

Diagnostic Value of Cord Blood Biochemistry

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Abstract

It is suggested that Umbilical cord blood can be utilized for biochemical screening. Since Cord blood reflects babies' biochemical milieu at birth and non red cell analyses in cord blood are influenced by maternal metabolism and placenta. Cord blood cannot be collected by parents and can be drawn by the doctor or nursing staff at the time of delivery from placental end of cord blood. It can be preserved as liquid or dried whole blood and Serum or whole blood may be analyzed for various biochemical analyses. There is risk of contamination from maternal blood exists but is found to be at a low but acceptable rate and can be reduced if careful withdrawal is done without squeezing the placenta and/or umbilical cord.

Keywords: *Umbilical Cord Blood; Maternal Metabolism; Placenta*

Umbilical cord blood (UCB)

Fetal growth and development occur quickly and dramatically during fetal time. The umbilical cord blood is in contact with most of the fetal tissues and it can reflect both normal physiological and pathological status of the fetus.

Umbilical cord blood (UCB) is responsible for transport of O₂/CO₂ and various other materials to mother and fetus via placenta and this regulates the intrauterine environment. Any changes in diagnostic and therapeutic potential UCB proteins such as alpha fetoprotein, adiponectin, leptin in monitoring fetal and neonatal disorders. Also, recent reports indicate that human UCB has the potential to serve as a source of biomarkers and biologically active molecules with diagnostic and predictive applications for diagnosing complications occurring during in utero infections of fetus. On the other hand, umbilical cord blood (UCB) can be obtained easily and poses only small risk to the donor.

In the past, the primary use of UCB used to be in bone marrow transplantation. Umbilical cord blood (UCB) is an easily available biofluid of diagnostic value. The diagnostic potential of UCB remains unexplored, though it can tell accurately about the health status of newborns. The diagnostic potential of UCB has recently been of interest for assessing the infant health in detection and identification of candidate biomarkers that are informative of existing or potential future adverse effects.

With increased awareness about the prevalence of newborn diseases and future long- term effects such as diabetes, obesity, and chronic heart and kidney diseases, it is now expected that newer methods for UCB screening for early diagnosis in neonates would come up in future.

Neonatal proteome

The neonatal proteome has not been compared with the adult serum proteome; the possible outcome of such comparison would be challenging, but promising!

Much less information is available regarding the cord blood proteome and more details are required in this context. The knowledge of cord blood proteome would help in expanding the prospects of infant health diagnostics.

Studies report that UCB proteome contains various house-keeping proteins and secreted or shed low-abundance proteins. During fetal development, many regulatory factors influence the fetus and the metabolic products from the fetus might be released into UCB [1].

The proteomic profiles of male and female fetuses are reported to be different and so is the case between those of fetal and adult serums. Possibly proteins in UCB serum proteome are produced and secreted by fetus and/ or placenta. Many of UCB proteins are important since their expression levels could reflect the physiological and pathological conditions of the fetus and the status of the pregnancy. Alpha-fetoprotein (AFP) is one such protein and its elevated levels have been shown to occur in maternal serum in several fetal abnormalities namely, spina bifida, Down's syndrome, trisomy 13 and trisomy 18 [2].

Recent proteomic biomarkers for status of the fetus include collagen alpha 1 (I), collagen alpha 1 (III), glyceraldehyde 3- phosphate dehydrogenase, and HSPG2 (For Down's syndrome) [3]; AFP; fibronectin and plasminogen activator inhibitor; and fibronectin [3-5] and apolipoprotein A-I.

Several proteins present in UCB have been identified that are absent from the adult serum. This reflects specific metabolic status of fetus and the correlation of these proteins with potentially important regulatory factors for the fetus.

Serum proteome from first, second and third trimester healthy human maternal subjects has been reported to be sequenced using tandem mass spectrometry. This revealed the functional annotation of the proteome to uncover a large number of metabolic, defense response, complement cascade, coagulation cascade, and pregnancy associated proteins present in maternal serum [6]. Also, majority of the maternal serum proteins (59%) have been reported in amniotic fluid (AF) proteome. They suggested that maternal serum proteins are involved in maternal and fetal development, innate immune defense, and hemostasis during gestation [7].

