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A review of fetal megacystis: from diagnosis to long-term prognosis

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Megacystis is a rare fetal condition characterized by an abnormal enlargement of the bladder, often associated with lower urinary tract obstructions (LUTO), genetic mutations (e.g., ACTG2 in Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome – MMIHS), or syndromic disorders such as Prune Belly Syndrome (PBS).

The aim – to evaluate prenatal diagnostic techniques, assess the effectiveness of prenatal and postnatal interventions, and analyze long-term renal and urological outcomes in neonates diagnosed with megacystis.

This systematic review consolidates available case reports to evaluate prenatal diagnosis, treatment strategies, and long-term outcomes of neonates diagnosed with megacystis. This review was conducted in accordance with the PRISMA 2020 guidelines. Studies were included if they provided prenatal or postnatal diagnoses, genetic findings, interventions, and clinical outcomes. Risk of bias was evaluated by applying the Joanna Briggs Institute (JBI) Critical Appraisal Checklist. Due to the heterogeneity of case reports, a narrative synthesis was performed, and findings were categorized based on intervention type and prognosis. A total of 20 case reports were included. The mean birth weight of affected neonates was 1152±532 g, with an average gestational age at diagnosis of 28±9.3 weeks. Prenatal interventions (n=5) demonstrated a 60% survival rate but were associated with preterm birth and oligohydramnios. Postnatal surgical management (n=8), including vesicostomy and catheterization, had a 75% survival rate, although some cases required long-term dependency on total parenteral nutrition (TPN) due to associated comorbidities. Cases where no intervention was performed (n=7) resulted in 100% mortality, with intrauterine demise or termination due to severe structural anomalies. The survival rates were compared across different intervention groups, highlighting that those cases managed postnatally showed significantly better survival outcomes, while fetal intervention success varied based on gestational age and underlying etiology.

This review highlights the need for standardized diagnostic protocols, genetic screening, and prospective cohort studies to improve treatment decision-making and long-term care for affected neonates.

The authors declare they have no conflict of interest.

Keywords: megacystis, lower urinary tract obstruction, megacystis-microcolon-intestinal hypoperistalsis syndrome, vesicoamniotic shunting.

Огляд фетального мегацистису: від діагностики до довгострокового прогнозу

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Мегацистис – це рідкісний стан плода, що характеризується аномальним збільшенням сечового міхура, часто пов'язаним з обструкцією нижніх сечовивідних шляхів (LUTO), генетичними мутаціями (наприклад, ACTG2 при синдромі мегацистису-мікроколон-кишкової гіперперистальтики – MMIHS) або такими синдромальними розладами, як синдром сливового живота (PBS).

Мета – оцінити методи пренатальної діагностики, оцінити ефективність пренатальних та постнатальних втручань та проаналізувати довгострокові ниркові та урологічні результати в новонароджених із діагнозом мегацистис.

Цей систематичний огляд об'єднує доступні звіти про випадки хвороби для оцінки пренатальної діагностики, стратегій лікування та довгострокових результатів лікування новонароджених із діагнозом мегацистис. Огляд було проведено відповідно до рекомендацій PRISMA 2020. Дослідження було охоплено, якщо вони надавали пренатальну або постнатальну діагностику, генетичні дані, втручання та клінічні результати. Ризик систематичної помилки оцінювався за допомогою контрольного списку критичної оцінки Інституту Джоанни Бріггс (JBI). Через неоднорідність звітів про випадки хвороби було проведено наративний синтез, а результати було класифіковано на основі типу втручання та прогнозу. Загалом було охоплено 20 звітів про випадки хвороби. Середня вага новонароджених із діагнозом становила 1152±532 г, середній гестаційний вік на момент постановки діагнозу 28±9,3 тижні. Пренатальні втручання (n=5) продемонстрували 60% виживання, але були пов'язані з передчасними пологам та олігогідрамніоном. Післяпологове хірургічне лікування (n=8), зокрема везикостомія та катетеризація, мало 75% виживаність, хоча в деяких випадках вимагалася тривала залежність від повного парентерального харчування (ППП) через супутні захворювання. Випадки, коли втручання не проводилося (n=7), призвели до 100% смертності з внутрішньоутробною смертю або перериванням вагітності через тяжкі структурні аномалії. Було порівняно показники виживання в різних групах втручання, при цьому було зазначено, що у випадках, коли лікування проводилося постнатально, спостерігалися значно кращі результати виживання, тоді як успішність втручання на плід змінювалася залежно від гестаційного віку та основної етіології. Цей огляд підкреслює необхідність стандартизованих діагностичних протоколів, генетичного скринінгу та проспективних когортних досліджень для покращення прийнятих рішень щодо лікування та довгострокового догляду за ураженими новонародженими.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: мегацистис, обструкція нижніх сечовивідних шляхів, синдром мегацистису-мікроколон-кишкової гіперперистальтики, везикоамніотичне шунтування.

