

Natural History and Perinatal Outcomes of Mild Versus Moderate Fetal Ventriculomegaly: A Retrospective Cohort Study

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Abstract

Objective: To compare the prenatal progression, associated anomalies, and perinatal outcomes between fetuses with mild (10-12 mm) and moderate (13-15 mm) ventriculomegaly (VM).

Methods: A retrospective cohort study was conducted on fetuses diagnosed with mild or moderate VM at a single tertiary center between October 2014 and January 2018. Maternal and neonatal clinical data were collected from electronic medical records. Participants were divided into two groups (Mild vs. Moderate VM) for comparison. Statistical analysis was performed using Wizard Pro, with a p-value < 0.05 considered significant.

Results: Among 46 included cases, the median ventricular measurement was 10.5 mm for the mild group (n = 24) and 14.1 mm for the moderate group (n = 21). Non- CNS anomalies were significantly more common in the moderate group (57.1% vs. 24%, p = 0.02). A clinically important trend showed that nearly half (47%) of moderate VM cases progressed to severe VM, compared to 17% of mild cases (p = 0.06). Neonatal death occurred exclusively in the moderate VM group (27.8% vs. 0%, p = 0.007). The rates of CNS anomalies, intrauterine growth restriction (IUGR), and NICU admission were not significantly different between the groups.

Conclusion: Moderate fetal ventriculomegaly carries a significantly higher risk of associated non-CNS anomalies, progression to severe ventriculomegaly, and neonatal mortality compared to the mild form. While mild VM generally follows a more benign course, vigilant fetal and neonatal follow-up is warranted. These findings are crucial for accurate prenatal counseling and prognostication.

Keywords: Ventriculomegaly; Hydrocephalus; Fetal Brain; Prenatal Diagnosis; Neurodevelopment; Congenital Anomalies; Retrospective Study

Introduction

Ventriculomegaly (VM), defined as a dilatation of the fetal lateral cerebral ventricles to an atrial diameter of ≥ 10 mm, is the most common central nervous system anomaly identified on prenatal ultrasound [1,2]. It is typically classified as mild (10 - 12 mm), moderate (13 - 15 mm), or severe (≥ 16 mm) [3]. The clinical significance of VM is highly variable and is primarily influenced by the severity of ventricular dilation, the presence of associated structural or chromosomal anomalies, and whether it is isolated or progressive [4,5]. While mild, isolated VM often has a favorable neurodevelopmental outcome, its association with aneuploidy, congenital infections, and other malformations necessitates a comprehensive prenatal workup [6,7].

The existing literature provides general prognostic data for VM; however, the specific natural history and comparative outcomes between the mild and moderate subtypes remain areas of clinical nuance. Moderate VM, in particular, presents a counseling dilemma, as it is less well-characterized than the mild form and may represent an intermediary state with a higher propensity for progression and associated abnormalities [8,9]. Accurate and detailed prognostic information is essential for clinicians to guide expectant parents through complex decision-making processes.

Objective of the Study

The objective of this study was to define and compare the prenatal progression, spectrum of associated anomalies, and perinatal outcomes in a cohort of fetuses diagnosed with mild versus moderate ventriculomegaly. We aimed to generate evidence-based data to refine prenatal counseling and management strategies for these distinct patient groups.

Materials and Methods

Study design and population

A retrospective cohort study was conducted at the Fetal-Maternal Unit of the Women Wellness Research Center, Hamad Medical Corporation, Doha, Qatar. The study included all cases diagnosed with mild or moderate fetal ventriculomegaly between October 2014 and January 2018. Cases with severe ventriculomegaly (>15 mm) at the time of initial diagnosis or with insufficient follow-up data were excluded.

Definitions and group allocation

Ventriculomegaly was diagnosed and classified based on the atrial diameter of the lateral ventricle measured in an axial plane at the level of the choroid plexus glomus [10]. Cases were allocated into two study groups: Mild Ventriculomegaly (10.0 - 12.0 mm) and Moderate Ventriculomegaly (13.0 - 15.0 mm). Isolated ventriculomegaly was defined as ventriculomegaly with no associated CNS or non-CNS anomalies identified on prenatal ultrasound.

Data collection

Maternal clinical data and neonatal outcomes were extracted from the hospital's Clinical Information System (Cerner; version 12.4.0). Detailed fetal ultrasound findings, including initial and follow-up scans, were obtained from the dedicated ultrasound database (Astraia Software GmbH). Collected data included maternal biodata, gestational age at diagnosis, serial ventricular measurements, associated CNS and non-CNS anomalies, results of genetic and TORCH screening, fetal outcomes (miscarriage, intrauterine fetal demise (IUID), therapeutic abortion, intrauterine growth restriction (IUGR)), delivery details, and neonatal outcomes (NICU admission, neonatal death, and significant morbidities).

