

# Postnatal outcome of isolated, nonprogressive, mild borderline fetal ventriculomegaly

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## Abstract

**Background** This study aimed to evaluate postnatal outcome of fetuses affected by nonprogressive, isolated, mild ( $\geq 10$  and  $\leq 12$  mm) borderline ventriculomegaly (BVM).

**Methods** We studied 25 consecutive fetuses with BMV and evaluated patients' characteristic, ultrasonographic findings, and the neurodevelopmental outcome at age  $\geq 24$  months.

**Results** The mean gestational age at diagnosis was  $23.84 \pm 5.02$  weeks (min–max; 17–34 weeks). In 16 cases, BVM was bilateral (16/25, 64 %), 4 left sided (4/25, 16 %), and 5 right sided (5/25, 20 %). Fourteen cases were males (14/25, 56 %), and 11 cases were females (11/25, 44 %). In two cases, ventriculomegaly was regressed 4 weeks after the initial diagnosis (2/25, 8 %), and in the remaining cases, ventriculomegaly persisted between initial measurement and 12 mm. The mean age of the infant at the time of the neurodevelopmental evaluation was 45.9 months (24–77 months). The neurodevelopmental outcome at the mean age of 45.9 months was completely normal in 16 infants (16/25, 64 %). The remaining nine infants (9/25, 36 %) had mild degree of neuromotor developmental delay.

**Conclusion** Prenatal counseling for isolated, nonprogressive, mild BVM should be mainly reassurance since it is not associated with severe neurodevelopmental delay. However, parents should be educated about the developmental

milestone of children to observe and detect mild neurodevelopmental delay which can be associated with mild BVM.

**Keywords** Ventriculomegaly · Borderline · Fetal · Prenatal · Ultrasonography · Neurodevelopmental outcome

## Introduction

Ventriculomegaly (VM) is the most common fetal intracranial anomaly diagnosed with ultrasonography (US). The prevalence of VM varies between 0.3 and 10 per 1,000 births, depending on the technique used for measurement, the evaluation of one or both ventricles [15, 18]. It is a descriptive term indicating the presence of excess fluid in the lateral ventricles of the fetal brain which can be isolated or the sole and subtle manifestation of underlying severe brain defects. Ultrasonographically, VM is diagnosed when the atrium width of one or both ventricles is greater than or equal to 10 mm. VM is defined severe when the ventricular width is greater than 15 mm and borderline when the measurement is between 10 and 15 mm [21]. Disagreement exists over the terminology of VM, and some authors have restricted the diagnosis of mild borderline ventriculomegaly (BVM) to measurements of 10–12 mm which were accepted in this paper [1].

Prenatal counseling for a fetus with isolated mild BVM is challenging for both obstetricians and parents due to the conflicting results of the previous studies which somehow put mild BVM into the gray zone between abnormal and anatomic variation [19]. Therefore, in fetus with mild BVM, it is important to collect data regarding patients' characteristics, prenatal findings, and postnatal outcome in order to offer appropriate prenatal counseling based on local perceptions and conditions. The aim of the present study is to

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report prenatal finding and midterm postnatal outcome of the 25 consecutive cases of isolated mild BVM.

## Materials and methods

We reviewed 25 consecutive cases of isolated mild borderline ventriculomegaly examined in our ultrasound unit between the years 2006 and 2010. Our prenatal diagnosis department provides detailed US examination for both referred patients with suspected anomalies and anomaly screening as a part of routine antenatal follow-up. The scans were performed transabdominally with Voluson 730 Pro equipped with a 5- to 8-MHz transabdominal transducer (GE, Healthcare). The ventricular atria were measured on an axial plane at the level of the thalami by positioning electronic calipers on the internal margins of the ventricular wall perpendicular to the long axis of the ventricles (Fig. 1) [2]. Mild BVM was defined as the diameter of one or both lateral ventricles  $\geq 10$  and  $\leq 12$  mm (Fig. 2).