Megacystis is characterized by an abnormally enlarged fetal bladder, a rare but significant finding during prenatal assessments. Its incidence varies, with reports indicating a prevalence ranging from 1 in 1,600 to 1 in 3,000 pregnancies [23,31]. The detection of megacystis often raises concerns due to its association with chromosomal abnormalities, structural anomalies, and potential progression to severe conditions such as renal failure and pulmonary hypoplasia [14,23].

The etiology of fetal megacystis is diverse, encompassing both obstructive and non-obstructive causes. Obstructive megacystis is frequently linked to lower urinary tract obstructions (LUTO), such as posterior urethral valves, leading to increased bladder pressure and subsequent renal impairment [11,31]. Non-obstructive causes include genetic syndromes like Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome (MMIHS), which is a condition associated with mutations in genes such as ACTG2 [16]. Other syndromic associations, such as Prune Belly Syndrome (PBS) and autosomal recessive polycystic kidney disease (ARPKD), have also been linked to megacystis, further emphasizing the heterogeneity of this condition [7]. The prognosis of fetal megacystis depends on multiple factors, including gestational age at diagnosis, bladder size, and the presence of oligohydramnios. Early detection before 14 weeks of gestation is often associated with a poor prognosis, particularly in cases where the bladder diameter exceeds 15 mm or there is associated oligohydramnios, significantly increasing the risk of perinatal loss [13,34]. Conversely, second-trimester diagnoses with preserved amniotic fluid levels have been correlated with better neonatal survival, particularly in cases without structural or genetic abnormalities [27]. Recent advancements in fetal imaging techniques have improved the ability to diagnose and characterize megacystis more accurately. Fetal MRI has emerged as an important adjunct to ultrasound, especially in cases where oligohydramnios limits the visibility of structures. It enhances the evaluation of renal parenchyma, urinary tract obstruction levels, and associated anomalies such as ureterocele or renal dysplasia [34,1]. Similarly, Doppler ultrasonography has proven valuable in assessing renal blood flow, ureteric jets, and bladder function, aiding in differentiating between obstructive and non-obstructive causes [13,27]. The combination of fetal MRI and ultrasound has been shown to improve diagnostic precision, as MRI is less affected

by maternal conditions or amniotic fluid levels, making it an essential tool when ultrasound findings are inconclusive [9]. These imaging advancements have significantly refined patient selection for prenatal interventions by providing detailed anatomical and functional insights.

The management of megacystis is highly variable, largely dependent on the underlying etiology and severity of obstruction. Prenatal interventions, such as vesicoamniotic shunting and fetal cystoscopy, are aimed at decompressing the bladder and preserving renal function [17]. However, the success of these procedures is inconsistent, with some studies highlighting the risks of preterm labor, fetal distress, and shunt displacement [29]. In cases where prenatal interventions are not feasible or unsuccessful, postnatal surgical interventions, such as vesicostomy, catheterization, and corrective urological procedures, remain the primary approach [19]. Pediatric nephrologists and urologists play a critical role in monitoring renal function and implementing early interventions to prevent long-term complications.

Given the variability in etiology, prognosis, and management approaches, a comprehensive systematic review is necessary to consolidate the existing evidence.

This review *aims* to evaluate prenatal diagnostic techniques, assess the effectiveness of prenatal and postnatal interventions, and analyze long-term renal and urological outcomes in neonates diagnosed with megacystis.

By synthesizing available data, this study seeks to identify gaps in current knowledge, refine clinical decision-making, and establish research priorities for improving patient care.

Additionally, this review aims to address the need for standardized prenatal and postnatal management protocols, emphasizing the role of genetic screening, patient selection for fetal interventions, and the impact of early surgical correction on long-term outcomes [29]. Through this synthesis, the study hopes to provide a framework for future clinical guidelines and research directions.