Statistical analysis

Data were anonymized and managed in a protected Microsoft Excel sheet. Statistical analysis was performed using Wizard Pro (version 1.9.25). Continuous variables were presented as mean $\pm$ standard deviation or median and range, and compared using the Student's t-test or Mann-Whitney U test, as appropriate. Categorical variables were presented as counts and percentages and compared using the Chi-square test or Fisher's exact test. A two-tailed p-value of < 0.05 was considered statistically significant.

Results

Study population and baseline characteristics

A total of 46 fetuses diagnosed with ventriculomegaly were included in the final analysis, comprising 24 (52.2%) in the mild group and 21 (45.7%) in the moderate group. One case (2.2%) was excluded from group comparisons due to reclassification. Maternal age and gestational age at the time of first diagnosis were not significantly different between the two groups ($p = 0.78$ and $p = 0.10$, respectively).

The median ventricular measurement at diagnosis was 10.5 mm in the mild group and 14.1 mm in the moderate group. The baseline characteristics of the cohort are summarized in table 1.

Variable	Mean	SD	Median	Range
Maternal Age	30,2	5,1	30	22
Gravida	3,3	2,8	3	17
Para	1,6	1,8	1	9
Gestational Age at 1st Diagnosis	26,0	5,4	27	24
Measurement of Lateral Ventricle (mm)	11,8	1,9	12	6
Gestational Age at Last Ultrasound Assessment	33,8	4,0	35	22
Measurement of Lateral Ventricle (mm)	17,2	10,3	13,5	36
Gestational Age at Delivery (Weeks) (N=39)	37,4	2,5	38	13
APGAR Score at 1 Minute (N=39)	7,3	3,0	9	9
APGAR Score at 5 Minutes (N=39)	8,6	3,0	10	10
Birth Weight (Grams) (N=39)	2.661,8	666,5	2.800	2.685

Table 1: Baseline maternal and fetal characteristics.

Associated anomalies and genetic findings

The overall prevalence of associated CNS anomalies was 54.3%, with no significant difference between the mild (48%) and moderate (57.1%) groups ($p = 0.34$). In contrast, non-CNS anomalies were significantly more frequent in the moderate group (57.1%) compared to the mild group (24%) ($p = 0.02$). The spectrum of these anomalies is detailed in figure 1.

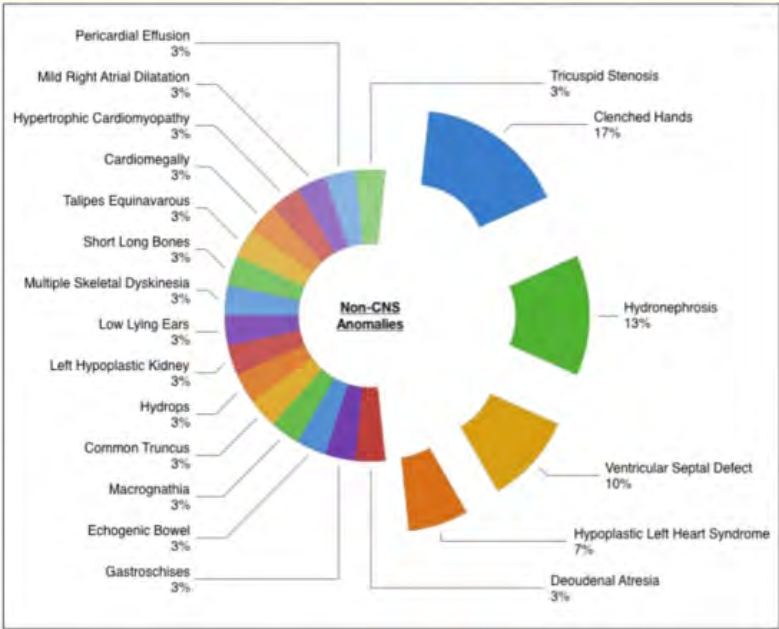


Figure 1: Spectrum and frequency of non-central nervous system (CNS) anomalies identified in the study cohort.

*Spectrum and frequency of non-central nervous system (CNS) anomalies identified in the study cohort.

Genetic testing was performed in 51.1% (23/45) of cases. Abnormal results were found in 35% (8/23) of those tested, with a similar distribution between the mild and moderate groups (Table 2). One case in the mild group tested positive for Cytomegalovirus (CMV) following TORCH screening.

Table 2: Distribution of genetic results among the two groups

Genetic Testing Details	Mild	Moderate
16.7 Mb Deletion in Chromosome 6 From Cytogenetic Band 6Q25.2 To 6Qter		1
Abnormal WES for VUS in One Gene Known to Cause X Linked Syndrome	1	
Chrmosome 9 Deletion	1	
Loss Of Short Arm Or Chromosome 16 Involving Band P 11.2		1
Normal	9	6
Trisomy 13		1
Trisomy 18	1	
Trisomy 21	1	
Trisomy 9 Mosaic		1

Table 2: Distribution of genetic testing results among the mild and moderate ventriculomegaly groups.

