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Fetal cerebral ventricular atria width of 8–10 mm: A possible prenatal risk factor for adolescent treated Attention Deficit Hyperactivity Disorder (ADHD)



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ABSTRACT

The purpose of our research was to study the in-utero and long term post-natal outcome of fetal isolated cerebral ventricular atria width between 8 and 10 mm.

We conducted a retrospective, observational, case–control study, of low risk pregnant women, between 1993 and 2001. One hundred and forty one fetuses with isolated cerebral ventricular atria width between 8 and 10 mm, corresponding to 2–4 standard deviations above the mean, and 309 controls, with atrial width below this level, were included for the analysis.

Clinical data concerning pre and post-natal outcome was retrieved from computerized medical records. Matching of cases with controls was based on age, with a ratio of 2–3 controls per case.

Statistical analysis included: *T*-test, Chi-Square, and Multiple Logistic Regression analysis. The study group was characterized by a predominance of male gender, left side involvement, and higher birth weight, compared to the control group.

Long term post-natal follow-up at a mean age of 12.7 years (± 1.9) demonstrated an adjusted odds ratio of 2.589 (95% CI 1.415–4.737, p = 0.001), being diagnosed as Attention Deficit Hyperactivity Disorder (ADHD), and treated by Methylphenidate (Ritalin®), during childhood, compared to the control group (23.6% and 10.0% respectively) (p = 0.001). Cerebral atria width was an independent factor, controlled for the only two significant variants between groups, gender and weight over 90th centile.

In conclusions, our preliminary results show that fetuses with prenatal finding of isolated cerebral ventricular atria width between 8 and 10 mm are more likely of being diagnosed and treated as ADHD during childhood.

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1. Introduction

Measurement of the fetal cerebral lateral ventricles at the atria level has been the cornerstone of fetal central nervous system evaluation for the last three decades (Cardoza, Goldstein, & Filly, 1988), Enlargement of the lateral ventricles has been

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found to be a sensitive marker for the detection of various structural brain abnormalities (Filly, Cardoza, Goldstein, & Barkovich, 1989).

Fetal biometric values within the range of two standard deviations (SD) are generally considered as predictors of a normal outcome. The cerebral atria width is exceptional, since most of the literature considers the 10 mm, corresponding to 3–4 SD above the mean, as the normal upper limit (Achiron, Schimmel, Achiron, & Mashiach, 1993; Alagappan, Browning, Laorr, & McGahan, 1994; Almog, Gamzu, Achiron, Fainaru, & Zalel, 2003; Cardoza et al., 1988; Farrel, Hertzberg, Kliewer, Harris, & Paine, 1994; Filly et al., 1989; Heiserman, Filly, & Goldstein, 1991; Kivilevitch, Achiron, & Zalel, 2010; Pilu, Reece, Goldstein, Hobbins, & Bovicelli, 1989).

In our daily experience, cerebral atria in the range between 8 and 10 mm, corresponding to 2–4 SD above the mean, is a prominent subjective sonographic finding, and constitutes a considerable part of the referrals for cerebral ventricular dilatation.

Our ability to counsel regarding this clinical problem is very limited since it based on scanty literature, originating from only tertiary centers, with a short postnatal follow up, and not controlled (Achiron et al., 1997; Bronsteen, Lee, Vettraino, Balasubramaniam, & Comstock, 2006; Farrel et al., 1994; Hertzberg et al., 1994; Sadan, Malinger, Schweiger, Lev, & Lerman-Sagie, 2007).

The aim of the present study was to evaluate the in-utero and long term post-natal outcome of fetuses with cerebral ventricular atria width between 8 and 10 mm, as an isolated finding, in an obstetric population of low risk for congenital malformation, compared to a matched for age control group.

2. Methods

We conducted a retrospective, observational, case–control study. The study period extended from 1993 to 2001. All examinations were performed by a single examiner (K.Z), an expert in fetal examination, at a secondary regional medical center. The study group comprised fetuses with cerebral atria width between 8 and 10 mm, as an isolated finding, presented at any stage of pregnancy.

2.1. Patients

Pregnant women were all of low risk for malformations, recruited during routine pregnancy examinations. It included women without any previous history of fetal, neonatal or family malformations/genetic diseases. Exclusion criteria were the presence or late appearance of any fetal abnormality (structural, chromosomal or infectious), or delivery before 34 weeks of gestation. Fetuses with sonographic markers for aneuploidy, with normal karyotype, and twin pregnancies were not excluded.

Our standard care included a second trimester anomaly scan at 19–24 weeks of gestation, and a third trimester fetal growth assessment at 30–32 weeks of gestation.

Unlike customary standard care, the study group was scheduled for an additional follow up visit. It was retrospectively compared with a similar low risk control group, matched for age, and with normal anatomic scans including atrial width below 8 mm. They followed standard care as above mentioned, and were randomly and consecutively recruited among women who had their second trimester anatomic screening examinations.

All patients provided a written informed consent for fetal anatomic examination as part of standard routine care at our institution, of which atrial width measurement constitutes an integral part. Phone consent for data analysis was obtained from all participants, in accordance with the Maccabi Health Services Review Board approval (number 2011054 from 4/1/2012). Consequently, a retrospective review of medical electronic charts was performed.

2.2. The sonographic examination

Both cerebral atria width were assessed routinely from 1996. The distal atrial width was measured in an axial plane, inclined laterally to include the Cavum Septi Pellucidi and the thalamus. Calipers were positioned perpendicular to the ventricle axis, at the level of the posterior edge of the choroid plexus, and between its inner margins as described in the literature (Cardoza et al., 1988; Pilu et al., 1989) (Fig. 1a). The proximal atrium was assessed at the same para-axial plane, by tilting the tranducer in a posterior- oblique direction from the axial plane, at the level of the Calcarine fissure (Fig. 1b). The fetal anatomic scan was based on the American Institute of Ultrasound in Medicine Practice 1996 guidelines (AIUM, 1996), but also included the visualization of the posterior fossa (cerebellar hemispheres and cistern magna), lips, orbits, four limbs (without fingers and toes) and the outflow of the great arteries from the heart. Documentation of 30–40 prints for each patient was archived. These data was used later for our study.

2.3. Outcome data

All patients had a postpartum pediatric examination, and data from subsequent visits was analyzed and compared for gender, birth weight, gestational age at delivery, incidence of preterm or post-date deliveries, mode of delivery, and incidence of large (neonatal weight above the 90th centile) or small (neonatal weight bellow the 10th centile) for gestational

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