienced at least one non-IVH component of the composite, and 114 (40.7%) experienced two or more components. Among the 149 infants with IVH, 92 also experienced at least one non-IVH component, whereas 57 had IVH without another composite component. Conversely, 36 infants without IVH experienced at least one non-IVH component.

During the observation period, 11 of 280 infants (3.9%) died and 4 (1.4%) were transferred to another healthcare facility. Ten of the 11 infants who died had experienced at least one component of the selected composite before death, whereas one infant died without a recorded composite event. All four transferred infants had experienced at least one component before transfer. The remaining 265 infants (94.6%) were discharged alive without external transfer. Complete numeric ward-level bed-day data were available for 259 infants. Median recorded in-hospital observation was 12 days (IQR, 8–22) overall, 16 days (IQR, 9–28.5) among infants with the selected composite outcome, and 8 days (IQR, 6–12) among infants without it (Mann–Whitney $p < 0.001$).

Association Between Biomarkers and the Composite Adverse Neonatal Outcome:

Comparisons of maternal and umbilical cord blood biomarkers according to the composite adverse neonatal outcome are presented in Table 4.

Maternal homocysteine concentrations tended to be higher among mothers whose infants developed the composite adverse neonatal outcome than among those without the outcome; however, this difference did not reach statistical significance ($p = 0.062$). Likewise, umbilical cord blood homocysteine concentrations did not differ significantly between the two groups ($p = 0.584$). Neonatal S100B concentrations were also comparable regardless of the occurrence of the composite outcome ($p = 0.598$).

Therefore, none of the evaluated biomarkers demonstrated statistically significant associations with the composite adverse neonatal outcome in the unadjusted analysis.

S100B and Intraventricular Hemorrhage:

Because of the proposed relationship between S100B and neurological injury, exploratory analyses were performed according to the presence and severity of IVH.

Neonatal S100B concentrations were numerically higher among infants with any-grade IVH than among those without IVH (85.0 ng/L [IQR, 58.0–115.2] vs. 72.1 ng/L [IQR, 53.1–102.6]); however, the difference did not reach statistical significance ($p = 0.092$).

Similarly, S100B concentrations did not differ significantly between infants with grade III–IV IVH and those without grade III–IV IVH (91.4 ng/L [IQR, 55.9–131.6] vs. 77.9 ng/L [IQR, 56.2–106.8]; $p = 0.560$).

Thus, no statistically significant association between neonatal S100B concentration and either the presence or severity of IVH was demonstrated in this cohort.

Maternal–Cord Homocysteine Correlation and Separate Adjusted Models:

Spearman correlation analysis demonstrated a strong positive correlation between maternal and umbilical cord blood homocysteine concentrations ($\rho = 0.663$, $p < 0.001$). Higher maternal homocysteine concentrations were associated with higher umbilical cord blood homocysteine concentrations, indicating a close maternal–fetal metabolic relationship at delivery.

Given this correlation, maternal and cord-blood homocysteine were evaluated in separate adjusted models to avoid interpreting mutually adjusted coefficients as the total association of either marker. A third model evaluated neonatal S100B; gestational age and birth weight were included in each model.

None of the three biomarkers was independently associated with the selected composite outcome in its separate adjusted model. Gestational age and birth weight were inversely associated with the selected composite in all three models (Table 6).

Combined Five-Variable Sensitivity Model:

A combined sensitivity model simultaneously included maternal homocysteine, cord-blood homocysteine, neonatal S100B, gestational age, and birth weight to estimate mutually adjusted associations. All 280 infants were included.

In the combined model, increasing gestational age was associated with lower odds of the selected composite (aOR 0.668 per 1-week increase, 95% CI 0.534–0.834; $p < 0.001$), and higher birth weight was also associated with lower odds (aOR 0.912 per 100-g increase, 95% CI 0.853–0.975; $p = 0.007$).

