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Diagnostic accuracy of prenatal ultrasound in fetal ventriculomegaly: autopsy based correlation

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Background: Ventriculomegaly (VM) is one of the most common abnormality detected by perinatal scans, and it is characterized by lateral ventricular enlargement with an atrial width of ≥10 mm, which can be visualized during second-trimester imaging. This entity can be associated with brain abnormalities and other malformations. In order to perform good prenatal counseling, the prenatal ultrasound diagnosis as well as the fetal autopsy additional findings are essential.

Aim: The retrospective observational study aimed to assess the correlation between prenatal ultrasound and autopsy findings during the second trimester (fetuses from 12 to 28 weeks of gestation) due to VM and its related structural abnormalities.

Objective: Our study included 35 fetal autopsy cases over a 2-year period following a fetal loss that occurred from elective terminations and spontaneous expulsions and was chosen for comparison. The cases were classified according to the degree of agreement on diagnostic performance at the level of various organ systems and specific malformations. An extensive perinatal autopsy protocol comprising external examination and internal examination of aborted fetuses with corresponding ultrasound imaging was studied. Cases were classified according to VM etiology as malformative, obstructive, destructive, syndromic or chromosomal, along with the presence of central nervous system (CNS) or extra-CNS abnormalities. The study is intended for compatibility with prenatal ultrasound findings and postmortem results to determine underlying reasons.

Results: Of the cases, three had isolated VM, 54% of cases had central nervous system abnormalities and 29% of fetuses had extra-brain deformities; in addition, cerebellar hypoplasia (n = 11 cases), corpus callosum anomaly (n = 13 fetuses) and the absence of cavum septum pellucidum (10 cases) were also observed. Autopsy revealed additional abnormalities; which was not picked up on imaging, including rhombencephalosynapsis and cytomegalovirus (CMV) inclusions. Diagnostic concordance between ultrasound and autopsy was good for central nervous system abnormalities (82%), but poor for gastrointestinal (60%), cardiovascular (63%), and syndromic abnormalities (38%).

Conclusion: This work emphasizes the convergence of prenatal imaging with postmortem fetal assessment such that to improve overall understanding of perinatal fetal assessment in different organ systems and their related anomalies. VM can be noticed by perinatal scans. However, the Fetopathological examination was

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essential for final report findings. Combining these two approaches significantly improve the understanding of etiology, diagnostic precision, and planning for genetic counseling for the pregnancies that are affected.

Keywords: prenatal ultrasound, fetal autopsy, ventriculomegaly (VM), central nervous system (CNS), cytomegalovirus (CMV), cardiovascular system (CVS), diagnostic concordance

Introduction

Fetal ventriculomegaly (VM) is represented as an abnormal enlargement of the cerebral ventricles identified by prenatal ultrasound. It is one of the most common abnormality of the central nervous system (CNS) diagnosed during the second trimester with an estimated occurrence of about two cases for every 1,000 live births (1). Based on the atrial size and lateral ventricles diameter; VM can be classified as mild (10–12 mm) moderate (13–15 mm) or severe (≥16 mm) either by magnetic resonance imaging (MRI) or by perinatal ultrasound scan. This condition has diverse etiology that includes cerebrospinal fluid (CSF) obstruction, destructive brain lesions; by which it leads to the parenchymal loss and abnormal neuronal development. In addition cytomegalovirus (CMV) infection, Chromosomal abnormalities and syndromic disorders even contribute to growth issues with neurodevelopmental and structural malformations. This study emphasize on the need for comparing prenatal ultrasound imaging results with postmortem findings to improve the diagnostic accuracy (2, 3). Although the ultrasonography findings is the primary method utilized for prenatal Diagnosis. Fetal autopsy remains the golden standard for confirming the severity of the congenital malformations and the type of structural abnormalities related to fetal VM; additionally the histopathology findings reinforce for further diagnosis.

The present study was designed to assess the concordance between prenatal ultrasound and fetal autopsy findings in the cases of fetal VM by classifying according to its etiological categories: as malformative, obstructive, destructive/clastic, syndromic and chromosomal, such that correlating the VM associated with CNS and extra-CNS malformations. This work aims to highlight how integrated the prenatal imaging and autopsy findings contributes to comprehensive fetal diagnosis for better genetic and prenatal counseling.

