Incidence of autism in high risk neonatal follow up

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ABSTRACT

The main characteristics of autism spectrum disorder (ASD) are persistent deficits in social interaction and social communication in multiple contexts, including nonverbal communicative behaviors.

Objective: To detect autism spectrum disorder (ASD) cases within the High Risk Neonatal Follow up Program (HRNFP), as an indicator of the prevalence of ASD and associated risk factors in the Kingdom of Saudi Arabia (KSA).

Methods: We conducted this retrospective medical chart review in a tertiary care hospital in Riyadh, KSA. All patients admitted to the HRNFP were seen at 3 years corrected age between January 2012 and December 2013. Patients diagnosed with ASD from the HRNFP were referred to the King Fahad Medical City (KFMC) Autism Program for further assessment. The following potential risk factors for ASD were documented: low birth weight, gestational age less than 33 weeks, and male gender.

Results: From the National Neuroscience Institute (Mohammed), Mental Health Department and Pediatric Neurology Department (Mahmoud), King Fahad Medical City, Riyadh, the Department of Psychiatry (Wahass), College of Medicine, Dammam University, Dammam, Kingdom of Saudi Arabia.

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and deficits in social reciprocity used for social interaction, and skills in developing, maintaining, and understanding relationships. The diagnosis of ASD, in addition to social communication deficits, requires the presence of restricted, repetitive, patterns of behavior and interests or activities.\(^1\) The High Risk Neonatal Follow up Program (HRNFP) is a program at King Fahad Medical City (KFMC), Riyadh, Kingdom of Saudi Arabia (KSA) involving a multi-disciplinary team of professionals who care for children with many risk factors for diseases and disabilities, such as low birth weight of 1250 grams or less, gestational age of 29 weeks or less, and grade III or IV intra ventricular hemorrhage. Autism spectrum disorder is increasingly being recognized as a public health problem of major importance.\(^2\) It is one of the leading disorders causing disabilities in the neonatal population.\(^3\) With current genetic testing, it is estimated that an etiology is identified in 15-20% of individuals with ASD; in others, the cause remains unknown.\(^4\) Advances in neonatal intensive care have dramatically increased survival in preterm infants, most strikingly among the sickest and most preterm.\(^5\) The contribution from the increasing number of survivors of extreme prematurity to this growing population of children with ASD has not been adequately evaluated.\(^6\) Prevalence studies for any disorder provide crucial information that may allow an estimation of the magnitude of the problem among the specified population; this in turn may assist policy makers in planning and decision making, as well as risk factor identification.\(^7\) Information on the prevalence of ASD in KSA is scarce and limited to small studies.\(^8,9\) In one study, it was found that the overall prevalence of autism in the primary school of Taif district whose age ranged from 7 to 12 years was 0.035%.\(^8\) According to a recent report from the Centers for Disease Control and Prevention (CDC),\(^7\) the rate of diagnosis has increased substantially, with one in 68 children identified with ASD; boys were almost 5 times more likely to be identified with ASD than girls. The average prevalence also varied by race and ethnicity.\(^7\) However, it is unclear whether this higher prevalence represents a true increase in disease burden or it could be attributed to changes in diagnostic practices and complex issues relating to service provision.\(^7,13,14\) The purpose of the present retrospective study was to estimate the incidence of ASD in the HRNFP at KFMC. We also sought to investigate the potential association of very low birth weight (VLBW) with ASD.

**Methods.** We conducted this retrospective medical chart review in a tertiary care hospital in Riyadh, KSA. The Institutional Review Board (IRB) at KFMC approved the study. All patients in the HRNFP were screened for developmental disorders at the corrected age of 18 and 36 months. Evaluation was performed qualitatively and quantitatively. Patients who were diagnosed with ASD in the HRNFP were referred to the Comprehensive Autism Program (CAP), for further assessment and recommendation. The diagnosis of ASDs was based on DSM IV criteria.\(^15\)

Using PubMed and Google, we carried out a manual search for previously published researchs. The results were documented and compared to our local results. Babies were evaluated and diagnosed with ASD in the CAP, which includes a multi-disciplinary team of psychologists, behavior specialized pediatricians, and speech therapists.