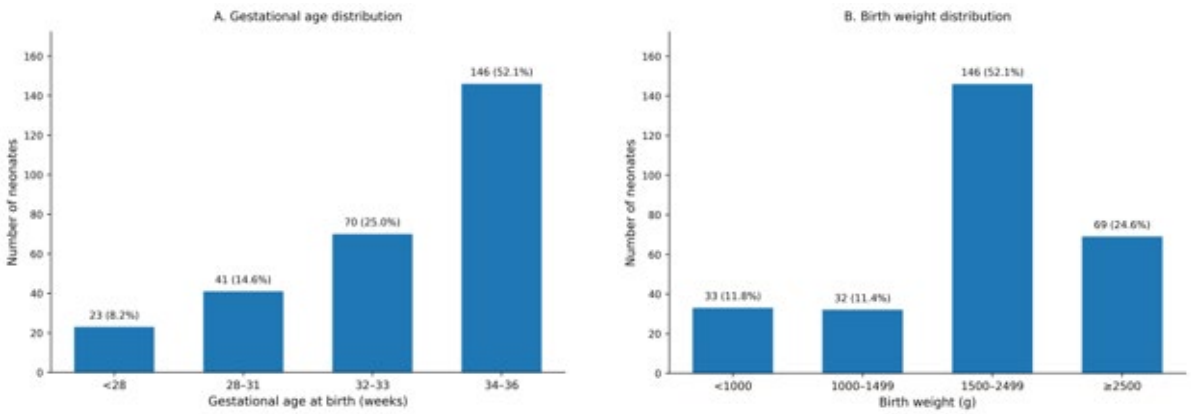


Figure 1. *Distribution of gestational age and birth weight in the study population (n = 280). (A) Distribution of gestational age at birth. (B) Distribution of birth weight. Values above the bars indicate n (%).*

