International Journal of Gynecology & Clinical Practices

Commentary   **Open Access**

Can Metabolomics Aid in the Clinical Management of Preterm Birth?

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The idea that the omic sciences (e.g. genomics, transcriptomics, proteomics, metabolomics) may revolutionize disease diagnostics and management has been much discussed in the last decade. All omics come together under the umbrella of *systems biology*, a strategy that may provide an enormous amount of new information on the biochemical and biological function of the human organism, including its response to disease and therapy. Individually, each omic has also the potential of unveiling new biomarkers, which may then be used not only to detect and follow disease in a human individual, but also to measure risk and predict disease early on. With this enticing promise in mind, a significant amount of research has been carried out in this quest for new biomarkers for diseases such as cancer, diabetes and cardiovascular disease. Following this trend, consistent efforts are being made in prenatal health research to use omics to seek predictive biomarkers of conditions such as preeclampsia and preterm birth (PTB, birth before 37 gestational weeks). The latter is the leading cause of neonatal deaths and the second cause of infant death under 5 years of age (after pneumonia), and, in particular, *metabolomics* (or *metabonomics*) has been increasingly used in the last 8-10 years to find PTB biomarkers in fetal, maternal or newborn biofluids, either during pregnancy (for predictive biomarkers) or postpartum (for a deeper understanding of the metabolism disturbances and adaptations of the PTB newborn). The hypothesis supporting this research is that the development patterns of PTB subjects, either in *utero* or after birth, are accompanied by specific metabolic deviations which may be picked up and quantified by metabolomics. These deviations are expected to in time translate into prenatal biomarkers of increased PTB risk or postnatal biomarkers of infant development.

Therefore, metabolomics studies have set out to analyze the metabolic profile (complex set of composing small compounds and their concentrations) of the biofluids collected during pregnancy (amniotic fluid, maternal blood/urine, cervicovaginal fluid) and at or postpartum (umbilical cord blood, maternal blood, newborn blood/urine), to find PTB biomarkers i.e. subsets of compounds the levels of which are associated to early or established PTB with statistical robustness. Recent metabolomic advances on breast milk composition have also been used to establish the point at which its full term nutritional characteristics are attained. The possibility of predictive biomarkers of PTB becoming measurable in maternal urine or blood during pregnancy is of added importance for the non-invasive clinical prediction and management of PTB. The excreted and circulating levels of several small molecules such as amino acids, organic acids, lipids have indeed been shown to be associated to *pre*-PTB stages and their use as predictive biomarkers is currently being further explored. In addition, the metabolic profile of the PTB newborn, though urine or/and blood, has provided a detailed description of the corresponding deviant metabolism, depending on gestational age, and a basis for follow-up until theoretical term time and even into infancy. Such longer-term studies are yet to be performed and consist of one of the great promises of metabolomic strategies in PTB research. The possible use of non-invasive biofluids such as urine or saliva as matrixes where deviant metabolic profiles are to be sought postpartum could easily lead to new follow-up protocols for the early detection of health complications associated to PTB.

As a rather sophisticated analytical strategy, metabolomics usually requires academic expertise and, therefore, the close interaction and collaboration between clinicians and academy are of paramount importance at all stages of PTB metabolomics research. A number of challenges have also been recognized, such as the necessary consideration of large enough cohorts (up to epidemiological level) for statistical robustness to be duly assessed, and the standardization of procedures in sampling and data handling, to enable adequate comparison of different cohorts and improved understanding of the effects of diet, lifestyle, culture on metabolism and, hence, metabolic biomarkers.

In spite of the challenges, metabolomics has clearly opened new avenues to find easily measurable prenatal and postnatal markers of PTB. The knowledge thus provided may in time prove extremely valuable in aiding the clinicians to devise improved management protocols for pregnancies at risk of PTB and assessment of health status and PTB-related health complications postpartum.

Competing Interests

The authors declare that they have no competing interests

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