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Complex neonatal neurological anomalies: A case report of hydrocephalus, hydranencephaly, and holoprosencephaly

Muhammad Ilham*, Febriani

Fakultas Kedokteran, Universitas Riau

Corresponding author: *Email: Ilhamharahap13@gmail.com

Abstract

Background: Hydrocephalus, hydranencephaly, and holoprosencephaly are severe neurodevelopmental disorders that significantly impact brain structure and function. Early identification and appropriate management are essential to reduce morbidity and mortality, yet clinical differentiation among these conditions remains challenging.

Purpose: To explore the pathophysiological mechanisms, clinical outcomes, and current management approaches for hydrocephalus, hydranencephaly, and holoprosencephaly, with a focus on improving diagnostic accuracy and therapeutic strategies.

Method: This retrospective study was conducted at Arifin Achmad Hospital, Pekanbaru, over a five-year period (July 2018–July 2023), reviewing medical records of neonates diagnosed with major neurological anomalies such as hydrocephalus, hydranencephaly, and holoprosencephaly, confirmed by imaging or clinical evaluation.

Results: The findings reveal that hydrocephalus is primarily characterized by abnormal cerebrospinal fluid accumulation, hydranencephaly involves near-complete cerebral hemisphere loss replaced by cerebrospinal fluid, and holoprosencephaly results from impaired prosencephalon division during early embryogenesis. Advances in genetic testing and neuroimaging have enhanced differential diagnosis, while early neurosurgical intervention and multidisciplinary care significantly improve survival and quality of life.

Conclusion: Understanding the distinct pathophysiology and outcomes of these disorders is crucial for effective patient care. Future research in genetic and neurodevelopmental pathways offers promising opportunities for targeted therapies and improved long-term management.

Keywords: Holoprosencephaly; Hydrocephalus; Hydranencephaly; Neurodevelopmental Disorders; Patient Management.

INTRODUCTION

Hydrocephalus, hydranencephaly, and holoprosencephaly are three distinct yet severe neurological conditions that significantly affect brain development and function. Hydrocephalus is defined as an abnormal accumulation of cerebrospinal fluid (CSF) within the ventricular system, which leads to increased intracranial pressure and secondary brain injury (McAllister, 2022). This disorder can result in clinical manifestations ranging from developmental delay and motor impairment to vision and cognitive disturbances, depending on the severity and timing

of onset (Chen, Luo, Reis, Manaenko, & Zhang, 2017). The prevalence of hydrocephalus is estimated at 85 cases per 100,000 individuals, with a greater burden among infants and the elderly due to congenital anomalies and age-related degenerative changes (Mori, Shimada, Kurisaka, Sato, & Watanabe, 2025). Hydranencephaly, in contrast, is an exceedingly rare congenital anomaly characterized by near-total absence of the cerebral hemispheres, which are replaced by CSF-filled sacs (Gezmu, Shifa, Kgwarae, & Siamisang, 2020).

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Although the brainstem and thalami may be preserved, higher cortical functions are severely impaired, resulting in symptoms such as macrocephaly, seizures, and profound neurodevelopmental deficits (Hermawan, Mahardhika, Sutantio, & Velies, 2022). The prognosis remains poor, as most affected infants succumb within the first year of life despite supportive management. The etiology of hydranencephaly is still debated, with evidence pointing toward vascular insults, such as bilateral occlusion of the internal carotid arteries during early gestation, as a major causative factor (Quek, Su, Tsao, Chen, Hu, & Chen, 2018). Other potential contributors include intrauterine infections, genetic mutations, and exposure to teratogenic agents (Omoto, Takahashi, Fujimori, & Kin, 2020). These uncertainties complicate prenatal counseling and highlight the necessity of improved diagnostic modalities to differentiate hydranencephaly from other severe forms of hydrocephalus (Chinsky, 2022).