**Statistical analyses.** Continuous variables are presented as mean±SD (normal distribution) and as median with interquartile range (skewed distribution). Categorical variables are presented as percentages with corresponding 95% confidence intervals (95% CI). The adjusted Wald method, which provides the best coverage for binomial CI when samples are less than 150,\(^16\) was used for computation of the 95% CI of reported prevalences. Pearson's Chi-Square test was used to detect univariate associations between VLBW and ASD. The IBM SPSS Statistics for Windows (Version 22.0, IBM Corp., Armonk, NY, USA) was used for statistical analyses.\(^17\)

**Results.** A total of 5 patients were diagnosed with ASD during the study period. All the diagnosed patients had VLBW (100%). The gestational age was less or equal to 29 weeks in 80% (n=4) of ASD patients (Table 1). In 2012, 59 patients were evaluated by the HRNFP, and 3 cases were diagnosed with ASD (Table 2) giving an ASD incidence rate of 5.1% (95% CI calculated by the adjusted Wald method: 1.2-14.5%). In year 2013, 48 patients were evaluated by the HRNFP and 2 cases were diagnosed with ASD (Table 2), giving an ASD incidence rate of 4.2% (95% CI: 0.4-14.8%). The total rate of ASD during the 2-year study period was 4.7% (95% CI: 1.7-10.8%).

**Discussion.** Low birth weight and gestational age have been identified in several studies as important perinatal risk factors for disturbances in social interaction, communication, and behavior,\(^18,19\) as well as later psycho affective disorders in adulthood.\(^20,21\) In a recent study,\(^22,23\) it was shown that preterm birth increased ASD risk.
Table 1 - Birth weight and gestational period for diagnosed autism spectrum disorder patients.

| No. | Date of birth | Birth weight | Gestation period | Year |
|-----|---------------|--------------|------------------|------|
| 1   | 31/1/2012     | 1022 grams   | 27               | 2012 |
| 2   | 2/10/2012     | 900 grams    | 28               | 2012 |
| 3   | 9/10/2012     | 680 grams    | 29               | 2012 |
| 4   | 2/4/2013      | 820 grams    | 26               | 2013 |
| 5   | 28/5/2013     | 1220 grams   | 33               | 2013 |

Table 2 - Rate of ASD in HRNFP patients in 2012 and 2013 and total rate.

| Year     | Number of patients seen in the HRNFP | Number diagnosed with ASD | Prevalence of ASD (% with 95% CI) |
|----------|--------------------------------------|---------------------------|----------------------------------|
| 2012     | 59                                    | 3                         | 1 in 20 (1.2-14.5)               |
| 2013     | 48                                    | 2                         | 1 in 24 (0.4-14.8)               |
| Total    | 107                                   | 5                         | 1 in 21 (1.7-10.8)               |

ASD - autism spectrum disorder, HRNFP - high risk neonate follow up program, 95% CI - 95% confidence interval

There is a lack of published studies describing the prevalence of autism in high risk children in KSA. The current study documented a substantial prevalence rate of ASD among HRFP patients (1 in 21), which is higher in comparison with the prevalence of ASD in the general population that ranges from 1 in 88 to 1 in 150 births.24

Higher autism spectrum traits were associated with very low birth weight adults as compared to term-born controls.25 Low birth weight and preterm birth place these infants at higher risk for disturbances in social interaction, communication, and other psycho affective disorders in adulthood.26 An Indian study27 evaluating perinatal and neonatal risk factors showed labor complications, preterm birth, neonatal jaundice, delayed birth cry and birth asphyxia to be associated with ASD with an odds ratio greater than 1.5.

Certain limitations of the present study need to be acknowledged. First, our limited sample size does not allow us to accurately estimate ASD prevalence with a narrow 95% CI. Second, the retrospective nature of our study does not provide definitive evidence regarding the potential causality of VLBW and early gestational age with ASD. Third, selection bias cannot be excluded given that the chart review was conducted in a tertiary care center. Consequently, the actual prevalence in the general population may be substantially lower. Fourth, other potential risk factors that might have been associated with a higher ASD prevalence were not collected including: maternal age, family history of ASD and number of prior spontaneous abortions, abnormal presentation, umbilical-cord complications, fetal distress, birth injury, or trauma, multiple birth, maternal hemorrhage, summer birth, low birth weight, small for gestational age, congenital malformation, low 5-minute Apgar score, feeding difficulties, meconium aspiration, neonatal anemia, ABO, or Rh incompatibility, and hyperbilirubinemia. Finally, the limited sample of ASD cases (n=5) prevents the investigation of the potential relationships between specific HRNFP diagnoses with ASD.

In conclusion, our findings indicate that the prevalence of ASDs was high in HRNFP patients at KFMC. Further investigations are required to evaluate which potential risk factors may be associated with the higher ASD incidence documented in this specific population.

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**ETHICAL CONSENT**

All manuscripts reporting the results of experimental investigations involving human subjects should include a statement confirming that informed consent was obtained from each subject or subject’s guardian, after receiving approval of the experimental protocol by a local human ethics committee, or institutional review board. When reporting experiments on animals, authors should indicate whether the institutional and national guide for the care and use of laboratory animals was followed. Research papers not involving human or animal studies should also include a statement that approval/no objection for the study protocol was obtained from the institutional review board, or research ethics committee.