Materials and methods

This retrospective descriptive study was conducted at the Department of Pathology, PSG Hospitals, Coimbatore, over a period of 2 years (January 2023–January 2025). A total of 35 fetuses diagnosed prenatally with VM were included for the assessment. Gestational age ranged between 12 and 28 weeks was chosen for the correlation. Ethical approval for the study was obtained from the Institutional Human Ethics Committee, and informed written consent was obtained from one or both parents before each perinatal autopsy procedure was performed. Clinical details were acquired from the hospital medical records, including maternal age, parity, consanguinity, previous obstetric history, associated illnesses, gestational age, and ultrasound findings. All prenatal ultrasonographic scan was performed by experienced obstetricians. Ventricular measurements and associated anomalies were measured, documented, and further cases were classified accordingly as VM severity (mild, moderate, or severe) and the type as (isolated or non-isolated).

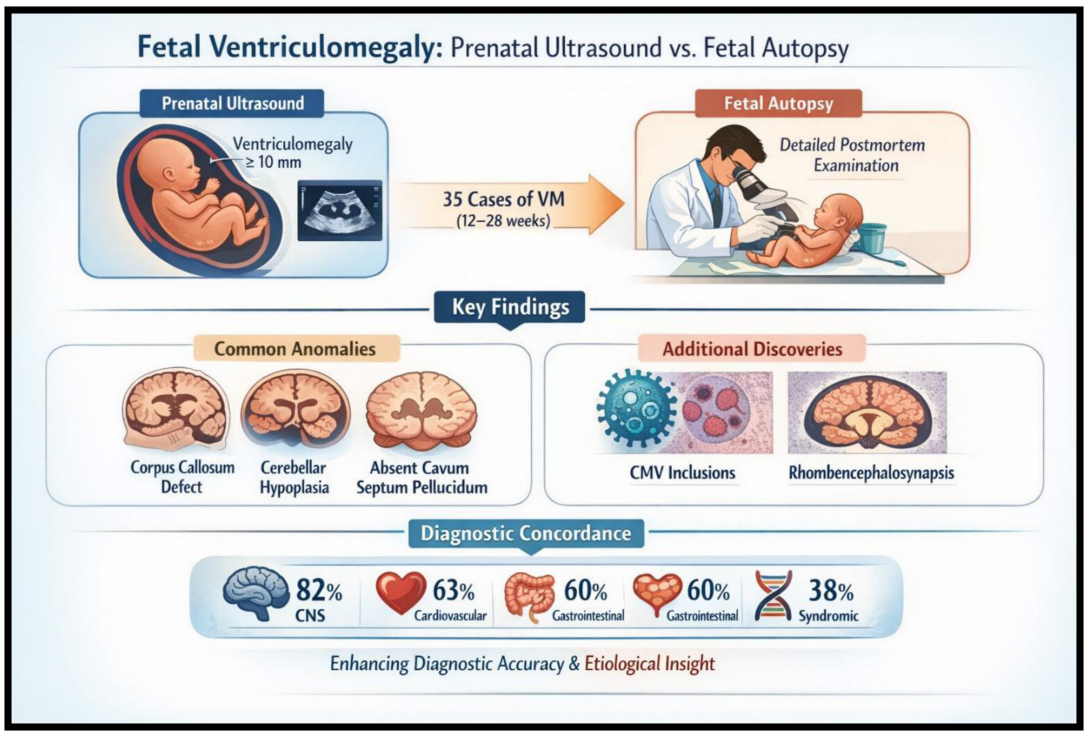
All fetal autopsies were conducted following the guidelines of The Royal College of Obstetricians and Gynecologists and the Royal College of Pathologists (4). Standardized procedures were included like external examination, foetogram, anthropometric measurements, and high-resolution photographic documentation. An “en bloc” organ removal technique was employed such that to preserve the organ integrity. To optimize the brain fixation, 40% neutral buffered formalin was gently infused through the anterior fontanelle until the fixative appeared from the nostrils. The brain was subsequently removed using a hinge calvarial incision that maintained the sagittal sinus. After removal, the brain was weighed and suspended in formalin for a minimum of 8 weeks before detailed examination. Subsequently coronal and sagittal sections were inspected for any structural anomalies, gyral and sulcal patterns, and color or texture changes and the same were reported.

Classification and analysis

VM cases were categorized according to etiological groups: malformative, obstructive, destructive (clastic), syndromic, and growth-restricted fetuses (**Table 1**). They were further divided into three categories based on anomalies associated:

1. Group I: VM associated with CNS anomalies only.
2. Group II: VM associated with extra-CNS anomalies.
3. Group III: Additional anomalies missed on ultrasound but identified during perinatal autopsy findings.