Prenatal progression and pregnancy outcomes

Progression of ventriculomegaly was more common in the moderate group, with 47% progressing to severe VM compared to 17% in the mild group, a difference that approached but did not reach statistical significance ($p = 0.06$). This progression is illustrated in figure 2. Intrauterine growth restriction (IUGR) was observed in 32.6% of the cohort, with a higher, non-significant trend in the moderate group (47.4% vs. 20.8%, $p = 0.065$).

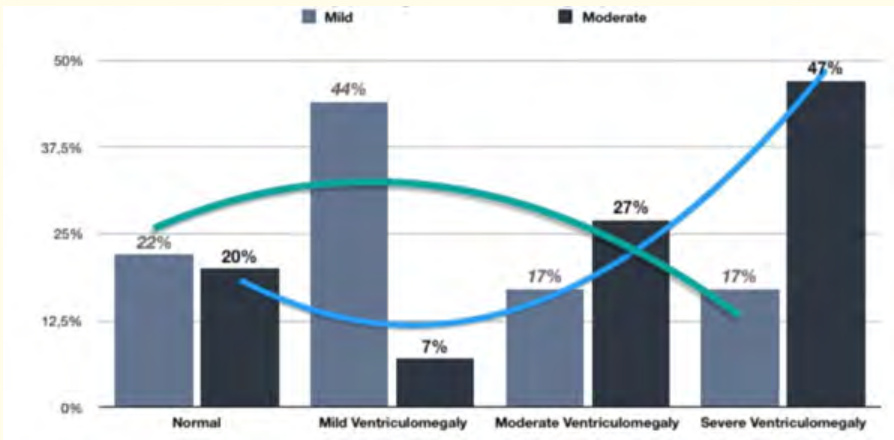


Figure 2: Progression of ventricular dilation from initial diagnosis to last ultrasound assessment in the mild and moderate ventriculomegaly groups.

*Progression of ventricular dilation from initial diagnosis to last ultrasound assessment in the mild and moderate ventriculomegaly groups.

Of the initial 46 pregnancies, there were 2 cases of intrauterine fetal demise (IUFD) (4.3%), 1 miscarriage (2.2%), and 1 therapeutic abortion (2.2%). Four patients (8.7%) were lost to follow-up.

Delivery and neonatal outcomes

The mean gestational age at delivery and mode of delivery were not significantly different between the two groups. Similarly, Apgar scores at 1 and 5 minutes and birth weight were comparable (Table 1).

The vast majority of neonates (71.8%) required admission to the NICU, with no significant difference between the groups. The indications for NICU admission were diverse, ranging from routine observation for further evaluation to significant congenital anomalies (Table 3). The most critical finding was a neonatal mortality rate of 27.8% (5/18) in the moderate VM group, compared to 0% (0/21) in the mild VM group (p = 0.007). The causes of neonatal death were all related to severe associated malformations (Table 4). Among survivors, only 7 neonates (17.9% of the delivered cohort) were assessed as normal at postnatal evaluation, while 6 (15.4%) had severe disability and developmental delay.

Table 3: Indication for each case who needed an Admission to the NCIU

Number of Neonates (N=28)	Neonatal Findings and Reason for NICU Admission
1	- Mild Respiratory Distress Requiring Nasal Cannula - To Rule Out Coarctation Of Aorta 3. Further Work Up [B/L Moderate Ventriculomegaly]
1	- Arthrogryposis, - Jejunal Atresia, - Overfolded Ears, - Multiple Joint Contractures Both Upper and Lower Limbs
1	- Baby Intubated: - Macrocephaly, - Ventriculomegally, - Cleft Palate
1	CPAP
1	- CPAP, - Abnormal Features, - Further Evaluation
1	- CPAP, - Neurology, - Cardiology Review
1	Further Evaluation
1	- Hydrocephalus Further Evaluation - On CPAP
1	- Hypotonia, - Cyanosis Attacks, - Poor Feeding
1	Intubated
1	Further Evaluation
1	- Investigations, - Impaired Renal Function
1	- Investigations, - Observe CNS Symptoms
1	Jaundiced For Phototherapy
1	- Major Cardiac Anomaly, - Asplenia, - Conginital Adrenal Hyperplasia
1	- Multiple Conginital Anomalies, - Cardiac, - Anorectal Malformation, - Tracheoesophageal Fistula
1	- Multiple Dysmorphic Features : - Weak Cry - High Arched Palate - Low Set Posterior Rotated Simple Ears - Clenched Fist - Toe Overlapping