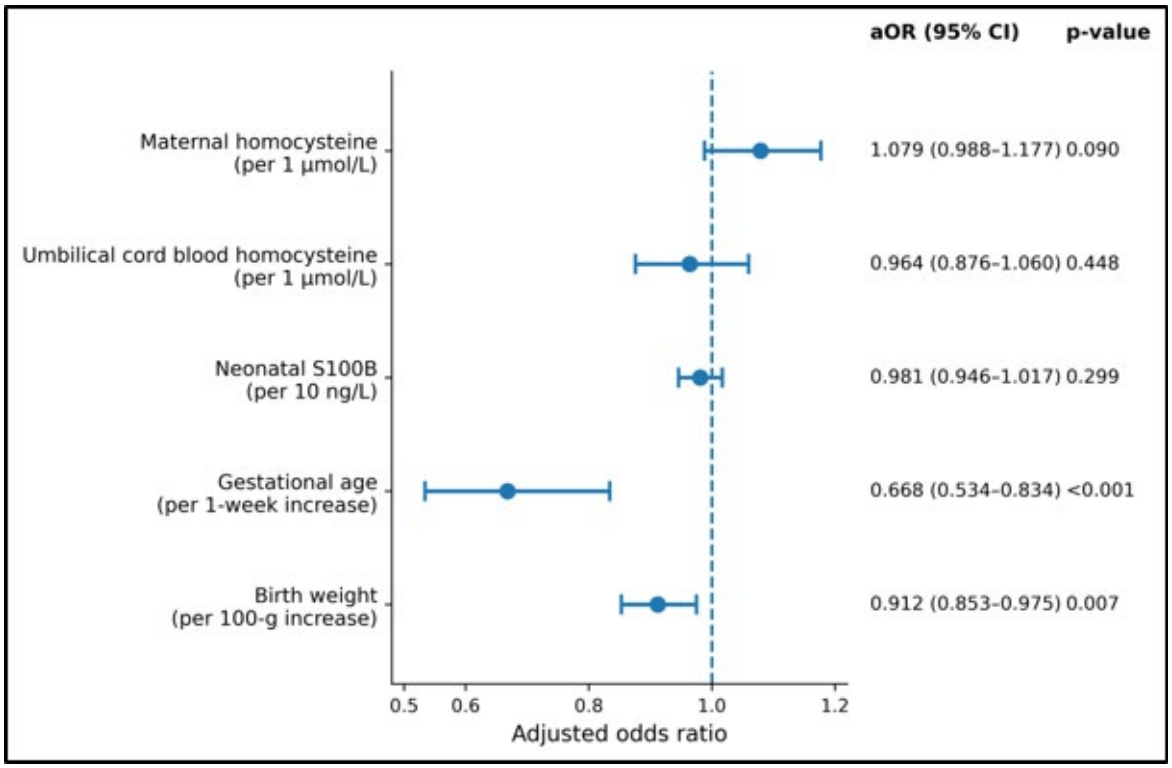


Figure 2. *Forest plot of adjusted odds ratios (aORs) and 95% confidence intervals (CIs) from the combined five-variable sensitivity model. The vertical dashed line indicates an aOR of 1.0.*

Table 1. *Maternal characteristics of the study population (n = 280).*

Parameter	**Me [Q1; Q3]**
Age, years	32.0 [27.0–36.0]
Height, cm	165.0 [160.0–168.0]
Weight, kg	71.0 [62.0–80.0]
Body mass index, kg/m²	27.0 [24.0–30.0]
Number of pregnancies	2.0 [1.0–4.0]
Number of deliveries	2.0 [1.0–3.0]

Table 2. *Clinical characteristics of preterm newborns (n = 280).*

Parameter	**Me [Q1; Q3]**
Gestational age, weeks	34.0 [32.0–35.0]
Birth weight, g	2170.0 [1660.0–2490.0]
Birth length, cm	44.5 [42.0–46.0]
Apgar score at 1 min	6.0 [5.0–6.0]
Apgar score at 5 min	7.0 [7.0–7.0]
Head circumference, cm	32.0 [30.0–34.0]

Table 3. *In-hospital neonatal complications in preterm newborns (n = 280).*

Complication	n	%
Intraventricular hemorrhage, any grade	149	53.2
IVH grade I	89	31.8
IVH grade II	48	17.1
IVH grade III	5	1.8
IVH grade IV	7	2.5
IVH grade III–IV	12	4.3
Congenital pneumonia	93	33.2
Invasive mechanical ventilation from birth	74	26.4
Neonatal pneumonia	45	16.1
Early-onset neonatal sepsis	4	1.4
Late-onset neonatal sepsis	2	0.7
Composite adverse neonatal outcome	185	66.1

Table 4. *Biomarker concentrations according to the composite adverse neonatal outcome.*

Parameter	Adverse outcome (n = 185), median [Q1–Q3]	No adverse outcome (n = 95), median [Q1–Q3]	p-value
Maternal homocysteine, μmol/L	10.30 [7.60–14.10]	9.09 [6.70–12.41]	0.062
Umbilical cord blood homocysteine, μmol/L	8.04 [5.67–11.13]	8.22 [6.61–10.51]	0.584
Neonatal S100B, ng/L	79.30 [56.30–105.30]	75.00 [54.57–107.05]	0.598

Table 5. *Neonatal S100B concentrations according to IVH status.*

Comparison	S100B, median [Q1–Q3], ng/L	p-value
Any-grade IVH (n = 149)	85.0 [58.0–115.2]	
No IVH (n = 131)	72.1 [53.1–102.6]	0.092
Grade III–IV IVH (n = 12)	91.4 [55.9–131.6]	
No grade III–IV IVH (n = 268)	77.9 [56.2–106.8]	0.560

Table 6. *Separate adjusted logistic regression models for the selected composite adverse neonatal outcome.*