The findings of this retrospective study with prenatal ultrasound results and perinatal fetal autopsy findings were reviewed and compared (3). Concordance can be defined as complete agreement between perinatal scan imaging



GRAPHICAL ABSTRACT |

and perinatal autopsy observations. The term "discordance" referred as additional findings or the results in contrast to fetal autopsy. Frequencies and percentages were represented to show the findings on descriptive analysis.

Results

From the prenatally diagnosed 35 fetuses with VM for a period of 2 years (January 2023–January 2025); was examined by standardized Autopsy procedure. The findings were correlated and evaluated. The mean gestational age during the termination of fetus was 21.9 weeks of gestation (from 12 to 28.4 weeks). VM by its type and severity is depicted on (**Figure 1**) as Isolated VM in 3 cases (9.4%), VM associated by CNS anomalies around 19 cases (59.4%), and VM with extra-CNS or multi-system anomalies in 10 cases (31.2%). Whereas, mild VM (10–12 mm) was the most commonly noticed in (15 cases, 46.9%), followed by moderate VM (13–15 mm, 10 cases) and severe VM with (≥16 mm, 7 cases) in accordance to the degree of ventricular dilatation. Bilateral VM imaged by ultrasound is shown in (**Figure 2a–d**). The examination also found non-isolated VM for more than 90% of cases, with the structural or syndrome abnormalities. As shown in (**Table 1**), malformative lesions was the largest etiological group with corpus callosum anomalies in (13 cases), followed by cerebellar hypoplasia in (11 cases) and absence of the cavum septum pellucidum with (10 cases). Fewer cases was reported on pontocerebellar hypoplasia with (4 cases), rhombencephalosynapsis by (3 cases), hydranencephaly of (2 cases), and a single cases were also observed for lobar holoprosencephaly, mild hypertrichosis, and hemispheric cyst.

Among 20 cases of Obstructive VM, Bilateral VM was found in (13 cases), Arnold–Chiari II malformation with (5 cases), and aqueductal atresia by (2 cases). Followed by clastic (destructive) etiology cases such as intraventricular hemorrhage of (16 cases), toxoplasmosis along with other infections such as rubella, cytomegalovirus, and herpes simplex virus (TORCH) associated with pulmonary hypoplasia with (2 cases), and one hydropic fetus were even found. Syndromic associations such as Joubert, Dandy Walker, Ellis van Creveld, DiGeorge (22q11.2 deletion), Apert, and Amniotic-band syndromes, were also presented among 8 cases. Growth-restricted fetuses was identified in (6 cases), multisystem malformations involved with potter facies, diaphragmatic hernia, talipes, and visceral malformations were also examined. **Table 2** shows the concordance between prenatal ultrasound diagnosis and perinatal autopsy findings; where highest was the Group I, showing VM with CNS anomalies by perinatal autopsy findings (**Figure 3a–d**), like corpus callosum agenesis/dysgenesis, cerebellar hypoplasia, absence of the cavum septum pellucidum, Arnold–Chiari II malformation, and holoprosencephaly. Additional findings detected by postnatal autopsy evaluation such as rhombencephalosynapsis, neuronal migration disorders, CMV inclusions, and germinal matrix hemorrhage. As defined in (**Table 3**), extra-CNS findings with variable levels of agreement among Group II was shown predominantly;

TABLE 1 | Etiological classification and distribution of VM cases based on main pathological groupings and associated conditions.

Main group	Condition	Case count
Malformative	Hydranencephaly	2
	Cerebellar hypoplasia (includes Arnold C II)	11
	Pontocerebellar hypoplasia	4
	Absent cavum septum pellucidum	10
	Rhombencephalosynapsis	3
	Corpus callosum anomalies (partial/complete/dysgenesis)	13
	Interhemispheric cyst type 2A	1
	Lobar holoprosencephaly	1
	Mild hypertrichosis	1
Obstructive	Aqueductal atresia ± hypoplastic cerebellum	2
	Marked/bilateral/single ventricle VM	13
	Arnold Chiari malformation (Type II ± meningocoel)	5
Clastic	Intraventricular hemorrhage (all grades, subtypes)	16
	Pulmonary hypoplasia with TORCH/CMV infection	2
	Hydropic fetus	1
	Autolysis (dolichocephaly, midfacial hypoplasia)	2
Syndromic	Joubert syndrome	1
	Dandy Walker malformation	1
	Ellis van Creveld syndrome	1
	DiGeorge syndrome (22q11.2 deletion)	1
	Apert/acrocephalosyndactyl syndrome	2
	Amniotic band syndrome	2
	Congenital obstructive airway syndrome (CHOAS) + CPAM	1
Growth-restricted/syndromic	Multisystem fetal syndromes (Potter face, talipes, imperforate anus, cardiac/renal defects, autolysis, diaphragmatic hernia)	6