There is a need to develop maternal serum proteome map so as to trace the changes in UCB proteome during healthy gestation and possibly these proteomic markers could serve as an important tool for maternal-fetal diagnostics [6].

Maternal-fetal interface

Maternal blood plays an important role During implantation, gestation and parturition. Factors like insulin-like growth factors (IGF-I), IGFBP-1, cytokines and vascular endothelial growth factor (VEGF) and placental growth factor (PGF) are present in maternal serum and they aid in embryonic implantation [6,7].

Since maternal blood supplies all the necessary vitamins, minerals, carbohydrates, lipids and amino acid required by developing fetus. During gestation, human chorionic gonadotropin subunit (beta- HCG), chorionic somatomammotropin hormone (CSH), pregnancy-associated-alpha-1-glycoproteins (PSG), and pregnancy- associated proteins (PAPP-A, PAPP-B and PAPP-C etc.) are present in maternal serum. These factors aid in fetal development and some of these placental proteins (e.g. beta HCG) prevent maternal immune-rejection of fetus [8]. During gestation and parturition, changes in blood coagulation system and fibrinolysis system of maternal plasma occur [9].

Also, pathologies of mother and/or placentas (namely, preeclampsia, Down syndrome, and preterm birth) can affect the dynamics and composition of maternal plasma. In preeclampsia, abnormal levels of maternal serum endothelin, soluble forms-like tyrosine kinase-1 (sFlt-1), angiotensin-II etc. have been reported [8,10-12].

In light of these discussed facts, it can be concluded that complex physiological changes occur in maternal blood during normal as well as abnormal gestations. Most changes observed in the maternal circulation in preeclamptic women are also present in the cord blood of their newborns, although these changes are less pronounced.

Detailed investigations of these changes that take place in maternal serum protein during healthy gestation are required for developing next generation biomarker-based diagnostics based on maternal-fetal proteins.

Amniotic fluid

Amniotic fluid (AF) being an extensively sequenced maternal body fluid. In maternal serum, a total of 47 AF proteins have been reported. AF also changes during gestation in a manner similar to maternal serum changes. The dynamics of AF during normal gestation have been explored by workers. The serial assessment of easily accessible body fluids like serum should be used instead of high-risk amniocentesis for maternal - fetal diagnostics.

Importance of cord blood

Cord blood is a readily accessible biofluid, since proteomic makeup of cord blood remains unexplored as compared to that of adults. Global screening for cord blood protein expression differences may be of help in exploring infant health outcomes associated with in utero exposures to environmental toxicants.

A maternal serum proteome map when derived in detail and standardization of changes occurring in the protein expression during healthy gestation could be of help in development of future maternal-fetal diagnostics.

Preeclampsia (PE) shares several similarities with atherosclerosis, namely, modifications in lipid milieu, amplified inflammatory processes and raised oxidative stress. These changes may result in disturbed cell activation and subsequent endothelial dysfunction. Studies have suggested that pregnant women who developed PE have a predisposition to develop, at long term [10,12] cardiovascular diseases. Changes in the inflammatory response and endothelial dysfunction have been observed in umbilical cord blood from mothers with PE [13] and they may have an increased risk of developing cardiovascular diseases in the future.

Despite several thousand publications on etiopathogenesis, prediction, diagnosis and treatment of preeclampsia, still many basic questions remain to be answered.

There is a need of studies to provide a basis for the development of diagnostic and prognostic biomarkers of preeclampsia that might be of help in reducing risk for developing future cardiovascular disease.

There is a need to identify novel epigenomic biomarkers in cord blood DNA to explore obesogenic experiences during fetal life and to profile the future risk of childhood obesity and future cardiometabolic disorders.

Conclusion

It is likely that in future UCB biochemical markers along with easily recordable clinical risk markers could help in predicting preeclampsia and developmental origins of adult disease.

Prospective cohort studies are required to define the possible role of umbilical cord blood to serve as a diagnostic window for human physiology and pathology.

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