Methodology

Eligibility criteria. This systematic review adhered to the PRISMA 2020 guidelines, confirming a transparent and organized method for the selection and synthesis of literature. The study included case reports and case series describing neonates diagnosed with megacystis and associated congenital anomalies. Studies were eli-

gible if they reported either prenatal or postnatal diagnoses of megacystis and provided comprehensive details regarding clinical presentation, genetic findings, interventions, and outcomes. Only peer-reviewed journal articles available in English were considered. Exclusion criteria included studies lacking detailed patient data, reviews, editorials, conference abstracts, and animal studies. Additionally, studies with incomplete follow-up or unclear diagnostic criteria were excluded.

Source of information and search strategy. A complete literature search was done in the PubMed directory and Web of Science to find relevant publications. Since these databases cover extensive coverage of biomedical literature and indexed case reports, they were selected. The search included Medical Subject Headings (MeSH) terms and related keywords such as «Megacystis», «Prune Belly Syndrome», «Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome (MMIHS)», «Congenital bladder distension», and «Lower urinary tract obstruction». The final search was conducted on 17-03-2025, and results were screened based on pre-defined inclusion and exclusion criteria.

Study selection process. The selection process involved two independent reviewers screening article titles and abstracts to determine their relevance. Full-text articles were subsequently reviewed, and any inconsistencies in selection were resolved through discussion and consensus. The study selection process was documented using the PRISMA flow diagram to ensure clarity and reproducibility.

Data collection and extraction. For data extraction, a standardized form was employed, capturing patient demographics (age, birth weight, gestational age), clinical features, genetic findings, interventions, and outcomes. To maintain accuracy, a double data entry system was used, and any discrepancies were addressed by cross-verification.

Outcomes and data items. The primary outcomes assessed in this review included the fatality rate, intervention success, and long-term prognosis, while secondary outcomes encompassed the presence of hydronephrosis, oligohydramnios, bladder size, and genetic findings.

Risk of bias assessment. Risk of bias was evaluated using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for case reports. Two independent reviewers assessed bias in

terms of case selection, outcome measurement, and reporting reliability.

Data synthesis and statistical analysis. Descriptive statistics were used to present the data, including frequencies and mean values with standard deviations. Given the nature of case reports and small sample size, no meta-analysis was performed. Instead, studies were grouped based on interventions, distinguishing prenatal and postnatal management approaches. Findings were presented through a narrative synthesis, and visual representation was provided in tables to summarize key clinical parameters, interventions, and outcomes.

Reporting bias and certainty assessment. To minimize reporting bias, both successful and unsuccessful interventions were included in the review. Studies that reported negative or unclear outcomes were not excluded, ensuring a comprehensive overview of clinical experiences. The GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) framework cannot be applied due to the nature of the included studies; however, findings were assessed based on their reproducibility and clinical significance to guide future research and clinical decision-making.

Reporting bias & certainty of evidence. To minimize publication bias, this review included both successful and unsuccessful cases, ensuring a balanced representation of clinical outcomes. However, the overall certainty of evidence remains low, primarily due to the retrospective nature of case reports and the absence of control groups for direct comparisons. Additionally, significant limitations were identified, including a small sample size, substantial heterogeneity in interventions, and incomplete follow-up data in several cases. These factors limit the generalizability of the findings and highlight the need for prospective studies with standardized outcome measures to strengthen clinical recommendations.

Results

Study selection and characteristics. A total of 20 case reports were included in this systematic review. The search strategy yielded an initial 89 records. After screening 26 full-text articles that were open to access, 20 studies met the eligibility criteria. The figure summarizes the selection process as per PRISMA flow chart. The included studies were published between 1998 and 2023, covering neonatal megacystis cases with

varied etiologies and management approaches. A summary of key clinical parameters extract-

ed from all case reports is presented in Table 1. *Risk of bias in studies.* The JBI Checklist was