with cardiovascular defects such as tetralogy of fallot, double-outlet right ventricle, and septal defects. However, Autopsy revealed additional findings on cardiomegaly, right aortic arch, myocardial necrosis, as well vascular congestion. The gastrointestinal and genitourinary systems was identified with moderate concordance by ultrasound diagnosis but fetal autopsy confirmed the findings with intestinal malrotation, posterior urethral valve, hydronephrosis, and renal cysts, and moreover identified Meckel's diverticulum and imperforate anus in few cases too. Placental and syndromic associations, including CMV/TORCH infections, Meckel–Gruber syndrome, and chromosomal abnormalities (Trisomy 13, 18, 21, and 22q11.2 deletion), were supported by fetal autopsy findings. The following findings include anomalies detected exclusively by fetal autopsy under Group III with subtle CNS and systemic abnormalities able to visualize prenatally, such as rhombencephalosynapsis, neuronal migration defects, germinal matrix hemorrhage, and microscopic CMV inclusions were also identified only by post-mortem findings and were also newly documented. Undetected anomalies of extra-CNS systems includes aortic narrowing, thoracic and cardiac findings, thymic hypoplasia, myocarditis, and vascular congestion, vertebral fusion, amniotic constriction bands, syndactyly, and hepatic fibrosis associated with chromosomal abnormalities like (9p11 q13 inversion and 22q11.2 deletion).

Overall concordance between prenatal ultrasound and autopsy was found varied across the various organ systems as shown in (**Figure 4**). The CNS malformations was the highest rate of agreement (82%, 18/22 cases) found, followed by musculoskeletal (67%), cardiovascular (CVS) (63%), gastrointestinal (60%), and genitourinary (57%) systems. Syndromic and placental abnormalities were observed on the lowest concordance of (38%).

Conclusion

Prenatal ultrasound findings was highly accurate for major CNS malformations indications, but less sensitive for subtle, multisystem malformations or chromosomal anomalies that required further histopathological confirmation by perinatal autopsy.

Discussion

This study was aimed to assess the concordance and discordance between prenatal ultrasonography outcomes with fetal autopsy findings of VM and its associated anomalies. The objective of this comparative analysis was to support and elaborate on fetal autopsy findings in addition to prenatal imaging by highlighting on diagnostic accuracy.

Over the course of the 2-year cohort, isolated ventriculomegaly (IVM) occurred in 8%–6% of the 35 fetuses, consisting of two moderate and one severe VM. However, previous studies found that the isolated VM rates to be greater (30%–45%) in population-based series (5–7). There is decrease in proportion in our study is most likely due to early pregnancy termination in addition to a smaller sample. About 91.4% of cases had non-IVM, which was usually associated with the central nervous system or irregularities across various systems. These findings of our study align with recent findings of VM indicating 55%–60%

