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Original Article

Risk factors for cerebrospinal fluid shunt infection in pediatrics: A meta-analysis

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ABSTRACT

Background: Placement of cerebrospinal fluid (CSF) shunt for diversion remains a primary treatment for patients with hydrocephalus despite its surgical complications, including shunt infection, that remain high and become a medical and social problem. The meta-analysis was conducted to investigate risk factors of shunt infection in pediatrics.

Methods: Literature was searched on PubMed, Scopus, and the Cochrane Library. The methodology used for this investigation was preferred reporting items for systematic reviews and meta-analysis.

Results: This meta-analysis included five publications. The only significant results were found in ages <6 months with relative risk (RR) of 33.06 (95% confidence interval [CI] 9.27–117,99; $P < 0.01$), Caucasian race with RR of 15.24 (95% CI 6.77–34.34), and African–American race with RR of 2.37 (95% CI 2.07–2.70). The other results provided were not significant, such as intraventricular hemorrhage (IVH) of prematurity as the etiology of hydrocephalus with RR of 4.71 (95% CI 1.07–20.82), presence of gastrostomy during shunt insertion with RR of 3.80 (95% CI 0.91–15.88), and comorbidity of respiratory diseases with RR of 0.22 (95% CI 0.11–0.43).

Conclusion: Younger age during the shunt placement procedure, Caucasian race, and African–American race have a significantly higher risk of CSF shunt infection. The previously reported higher risk of shunt infection in cohort studies, such as IVH of prematurity and the presence of gastrostomy, were not significant in this study. Primary studies regarding shunt infection are advocated to be performed in a more extensive population with further risk factors included in the analysis.

Keywords: Hydrocephalus, Pediatrics, Risk factors, Shunt infection

INTRODUCTION

Complications are frequent following cerebrospinal fluid (CSF) shunt placement. Infection is one of the most frequent and serious side effects, occurring in 5–25% of cases.[14,21] Shunt infection following shunt placement has been reported to have serious morbidity and mortality, including increased expenses for shunt revision, hospital readmission, prolonged antibiotic use, and related operations.[12,14]

Several studies with observational methods have previously been carried out to identify risk factors in the occurrence of shunt infections. Despite its various reports, there has been no systematic review and meta-analysis methods ever conducted as the basis for the strongest scientific evidence regarding shunt infection in pediatrics. The authors aim to collect studies that reported risk factors of shunt infection and analyze using a combined proportion system to assess the factors that provide the most impactful and significant role in shunt infection. The results of this research would be beneficial in predicting the incidence of shunt infections more accurately and developing prevention strategies.

MATERIALS AND METHODS

Literature search strategy

The journal search strategy was carried out according to the preferred reporting items for systematic review and meta-analysis protocol (PRISMA) guidelines [Figure 1]. Journal data were collected through several databases, such as PubMed, Cochrane, and EMBASE.

Study selection criteria

The authors reviewed published studies in the database. We excluded all unpublished studies or articles-in-press and used the keywords [Table 1]. The articles searched had no limitations on the year published. To minimize bias, we manually searched the references mentioned in the appropriate articles to find further primary studies. Subjects were patients who underwent a primary CSF shunt procedure with age <16 years. Exclusion criteria were subjects with age >16 years, and the shunt procedure was not the first shunt procedure for the patient. Articles in indonesian or English were acceptable for this study and had no publication year restrictions. The data studied included age, hydrocephalus etiology, gastrostomy presence, race and ethnicity, comorbidity, and bias. Statistical averages and percentages for all populations and characteristics were examined and described descriptively.

Analysis

RevMan version 5.4 from the Cochrane review was used. A forest plot was generated to show visual statistics between variables. Pooled effect sizes and matching 95% confidence intervals (CIs) were computed for relevant outcome measurements. Cochran's Q test and the I^2 statistic were used to evaluate the heterogeneity among the studies. When necessary, subgroup and sensitivity analyses were carried out to investigate the causes of heterogeneity and evaluate the reliability of the results.