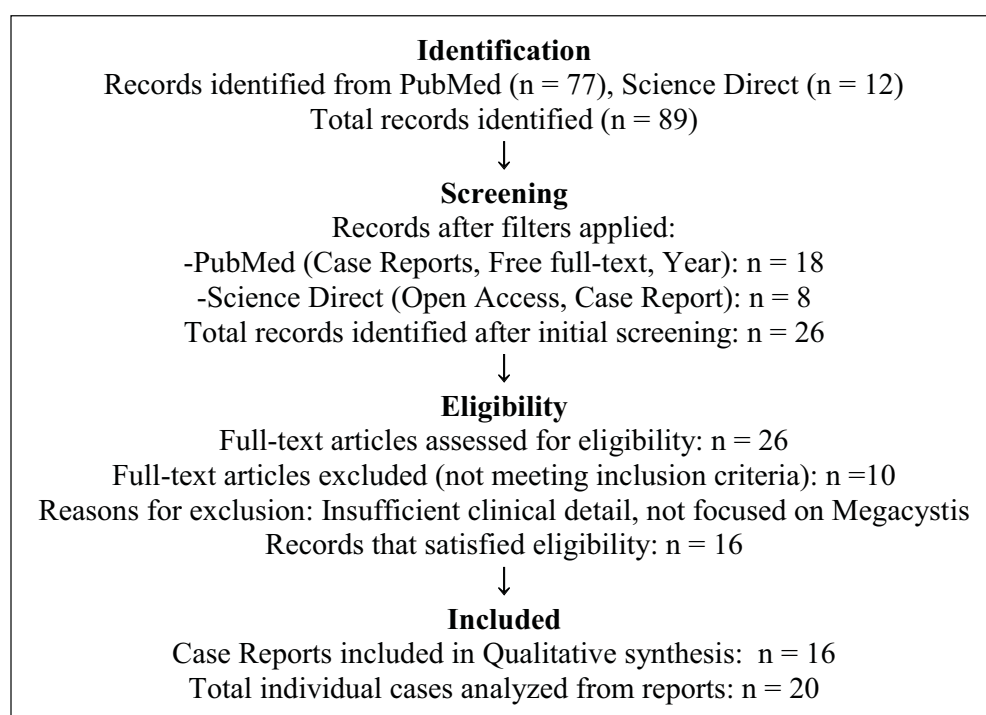


Fig. PRISMA Flow Diagram of Literature Selection Process for Case Reports on Neonatal Megacystis

Summary of clinical parameters from all case reports

Table 1

Parameter	(Mean $\pm$ SD for Continuous Data, % (n/N) for Categorical Data)
Number of cases (N)	20
Birth weight (g)	1152 $\pm$ 532
Intrauterine age at diagnosis (weeks)	28 $\pm$ 9.3
Time of corrective intervention (weeks)	22 $\pm$ 12.7
Fatality rate	45% (9/20)
Hydronephrosis	50% (10/20)
Oligohydramnios	20% (4/20)
Megacystis-Microcolon-Intestinal Hypoperistalsis Syndrome (MMIHS)	15% (3/20)
ACTG2 gene mutation	5% (1/20)
Imperforate anus	20% (4/20)
Distended abdomen	35% (7/20)
Posterior urethral valve	15% (3/20)
Prune belly syndrome (PBS)	20% (4/20)
Bladder size (mm ³)	484 $\pm$ 119.8
Racial distribution reported	40% (5/20)

Table 2

Risk of bias assessment using jbi checklist

Study (Author, Year)	Patient selection	Outcome measurement	Follow-up completeness	Overall bias risk	References
Cadoret F. et al., 2020	Low	Low	Moderate	Low	[4]
Vasconcelos, 2014	Low	Moderate	Low	Moderate	[33]
Fuman She, 2017	High	Moderate	High	High	[30]
Machado L., 2012	Low	Low	Low	Low	[25]
Ali Thomas, 2023	Low	Low	Moderate	Low	[32]
Hoshino T., 1998	High	High	High	High	[18]

applied to evaluate the risk of bias in individual case reports. Table 2 summarizes the risk of bias evaluation across included studies.

Table 3 presents detailed clinical information from 16 included case reports, collectively describing 20 cases of neonatal megacystis.

Synthesis of Results. Results were categorized based on intervention type and their impact on survival and morbidity (Table 4).

Discussion

Interpretation of findings in the context of existing evidence. This systematic review synthesizes evidence from 20 case reports, offering valuable insights into the prenatal and postnatal management, genetic associations, and clinical outcomes of neonates diagnosed with megacystis. The findings emphasize the crucial role of early detection, as first-trimester diagnoses are often associated with a poor prognosis, particularly in cases linked to genetic anomalies such as ACTG2 mutations, PBS, or MMIHS. This aligns with prior research, which suggests that megacystis diagnosed before 14 weeks of gestation carries a significantly higher risk of mortality compared to cases detected later in pregnancy [7,15,26].