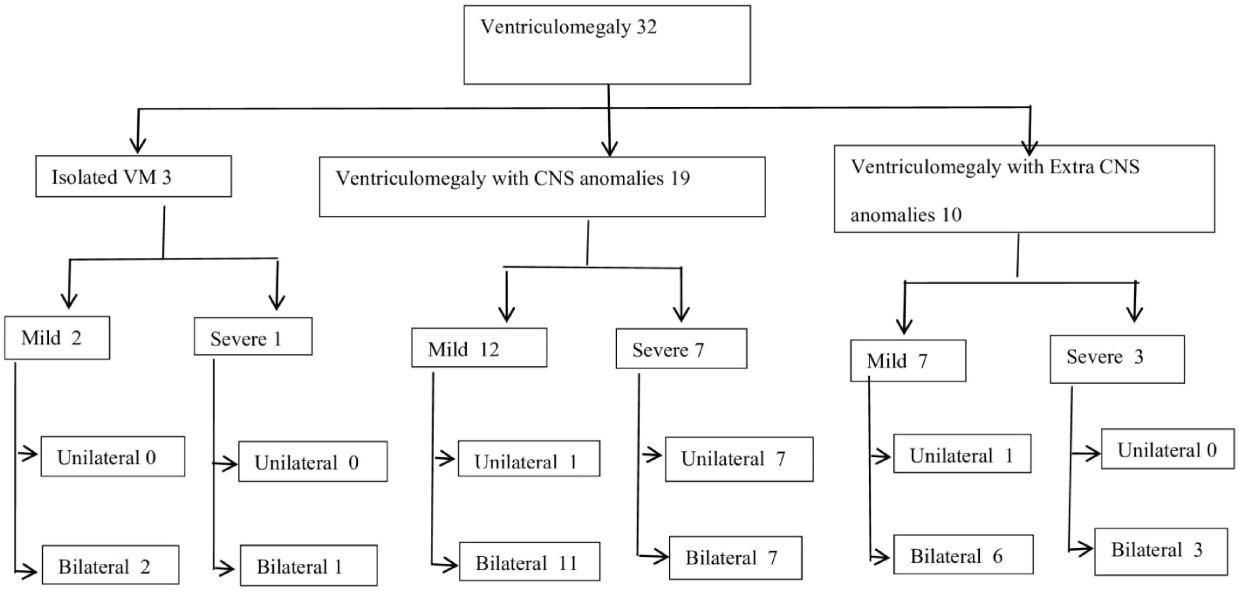


FIGURE 1 | Classification of ventriculomegaly (VM) by type and severity.