Model	Variable	Adjusted OR	95% CI	p-value
A	Maternal homocysteine, per 1 μmol/L	1.057	0.989–1.130	0.100
A	Gestational age, per 1-week increase	0.681	0.548–0.846	<0.001
A	Birth weight, per 100-g increase	0.913	0.854–0.976	0.008
B	Umbilical cord blood homocysteine, per 1 μmol/L	1.021	0.949–1.099	0.574
B	Gestational age, per 1-week increase	0.686	0.552–0.852	0.001
B	Birth weight, per 100-g increase	0.908	0.850–0.971	0.004
C	Neonatal S100B, per 10 ng/L	0.981	0.947–1.016	0.278
C	Gestational age, per 1-week increase	0.674	0.540–0.841	<0.001
C	Birth weight, per 100-g increase	0.906	0.848–0.968	0.003

Note: *Model A included maternal homocysteine, gestational age, and birth weight; Model B included cord-blood homocysteine, gestational age, and birth weight; Model C included neonatal S100B, gestational age, and birth weight. n = 280 in each model. S100B is scaled per 10 ng/L, gestational age per 1 week, and birth weight per 100 g. These post hoc models are exploratory. OR, odds ratio; CI, confidence interval.*

Table 7. *Combined five-variable sensitivity model for the selected composite adverse neonatal outcome.*

Variable	Adjusted OR	95% CI	p-value
Maternal homocysteine, per 1 μmol/L	1.079	0.988–1.177	0.090
Umbilical cord blood homocysteine, per 1 μmol/L	0.964	0.876–1.060	0.448
Neonatal S100B, per 10 ng/L	0.981	0.946–1.017	0.299
Gestational age, per 1-week increase	0.668	0.534–0.834	<0.001
Birth weight, per 100-g increase	0.912	0.853–0.975	0.007

OR, odds ratio; CI, confidence interval. The model included 280 infants, of whom 185 (66.1%) experienced the selected composite. Gestational age and birth weight are expressed per 1-week and per 100-g increase, respectively; S100B is expressed per 10-ng/L increase. VIFs were <3 for all included predictors. Hosmer–Lemeshow goodness-of-fit p = 0.771. This combined model is a post hoc sensitivity analysis.

Table 8. *Sensitivity analysis excluding grade I–II IVH.*

Variable	Adjusted OR	95% CI	p-value
Maternal homocysteine, per 1 µmol/L	1.022	0.946–1.105	0.580
Umbilical cord blood homocysteine, per 1 µmol/L	0.973	0.890–1.065	0.555
Neonatal S100B, per 10 ng/L	0.981	0.951–1.012	0.236
Gestational age, per 1-week increase	0.665	0.548–0.806	<0.001
Birth weight, per 100-g increase	0.942	0.882–1.007	0.079

Outcome: modified composite adverse neonatal outcome excluding grade I–II IVH (n = 129/280, 46.1%). The same covariates and scaling as in the combined five-variable sensitivity model were used.

Table 9. *Sensitivity analysis adding in-hospital death to the selected composite outcome.*

Variable	Adjusted OR	95% CI	p-value
Maternal homocysteine, per 1 µmol/L	1.079	0.989–1.177	0.087
Umbilical cord blood homocysteine, per 1 µmol/L	0.961	0.874–1.056	0.409
Neonatal S100B, per 10 ng/L	0.981	0.947–1.017	0.308
Gestational age, per 1-week increase	0.674	0.541–0.840	<0.001
Birth weight, per 100-g increase	0.915	0.856–0.978	0.009

Outcome: selected composite adverse neonatal outcome plus in-hospital death (n = 186/280, 66.4%). The same five covariates and scaling as in the combined sensitivity model were used.

Maternal homocysteine (aOR 1.079, 95% CI 0.988–1.177; p = 0.090), cord-blood homocysteine (aOR 0.964, 95% CI 0.876–1.060; p = 0.448), and neonatal S100B (aOR 0.981 per 10-ng/L increase, 95% CI 0.946–1.017; p = 0.299) were not independently associated with the selected composite.

