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Metabolomic Research to Identify Intermediate Infants that Might Need a Diagnostic Tool

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Abstract

Finding metabolic markers connected to healthy and disease states using urine metabolomics is gaining popularity. The study comprised 31 late preterm (LP) neonates who were admitted to the neonatal intensive care unit (NICU) and 23 healthy LPs who were age-matched and admitted to the maternity ward of a tertiary hospital. On the first and third days of the neonates' lives, urine metabolomic analysis using proton nuclear magnetic resonance (1H NMR) spectroscopy was conducted. Both univariate and multivariate statistical analysis were used to examine the data. The NICU-admitted LPs were found to have a distinct metabolic pattern of increased metabolites on their first day of life. When LPs with respiratory distress syndrome (RDS) presented, their metabolic profiles were distinctive. The inconsistencies most likely reflect abnormalities in the gut microbiota, which may be brought on by dietary changes or medical procedures like the administration of antibiotics and other drugs. For seriously unwell LP neonates or those who are at a high risk for negative outcomes later in life, including metabolic concerns, altered metabolites may be used as biomarkers. The identification of novel biomarkers may provide a personalized strategy by revealing prospective drug discovery targets and the best window of opportunity for intervention.

Keywords: Late preterm neonates; Neonatal intensive care unit/ NICU; Urine metabolomics

Introduction

The term "late preterm" (LP) neonates refers to infants born between 340 and 366 weeks gestation. They make up almost 75% of preterm newborns and 9.1% of all neonates in the United States. Compared to term newborns, late preterms have a higher risk of morbidity and mortality [1]. Sepsis, intraventricular haemorrhage, periventricular leukomalacia, neurodevelopmental impairment, feeding problems, hypoglycemia, impaired immune response, respiratory disorders like respiratory distress syndrome (RDS), transient tachypnea of the newborn, pneumonia, apnea, and pulmonary hypertension are some of the associated morbidities [2].

A rapidly developing area of system biology, "metabolomics" is the systematic examination of a wide variety of tiny endogenous molecules (1500 Da) in a biological sample. Small molecules including peptides, lipids, organic acids, vitamins, amino acids, medicines, and other compounds can be quantified in order to identify metabolic abnormalities and signatures that are connected to states of health and sickness [3]. Metabolomics is essential in the context of the precision medicine approach because changes in an individual's metabolic profile take place much sooner than any clinically identifiable indication or symptom. The metabolome has the strongest correlation to the clinical phenotype since it is the product of biochemical processes controlled by proteins derived from gene expression. As a result, metabolomics is increasingly being used as a technique for the validation of novel biomarkers for the early diagnosis or prognosis of pathophysiological disorders [4].

Blood has undergone extensive metabolomic analysis, but other methods that profile metabolites using non-invasive matrices are becoming more and more common. Since faecal metabolites reflect gut microbial makeup, one such strategy is the use of a faecal metabolomic profile to forecast illness outcomes [5]. Early gut colonisation in infants is known to have long-term health effects on immune system development, growth, cognitive development, and the beginning of childhood disorders like obesity, asthma, and allergies. Numerous researches have also discussed the effects of delivery method, use of antibiotics, and early life feeding practises on the infant faecal metabolome. Additionally, distinct faecal metabolomes between formula-fed and breast-fed infants have been found [6].

Materials and Methods

Study population

The University General Hospital of Patras' neonatal ward, neonatal intensive care unit (NICU), and pharmacy department at the University of Patras all participated in the current study. The study initially included 51 neonates hospitalized to the NICU and an additional 23 age-matched healthy LPs admitted to the maternity unit between April 2017 and December 2018 [7]. Urine was taken as a biological sample from each newborn in order to track the metabolic changes that occurred over the first few days after delivery, notably on the first and third days of life, and compare them to the metabolism of infants with normal LP. For urine metabolomic analysis, proton nuclear magnetic resonance (1H NMR) spectroscopy was employed. Both univariate and multivariate statistical analysis were used to examine the data. In a prior investigation, our research team collected clinical and NMR data from 18 healthy, age-matched LP infants [8].