Holoprosencephaly represents another major congenital brain malformation, occurring when the prosencephalon fails to divide into bilateral hemispheres during embryonic development. This condition encompasses a clinical spectrum ranging from lobar holoprosencephaly, which is the most severe, to lobar forms with relatively preserved cerebral architecture (Kruszka & Muenke, 2018). Associated craniofacial anomalies, such as cyclopia, cleft lip, and hypotelorism, are frequently observed. Genetic syndromes, particularly chromosomal abnormalities such as trisomy 13, are strongly associated with holoprosencephaly (Lies, Beckwith, Mills, Butler, Ezaki, & Oishi, 2019). Epidemiological studies demonstrate that holoprosencephaly affects approximately 1 in 10,000 to 20,000 live births, but the incidence may be underestimated due to frequent pregnancy losses. Survival rates vary widely depending on the subtype and severity, with most lobar cases being incompatible with long-term survival. Recognition of these statistics underscores the importance of prenatal imaging and genetic counseling in high-risk pregnancies (Pober, Greene, & Holmes, 2016).

The advent of prenatal neuroimaging has transformed the ability to identify and classify these conditions before birth. Ultrasonography remains the

first-line modality, while MRI and advanced techniques such as four-dimensional ultrasound provide superior resolution and aid in differentiating central nervous system anomalies (Afdhalurrahman, 2023). Early identification allows clinicians to provide tailored counseling to families and plan perinatal management strategies more effectively (Dorner, Burton, Allen, Robinson, & Soares, 2018). Differentiating between hydranencephaly and severe hydrocephalus is especially crucial for determining prognosis and management. In cases of severe hydrocephalus, surgical interventions such as ventriculoperitoneal shunting may prolong survival and improve quality of life (Pindrik, Schulz, & Drapeau, 2022). By contrast, hydranencephaly offers little surgical benefit due to the absence of cortical structures (Sutton, Bruce, & Schut, 2020). This clinical distinction highlights the importance of accurate diagnosis, as misclassification can result in unnecessary procedures and unrealistic expectations.

RESEARCH METHOD

This retrospective case study was conducted at Arifin Achmad Hospital, Pekanbaru, focusing on neonates diagnosed with major congenital neurological anomalies including hydrocephalus, hydranencephaly, and holoprosencephaly. The study period spanned five years, from July 2018 to July 2023, and included data collected from the perinatology department's medical records. All cases that met the inclusion criteria neonatal head anomalies confirmed by imaging or clinical evaluation were identified and reviewed systematically. Patient medical records were examined to obtain comprehensive information regarding diagnostic findings, treatment approaches, and clinical outcomes. Neuroimaging, including CT and MRI, played a critical role in differentiating between hydrocephalus, hydranencephaly, and holoprosencephaly. The importance of accurate imaging in distinguishing these conditions has been emphasized in prior studies, as correct classification significantly impacts prognosis and management strategies. In addition, local studies have highlighted the role of CT-scan interpretation and neuroimaging features in pediatric hydrocephalus, which were used as comparative references in this analysis.

Muhammad Ilham*, Febriani

Fakultas Kedokteran, Universitas Riau

Corresponding author: *Email: Ilhamharahap13@gmail.com

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Data collection was carried out by trained researchers using standardized forms to ensure uniformity and accuracy. Parameters extracted included demographic data, antenatal history, delivery details, presenting symptoms, imaging results, interventions performed, and survival outcomes. These variables were chosen based on prior recommendations from neonatal neurological research, which highlight the importance of correlating clinical features with radiological evidence for diagnostic reliability. Similar methodological approaches are supported in neurology clinical guidelines and pediatric neuroimaging studies, ensuring validity and comparability of findings.

Ethical approval was obtained from the institutional review board of Arifin Achmad Hospital prior to initiation of the study. Patient confidentiality was strictly maintained by anonymizing personal identifiers and securing access to medical records. All procedures were conducted in accordance with established ethical standards for human subject research, as outlined in previous neonatal neurological investigations. The collected dataset was then analyzed descriptively to identify prevalence, diagnostic patterns, and potential underlying etiological factors contributing to the observed cases.

RESEARCH RESULTS

Table 1. Survival Outcomes of Neonates with Head Anomalies (2018–2023)

Outcome	Number of Cases	Percentage
Survived	32	84%
Died	6	16%

Table 1 illustrates the overall survival outcomes for neonates with head anomalies. Out of 38 cases, 32 neonates (84%) survived, while 6 neonates (16%) died, with mortality attributed to severe anomalies or complications such as sepsis. This survival rate emphasizes the effectiveness of early diagnosis and surgical management, particularly in hydrocephalus cases, while also reflecting the severity of conditions like holoprosencephaly.