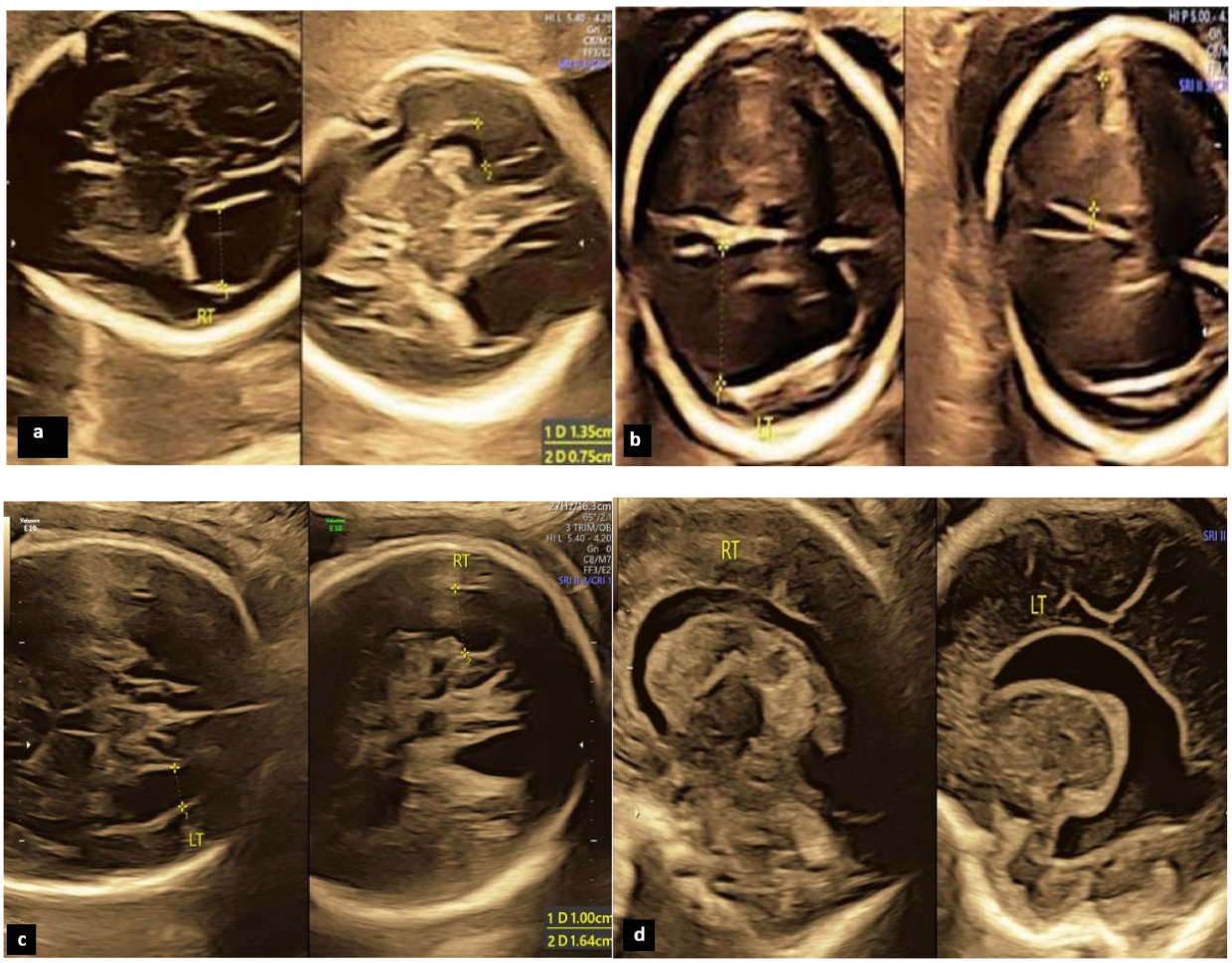


FIGURE 2 | (a–d) Prenatal ultrasound (USG) images showing varying presentations of VM: (a) USG with 24 weeks Fetus showing complete agenesis of the corpus callosum with asymmetric left lateral VM, (b) USG image with Fetus at 22 weeks 3 days demonstrating Gross bilateral VM with absent cavum septum pellucidum and corpus callosum, (c) USG with Both lateral ventricles appear dilated, and (d) USG showing Right lateral ventricle of intraventricular hemorrhage extending onto the parenchyma.

TABLE 2 | Group I; prenatal ultrasound and autopsy correlation for VM cases with CNS anomalies.

Organ system	Prenatal main diagnosis	Correlated autopsy findings
CNS	VM (bilateral, colpocephalic, obstructive, secondary)	Hydranencephaly Cerebellar hypoplasia (global, vermian) Absent cavum septum pellucidum Corpus callosum agenesis/dysgenesis Arnold Chiari malformation Rhombencephalosynapsis CMV inclusions Germinal matrix hemorrhage Neuronal migration disorder Dandy Walker malformation Holoprosencephaly
	Arnold Chiari malformation Type II (often with VM)	Lumbosacral meningomyelocele Aqueductal stenosis Cerebellar vermian hypoplasia Spinal dysraphism Aortic narrowing
	Agenesis/dysgenesis of corpus callosum	Interhemispheric cyst Parieto-occipital nodularity Small kidneys Absent pancreas body and tail
	Cerebellar hypoplasia (Joubert or CMV-related)	Pituitary hypoplasia Adrenocortical and renal CMV inclusion Necrosis Neuronal loss