Variance inflation factors were <3 for all variables in the combined model, indicating no evidence of problematic multicollinearity. The Hosmer–Lemeshow test showed no evidence of poor calibration (p = 0.771). The biomarker conclusions were consistent with the separate adjusted models.

Sensitivity Analysis Excluding Grade I–II IVH:

Because low-grade IVH accounted for most IVH events, a sensitivity analysis used a modified composite excluding grade I–II IVH while retaining grade III–IV IVH, invasive mechanical ventilation from birth, congenital pneumonia, neonatal pneumonia, EOS, and LOS. The modified composite occurred in 129 of 280 infants (46.1%).

In the combined five-variable sensitivity model for the modified outcome, gestational age remained associated with lower odds (aOR 0.665 per 1-week increase, 95% CI 0.548–0.806; p < 0.001). The birth-weight association was attenuated (aOR 0.942 per 100-g increase, 95% CI 0.882–1.007; p = 0.079). Maternal homocysteine (aOR 1.022, 95% CI 0.946–1.105; p = 0.580), cord-blood homocysteine (aOR 0.973, 95% CI 0.890–1.065; p = 0.555), and neonatal S100B (aOR 0.981 per 10-ng/L increase, 95% CI 0.951–1.012; p = 0.236) were not associated with the modified composite.

Sensitivity Analysis Including In-Hospital Death:

To examine whether exclusion of death from the morbidity composite altered the findings, in-hospital death was added to the selected composite. The death-inclusive outcome occurred in 186 of 280 infants (66.4%); 10 of 11 deaths had already met at least one morbidity component and one additional infant was classified by death alone.

In the combined five-variable model, maternal homocysteine (aOR 1.079, 95% CI 0.989–1.177; p = 0.087), cord-blood homocysteine (aOR 0.961, 95% CI 0.874–1.056; p = 0.409), and neonatal S100B (aOR 0.981 per 10-ng/L increase, 95% CI 0.947–1.017; p = 0.308) remained non-significant. Gestational age (aOR 0.674, 95% CI 0.541–0.840; p < 0.001) and birth weight (aOR 0.915 per 100-g increase, 95% CI 0.856–0.978; p = 0.009) remained associated with lower odds of the death-inclusive outcome.

Discussion.

This prospective multicenter cohort study examined maternal–newborn biochemical relationships and their associations with in-hospital neonatal outcomes following preterm birth. The main findings were a strong positive correlation between maternal and cord-blood homocysteine concentrations and the absence of independent associations between maternal homocysteine, cord-blood homocysteine, or neonatal S100B and the selected composite outcome in separate adjusted models. Gestational age and birth weight were associated with lower odds of the selected composite. The combined five-variable model and sensitivity analyses excluding low-grade IVH or adding death yielded consistent biomarker conclusions. Because the exact composite and model specification were not prospectively documented before outcome review, these analyses should be regarded as post hoc and exploratory.

The strong correlation between maternal and umbilical cord blood homocysteine concentrations represents an important finding and supports a close maternal–fetal metabolic relationship at delivery. Homocysteine metabolism is closely related to folate, vitamin B12, vitamin B6, and methionine metabolism, and elevated maternal homocysteine concentrations have been associated with adverse pregnancy outcomes, impaired placental function, and fetal growth restriction [4-6]. Because maternal and cord-blood homocysteine reflect related points in the same pathway, we evaluated them in separate adjusted models. Neither marker was independently associated with the selected composite after adjustment for gestational age and birth weight; the combined mutually adjusted model produced the same overall conclusion.

S100B has been investigated as a biomarker of neurological

stress and brain injury in premature neonates, including in relation to IVH and other forms of neonatal brain injury [7-11]. In the present cohort, neonatal S100B concentrations were numerically higher in infants with any-grade IVH than in those without IVH, but the difference did not reach statistical significance. S100B concentrations also did not differ significantly between infants with and without grade III–IV IVH. Thus, our findings did not demonstrate a statistically significant association between a single early neonatal S100B measurement and either the presence or severity of IVH. Interpretation should account for the relatively small number of infants with severe IVH and the use of a single S100B measurement during the first 12–24 h of life.

