Singapore Journal of Obstetrics and Gynaecology
November 2004; 35(3): 165-168

Antenatally diagnosed isolated borderline fetal ventriculomegaly - Is it associated with an increased risk of Trisomy 21?

JJ Chee
J Tan
GSH Yeo

ABSTRACT

Objective:
The finding of isolated borderline fetal ventriculomegaly on antenatal ultrasonography has been associated with chromosomal abnormalities in some studies. This study aims to establish the risk of Trisomy 21 and determine the likelihood ratio for Trisomy 21 of such abnormality in our population.

Methods & Materials:
All cases of isolated borderline fetal ventriculomegaly with lateral ventricles measuring between 10 and 15 mm on antenatal ultrasonography were registered with the hospital based Birth Defect Registry and the karyotypic outcomes of these cases were studied. Using Howard Cuckle's formula that predicts the age-related Down syndrome risk, the predicted risk of Trisomy 21 for that population was compared to the actual incidence of Trisomy 21 to derive the likelihood ratio.

Results:
In tbe 6 $^{1}/_{2}$ year period between 1st June 1996 and 31st December 2002, there were 130 cases of antenatally diagnosed isolated borderline ventriculomegaly among 94349 deliveries, resulting in an incidence of 13.78 cases in 10 000. Out of these 130 cases, there was 1 case of Trisomy 21, diagnosed on amniocentesis. The maternal age was 35. The calculated background risk of Down syndrome in this cohort of patients was 1.28. The actual incidence of Down syndrome in this same cohort is 1. The calculated likelihood ratio for Trisomy 21 in the presence of isolated borderline ventriculomegaly was thus calculated to be 0.78.

Conclusion:
Our results suggest that the presence of isolated borderline fetal ventriculomegaly on antenatal ultrasound in our population does not increase the risk of Trisomy 21 in that pregnancy. However, given the small numbers, a larger cohort of subjects should be analysed.

Keywords: isolated borderline ventriculomegaly, chromosomal abnormalities, antenatal ultrasound screening

Department of Maternal Fetal Medicine
KK Women's and Children's Hospital
100 Bukit Timah Road
Singapore 229899
Correspondence:
Dr J J Chee
Department of Maternal Fetal Medicine
KK Women's and Children's Hospital
100 Bukit Timah Road
Singapore 229899

INTRODUCTION

Fetal cerebral ventriculomegaly, especially when isolated and mild, is an ultrasonic finding with uncertain prognosis[1,2]. Identification presents with a counselling dilemma[3] because it can represent a normal physiologic variant or can be the epiphenomenon of a heterogenous group of pathologic processes that include increased intra ventricular pressure, primary neuronal loss and abnormalities of brain development [4].

Isolated borderline ventriculomegaly is difficult to manage and counsel for the following reasons. Firstly, the average gestational age at diagnosis is rather advanced, near or beyond fetal viability. Secondly, the exclusion of associated (chromosomal or structural) anomalies is not simple and may not be the main determinant of the prognosis. Thirdly, the risk of developmental delay still remains unclear and this poses much difficulty in explanation of prognosis to the parents.

Objectives:
The etiology of isolated mild ventriculomegaly often remains unknown and does not appear to be associated with either obstruction or atrophy. However, the finding of isolated borderline fetal ventriculomegaly has been associated with chromosomal abnormalities in some studies. This study aims to establish the risk of Trisomy 21 and determine the likelihood ratio for Trisomy 21 of such abnormality in our population.

Materials and Method:
This is a prospective, cross-sectional study based in KK Women's & Children's Hospital over a 6 $^1/_2$ year period between 1st June 1996 to 31st December 2002.

The transverse diameter of the ventricular atrium of the fetal brain at the level of the glomus of the choroid plexus was measured. (Fig 1) Presence of ventriculomegaly was screened for by a team of trained sonographers. All cases of fetal ventriculomegaly detected were then referred to obstetricians with specific training in Maternal-Fetal medicine and prenatal ultrasonographic diagnosis. These specialists will confirm the finding and carry out a detailed fetal survey, including targeted ultrasonographic examination of the central nervous system, fetal echocardiogram, and ultrasonographic markers of aneuploidy.