In each case, a thorough sonographic evaluation of fetal anatomy was performed, including fetal echocardiography. Fetal magnetic resonance imaging (MRI) was performed for all cases. The fetuses that had another major malformation diagnosed either with US and MRI were excluded from the study. Follow-up US was performed in each case and those fetus with progressive hydrocephaly were excluded. Additionally, cases whose diagnosis refuted or upgraded on MRI were also excluded. Screening for perinatal infections (TORCH) was also a routine part of the evaluation. Data on pregnancy outcomes were available in all cases. Detailed neonatal examinations of all newborn were conducted in the first week of life, including general and neurological clinical assessment and a cerebral transfontanelar US in

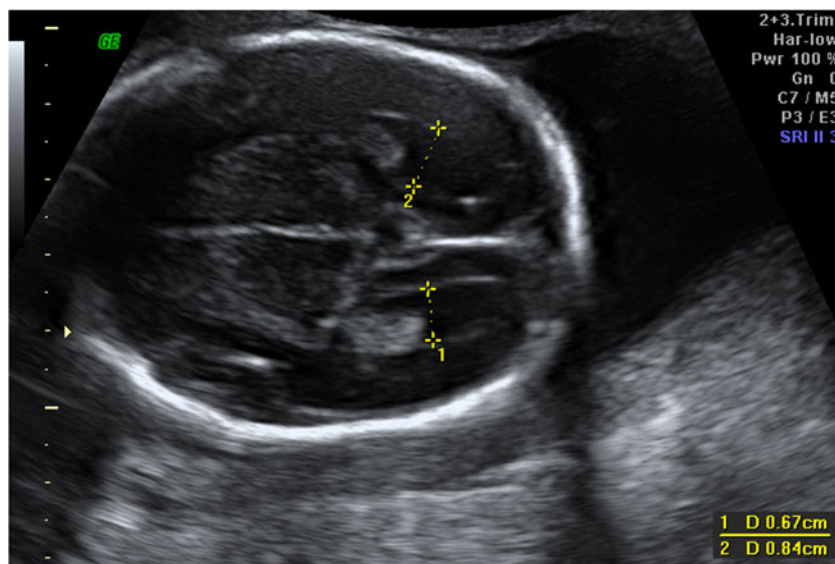
order to confirm the prenatal diagnosis. BVM was defined as isolated when prenatal and postnatal evaluation revealed no other cranial or extracranial malformation, perinatal infection, or karyotype abnormalities. All the surviving neonates were at least 24 months old at the time of the study.

Since 68 % (17/25) of our patients were referred from the distant areas of our country or resided in different cities, we obtained all the data by means of telephone interview with the parents. Information about neurological development status of patients included in the study was evaluated by a pediatric neurologist using the Battelle Developmental Inventory Screening Test (BDIST). The questionnaire included the evaluation of locomotor activities and coordination of movements, hearing and visual functions, development and quality of speech and socialization skills, learning performance, and evolution of diagnosed neurodevelopmental anomalies or new pathologies and their treatments.

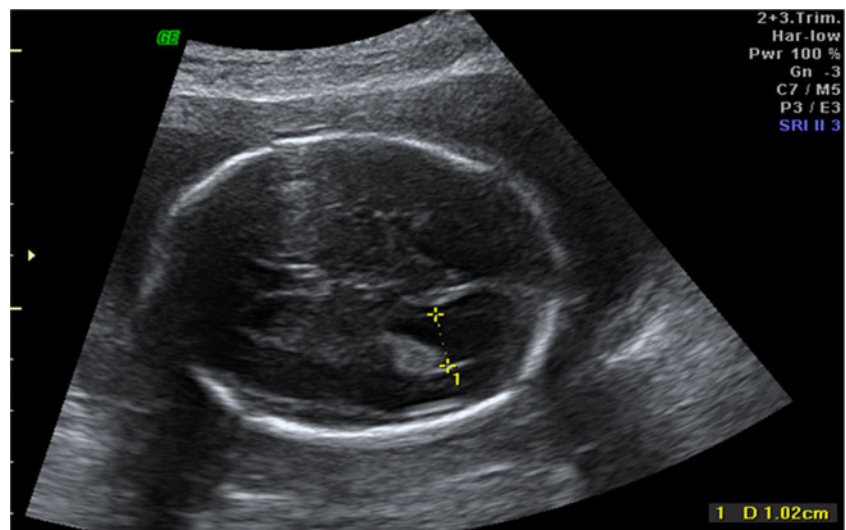
We defined severe neurodevelopmental outcomes as: cerebral palsy (with or without the need for orthopedic help, urinary incontinence, daily enema, etc.), epilepsy, bradycardia with prosthesis, mono-/bilateral blindness, and mental retardation. Mild anomalies were: moderate motor skill problem (with or without tone and reflex anomalies), squint, nystagmus, mild speech difficulty, moderate learning problems, and ventriculoperitoneal shunt with normal motor development [23].

