



ASD and Preterm Low Birth Weight Infant- A Risk Factor

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Introduction

Autism spectrum disorders (ASD) research and initiatives need to focus particular attention to premature, low birth weight infants in order to expand our knowledge base. Current research exploring premature and low birth weight populations provide direction, for researchers and providers, in terms of risk factor considerations. This paper reviews current data about ASD and recent research in the field related to ASD, prematurity and low- birth weight infants. In addition, next steps are recommended to improve our understanding of ASD. It is believed that improving our knowledge of premature, low birth weight infants will enhance our overall knowledge of ASD.

What We Know

ASD is a range of development disabilities. ASD can cause behavioral, communication and social changes [1]. The American Academy of Pediatrics (AAP) recommends that children get formally screened using standardized tools between 18 and 24 months with developmental surveillance [2]. In the United States, ASD is estimated to occur in 1% of children [3]. The total number of individuals diagnosed with autism is unclear but appears to be rising. It is unclear if the increase in diagnosis is based on more individuals developing the disorder, improvements in diagnostic abilities, or a more inclusive definition among clinical providers [1]. The Autism and Developmental Disabilities Monitoring Network (ADDMN) identifies a prevalence rate of 1 in 68 children (8 years of age) noting that overall ASD prevalence varies across sites [4].

Similar to prevalence rates, the etiology of ASD is also unknown. Research connects ASD to gene risk factors and children who have siblings with ASD are at higher risk for developing ASD [1]. There are also genetic and chromosome related conditions (fragile X syndrome and tuberous sclerosis) associated with ASD [1]. Children born to older parents have an increased risk for developing ASD [1]. In addition, there is a focus on specific periods of risk that provide some clues for the causes of ASD. Researchers are exploring the prenatal, perinatal, and postpartum timeframes to identify possible causes for ASD [1]. Particularly, in pregnancy the use of Valproic Acid and Thalidomide are associated with higher ASD risk. Although there is heightened public concern about vaccines, research findings show that there is no link between vaccines and ASD [5,6].

There is knowledge about the basic characteristics of individuals with ASD that derives from standard screening and diagnostic protocols. Positive screens for ASD occur more frequently in white, male children [7]. Although boys are 5 times more likely to be diagnosed than girls, ASD diagnosis occurs across gender, race, ethnicity and socioeconomic backgrounds [1]. Children tend to be diagnosed after the age of 4 but some can be diagnosed as early as 2 years old [1]. Infants that have frequent hospital admissions, behavior

problems, cognitive and language delays and infants with mothers who have low maternal education have more positive ASD screens [7]. More demographic information is being gathered about ASD characteristics. The Study to Explore Early Development (SEED) is a large, longitudinal, six multisite research study with a goal to gather additional information and identifying risk factors for ASD [1].

Currently, there are information networks gathering community data on the characteristics and frequency of ASD in children. The ADDMN is a collaborative network in 14 state sites collecting ASD data using a single, standard tracking method [8]. The goal of the ADDMN is to identify the number of children with ASD in their network area, provide information about ASD characteristics, determine ASD commonality and changes among groups of children, and understand the impact of ASD in families and communities [8]. The ADDMN may reduce gaps in knowledge related to prevalence, characteristics, and the impact of ASD on families and communities.

ASD experts, organizational representatives, stakeholders, and affected families convened to develop the ASD executive summary. The ASD executive summary identifies key areas of exploration in terms of prevalence and change (CDC, 2011):

- Examining different types of data systems to understand ASD trends
- Understanding the challenges of ASD for families and communities
- Continuing political & legislative pressures to gain momentum and address the needs of ASD
- Knowledge of the complex intrinsic and extrinsic identification factors to validate symptomology across ASD populations
- Better understanding for the causes of ASD in order to modify risk factors
- Examining biological and environmental factors alone an in conjunction when considering causes for ASD
- Focusing on both individual and population risks with three factorial conditions: prevalence in the population, substantial increase over time, and strong association with ASD diagnosis

The executive summary provides a framework for developing the next steps for practice and research. In order to better understand ASD, more focus needs to be on understanding causal factors through the examination of all data collection systems. In considering causal factors, there needs to be comprehensive evaluation of biological, individual-population and environmental factors. Research needs to provide data on causal factors to help medical providers mitigate risks, and more support is needed for families to help address the needs of ASD individuals across the lifespan.

Premature and Low Birth Weight Infants

Premature, low birth weight infants are a population gaining increased awareness in ASD discussions. Premature, low birth weight infants have their own unique neurodevelopmental needs and outcomes. In considering the framework provided by the ASD executive summary, premature and/or low birth weight births are significant causal factors when evaluating biological and environmental considerations [3]. The premature and low birth weight populations are often overlooked in terms of their contribution to the larger ASD discussion.

Biological

Factors that increase the risk of Autism Spectrum Disorder (ASD) for infants include prematurity and low birth-weight [9,10]. Similar to ASD in the general population, the actual prevalence of ASD for the preterm and low-birth weight population is not known. One reason for the lack of knowledge on prevalence rates for this group is the use of general screening tools [7]. General screening tools may result in false positive screens in a premature, low-birth weight population with high rates of neurodevelopmental impairments [7].

Birth weight, gestational age, and small for gestational age (SGA) are considered to be factors for ASD and pervasive developmental disorder [9]. Infants with birth weights less than 2500 grams and a gestation of less than 33 weeks have approximately two times the risk for developing ASD [10]. In this population, gender and magnitude vary where low birth weight girls have a 4 times increase risk of developing ASD with mental retardation [10]. It is worthy to note the prevalence of ASD is lower in premature, low birth weight infants compared to other developmental disabilities [10].

