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Biomedical and Psychosocial Determinants of Early Neurodevelopment After Preterm Birth

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Abstract

Prematurity and them related conditions are subject of scientific discussion. From the point of view optimization of postpartum processes, timely assessment of individual biomedical and psychosocial conditions and management of preventive intervention is very important, because of its linkage to issues of preterm infants and their families in long-term perspectives. The goal of the literature review is to bring together existing body of knowledge on biomedical, psychological, and social issues of premature infants related to early neurodevelopment in order to achieve better systemic vision. For this goal scientific articles related to neurological development delay of premature children and the possibilities of their timely identification were processed using electronic scientific search systems. Diagnostic tools to identify at-risk children and early intervention programs discussed in the article, significantly improve the chances of premature child development. In the article Introduced materials are to support: Clinicians to make correct decisions regarding important components of premature infants; Healthcare policy makers to plan targeted programs and activities; Public to better understand prematurity issues, especially in case of prematurely-born family members.

Keywords

child, neurodevelopment, prematurity, motor skills, cognitive skills, social determinants

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Introduction

For the past 25 years, preterm delivery (pregnancy finished before 37 weeks) remains high in developed countries as well as countries in transition.[1,2]

For the newborn, this state is complemented with development problems arising from immature organ system, which, on later stages of ontogenesis, is reflected on motoric, cognitive, and nervous systems. For parents, preterm delivery is associated with unexpected stress, where post-traumatic period is quite long. Stressful condition can damage mother-child interaction and support development delay. In long-term perspective lack of neurodevelopment issues, limit possibilities of individuals for education, and therefore, possibilities for better income, resulting into social and economic status. Mentioned points emphasize prematurity's importance for improvement of population health. To reduce impact of such consequence, timely diagnosis of health-related issues and provision of health promotion is required.

Interesting point, when describing the issue related to preterm child neurodevelopment, as the preterm birth itself,[3] is its multicausality. This paper discusses the following issues related to prematurity: *Bio-medical factors*, such as neurodevelopment and them related clinical issues; *Psychosocial* characteristics, which encompass emotional development of the child, and *related social*

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components as well as *parent stress factor impact*, caused by preterm delivery and its consequences.

Methodology

Data Selection Strategy

To process actual scientific information about the problematic issues related to neurodevelopment and their diagnostic possibilities at an early stage of ontogenesis the standard search strategy of Cochrane Neonatal to search the Cochrane Central Register of Controlled Trials (CENTRAL 2018, Issue 5), MEDLINE via PubMed 2000 to 2022 was used. Additionally, clinical trials databases, conference proceedings, and the reference lists of retrieved articles for randomized controlled trials (RCTs) and quasi-RCTs was searched, with key words "prematurity"; "preterm birth"; "premature infant's neurodevelopment."

Ethical Approval and Informed Consent

Ethics approval or informed consent was not required as the paper reviewed the work of various researchers.

Biomedical Factors of Early Neurodevelopment

The fetal brain is particularly vulnerable during third trimester of pregnancy, when it is going through the biggest growth and development.[4,5] Hence, children born exceptionally preterm are at high chance of disruptions in typical brain advancement (eg, abnormal myelination) and brain harm (eg, intraventricular hemorrhages [IVHs]).[5] Brain harm procured early in life can lead to neurodevelopmental impairments (NDI) and can considerably affect encourage cognitive and study function.[6]

Preterm survivors compared with those born full term are more likely to have the following neurodevelopment disabilities: Impaired cognitive skills; Motor deficits including mild fine or gross motor delay, and cerebral palsy (CP); Sensory impairment including vision and hearing losses; Behavioral and psychological problems.

Neurodevelopmental Impairment

Approximately 15% to 25% of surviving early preterm infants (EPT infants) have major disability as severe Neurodevelopmental impairment (NDI). Evaluated at 18 to 24 months corrected age the relative frequencies for disability list are as follows: Significant cognitive and/or motor impairment: 10% to 15%; Cerebral palsy (CP): 6% to 12%; Hearing loss requiring amplification devices: 1% to 3%; Blindness: 1% to 2%.[7]

Neurodevelopmental impairment is a significant long-term complication associated with preterm birth. The risk of NDI increases with decreasing gestational age (GA) and birth weight (BW).[8] Children who are born extremely (<28 week GA) or very preterm (28-32 week GA) are more likely than children who were born at term to have behavioral and emotional problems. A study from the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network of extremely preterm infants born between 2008 and 2012 reported one-third of the cohort had behavioral problems and one-quarter had deficits in socioemotional competence at 18 to 22 months corrected age.[9] Infants with severe NDI at 18 to 24 months are likely to have persistent disability throughout childhood.[10] However, some may have improvement in cognitive function.[11] Infants with milder disability are more likely to improve as they age.