All datasets were subjected to normality tests using the Shapiro–Wilk method and data were reported either as mean+standard deviation (for normally distributed data) or proportions. Comparison of variables between the two groups was made using Student's *t* test for normally distributed data and  $\chi^2$  test for proportions. A two-tailed *p* value of  $<0.05$  was considered statistically significant.

**Fig. 1** Sonographic measurement of both normal lateral ventricles at 22 weeks of gestation



**Fig. 2** Borderline lateral ventriculomegaly at 22 weeks. *Calipers* indicate measurement of the ventricle from medial to lateral wall



## Results

A total of 31 patients were included in the study. One fetus died in utero at 24 weeks, and another fetus was reported to be born at 25 weeks due to preterm rupture of the membranes and died at the first postnatal day. Three patients were lost in follow-up. One fetus was born at 29 weeks and excluded from the study. The 25 term, live-born infants who fulfilled all the inclusion criteria were evaluated in the final analysis.

The maternal age was  $26.28 \pm 5.15$  (min–max, 18–39), and the mean age at diagnosis was  $23.84 \pm 5.02$  weeks (min–max, 17–34 weeks). Indications for prenatal diagnosis unit referral were: diagnosis of ventriculomegaly by referring obstetrician ( $n=15$ , 60 %), routine fetal anatomy screening ( $n=6$ , 24 %), advanced maternal age ( $n=2$ , 8 %), abnormal serum screening for Down syndrome ( $n=1$ , 4 %), and history of having a baby with congenital cardiac defect ( $n=1$ , 4 %). Karyotype analysis was performed prenatally in 11 cases (11/25, 44 %; six umbilical cord blood sampling and five amniocentesis). In the rest, the karyotype was studied postnatally according to neonatal clinical findings and all revealed normal karyotype. Mild BVM was bilateral ( $n=16$ , 64 %), left sided ( $n=4$ , 16 %), and right sided ( $n=5$ , 20 %). Fourteen cases were males (14/25, 56 %), and 11 cases were females (11/25, 44 %). Clinical data of the cases were summarized in Table 1.

At least one additional ultrasound examination was performed in all cases after the initial diagnosis, and all the control US examinations were performed at third trimester. In two cases diagnosed at early second trimester, two follow-up US examinations were performed at late second trimester and third trimester. In two cases, ventriculomegaly was regressed 4 weeks after the initial diagnosis (2/25, 8 %), and the remaining cases of ventriculomegaly persisted between the initial measurements and  $\leq 12$  mm.

The main age of the infant at the time of the neuro-developmental evaluation with BDIST was 45.9 months (24–77 months). Head circumference measurements were within normal limits in all cases in neonatal period. We collected follow-up data when the infants were at least 24 months old by means of interviews with the parents. The neurodevelopmental outcome was completely normal in 16 infants (16/25, 64 %). There were nine abnormal neurodevelopmental outcomes, all of which were classified as mild neurodevelopmental delay. Among these, one case was found to have personal and social skill impairment diagnosed as autism and required special education, and two cases had neuropsychiatric symptoms consistent with attention deficit and hyperactivity disorder. No cases with severe neuromotor impairment were detected. Out of nine cases showing neurodevelopmental delay, five were males (5/14, 35.7 %) and four were females (4/11, 36.4 %). Mild BVM was bilateral in six cases (6/9, 66.7 %) and unilateral in three cases (3/9, 33.3 %) in the group showing neurodevelopmental delay. There were no statistically significant differences between normal and abnormal postnatal outcome groups with regard to maternal age, gestational age at diagnosis, ventricular width, fetal gender, and site of the affected ventricle. Patients' characteristic and sonographic findings in relation to postnatal neurodevelopmental outcome were shown in Table 2.