Quality assessment

A bias analysis (confounding, selection, information, and reporting bias) was conducted on five included studies. Authors assessed the bias based on the modified Cochrane collaboration tool: Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) [Figure 2].[20]

Protocol registration

The protocol for this systematic review and meta-analysis was filed with the relevant registry International prospective register of systematic reviews (PROSPERO) to guarantee transparency and adherence to standards. PROSPERO has already received the study's registration (ID: 598408). In Figure 1, the PRISMA flowchart is explained.

RESULTS

Characteristics of included studies

Five studies were included after conducting a literature search. The research flow diagram is shown in Figure 1. The search was conducted in July 2024. After removing duplicates, 184 articles were excluded from the abstract review and a further 104 articles were in the full-text review. Of the remaining studies, we continued with a meta-analysis for five eligible. The five studies included retrospective cohort studies conducted in the United States and involved multicentres, with the average population size of these five studies being 2,568.2 pediatric patients. The average duration of observation carried out to identify the onset of shunt infection from the five studies was 291.2 days of observation, with the shortest observation duration carried out by Alvi *et al*.[1] in 2022 for 30 days. CSF shunt infections occurred at an incidence rate of 1162 incidents from 12,841 populations studied in the five literature in this meta-analysis, or 9.04%. These five studies did not report the duration of shunt infection calculated from when the shunt was placed. Research demographic data are shown in Table 2.

Risk of bias assessment

As shown in Table 2 every study analyzed this way had a cohort design. The total risk of bias in the included studies was minimal, according to the evaluation of cohort studies using the (ROBINS-I).[20]

Meta-analysis of measured outcomes

A total of three studies in the <6 months group, two studies in the 6–12 months group, and two studies in the more than 12 months group were reported. The analysis showed a significant increase in the risk of infection in the age group <6 months with RR 33.06 (95% CI 9.27–117.99; $P < 0.01$)