The strong maternal–cord homocysteine correlation is relevant to model interpretation. Simultaneous inclusion of both measurements estimates their mutually adjusted associations and can attenuate the apparent association of either correlated marker. For this reason, the separate biomarker models were emphasized, while the original combined five-variable model was retained only as a sensitivity analysis. The lack of an independent biomarker association was consistent across both approaches.

Across the three separate adjusted models, increasing gestational age and birth weight were associated with lower odds of the selected composite outcome, whereas maternal homocysteine, cord-blood homocysteine, and neonatal S100B were not. These findings should be interpreted as associations within post hoc models rather than as evidence of predictive or prognostic performance. The associations with gestational maturity are consistent with the well-established relationship between gestational age and neonatal morbidity among preterm infants [12].

The composition of the selected outcome also warrants consideration. IVH was the most frequent component, occurring in 149 infants, and most cases were grade I–II. Nevertheless, morbidity was not limited to low-grade IVH: 128 infants experienced at least one non-IVH component of the composite, and 114 experienced two or more components. Because the individual components represent clinically and pathophysiologically heterogeneous events, the composite should be interpreted as an exploratory summary measure of in-hospital neonatal morbidity rather than as a single pathophysiological endpoint.

Sensitivity analyses addressed two concerns about outcome definition. Excluding grade, I–II IVH reduced the event rate to 129/280 (46.1%) without creating an independent association for any biomarker. Adding in-hospital death increased the event rate from 185 to 186 infants because 10 of the 11 deaths had already experienced a morbidity component; again, the biomarker findings were unchanged. These analyses support the robustness of the null biomarker associations to these alternative outcome definitions, while not resolving the broader limitations of a heterogeneous post hoc composite.

Several limitations should be considered. First, the selected composite combined neurological, respiratory, and infectious complications that differ in pathophysiology and clinical severity, and its exact composition was not documented in a time-stamped statistical analysis plan before examination of the outcome data. It should therefore be regarded as a post hoc exploratory endpoint. Second, follow-up extended from birth until discharge, transfer, or death, resulting in unequal observation periods. Among 259 infants with complete numeric ward-level bed-day data, median recorded observation was longer in infants with the composite outcome (16 days [IQR, 9–28.5]) than in those without it (8 days [IQR, 6–12]). This creates differential time at risk for later-occurring events, particularly neonatal pneumonia and LOS. Standardized dates of onset were not available for all outcome components, so a fixed 28-day or time-to-event sensitivity analysis could not be performed. Third, pneumonia and neonatal sepsis were identified according to the clinical protocols of the participating centers and were not restricted exclusively to culture-confirmed infection; therefore, some diagnostic heterogeneity cannot be excluded.

Fourth, although this was a two-center study, an individual-level center identifier was not retained in the final analytical dataset and could not be reconstructed reliably from the available study variables. Consequently, center-specific recruitment and outcome frequencies could not be reported, and center effects could not be assessed; this is a major limitation because center-level practices may differ. Fifth, although manufacturer assay specifications are now reported, specimen-level storage duration, exact freeze–thaw counts, assay batch identifiers, replicate optical-density values, study-specific coefficients of variation, and formal laboratory blinding status were not retained in the analytical dataset. The documented preanalytical processing and manufacturer protocols therefore cannot fully reconstruct all laboratory workflow details. Sixth, the number of infants with severe IVH and neonatal sepsis was small, limiting outcome-specific analyses. Finally, homocysteine and S100B were measured at defined single time points, limiting evaluation of temporal biomarker trajectories.