Table 2. Prevalence of Neonatal Head Anomalies

Type of Anomaly	Number of Cases
Holoprosencephaly	3
Hydrocephalus	30
Hydranencephaly	5

Table 2 presents the prevalence of specific anomalies, confirming hydrocephalus as the predominant condition, followed by hydranencephaly and holoprosencephaly. The disproportionate representation of hydrocephalus aligns with previous reports identifying it as the most frequently encountered neonatal cranial abnormality in both national and international contexts.

Table 3. Annual Incidence of Neonatal Head Anomalies (2019–2023)

Year	Number of Cases
2019	7
2020	9
2021	8
2022	7
2023	9

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Table 3 illustrates the temporal distribution of these cases over the five-year period. While hydrocephalus cases were consistently reported each year, hydranencephaly and holoprosencephaly occurred sporadically, with no clear upward or downward trend. This variability suggests that while hydrocephalus remains a constant clinical burden, rarer anomalies present unpredictably, making long-term planning for neonatal intensive care challenging. While survival outcomes for hydrocephalus and some hydranencephaly cases were encouraging, the uniformly poor prognosis of holoprosencephaly remains a significant clinical challenge. These findings underscore the need for continued surveillance, timely neurosurgical interventions, and supportive perinatal care to optimize neonatal outcomes.

DISCUSSION

The analysis emphasized not only the distribution of cases but also the outcomes and survival rates. Hydrocephalus emerged as the most prevalent anomaly, with 30 cases recorded across the five-year study period. This high proportion aligns with previous studies that identify hydrocephalus as the leading congenital head anomaly among neonates. Of these cases, the majority required neurosurgical intervention, specifically ventriculoperitoneal (VP) shunt placement, to relieve intracranial pressure and preserve neurological function. The significance of shunting procedures has also been reinforced by clinical investigations describing how altered CSF dynamics lead to progressive neurological impairment if untreated (McAllister & Chovan, 2018). Hydranencephaly was identified in five cases, making it the second most frequently diagnosed anomaly. Despite its rarity, the survival outcome was notable: four infants survived, while one succumbed early, likely due to complications associated with the profound cerebral malformation. Hydranencephaly, though uncommon, carries a highly variable prognosis depending on the extent of associated brainstem preservation (Apriyanto, Agung, & Sari, 2023). Case reviews in the modern treatment era have shown that some infants with hydranencephaly can achieve prolonged survival under careful supportive care, although quality of life remains compromised (Akutsu, Azumi, Koyama, Kawamura, Taniguchi, & Kohmura, 2020). Similarly, rare presentations such as microhydranencephaly reported in perinatal imaging

literature highlight the challenges in early differential diagnosis. Holoprosencephaly, in contrast, was observed in three cases during the study period. Unfortunately, all affected infants did not survive, underscoring the poor prognosis commonly reported in the literature (Golomb, Wisoff, Miller, Boksay, Kluger, Weiner, & Graves, 2020).

Craniofacial abnormalities and fetal head anomalies represent a spectrum of congenital disorders that significantly impact neonatal morbidity and mortality. These conditions often demand a multidisciplinary approach encompassing genetics, neurosurgery, pediatrics, and rehabilitation medicine to ensure accurate diagnosis and tailored management strategies. Hydrocephalus, hydranencephaly, and holoprosencephaly, as observed in this study, highlight the diversity of structural malformations that can occur in early neurodevelopment, with outcomes largely dependent on the timing of diagnosis and intervention. Literature on intraventricular abnormalities illustrates the complexity of associated pathologies and their impact on neonatal survival (Muhammad, Samaha, & Omar, 2023).

Amniotic Band Syndrome (ABS) has historically been linked to craniofacial and intracranial anomalies through the theory of premature rupture of the amniotic sac. However, recent evidence suggests that many ABS-associated defects may have a germline etiology rather than purely mechanical disruption. ABS involving craniofacial regions is rare but may present with cleft lip, atypical clefts, or ocular abnormalities, reflecting its heterogeneous phenotypic spectrum (Ayu, 2016). Intracranial pathologies associated with ABS, including hydrocephalus and agenesis of the corpus callosum, further complicate neonatal outcomes. More recent reviews have detailed complex craniofacial manifestations of ABS and emphasized the need for early surgical planning (Lies, Beckwith, Mills, Butler, Ezaki, & Oishi, 2019).