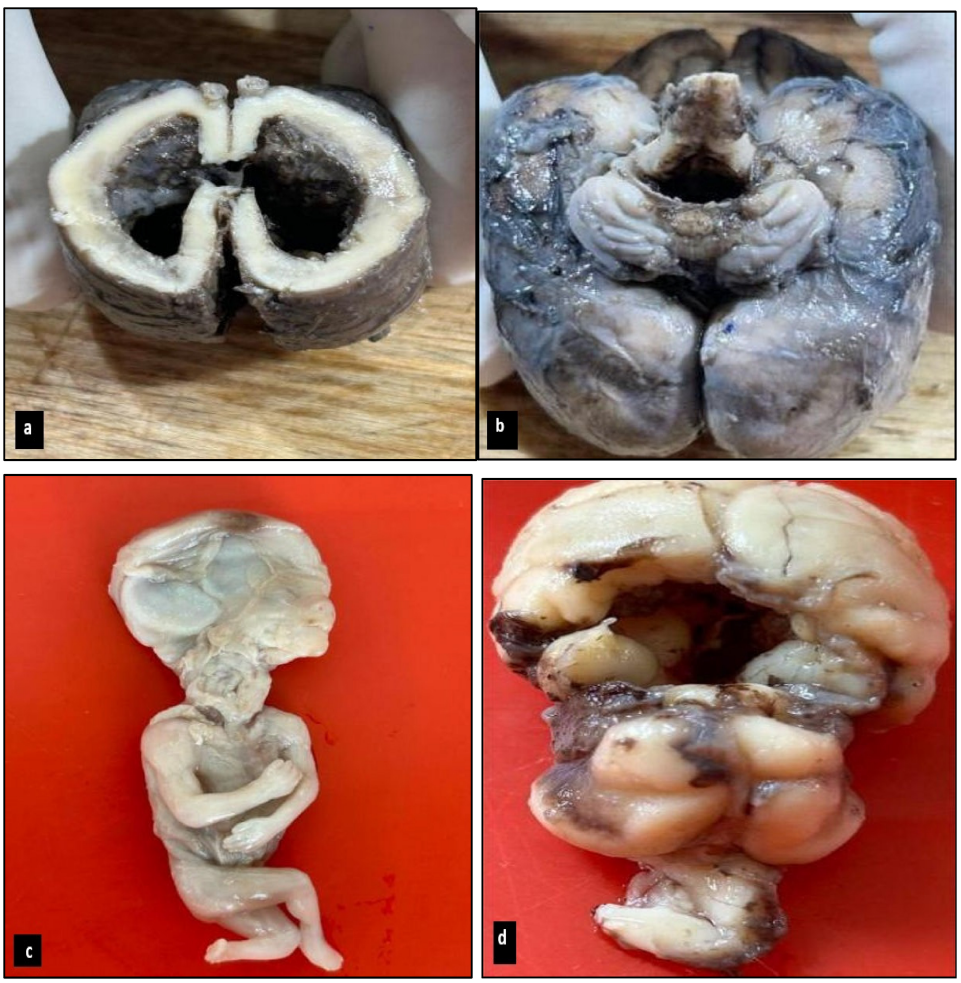


FIGURE 3 | (a–d) Shows fetal autopsy brain specimen: (a) Coronal section of fetal brain depicting bilateral gross VM, (b) Bilateral gross VM and cerebellar hypoplasia, due to cytomegalovirus (CMV) infection, (c) Growth restricted fetus with hydranencephaly, and (d) Fetal brain specimen exhibiting central nervous system (CNS) malformations typical of Meckel-Gruber syndrome with alobar holoprosencephalneuronal migration disorder.

TABLE 3 | Group II; prenatal ultrasound and autopsy correlation for VM cases with extra-CNS congenital anomalies.

Organ system	Prenatal main diagnosis	Autopsy findings
Cardiovascular system (CVS)	• Tetralogy of fallot double outlet right ventricle • Atrial septal defect • Ventricular septal defect	• Cardiomegaly, right aortic arch, pulmonary hypoplasia • Persistent left SVC, Myocardial necrosis • Lymphocytic myocarditis, Vascular congestion in heart, liver, kidneys
Musculoskeletal	• Syndactyly, polydactyly Syndromic: • Joubert, apert syndrome.	• Vertebral fusion or segmentation defects • Limb constriction bands (amniotic band sequence) • Rocker-bottom feet, dolichocephaly
Gastrointestinal	• Imperforate anus Intestinal malrotation	• Posterior urethral valve, Jejunal volvulus • Meconium impaction, Meckel's diverticulum • Atresia of rectum or other gut segments
Genitourinary	• Posterior urethral valve (PUV) hydronephrosis • Hydroureter	• Bilobed hypoplastic lungs, cerebellar hypoplasia • Aortic coarctation, renal cortical cysts • Pelvicalyceal dilatation, bladder distension • Hypoplastic bladder, imperforate anus, small hypoplastic kidneys/absent pancreas body and tail
Placental/ Syndromic Associations	• CMV infection, TORCH infection • Meckel–Gruber syndrome • Ellis–van Creveld syndrome • DiGeorge syndrome (22q11 deletion) • Chromosomal anomalies (Trisomy 13,18,21, structural rearrangements)	• Polycystic kidneys, ductal plate malformation in liver • Pulmonary hypoplasia, thymic agenesis/hypoplasia • Cardiac and skeletal anomalies • Hepatic fibrosis, chromosomal deletions (9p11-q13 inversion, 22q11.2 deletion) • Fryns or Pallister-Killian syndrome features

of cases accompanied by other abnormalities like mid line abnormalities of the corpus callosum and posterior fossa (7–10).

Within our series, the predominant anomalies involved the corpus callosum (13 cases), cerebellum (11), and cavum septum pellucidum (10), consistent with prior observations that these structures are particularly vulnerable during fetal brain development. Rare entities such a rhombencephalosynapsis (3 cases) and holoprosencephaly (1 case) align with our study findings. Obstructive types, including aqueductal atresia (2) and Arnold–Chiari II malformation (5), were less frequent, in agreement with studies who reported that CSF-flow obstruction accounts for a minority of VM cases. Similarly, the clastic (destructive) forms associated with intraventricular hemorrhage and CMV infection support the pathophysiological mechanisms described. Extra-CNS abnormalities involving the cardiac, renal, or skeletal systems were also common, corroborating reports.