Despite these limitations, the study provides prospective data integrating paired maternal and umbilical cord blood homocysteine measurements, neonatal S100B, and clinically relevant in-hospital neonatal outcomes within the same preterm cohort. The strong maternal–cord homocysteine correlation demonstrates a close maternal–fetal metabolic relationship, whereas homocysteine and S100B were not independently associated with the selected composite after adjustment for gestational age and birth weight. Future studies should prespecify clinically coherent endpoints, standardize observation windows, retain center and laboratory process identifiers, and evaluate serial biomarker measurements in relation to specific neonatal complications.

Conclusion.

This prospective multicenter cohort study demonstrated a strong positive correlation between maternal and umbilical cord blood homocysteine concentrations, indicating a close maternal–fetal metabolic relationship at delivery. In separate adjusted models, maternal homocysteine, cord-blood homocysteine, and neonatal S100B were not independently associated with the selected composite of in-hospital neonatal morbidity. Gestational age and birth weight were associated with lower odds of the composite across the separate models, and the biomarker conclusions were

unchanged in the combined model and in sensitivity analyses excluding grade I–II IVH or adding in-hospital death. These post hoc findings support further investigation using prespecified outcome definitions, standardized follow-up windows, and serial biomarker measurements.

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Conflict of Interest.

The authors declare no conflict of interest.

Author Contributions (CRediT):

Conceptualization: S.I., D.S.;
Methodology: S.I., I.A.;
Investigation: S.I., N.B., I.A., G.A.;
Data curation: I.A.;
Formal analysis: D.S.;
Writing—original draft preparation: G.A.;
Writing—review and editing: All authors;
Supervision: S.I.;
Funding acquisition: I.A.

Ethical Approval.

The study protocol was approved by the Local Ethics Committee of the Center of Perinatology and Pediatric Cardiac Surgery, Almaty, Kazakhstan (Protocol No. 26, 31 October 2024).

Informed Consent.

Written informed consent was obtained from all participants included in the study.

Data Availability Statement:

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Цель исследования.

Изучить взаимосвязь между концентрациями гомоцистеина у матери и в пуповинной крови, а также оценить ассоциации гомоцистеина и неонатального S100B с внутригоспитальными неонатальными исходами у недоношенных новорожденных.

Материал и методы: В проспективное многоцентровое когортное исследование включены 280 пар «мать–новорожденный» при одноплодных преждевременных родах в сроке 22+0–36+6 недель. Определяли концентрации гомоцистеина в сыворотке крови матери и пуповинной крови, а также S100B у новорожденных. Выбранный комбинированный исход, включавший ВЖК, инвазивную ИВЛ с рождения, врожденную или неонатальную пневмонию, ранний или поздний неонатальный сепсис, анализировался post hoc. Для каждого биомаркера отдельно построены скорректированные логистические модели с учетом гестационного возраста и массы тела при рождении; объединенная пятифакторная модель использована как анализ чувствительности.

Результаты: Комбинированный исход зарегистрирован у 185 из 280 новорожденных (66,1%). Между концентрациями гомоцистеина у матери и в пуповинной крови выявлена сильная положительная корреляция ($\rho = 0{,}663$; $p < 0{,}001$). В отдельных скорректированных моделях гомоцистеин матери (скорректированное ОШ 1,057; 95% ДИ 0,989–1,130; $p = 0{,}100$), гомоцистеин пуповинной крови (ОШ 1,021; 95% ДИ 0,949–1,099; $p = 0{,}574$) и S100B (ОШ 0,981 на каждые 10 нг/л; 95% ДИ 0,947–1,016; $p = 0{,}278$) не были независимо ассоциированы с комбинированным исходом. Более высокий гестационный возраст и большая масса тела при рождении ассоциировались с меньшей вероятностью исхода во всех трех моделях.

Заключение: Концентрации гомоцистеина у матери и в пуповинной крови тесно взаимосвязаны, что подтверждает выраженную метаболическую связь между матерью и плодом. Однако гомоцистеин матери, гомоцистеин пуповинной крови и неонатальный S100B

не были независимо ассоциированы с выбранным комбинированным показателем внутригоспитальной неонатальной заболеваемости после учета гестационного возраста и массы тела при рождении.