Psychosocial Factors of Early Neurodevelopment

Social determinants of health for preterm-born children remain poorly studied. Components for socio-economic status, such as family income, parent's education, and the use of health services related to this subject have to be discussed in this article.

Although the association between preterm birth and NDI is well established, far less is known about the role of environment and experience in moderating the association. Some studies have reported that certain environmental factors (eg, higher maternal education level, parental interventions, home environment, and daycare environment) have beneficial effects on cognition, speech, and language development.[12]

Mother and premature infant social determinants can affect health of premature infant, including biomedical, psychosocial implicature in it in individual lives, learning processes, working abilities, generally influencing health wellbeing.[13] In a long-term perspective, low social status, expressed with poverty and low education of the mother, from pregnancy to motherhood can be reason for diverse pregnancy outcome with preterm birth and for future health and social development status of premature infant as well.[14] It results from lack of goods, limited access to quality health care services, neighborhood poverty, from lack of health promoting activities.[15]

Mother's Social Characteristics and Preterm Child's Neurodevelopment

According several study results, indicators of social determinants such as race/ethnicity, health care services availability, urban/rural region living, has impact on

premature infant health state. Millenium cohort study of preterm infants in the United Kingdom with 13 267 singleton children through lineal regression model analysis confirmed evidence-based relationship between family's socioeconomic status and preterm children cognitive development. Namely low status of this characteristic tended to child low development. According study results poverty level impact was so strong that term children from low-income families had lower cognitive scores than preterm children who were not living in poor families.[16]

Results of European preterm cohorts, with 20 839 extremely preterm born children showed, that children standardized mean differences for cognitive scores with mothers of high education degree is 0.24 (95% CI 0.02-0.46) lower and for premature infants when mothers had only primary education 0.57 (95% CI 0.34-0.76).[17]

Parental Stress Caused by Premature Birth and Its Impact on Child Development

Preterm birth of child is stressful event for parents. This event consequence can impact parents' health situation and action and persist for many years.[18] Posttraumatic stress of parents can affect the relationship to child and their health outcome.

Prospective cohort study "Hamburg study of VLBW and full-term infant development" aimed to discover birth-related traumatic stress symptoms. In the study recruited were parents from 3 largest perinatal medical care centers in Hamburg (Germany). During 4 to 6 weeks after the birth, while the child treatment in the NICU they were asked to participate in the study. Results showed that preterm birth might often lead to parental traumatization causing further mental health problems.[13]

Switzerland study about parental stress experience after preterm birth used mixed (qualitative and quantitative) methodology to compare after birth stress among parents with preterm and full-term babies. Data were collected between 2011 and 2012. Sample for quantitative analysis was 190 (77 fathers; 113 mothers) parents. Study reported statistically significant result for more parenting stress during first year after preterm birth and greater anxiety about the child in the first 2 years. Mothers experienced significant ($>.05$) more stress than fathers.[19]

Preterm Child-mother interaction is complex. Interactional behavior is different for pre- and full-term infants.[20] Early psychological and informational support after arising sudden event (preterm labor) can help parents to make timely and correct decision for infants' optimal development.

Identifying At-Risk Infants

Gestational age (GA) is factor for risk assessment of NDI in preterm infants. Additional risk factors include male sex, twin pregnancy, congenital malformations, comorbid neonatal conditions, socioeconomic factors, and lack of adequate antenatal care.