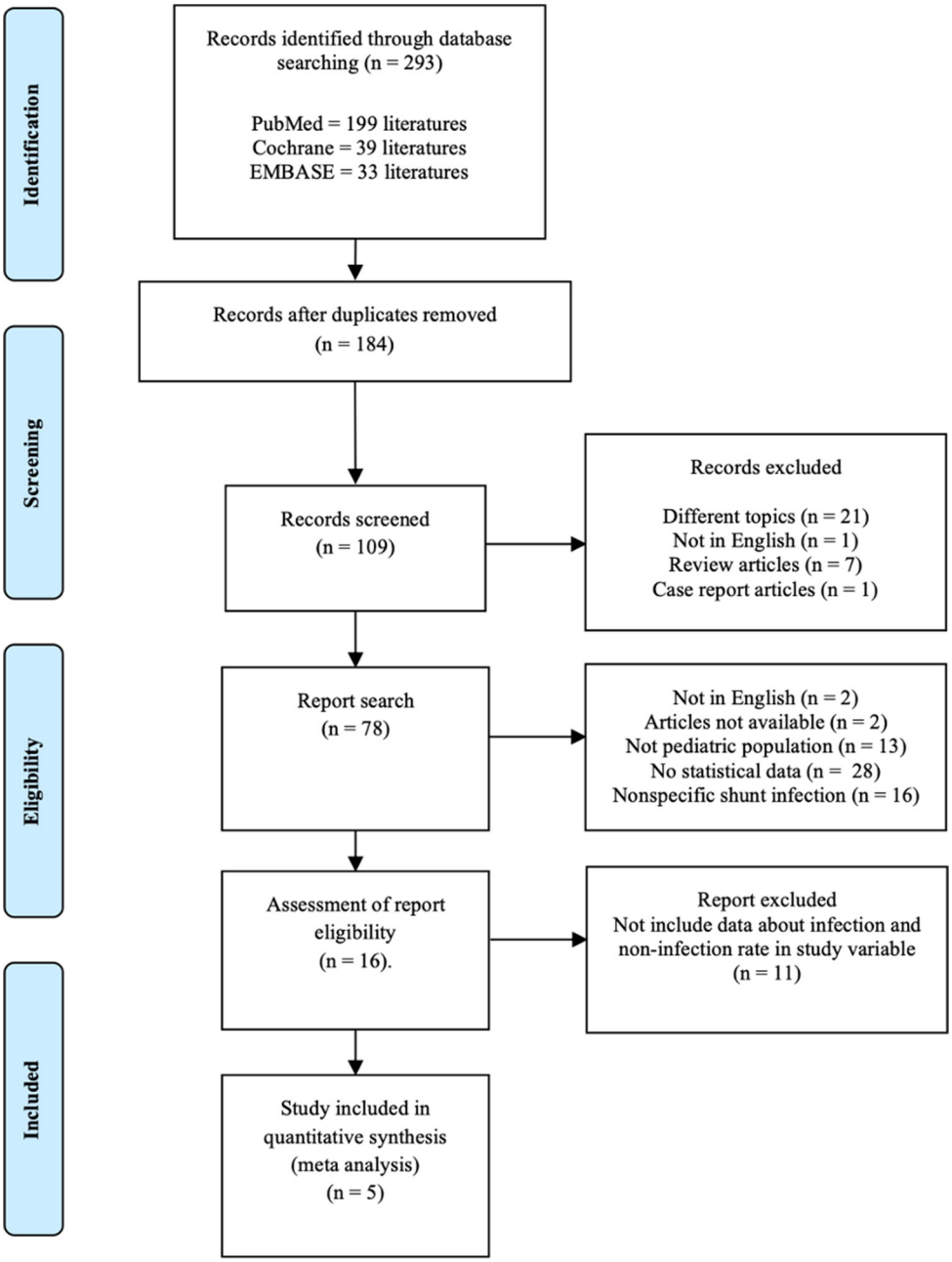

Figure 1: Literature search flow.

and at age more than 12 months at the time of CSF shunt installation with RR 3.58 (95% CI 1.37-9.36; $P < 0.01$ [Figure 3].

Four of the five meta-analysis studies reported the incidence of infection after CSF shunt installation in the hydrocephalus group with intraventricular hemorrhage (IVH) of prematurity etiology, three studies in the congenital hydrocephalus etiology group, and four studies in the central nervous system (CNS) tumor etiology group. The relative risk meta-analysis test showed no significant results in all groups [Figure 4].

Two studies in this meta-analysis were analyzed for the incidence of infection after CSF shunt installation in population groups using gastrostomy. The CSF shunt infection risk was not significant in the hydrocephalus group employing gastrostomy (RR = 3.8; 95% CI 0.91–15.88; $P = 0.07$) [Figure 5].

Two studies in this meta-analysis were analyzed for the incidence of infection after CSF shunt installation in populations with comorbid malignancies. The result demonstrated a significant RR of CSF shunt infection with respiratory comorbidity (RR = 0.22; 95% CI 0.11–0.43; $P < 0.01$) [Figure 6].

Three studies in this meta-analysis analyzed the incidence of infection after cerebrospinal fluid (CSF) shunt installation in population groups of Caucasian race, three studies in population groups of African–American race, and two studies in population groups with Latin ethnicity. There were 500 incidents of infection from a total of 4775 hydrocephalus groups with Caucasians compared to 484 incidents of infection from a total of 3871 hydrocephalus populations other than Caucasians. The relative risk results demonstrated a significant risk in the probability of CSF shunt infection in the Caucasian hydrocephalus group with an RR of 15.24 (95% CI 6.77–34.34; $P < 0.01$) and African–American hydrocephalus group with an RR of 2.37 which was statistically significant (95% CI 2.07–2.7; $P < 0.01$) [Figure 7].

Table 1: Keywords search strategy.