Ключевые слова: преждевременные роды, гомоцистеин, S100B, неонатальные исходы, недоношенность.

რეზიუმე

კვლევის მიზანი: დედის და ჭიპლარის სისხლში ჰომოცისტეინის კონცენტრაციებს შორის კავშირის შესწავლა და ჰომოცისტეინისა და ნეონატალური S100B-ის ასოციაციების შეფასება დღენაკლულ ახალშობილთა ჰოსპიტალიზაციის პერიოდში განვითარებულ ნეონატალურ გამოსავლებთან.

მასალადამეთოდები:პროსპექტიულმრავალცენტრულ კოჰორტულ კვლევაში ჩართული იყო 280 დედა–ახალშობილის წყვილი ერთნაყოფიანი ნაადრევი მშობიარობით, გესტაციის 22+0–36+6 კვირაზე. შეფასდა დედის შრატისა და ჭიპლარის სისხლის ჰომოცისტეინი და ახალშობილის S100B. შერჩეული კომბინირებული გამოსავალი, რომელიც მოიცავდა ინტრავენტრიკულურ სისხლჩაქცევას, დაბადებიდან ინვაზიურ მექანიკურ ვენტილაციას, თანდაყოლილ ან ნეონატალურ პნევმონიას და ადრეულ ან გვიან დაწყებულ სეფსისს, გაანალიზდა post hoc. თითოეული ბიომარკერისთვის ცალ-ცალკე აშენდა კორექტირებული ლოგისტიკური მოდელი გესტაციური ასაკისა და დაბადების წონის გათვალისწინებით; ხუთცვლადიანი გაერთიანებული მოდელი გამოყენებულ იქნა მგრძნობელობის ანალიზად.

შედეგები: შერჩეული კომბინირებული გამოსავალი აღინიშნა 280 ახალშობილიდან 185-ში (66.1%). დედისა და ჭიპლარის სისხლში ჰომოცისტეინის კონცენტრაციებს შორის გამოვლინდა ძლიერი დადებითი კორელაცია ($\rho = 0.663$; $p < 0.001$). ცალკეულ კორექტირებულ მოდელებში დედის ჰომოცისტეინი (aOR 1.057; 95% CI 0.989–1.130; $p = 0.100$), ჭიპლარის სისხლის ჰომოცისტეინი (aOR 1.021; 95% CI 0.949–1.099; $p = 0.574$) და ნეონატალური S100B (aOR 0.981 ყოველ 10 ng/L-ზე; 95% CI 0.947–1.016; $p = 0.278$) დამოუკიდებლად არ იყო დაკავშირებული კომბინირებულ გამოსავალთან. უფრო მაღალი გესტაციური ასაკი და დაბადების უფრო მაღალი წონა ყველა მოდელში დაკავშირებული იყო გამოსავლის ნაკლებ ალბათობასთან.

დასკვნა: დედისა და ჭიპლარის სისხლში ჰომოცისტეინის კონცენტრაციები მჭიდროდ იყო დაკავშირებული, რაც დედა–ნაყოფის ახლო მეტაბოლურ ურთიერთკავშირს ადასტურებს. თუმცა დედის ჰომოცისტეინი, ჭიპლარის სისხლის ჰომოცისტეინი და ნეონატალური S100B გესტაციური ასაკისა და დაბადების წონის გათვალისწინების შემდეგ დამოუკიდებლად არ იყო დაკავშირებული ჰოსპიტალიზაციის პერიოდის შერჩეულ კომბინირებულ ნეონატალურ ავადობასთან.

საკვანძო სიტყვები: ნაადრევი მშობიარობა, ჰომოცისტეინი, S100B, ნეონატალური გამოსავლები, დღენაკლულობა.