All cases of isolated borderline fetal ventriculomegaly with lateral ventricles measuring between 10 and 15 mm on antenatal ultrasonography were registered with the hospital based Birth Defect Registry and the karyotypic outcomes of these cases were studied. Using Howard Cuckle's fommula that predicts the age related Down syndrome risk, the predicted risk of Trisomy 21 for that population was compared to the actual incidence of Trisomy 21 to derive the likelihood ratio. (Table 1)

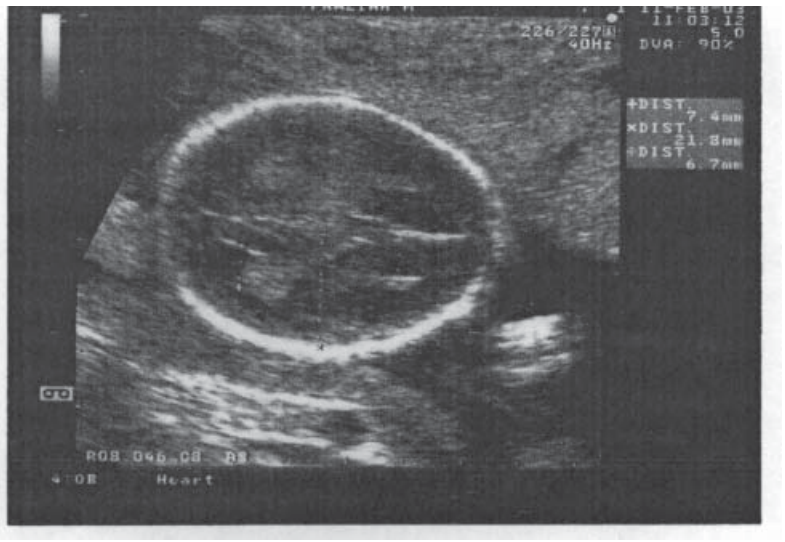

Figure 1 : This figure shows the measurement of the anterior and posterior ventricles.

Table I: Computation of Likelihood Ratio

Age	Age related risk	Total Number	Accum Age Related Risk	Actual Risk
16	0.000592533	0	0	
17	0.000595697	0	0	
18	0.000599922	2	0.001199844	
19	0.000605564	0	0	
20	0.000613099	5	0.003065495	
21	0.000623161	6	0.003738967	
22	0.000636598	6	0.00381959	
23	0.000654543	0	0	
24	0.000678506	4	0.002714022	
25	0.000710506	10	0.007105062	
26	0.00075324	3	0.002259721	
27	0.000810308	4	0.003241233	
28	0.000886518	3	0.002659553	
29	0.000988289	10	0.009882887	
30	0.001124196	13	0.014614544	
31	0.001305688	5	0.006528441	
32	0.001548056	15	0.023220841	
33	0.001871718	5	0.009358591	
34	0.002303942	3	0.006911826	
35	0.002881141	10	0.028811407	1
36	0.003651941	9	0.032867472	
37	0.004681281	4	0.018725125	
38	0.006055879	7	0.042391151	
39	0.007891539	2	0.015783078	
40	0.010342909	3	0.031028728	
41	0.01361651	1	0.01361651	
42	0.017988131	0	0	
43	0.023826064	0	0	
44	0.031622137	0	1	
46	0.055936168	0	0	
		Likelihood ratio	1.283544086	1 0.7790928

Results:

There were 130 cases of isolated borderline ventriculomegaly in the 6 ½ year period between 1st June 1996 to 31st December 2002. In the same period of time, there were 94349 deliveries, giving an incidence of 13.78 cases in 10 000.

Out of these cases, there was 1 case of Trisomy 21, diagnosed on amniocentesis. The maternal age was 35. The calculated background risk of Down syndrome in this cohort of patients was 1.28. The actual incidence of Down syndrome in this same cohort is 1. The calculated likelihood ratio for Trisomy 21 in the presence of isolated borderline ventriculomegaly was thus calculated to be 0.78.