Keywords of literature search		
1		Pediatrics
2		Children
3		Neonates
4		Hydrocephalus
5		Ventriculomegaly
6		Cerebrospinal fluid
7		CSF shunt
8		Ventriculoperitoneal shunt
9		Ventriculoarterial shunt
10		Shunt infection
11		Early infection
12		Late infection
13		Risk factor
Combination of a boolean operator		
14		(#1 OR #2 OR #3)
15		(#4 OR #5 OR #6 OR #7 OR #8 OR #9)
16		(#10 OR #11 OR #12)
17		#13 AND #14 AND #15 AND #16

CSF: Cerebrospinal fluid, "or": regular

DISCUSSION

Age

This study obtained significant results in the age group of <6 months with an RR of 33.06 (95% CI 9.27–117.99; $P < 0.01$). This finding is consistent with earlier retrospective reports. There are several hypotheses to expound the relation of age and risk of CSF shunt infection. One of the established theories is an underdevelopment of the cellular and humoral immune systems in children under 12 months of age, where immunoglobulins in newborns are dominated by immunoglobulin G (IgG) obtained from maternal through the placenta. Maternal IgG concentration will decrease progressively due to physiological catabolism processes until 12 months of age. Maternal IgG has limited capacity because it relies on maternal history of antigen exposure. Antibody production begins in the 3rd month of life, and at the age of 4–6 years, the IgG levels will be equivalent to

Table 2: Demographic summary of the studies.

Author	Publication year	Country	Study type	Observational duration (days)	Population	Infection rate *n* (%)
Alvi *et al.*[1]	2022	USA	Cohort	30	3919	89 (2.3)
Beckman *et al.*[2]	2015	USA	Cohort	180	539	47 (8.7)
Simon *et al.*[18]	2014	USA	Cohort	356	1036	102 (10.8)
Kestle *et al.*[10]	2011	USA	Cohort	178	1004	89 (5.7)
Simon *et al.*[19]	2009	USA	Cohort	712	7071	825 (11.7)

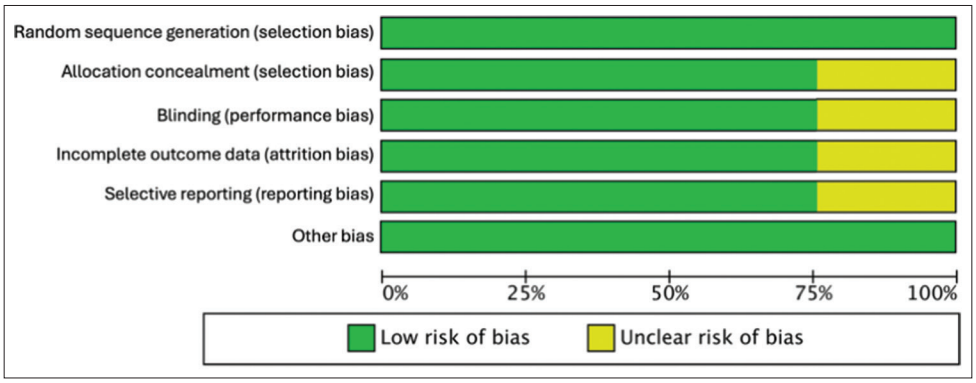

Figure 2: Bias analysis summary.