The available clinical tools to predict outcome include:

Neuroimaging (cranial ultrasonography and magnetic resonance imaging, Electroencephalography).
Early childhood clinical assessment during the first 2 years of life consisting of neurologic examination and formal evaluation of cognitive and motor function, language, and social development and behavior.[21]

Neuroimaging

Improvements in cranial ultrasonography and magnetic resonance imaging technology and application (MRI) have improved the identification of brain damage in premature newborns and the comprehension of the relationships between brain damage and neurodevelopmental outcomes.[22] Neuroimaging is used to identify preterm infants with significant brain injury, with high probability of NDI. In contrary, same method is not used successfully to predict changes in cognitive functions later in life. As a result, neuroimaging should not be used as the sole accurate predictor of long-term neurodevelopmental outcome for individuals.

Kidokoro et al[4] created a scoring system applicable to an MRI scan performed at term comparable age in order to evaluate and prevent early macrostructural brain damage (TEA). The approach has been verified for MRI scans performed between 29 and 35 weeks GA, and results showed a correlation between behavioral and neurodevelopmental outcomes at 1 year (CA) corrected age on the Bayley scales and neurosensory motor developmental assessment techniques.[23] A term-equivalent age MRI scan was performed (TEA). The system has been validated for MRI scans performed between 29 and 35 weeks gestational age (GA), and the scan scores were linked to behavioral and neurodevelopmental outcomes at 1 year corrected age (CA) on the Bayley Scales of Infant and Toddler Development and neuro-sensory motor developmental assessments.[23] Shortcoming of these methods are that, they are not provide useful information regarding individual sensory domains (auditory, visuospatial) contributing to child's development.[24] Specifically, because the ability to interact with the environment requires visuospatial attention and processing, deficiencies in this area can have a negative impact on

the growth of cognitive, motor, and behavioral abilities.[25,26] Neonatal MRI studies have shown that most of VPI (GA weeks) have white matter abnormalities increasing ventricular size, decreasing white mater volume, increased intensity of white matter signal, and evidence of decreasing myelination.[27]

In addition, there is evidence that these findings are useful in predicting long-term neurodevelopmental outcome based on studies that have shown correlation between neurodevelopmental outcome and either seriously abnormal or normal MRI scans at term equivalent for study cohorts.[22]

A prospective cohort research from a single location, however, found that only motor skills and behavior, not cognition, were linked with MRI findings at term with regard to short-term neurodevelopmental outcome at 2 years of age.[28] In this study, environmental factors (such as maternal level of education) were more predictive of cognitive function as children grew older.[28]

In addition, not all children with white matter abnormalities on term MRI had severe impairment, and severe neurologic impairment occurred in children without white matter abnormalities. As a result, the use of neuroimaging alone is insufficient to determine long-term outcome and follow-up intervention for individual patients.[29]

Formal Clinical Assessment

Early clinical assessments in preterm survivors with high risk of NDI, found moderate to severe impairments. Children with significant NDI in early childhood often have persistent disability at school age and may benefit from early intervention.[30] The formal clinical assessment for NDI during the first 2 years of life includes all of the following:

Detailed neurologic examination, focusing on identifying motor deficits
Visual assessment
Hearing assessment
Standardized tests for cognitive and motor function, language, social development, and behavior.

Eye Tracking Data Processing and Analysis

It has been a long time since there was a good test to identify and acknowledge visuospatial issues in children. An eye tracking-based method was created to measure visuospatial attention and processing starting at age one in order to close this gap.

The new technique tracks eye movements in reaction to different visual stimuli. Children born before 29 weeks GA who had no obvious brain abnormalities responded to visual stimuli more slowly than children born at term.[31] Independent of brain injury, impaired visuospatial attention and processing was observed in 8% to 23% of infants born between 26 and 32 weeks GA.[32] The MRI findings weren't made known to any of the subjects. Eye movements were recorded during the presentation of a number of visual stimuli for this assessment.

According to the study's findings, cerebral visuospatial function in the first year of life is correlated with early structural brain assessments. In comparison to normative benchmarks from 1 to 2 years CA, this translates into a corresponding connection with functional visuospatial changes. At 1-year CA, children, especially those with moderate to severe brain injury, appear to be more susceptible to visuospatial attention and motion processing problems. After that point, the majority of their functional performance remained abnormal or normalized. Both patterns have been linked to perinatal risk factors for respiratory or cardiovascular failure. The absence of correlations at 2 years CA suggests that the relationship between early brain macrostructure and brain function in the visuospatial domain cannot be regarded as clinically important in extremely preterm-born children after the first year of life. However, it is well known that children born preterm are at high risk of growing into deficit in multiple neurodevelopmental domains at later developmental stages, for example, at preschool[33] and school age.[34,35] Moreover, study results showed that the rate of abnormalities compared with normative age-related visuospatial development increased, despite the finding that overall attentional and motion RTs from 1 to 2 years CA became faster; this warrants a longer and more elaborate follow-up than the one presented here. Study found that, comprehensive MRI scoring, quantitative functional visuospatial assessment provides new bright perspective in understanding and managing very preterm population in the first year of life.