Management of these anomalies requires coordinated care across multiple specialties. For example, genetic testing provides valuable insights into underlying mutations such as IRF6 and P63, which are implicated in craniofacial malformations. Likewise, ophthalmologists and plastic surgeons play a role in reconstructive planning, while neurosurgeons are central to treating intracranial

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pathologies like hydrocephalus with ventriculoperitoneal shunts (Chang, Asada, Mimura, & Suzuki, 2019). Evidence from prior clinical studies supports the efficacy of such integrated approaches in improving long-term survival and functional outcomes (Penar et al., 1995). In parallel, surgical literature continues to refine techniques for neonatal hydrocephalus, offering new perspectives on shunt design and perioperative management (Inayat, Rahman, & Hurairah, 2016).

Prenatal imaging remains the cornerstone of early detection. Ventriculomegaly, characterized by lateral ventricular enlargement, is often identified through ultrasonography in the second or third trimester. Although ventriculomegaly and hydrocephalus are sometimes used interchangeably, the latter specifically involves pathological dilatation due to elevated CSF pressure. Differentiating between these conditions is critical, as ventriculomegaly may be benign in some cases, whereas hydrocephalus typically requires surgical intervention. Four-dimensional ultrasound has been increasingly applied to improve diagnostic precision for fetal CNS anomalies and may enhance early prenatal counseling. Prospective studies have further highlighted how antenatal ventriculomegaly findings correlate with neonatal outcomes and survival rates (Donsu & Saifudin, I. (2024).

The association of ventriculomegaly with other congenital anomalies underscores its diagnostic importance. Studies indicate that 10% to 76% of ventriculomegaly cases are accompanied by additional structural or genetic abnormalities. Advanced imaging modalities such as fetal MRI complement ultrasound by detecting subtle malformations that may be missed during routine scans. Such findings allow clinicians to counsel families regarding prognosis, potential interventions, and long-term outcomes (Ahmed, Hassanien, Al Darf, & Al Ashwah, 2022). Recent reviews also describe impaired neural differentiation in experimental hydrocephalus models, which provide insight into possible molecular mechanisms underlying these anomalies (Emmert, Iwasawa, Shula, Schultz, Lindquist, Dunn, & Goto, 2019).

The survival rates observed in this study—84% overall survival, with the highest survival among hydrocephalus cases—are consistent with published outcomes emphasizing the benefits of early

neurosurgical intervention (Ryan, Start, Cathcart, Hughes, Denona, Higgins, & McAuliffe, 2022). Conversely, the universally fatal outcomes in holoprosencephaly mirror international data indicating the poor prognosis of this malformation. These results highlight the disparities in prognosis between different head anomalies and emphasize the need for condition-specific management strategies (Miche, Zernikow, von wickel, Hillebrand, & Jorch, 2025). In addition, differential diagnosis reviews and prospective management strategies proposed in prenatal obstetric practice support early multidisciplinary planning to improve outcomes in severe congenital anomalies (Saporta, Shy, Patzko, Bai, Pennuto, Ferri, & Shy, 2022). In conclusion, congenital head anomalies such as hydrocephalus, hydranencephaly, and holoprosencephaly require multidisciplinary management and early detection to optimize outcomes. Integration of prenatal imaging, neurosurgical expertise, genetic counseling, and supportive care frameworks forms the backbone of effective treatment (Rigotti, Inglese, & Gonen, 2017). Future research should focus on improving diagnostic precision, expanding access to fetal imaging, and exploring genetic underpinnings that may better explain the etiology of these anomalies. Such efforts could lead to more targeted therapies and improved survival for affected neonates and their families.

CONCLUSION

Understanding the pathophysiology, diagnostic challenges, and clinical outcomes of hydrocephalus, hydranencephaly, and holoprosencephaly is critical for guiding management strategies and providing comprehensive support to affected neonates and their families. These congenital anomalies vary widely in severity and prognosis, with hydrocephalus demonstrating better survival rates due to the availability of surgical interventions, while hydranencephaly and holoprosencephaly remain associated with significant morbidity and mortality. Multidisciplinary care, incorporating neurosurgery, genetics, perinatology, and rehabilitative medicine, is essential for optimizing treatment pathways and improving quality of life for survivors.

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