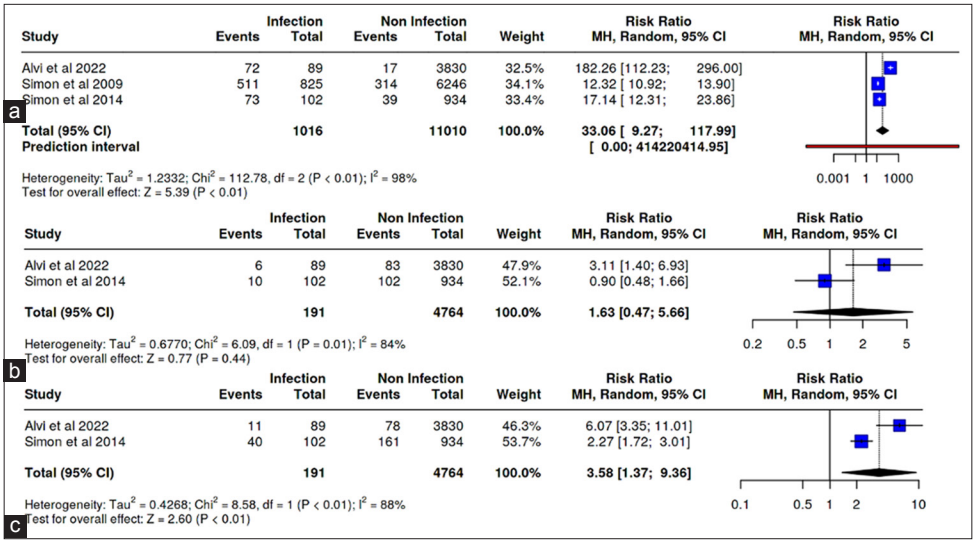

Figure 3: Forest plot of the RR on age groups (a) <6 months, (b) 6-12 months, and (c) more than 12 months. MH: Mantel-Haenszel analysis, CI: Confidence interval, RR: Relative risk.

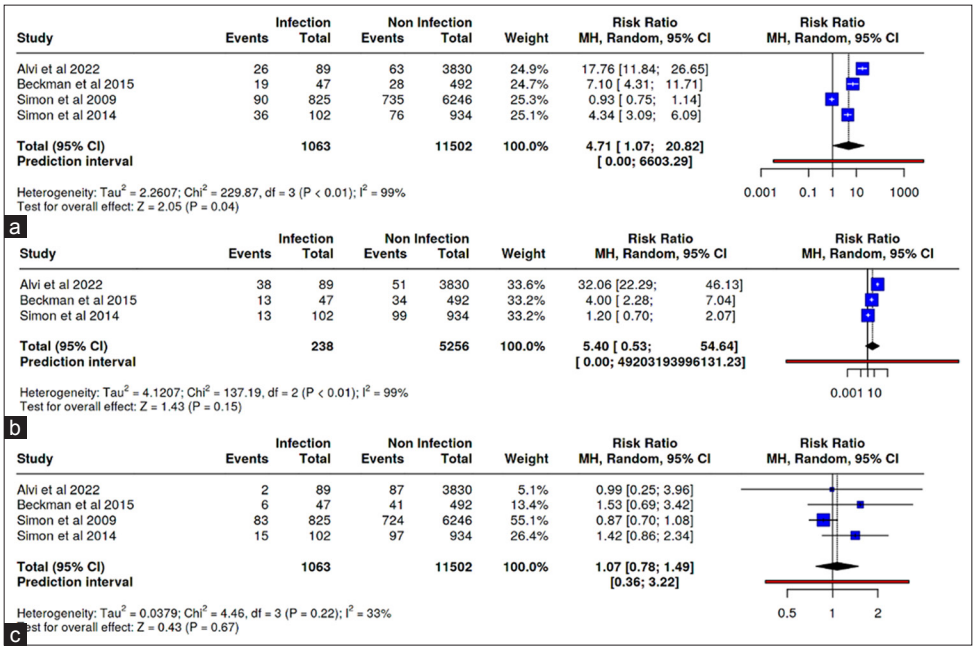

Figure 4: Forest plot of the RR on etiology of (a) intraventricular hemorrhage of prematurity, (b) congenital hydrocephalus, and (c) tumor. MH: Mantel-Haenszel analysis, CI: Confidence interval, RR: Relative risk.

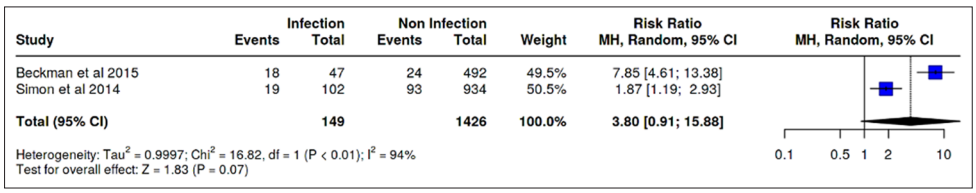

Figure 5: Forest plot of RR of gastrostomy status. MH: Mantel-Haenszel analysis, CI: Confidence interval, RR : Relative risk