Cranial Ultrasonography

Cranial ultrasonography is the primary neuroimaging modality used to evaluate intracranial pathology in preterm infants and predict long-term outcome.[22] Study found that ultrasonography is not sensitive method to detect abnormalities in posterior fossa, especially during first month of life.[36]

Although patients with neonatal cranial ultrasound abnormalities compared with those with normal studies are more likely to have long-term neurodevelopmental outcome impairment, approximately one-fourth of early preterm infants with an ultrasound may still have cognitive and psychomotor delay.[37]

Neurodevelopmental Assessment

Screening for cognitive and motor impairment is imperative to identify infants who would benefit from early intervention and special educational accommodations. Preterm infants are also at risk for difficulties with complex language function. The general pediatrician may use screening tools such as the Ages and Stages Questionnaire and Child Behavior Checklist to screen development and behavior prior to referral for a neurodevelopmental assessment.[38]

Early Intervention Programs

Early intervention (EI) programs appear to be effective at improving neurodevelopment for preterm infants through early childhood. In a meta-analysis of 16 randomized and quasi-randomized trials, EI improved cognitive function in infancy and preschool age.[39] A subsequent randomized trial found that a preventive EI program had minimal long-term effects of neurodevelopment (with the exception of improved achievement in mathematics); however, parents in the EI group were less likely to experience depressive symptom.[40] There is also evidence that EI programs may improve the early childhood outcome of high-risk preterm children, especially those from marginalized socioeconomical groups.[41]

Discussion

Improved screening methods and timely treatment contributed that preterm-born children will develop subtle late effects in academic and psychological functioning.[35,42] These subtle late effects have received increased attention recently and have been found to persist into adolescence[43,44] and into adulthood.[45] They span social, academic, and cognitive domains, and place a significant toll on economic, health care, education, and mental health systems. Impairments in cognitive functioning have been well documented in late preterm,[46] very preterm, and extremely preterm children[10] and differences in motor, cognitive, and attentional functioning have been identified as early as toddlerhood.[47,48]

Not all preterm survivors will have neurodevelopmental impairment, as a result, it would be optimal to identify those survivors at the greatest risk for significant neurodevelopmental disability who would most benefit from ongoing costly comprehensive neurodevelopmental assessment and early intervention services.

Early detection of neurodevelopmental defects is necessary to prevent health complications. Modern diagnostic tools allow continuous observation of development processes. Timely professional bio-psycho-social support can help parents to make right decisions for further participation supporting their child, with is highly important for newborn survival and developing. Further population-based research about psychosocial impact on preterm child's neurodevelopment is required.

The importance for investment in early life prevention to avoid later complications is widely accepted.

Based on study results, described in article, families' social circumstances need to be considered when evaluating the health consequences of preterm newborns.[49] The social context should be considered in routine follow-up care of children born preterm. Health policy maker have obligation to care for health equity and reduce disparities with thoughtful intent in the appropriate cultural context through optimization of infant development health care providers; Making available for families with preterm infants to support child development with parents health education, nurses home visit programs; Stress coping support through professionals.[50]

Conclusion

To correctly manage the process of infant development, it is of prime importance to ensure mitigation of stress of parents caused by preterm delivery, timely implementation of interventions and due monitoring. Focusing on biomedical resources as well as psychological and social resources of the family.

Author Contributions

Kvaratskhelia N: Contributed to conception psychosocial factors, analysis and interpretation; drafted manuscript; critically revised and design manuscript.
Rurua N. Contributed to conception biomedical factors, analysis and interpretation; critically revised manuscript.
Vadachkoria S: Contributed to conception biomedical factors, analysis and interpretation; critically revised manuscript.

Declaration of Conflicting Interests

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