Discussion:

Our study showed that isolated borderline fetal ventriculomegaly is not associated with increased risk of Trisomy 21 in our population. The main strength of this study is that it is by far the largest series of isolated borderline fetal ventriculomegaly[4,5,6] reviewed. The strict diagnostic criteria, the high standards of ultrasonography perfomed by specialists and the good data collection by the Birth Defect Registry in a prospective manner add to the robustness of our study.

However, the true significance of isolated borderline fetal ventriculomegaly remains to be determined. Comparison with studies in the literature for isolated ventriculomegaly suggests that the association between this finding and Trisomy 21 is higher than our finding. In our series, only 0.8% (1/130) risk of Trisomy 21 was noted. A review of 6 published studies of isolated mild ventriculomegaly by Vergani et al[5] showed the overall risks of chromosomal anomalies to be 2.7% (4/148). A similar review of 9 studies by Pilu et al[6] showed the risk of chromosomal anomalies in fetuses with isolated cerebral borderline ventriculomegaly to be 3.8% (9/234). Although we also acknowledge that Trisomy 21 was not the only chromosomal abnormality found in these two series, the autlhors of both papers do concede that Trisomy 21 was most frequently encountered.

It is also difficult to draw conclusions as the avaiiable literature has many shortcomings. For one, the number of cases studied so far is small. In the two series mentioned above, the largest number of cases in a single study is only 48. Another major shortcoming of the available experience, including ours, is the lack of proper postnatal follow-up to determine the association of isolated borderline fetal ventriculomegaly and neurodevelopmental abnormalities[7]. Not only the duration of postnatal follow-up is grossly disparate, the modalites for assessment varies greatly too. A well-planned prospective study on postnatal development of babies with antenatal diagnosis of isolated borderline ventriculomegaly, using objective evaluation up till the third year of life is clearly needed.

Until further substantive data is available, the prognosis of isolated borderline fetal ventriculomegaly remains diffcuit to predict. Suffice to say, for now the decision for karyotyping in such cases should be based on a combination of clinical factors (eg, maternal age, past history or family history of Down syndrome), laboratory screening tests (eg, first and/or second trimester maternal serum screening) and ultrasonographic findings (eg, other soft markers of chromosomal anomaly).

Conclusion:

Our results suggest that the presence of isolated borderline fetal ventriculomegaly on antenatal ultrasound in our population does not increase the risk of Trisomy 21 in that pregnancy. However, given the low incidence of this condition, a larger cohort of subjects should be analysed.

REFERENCES

1. *Greco P, Vimercati A, Selvaggi L. Isolated mild fetal cerebral ventriculomegaly. Prenat Diag 2002 Feb: 22(2): 162-3*

2. *Eizenberg V, Yagel S. The clinical significance of fetal isolated cerebral borderline ventriculomegaly: report of 31 cases and review of the literature. Ultrasound Obstet Gynecol 1999: 14(5):320-6*

3. *Greco P, Vimercati A, De Cosmo L, Laforgia N. Mild ventriculomegaly as a counselling challenge. Fetal Diagn Ther 2001 Nov-Dec;16(6):398-401*

4. *Kelly EN, Allen, Seaward G, windrim R, Ryan G. Mild ventriculomegaly in the fetus, natural history, associated findings and outcome of isolated mild ventriculomegaly: a literature review. Prenat Diagn 2001 Aug:21(8): 697-700*

5. *Vergani P, Locatelli A, Strobelt N, Cavallone M, Ceruti P, Paterlini G. Clinical outcome of mild fetal ventriculomegaly. Am J Obstet Gynecol. 1988 Feb; 178(2):218-222*

6. *Pilu G, Falco P, Gabrielli S, Perolo A, Sandri F, Bovicelli L. The clinical significance of fetal isolated cerebral borderline ventriculomegaly: a report of 31 cases and review of the literature. Ultrasound Obstet Gynecol 1999;14:320-326*

7. *Mercier A, Eurin D, Mercier PY, Verspyck E, Marpeau L, Marret S. Isolated mild fetal cerebral ventriculomegaly:a retrospective analysis of 26 cases,. Prenat Diagn 2001;21:589-595*