## Discussion

With the improvement of diagnostic US, and the addition of fetal MRI to the diagnostic armamentarium of prenatal medicine specialist, diagnosis of isolated mild BVM has been increased. In clinical practice, major concern for the perinatologist and the child neurologist dealing with the fetus with borderline ventriculomegaly (BV) is to ascertain

**Table 1** Clinical data of cases with isolated mild borderline ventriculomegaly

Case	Sex	Maternal age	Gestational age (weeks)		Diameter of ventricles	Follow-up sonogram	Birth weight (kg)	Outcome
			At diagnosis	At delivery				
1	M	24	32	38	11/9	Stable	2,900	Normal
2	F	34	19	40	10/10.1	Stable	3,200	Autism, necessitating special education
3	M	39	20	39	9/10.5	Stable	3,400	Mild gross motor skill disabilities
4	K	24	20	37	11/11	Stable	2,870	Normal
5	M	26	21	38	5/10.2	Stable	3,150	Mild speech disabilities
6	M	18	34	40	12/12	Stable	3,800	ADHD, mild speech disabilities
7	M	26	21	37	11.4/11	Stable	3,300	ADHD, mild fine motor skill disabilities
8	M	24	23	39	5.8/10.6	Stable	2,900	Normal
9	M	26	33	39	12/11.7	Stable	3,100	Normal
10	F	23	26	39	10.2/10.3	Stable	3,200	Mild, speech, gross motor, and fine skill disabilities
11	F	27	18	41	11/11	Stable	3,000	Mild speech disabilities
12	M	20	20	36	12/12	Resolved	3,700	Normal
13	M	35	19	38	10.1/10.2	Resolved	3,800	Normal
14	M	29	22	40	9/10.2	Stable	3,900	Strabismus, mild fine motor skill disabilities
15	F	25	17	37	12/12	Stable	3,300	Normal
16	M	27	34	39	8/11.6	Stable	3,200	Normal
17	F	24	24	39	10.2/10.4	Stable	3,400	Mild speech impairment
18	F	35	19	40	10.6/10.6	Stable	3,500	Normal
19	F	21	27	38	11/10.5	Stable	3,350	Normal
20	M	30	23	38	11.2/5.6	Stable	3,650	Normal
21	F	26	22	37	11.6/11	Stable	2,800	Normal
22	F	28	26	39	11.8/11.5	Stable	3,500	Normal
23	F	25	26	39	10.6/9.3	Stable	3,600	Normal
24	M	21	26	40	11.7/9.7	Stable	3,100	Normal
25	M	20	24	39	10.4/10.4	Stable	2,950	Normal

*M* male, *F* female, *ADHD* attention deficit hyperactivity disorder

whether the BV isolated or associated with cranial or extracranial defects [6, 22]. It is reported that about 13 % of fetus

diagnosed ultrasonographically as having isolated BV was found to have associated defects postnatally [11]. Recently,

**Table 2** Patients' characteristic and sonographic findings in relation to postnatal neurodevelopmental outcome

Variables	Postnatal outcome		<i>p</i>
	Normal ( <i>n</i> =16) $\bar{x} \pm SD$	Abnormal ( <i>n</i> =9) $\bar{x} \pm SD$	
Maternal age	25.69±4.60	27.33±6.16	0.462
Gestational age at diagnosis	24.44±5.16	22.78±4.87	0.618
With of the enlarged ventricle	11.19±0.62	10.68±0.65	0.889
	<i>n</i> (%)	<i>n</i> (%)	
Gender			
Male	9(64.3)	5 (35.7)	
Female	7 (63.6)	4 (36.4)	0.973
Affected ventricle			
Right	2 (12.5)	3 (33.3)	
Left	4 (25)	0 (0)	0.172
Bilateral	10 (62.5)	6 (66.7)	



fetal MRI gained wide acceptance in the evaluation of borderline intracranial lesion in prenatal period albeit with questionable benefit. Working on the subject, Parazini et al., at their large series, had shown that MRI of fetal brain had significantly changed management in 1.1 % of cases with seemingly isolated BV [13]. In contrast, Solomon et al. [17] argued that MRI changes management strategies in 6 % of cases. Certainly, diagnostic contribution of the MRI in mild BVM is largely dependent on the expertise and experience of the US operator, the power of the US device, and study protocol. As a result of strict study protocol including experienced operators, follow-up US examinations, and routine MRI, no additional cranial or extracranial malformation was detected postnatally in the present study.