Discussion

The goal of the current study was to ascertain if LP newborns admitted to the NICU, especially those with RDS, have a distinctive urine metabolic fingerprint from healthy LP neonates or LP neonates admitted to the NICU without RDS. Based on data retrieved from the

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urine NMR spectrum at two different time points, the metabolomic analysis indicates the existence of differential metabolic profiles between the investigated categories as early as the first day of life [9]. Our results showed that several metabolite levels were abnormal in various metabolic pathways and indicated as possible biomarkers for newborn RDS or NICU hospitalizations. The metabolic disparities reported in this study may have clinical relevance given that metabolic immaturity early in life is linked to poorer growth outcomes and metabolic illness in the long run.

It has been noted that due to changes in food, metabolism, and gut microbiota composition, the size and chemical diversity of the measured metabolome in healthy newborns are smaller and simpler than those of children and adults. Due to the rapid cell growth and division, higher levels of essential amino acids, collagen-associated amino acids, and acylcarnitines in neonatal urine may indicate greater neonatal requirements. It is also widely known that in neonates, time-dependent changes to metabolic fingerprints and biochemical pathways occur [10]. Diet has been identified as a significant environmental component that modifies the gut microbiota's metabolic activity. Since milk is the first food to enter the digestive tract, its composition directly affects the gut flora and newborn neurodevelopment. This is because the presence of probiotics, microorganisms, and immunomodulatory compounds as well as critical nutrients for bacterial proliferation—such as carbohydrates, proteins, iron, and human milk oligosaccharides (HMOs)—is provided. The human microbiome is first colonized by bacteria while a person is still a fetus, and maternally produced microbial metabolites that are passed on to newborns through human milk have an impact on the microbiome of the newborn and may have health effects on the child. Early infancy appears to be a window of opportunity when a healthy microbiome composition is linked to and profoundly influenced by the style of feeding.

Additionally, it has been noted that various feeding methods, including breastfeeding, formula feeding, and mixed feeding, change the metabolic profiles of newborns. Evidence points to the microbiome having a greater impact on metabolic activity in adolescence than in adulthood. The development of metabolic syndromes, such as obesity, insulin resistance, type 2 diabetes mellitus, hypertension, cardiovascular diseases, and gastrointestinal diseases, later in life is linked to the regulation of infant metabolism and gut immune system function by nutritional strategies during the early stages of infant development.

The microbial diversity is decreased as a result of these dysbiotic alterations. Several physiological activities, including gene expression, DNA and protein synthesis, cell proliferation, apoptosis, and the immunological response, depend on glutathione for protection against free radicals. Oxidative stress, which is involved in chronic illnesses such as neurological, haematological, respiratory, cardiovascular, and metabolic diseases, is exacerbated by glutathione deficiency.

When compared to neonates admitted to the NICU without RDS, their myo-inositol levels were greater on the first day and lower on the third day. In addition to playing a significant part in glucose transport and metabolism, myo-inositol also plays a part in intracellular insulin signaling.

It also functions as a structural lipid in phosphatidylinositol and cell membranes, which means that it is essential for lipid synthesis, cell development, and cell morphogenesis. Prematurity has an impact on myo-inositol-related metabolic pathways, raising the possibility of future cardiometabolic illness.

Conclusion

The diagnosis, treatment, and prognosis of outcomes in late preterm infants with RDS may all be significantly affected by the overall findings. The discovery of altered metabolites and metabolic pathways in late preterm neonates with RDS can offer important insights into the pathophysiology of the condition and serve as biomarkers for risk assessment and early diagnosis. In addition to making diagnoses easier, the identification of novel biomarkers may also open up new doors for personalized treatment in the neonatal population by revealing prospective targets for drug discovery and providing windows of opportunity for intervention.

In conclusion, our results support the use of NMR-based urine metabolomics for better understanding the relationship between mild preterm, neonatal illnesses, integrated metabolism, nutrition, and medical conditions. The study of newborn metabolic maturation and the discovery of early biomarkers helpful for diagnosis, specialised care of neonatal illnesses, and early outcome prediction may be improved by knowledge about the metabolic status of LP infants.

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