	○ Bilateral Talipes
1	• Neurology Consultation, • Small PDA
1	• Neurosurgery Consultation, • Ultrasound And Further Evaluation
1	• Observation, • Investigations, • Neurology Team Review
1	• Observation, • Preparation For Surgery, • Investigations, • Neurology and Cardiology Team Review
1	• Phototherapy, • Neurology & Cardiology Referral (? Dextrocardia)
1	• Respiratory Distress, • Dysmorphic Features, • On Nasal Canula
1	• Rule Out Sepsis, • Neonatal Hypoglycemia Recurrent.
1	Rule Out Sepsis
1	Short Episode Of Apnea With Desaturation
1	• Subglial Hematoma, • TTN, • Lactic Acidosis (Mother Gbs+Ve)
1	Further Evaluation

Table 3: Indications for admission to the neonatal intensive care unit (NICU).

Table 4: Neonatal death details	
Findings of Neonatal Death Cases.	Time of ND
Agenesis of Corpus Callosum and Hypoplastic Left Heart Syndrome	During Delivery
Cerebral Partial Lissencephaly/Pachygyria Anomaly	3 months of life.
Pulmonary Hage And Infantile Polycystic Kidney	4 months of life
Multiple Cong Anomalies (Trisomy 9 Syndrome)	5 months of life.
Huge Interhemispheric Supratentorial Cyst Occupying Most of The Midline Anterior and Middle Cranial Fossa	1 hour of life.
Multiple Abnormalities in The Supratentorial Brain, Ocular Hypotelorism, Abnormal External and Possibly Also Middle and Inner Ears	4 hours of life.
Complete Agenesis of The Corpus Callosum. Simplified Cerebral Gyral Pattern. Hypoplasia of The Cerebellum	??

Table 4: Findings and timing of neonatal death cases.

Discussion

This retrospective cohort study provides a detailed comparison of the prenatal characteristics and perinatal outcomes between fetuses with mild and moderate ventriculomegaly. Our principal findings indicate that moderate ventriculomegaly is a distinct clinical entity with a significantly higher risk profile compared to the mild form. Specifically, moderate VM was associated with a greater burden of non-CNS anomalies, a strong tendency to progress in severity prenatally, and a substantially higher rate of neonatal mortality.

The significantly higher incidence of non-CNS anomalies in the moderate VM group (57.1% vs. 24%, p = 0.02) is a critical finding that underscores the importance of a detailed, systematic anatomical survey in these cases. This suggests that moderate VM may less

frequently be an “isolated” finding and is more often a marker of a broader syndromic or chromosomal condition. This aligns with literature suggesting that the risk of associated anomalies increases with the severity of ventriculomegaly [11,12]. Furthermore, the trend we observed-where nearly half of the moderate cases progressed to severe VM compared to only a fifth of mild cases-highlights the volatile nature of moderate VM. This progression risk is a key factor for prenatal counseling and supports the recommendation for more vigilant serial ultrasound monitoring in these pregnancies [13].

The most stark outcome difference was in neonatal survival. The 27.8% mortality rate in the moderate group, contrasted with no deaths in the mild group, underscores the serious prognosis associated with moderate VM, particularly when other anomalies are present. All neonatal deaths in our cohort were attributable to severe associated structural malformations, reinforcing that the outcome is often dictated by these concomitant conditions rather than the ventriculomegaly itself [14]. This finding is consistent with studies that report a graded increase in adverse outcomes with increasing ventricular diameter [15]. However, it is noteworthy that rates of NICU admission were equally high in both groups, reflecting the universal need for specialized neonatal assessment and potential intervention in all cases of prenatally diagnosed VM, regardless of initial severity.

Strengths and Limitations

The strengths of our study include its well-defined cohorts based on standardized ventricular measurements and comprehensive collection of perinatal outcome data from a single tertiary center. However, the findings must be interpreted in the context of several limitations. The retrospective design introduces the potential for selection and information bias. The relatively small sample size, particularly in the moderate group, may have limited the statistical power to detect significant differences in some outcomes, such as the rate of progression ($p = 0.06$) and IUGR ($p = 0.065$), where strong clinical trends were observed. Furthermore, the loss of four patients to follow-up may have influenced the final outcome analysis.

Conclusion

In conclusion, our study demonstrates a clear prognostic distinction between mild and moderate fetal ventriculomegaly. Moderate ventriculomegaly is associated with a significantly higher risk of non-CNS anomalies, a strong tendency for prenatal progression, and substantial neonatal mortality. These findings underscore that moderate ventriculomegaly should not be considered a simple intermediate but rather a condition warranting heightened surveillance and comprehensive counseling about potential complex outcomes. While mild ventriculomegaly follows a more benign course, it still necessitates systematic evaluation and follow-up. Future prospective, multi-center studies with larger cohorts and long-term neurodevelopmental follow-up are needed to further refine management and counseling for these patients.

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