Prenatal interventions, such as vesicoamniotic shunting and intrauterine laser fulguration, demonstrated moderate success in selected cases. However, these interventions also presented risks, including preterm birth, oligohydramnios, and fetal distress, underscoring the variable efficacy of fetal interventions for LUTO [2,16]. Postnatal surgical interventions, including vesicostomy, catheterization, and transurethral excision of urethral polyps, were associated with higher survival rates (75%) when compared with cases managed conventionally. This reinforces the importance of early surgical correction in neonates where feasible [17,22]. However, long-term follow-up data

remain sparse, limiting the ability to assess renal function, bladder compliance, and overall quality of life in surviving patients.

Limitations of the included evidence. Despite the clinical relevance of megacystis, the available literature primarily consists of case reports and small case series, leading to several limitations:

- **Heterogeneity of Data:** There was considerable variability in gestational age at diagnosis, underlying etiology, and intervention strategies, making direct comparisons across cases difficult [22,26].

- **Lack of Standardized Management Protocols:** Differences in prenatal diagnostic criteria and postnatal treatment approaches introduce selection bias and hinder the development of generalizable treatment guidelines [16,22].

- **Limited Long-Term Follow-Up:** Most studies did not provide long-term postnatal data, with few addressing outcomes such as renal function, bladder capacity, or developmental milestones [2,17].

These limitations highlight the need for well-structured, large-scale cohort studies or registries that can systematically evaluate treatment strategies and long-term patient outcomes.

Limitations of the review process. Although this review followed PRISMA 2020 guidelines, certain methodological constraints should be acknowledged:

- **Database Restriction:** Only studies indexed in PubMed, Web of Science, and Scopus were considered, which may have excluded relevant but non-indexed reports from other sources.

- **Exclusion of Unpublished Data:** Institutional case records and unpublished clinical experiences were not included, potentially introducing publication bias.

- **Inability to Perform Meta-Analysis:** The heterogeneous nature of case reports prevented

Table 3

Summary of individual case reports

Author (year)	Outcome	Intervention	References
Cadoret F. et al. (2020)	The possibility of an iatrogenic cause of megacystis in a female fetus should be considered if the mother received a significant dosage of opiates during the second half of her pregnancy. The megacystis was succeeded by spontaneous bladder rupture at the 30 th week of gestation, resulting in a favorable maternal-fetal outcome	Resuscitation, paracentesis	[4]
Vasconcelos (2014)	Intrauterine intervention at the 19 th week of gestation. The delivery took place at the 34 th week of gestation	Laser intrauterine fulguration	[33]
She Fuman (2017)	The fetus was detected with trisomy 18 during amniocentesis. Pathology confirmed posterior urethral obstructive megacystis	No intervention	[30]
Machado L. (2012)	During the newborn phase, the diagnosis was validated, necessitating vesicostomy and TPN. At 12 months, the infant had normal physical and neurological development but required parenteral feeding and vesicostomy	Vesicostomy, TPN	[25]
Thomas Ali (2023)	A subsequent postnatal evaluation utilizing a micturating cystourethrogram (MCUG) alongside a retrograde urethrogram revealed a pediculated urethral polyp as the aetiology	Transurethral excision of urethral polyp	[18]
Hoshino T (1998)	Prune belly syndrome, no intervention performed	No intervention	[32]
Ome Marie (2013)	Subsequent ultrasound assessments indicated a viable fetus exhibiting continuous megacystis and anhydramnios	Termination of pregnancy	[28]
Buinoiu Natalia (2018)	A case of MMIHS identified prenatally in a female fetus exhibiting megacystis, dilated intestine, and elevated amniotic fluid levels	Laparotomy and temporary catheterization	[3]
Chen Chih Ping (2012)	Fetal MRI and USG revealed distal colon dilation, pelvic cystic masses, and a perineal cyst	Termination of pregnancy	[6]
Işgüder Çiğdem Kunt (2020)	Third documented instance of overlap between PBS and URSM. The newborn presented with left renal agenesis, right renal cystic dysplasia, bilateral clubfoot, lumbar scoliosis, and the absence of abdominal wall musculature, internal genitalia, urethral, vaginal, and anal orifices	Umbilical catheterization	[5]
Caroll S.G. (2001)	Fetal vesicocentesis at 10–14 weeks of gestation was performed. Later, the pregnancy was terminated	Vesicocentesis	[20]
Deng Lu Hau (2013)	The male fetus exhibits multicentric paraspinal neuroglial heterotopia in the retropharyngeal and retroperitoneal regions, accompanied by right renal agenesis, left renal hypoplasia, and Müllerian agenesis. Further discoveries comprised bilateral preaxial polydactyly of the hands, megacystis, rectovesical fistula, and imperforate anus. The karyotype shown 46, XX.	Termination of pregnancy	[10]
Lim Jennifer (2021)	Voiding cystourethrogram presented an infrequent picture of MMIHS in a male neonate. This was the characteristic of MMIHS and may aid early diagnosis	Urinary catheter	[24]
Karucuoglu Umit (2014)	Successful treatment of lower urinary tract obstruction with peritoneal-amniotic and vesicoamniotic shunting	Peritoneal-amniotic shunting	[20]
Fette Andreas (2015)	PBS is associated with other comorbid urological and non-urological conditions	Suprapubic cystotomy	[12]
Clark Paul (2007)	Recent genetic links to MMIHS suggest that interventional strategies targeting enteric smooth muscle function and development can detect the disorder earlier and follow it	Catheterization	[8]