Fetal infections (TORCH), especially toxoplasmosis and cytomegaloviruses (CMV), may cause ventricular dilatation. Moreover, mild BVM may be the only manifestation of cerebral involvement in CMV infection [14], and its presence can radically change the management of pregnancy. In accordance with previous study [9], no single case with perinatal infection was detected in our study group. In view of the potential of treatment, and the simplicity and safety and the low cost of the screening test, maternal serum CMV and *Toxoplasma* studies should be performed in the differential diagnosis of isolated mild BVM [6, 11].

The relationship between chromosomal abnormalities and isolated mild BVM is controversial and biased by the study populations assessed. Depending on the maternal age and baseline risk, it was suggested that karyotype abnormalities were found in 2.8 % of cases with BV [11]. In our study group, no karyotype abnormality was detected. This finding probably reflects relatively low maternal age ( $26.28 \pm 5.15$ ), the small number of women over 35 years age (one case), and our strict selection criteria. However, the decision to perform karyotype analysis should be based on the patients' characteristic (age, previous history of child with chromosomal abnormalities) and baseline risk (local prevalence, results of screening test).

There is a wide variation in the reported incidence of neurodevelopmental delay in children with isolated mild BVM mainly resulting from study designs, patient selection criteria, methods for data collection, timing of neurodevelopmental evaluation, and time to follow-up [12]. Our results showed that 16 of 25 children with isolated mild BVM had completely normal postnatal outcome (64 %). The remaining nine children had showed mild degree of neuromotor impairment. Of these, three cases had isolated mild speech impairment, and the other children showed some combination of speech, fine motor, and gross motor impairment. However, no case was found to have severe neurodevelopmental impairment. Despite the accumulating data concerning with borderline ventriculomegaly (10–15 mm), minority of this literature deal with “mild isolated

borderline ventriculomegaly.” Gómez-Arriaga et al. [8] in their study using BDIST structured interview reported that children with isolated mild BVM showed neurodevelopmental delay: 66 % in social–personal skill, 56 % in gross motor skill, 39 % in adaptive behavior, and 28 % in fine motor skill. Similarly, Broomley et al. [1] reported 19.2 % abnormal neurodevelopmental outcome. At the other end of the spectrum, some authors reported 100 % normal postnatal outcome and argued that mildest form of borderline ventriculomegaly represents normal variant [4, 10, 19, 20]. Melchiorre et al. [11], in their comprehensive analysis, reported overall 11 % risk of neurodevelopmental delay in fetus with isolated borderline ventriculomegaly (10–15 mm). Despite the conflicting results of these studies, the common denominator is the lack of an increased prevalence of severe neuromotor delay. We found that normal and abnormal neurodevelopment outcome cases were tended to distribute equally with regard to bilaterality/unilaterality and male/female, parameters which were consistent with previous literature [5, 11]. In contrast to severe NDD, milder form of neurodevelopmental delay is amenable to improvement by family stimulation, and thus, environment into which the affected child born may affect postnatal development. Therefore, when interpreting results of the studies dealing with child neurodevelopment, parental attitude, and quality of prenatal counseling should be taken into consideration. Regrettably, there is no study addressing the relationship between sociodemographic background and mental health status of the families and neurodevelopmental outcome of children affected by congenital brain anomalies.

In the present study, three children showed neuropsychiatric and adaptive disorders consistent with attention deficit hyperactivity disorder (cases 6 and 7), necessitating methylphenidate use, and autism (case 2). Several case series have suggested that isolated mild VM is associated with neuropsychiatric disorders, including autism, attention deficit and hyperactivity disorder, learning disabilities, and schizophrenia [7, 16, 24]. However, there is no solid evidence suggesting an increased incidence compared with normal population.

Previous studies demonstrated that the developmental stimulation that mothers provide can be increased and this can result in improvement of child development [3]. Since maternal knowledge and vigilance for neurodevelopmental milestone were notoriously poor in developing and underdeveloped countries [3] and early detection and stimulation of these children have prognostic implication, strict follow-up schedules and maternal educational program should be implemented before hospital discharge.

We acknowledge two limitations in our study. Firstly, the retrospective nature of the study, but it was based on detailed collected data. Secondly, parts of our results are based on a developmental screening test conducted on parents, so

further studies are needed to confirm these results through full assessment.

In conclusion, prenatal counseling for isolated, nonprogressive BVM should be mainly reassurance since it is not associated with severe neurodevelopmental delay. However, parents should be educated about the developmental milestone of their children to observe and detect mild neurodevelopmental delay which can be associated with BVM.

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