As shown in (**Figure 4**), the present study demonstrated a high level of agreement between prenatal ultrasound and autopsy for CNS malformations (82%), consistent with prior data showing the strong diagnostic accuracy of ultrasound in detecting major brain defects. However, concordance for other organ systems was lower musculoskeletal (67%), cardiovascular (63%), gastrointestinal (60%), and syndromic/placental (38%) highlighting ultrasound's limitations for smaller or histopathological lesions, as noted.

The perinatal autopsy findings of our study also showed microscopic and subtle findings, such as neuronal migration disorders,rhombencephalosynapsis, Phenotypic analysis, genetically mediated or syndromic conditions, CMV inclusions, which were invisible on ultrasound imaging. These findings confirm that fetal autopsies are necessary for final interpretation; However, prenatal ultrasound is reliable for significant CNS abnormalities.

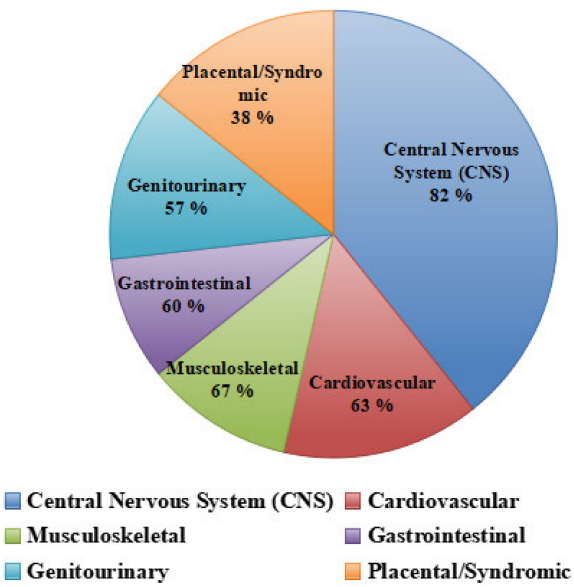


FIGURE 4 | Organ-system concordance: CNS: blue segment representing cases involving CNS anomalies (82%), cardiovascular: red segment representing cases with cardiovascular anomalies (63%), musculoskeletal: green segment representing cases with musculoskeletal anomalies (67%), gastrointestinal: purple segment representing cases with gastrointestinal anomalies (60%), genitourinary: cyan segment representing cases with genitourinary anomalies (57%), placental/syndromic: orange segment representing cases identified as placental or syndromic anomalies (38%.

Better agreement would result from detailed fetal analysis, which can be enhanced by introducing three-dimensional ultrasound and MRI for prenatal ultrasound.

Conclusion

A fetal autopsy and prenatal ultrasound act as complementary diagnostic methods. However, perinatal autopsy findings confirm, improve, and broaden the diagnostics, improves recurrence risk assessment, make genetic counseling easier, and eventually improve prenatal and postnatal care for families with VM.

Clinical relevance

Prenatal imaging scan reporting and fetal autopsy findings, when combined, increase the diagnostic potential is increased with more accuracy and the various causes will be better understood, which contributes for improved genetic counseling.

Ethical statement

After reviewing and discussing the study, the PSG IMS&R Institutional Human Ethics Committee gave its approval with specified sample size and it was decided by consensus. The approval number was (PSG/IHEC/2025/Appr/Exp/288). Hereby, we declare guidelines were followed as per Helsinki for conducting the study.

Strengths and limitations of the study

This retrospective study on fetal VM shows around 82% concordance with perinatal ultrasound scan findings, which is strongly validated, likewise, for spinal cord abnormalities and cerebellar hypoplasia as well as corpus callosum agenesis. Nevertheless, the retrospective design is at low rates for few cases with isolated VMs (9%), and the small sample size (n = 35) performed was the limitation of the study. Further genetic testing and MRI evaluations have not yet been evaluated.

Author contributions

Mrs K. Radhika helped with the study's design, conception, data collection, investigations, interpretation and ethical approval.

Dr Umamaheswari and Dr Lalitha made contributions to the data interpretation and study design.

Dr Amudha and Dr Kavitha helped with the study's design, data collection and submission for ethical approval.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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