Table 4

Risk of bias assessment using jbi checklist

Intervention type	No. of cases	Survival rate	Major complications
Prenatal interventions* (Laser fulguration, Vesicocentesis, Shunting)	5	60%	Preterm birth, oligohydramnios, risk of fetal distress
Postnatal surgical management** (Vesicostomy, Catheterization, Excision)	8	75%	Chronic renal insufficiency, dependency on total parenteral nutrition (TPN), risk of bladder dysfunction
No intervention [#] (poor prognosis cases)	7	0%	Intrauterine demise, pregnancy termination due to severe structural abnormalities, poor fetal prognosis

Notes: * – prenatal interventions showed a moderate survival rate but carried risks of preterm delivery and complications such as oligohydramnios; ** – postnatal surgical management was associated with a higher survival rate (75%), but complications included long-term renal insufficiency and TPN dependency; # – non-intervened cases resulted in 100% mortality, with most cases terminated due to severe fetal anomalies.

a formal meta-analysis, limiting the ability to quantitatively compare survival rates across different interventions.

These factors should be considered when interpreting the findings, as they may not fully capture the broader spectrum of clinical experiences with megacystis.

Implications for clinical practice, policy, and future research

Clinical Practice

- Early genetic screening should be integrated into the management of fetuses diagnosed with megacystis, especially in cases with oligohydramnios or multiple congenital anomalies [16].

- Prenatal intervention decisions should be individualized, taking into account fetal viability, parental preferences, and the availability of specialized fetal surgery teams [17].

- Postnatal surgical approaches should focus on preserving renal function, with early interventions such as vesicostomy or catheterization aimed at preventing obstructive uropathy [2,17].

Policy recommendations

- Development of standardized guidelines for the diagnosis, risk stratification, and management of megacystis to ensure uniformity in clinical practice [22].

- Establishment of multidisciplinary fetal medicine teams, comprising pediatric urologists, maternal-fetal medicine specialists, and geneticists, to improve decision-making in complex cases.

Future research directions

- Prospective Cohort Studies: To assess long-term renal function, bladder capacity, and

neurodevelopmental outcomes in neonates diagnosed with megacystis.

- Comparative Studies on Prenatal vs. Postnatal Interventions: To evaluate whether fetal interventions such as vesicoamniotic shunting offer better survival and renal outcomes compared to early postnatal surgical management.

- Genetic and Biomarker Research: To identify predictors of disease progression and develop personalized treatment approaches based on genetic profiling and fetal imaging markers.

Conclusions

This systematic review underscores the complexity of managing fetal megacystis, emphasizing the need for early detection, individualized treatment approaches, and multidisciplinary collaboration. While both prenatal and postnatal interventions have demonstrated potential benefits, gaps remain in long-term outcome data and standardized management protocols. Upcoming studies must concentrate on large-scale prospective studies and genetic investigations to enhance diagnostic accuracy, optimize treatment pathways, and improve survival outcomes for affected neonates.

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