Similar studies have confirmed the link between ASD, birth weight and gestation. Moore et al. examine infant birth weight stratified by gestational age and found an association between ASD and small for gestational age (SGA) infants and large for gestational infants (LGA) [11]. Preterm (less than 34 weeks) SGA infants and term (39-41 week) LGA infants have a significantly higher risk for ASD while preterm (less than 32 weeks) LGA infants are protected against ASD [11]. Another study shows that ASD is 3 times more prevalent in infants less than 27 weeks gestation and that each week of shortened gestation increases ASD risk [12].

Population-Individual Factors

The unique complications of preterm infants may reduce recognition of early ASD behaviors. Limperopoulos et al. found high rates of ASD features with many infants having challenges with internalizing behaviors problems, socialization and communication resulting in positive initial ASD screens [13]. Risk factors for higher scores on ASD screens include low birth weight, gestational age, male infants, chorioamnionitis, and illness severity [13].

Preterm infant behaviors may serve as precursor to ASD. Developing a set of clinical, developmental, differential diagnosis proves more challenging for preterm infants because of their unique complications [14,15]. Precursory behaviors can vary among infants but the highest ASD risks are associated with cognitive and language deficits and these risks increase with multiple impairments and high severity for these impairments [15].

In preterm infants, ASD related behaviors are identified as delays in behaviors that limit adaptive exploration and social engagement [15]. Parents of ASD children report perseveration with objects, vocalization, noise sensitivity, difficulty with eye contact and problems adapting to routine changes, however these behaviors are commonly seen in premature infants [15]. In premature infants, behaviors that mimic ASD risk behaviors (i.e., less empathy, pretend play) may be delayed onset behaviors rather than impairments. In addition, motor behaviors such as toe walker may be a result of hypertonic low extremities rather than ASD risk behavior [14]. It is not clear if these infants will later develop ASD, but it is important to follow these infants closely to determine if these behaviors are pre-ASD development. Understanding pre-ASD development and distinguishing between pre-ASD and expected social functioning delays in premature infants would significantly contribute to ASD findings. In cases where premature infants experience impairments in social functioning, these areas can be addressed with targeted interventions [14].

Environment

There are many environmental considerations for premature, low birth weight infants. Prenatal and postnatal (NICU and home) environments are significant considerations for low birth weight infants. Although research on ASD examines both prenatal and postnatal environments, many focus on postnatal factors for ASD.

The association between birth SGA, birth weight and ASD may be explained by neurodevelopmental insult in the prenatal and postnatal period and this may cause impairments in growth and brain development [9,11]. Particular attention is given to intrauterine growth retardation caused by placenta deficiency as it reduces oxygen and nutrients to the fetus and contributes to poor neurodevelopmental outcomes [9,11].

Based on technological advances the newborn intensive care (NICU) environment and increased length of stay for chronically ill infants the risks for ASD in premature low birth weight populations are increased. In infants less than 34 weeks, high frequency ventilation and intracranial hemorrhage are factors associated with ASD [12]. Similarly, Lampi et al. identifies postnatal complications as mediating intrauterine growth retardation and prematurity increasing risks for ASD [9]. In addition, the environment of the newborn intensive care (NICU) can have negative impacts on neurodevelopmental outcomes as it adversely impacts social, emotional and physiological maturation [9]. The postnatal environment of the NICU can have significant impact on ASD risk for premature, low birth weight infants.

Although the NICU environment can impact neurodevelopmental outcomes for premature low birth weight infants and increase ASD risks, there are interventions that may serve as a protective buffer. Infant brain development is influenced by health, nutrition, quality of care, and attachment bonds [15]. The interactions between a mother and infant can support social and emotional competencies for the infant [15]. In addition, breastfeeding provides optimal nutrition for brain development and provides the quality interactional experiences to support social, emotional, and physiological maturation and overall brain development [15]. The quality of interpersonal interactions and optimal nutrition in the NICU and home environments may mitigate the negative environmental experiences of the NICU and subsequent ASD risks.

Next Steps

The ASD executive summary identifies a need for collaboration between stakeholders and professionals, promotes improvement in data systems for better prevalence understanding, and encourages better use of existing data to improve services and support to families (CDC, 2011). In considering next steps for practice, ASD screening guidelines are needed specifically for preterm low birth weight infants and emphasis on early screening requirements and rigorous follow-up procedures [16]. The use of multiple ASD screens in premature infants may increase detection of ASD in the premature, low birth weight populations [7]. In order to understand the unique behavioral presentation of preterm low birth weight infants it may be necessary to develop ASD screening and diagnostic tools specific for low birth weight preterm infants [13,14].

In terms of next steps for research, enhanced understanding of brain development for late pre-term infants may improve our understanding of outcomes for ASD [16]. There is more information needed about the prenatal and genetic risk factors that effect fetal growth and premature birth [9,11]. In addition, more investigation of maternal metabolic disorders that lead to preterm SGA and term LGA is needed to inform providers about how to address pre and post pregnancy weight gain [11]. As we know infant brain development is influenced by quality interactions and optimal nutrition, more information about how families can support the needs of a rapidly growing infant through optimal parenting practices are also needed [15]. More support is needed to families also need on how to address the needs of ASD individuals throughout their lifespan [3];

Conclusion

There is much still to learn about ASD. There are collaborative networks in place gathering information to help reduce the gaps in information. Understanding the unique challenges of preterm low birth weight infant and how these challenges may or may not contribute to ASD risks may help reduce some of the information gaps related to ASD. In considering a framework for causal factors that includes biological, population-individual, and environmental conditions it appears that prematurity and low birth weight may be a strong causal factor for ASD. More awareness of this population is needed particularly its contribution to ASD research and practice.

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