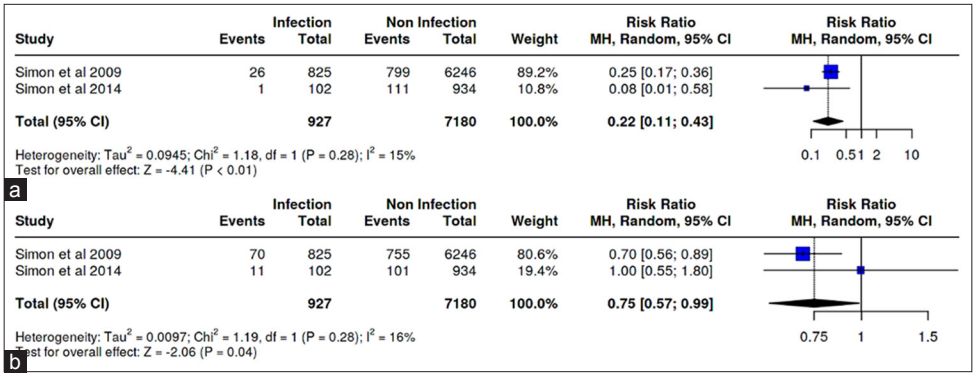

Figure 6: Forest plot of RR of comorbid conditions, (a) malignancy and (b) respiratory. MH: Mantel-Haenszel analysis, CI : Confidence interval, RR: Relative risk.

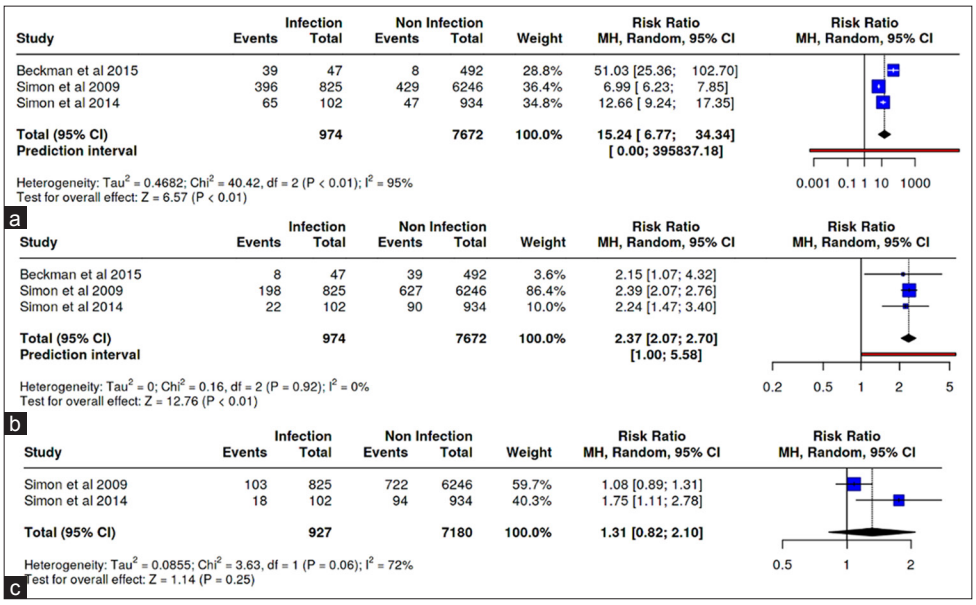

Figure 7: Forest plot of RR regarding the race of (a) Caucasian, (b) African-Americans, and (c) Latinos. MH: Mantel-Haenszel analysis, CI: Confidence interval, RR: Relative risk.

adult IgG levels.[13] Newborns are susceptible to infection by Gram-negative pathogens; this finding is related to the absence of maternal immunoglobulin M (IgM) transport across the placenta, where IgM is the main antibody against Gram-negative pathogens.[3,13] Another established theory is the vulnerability and immaturity of the skin barrier with a higher density of skin bacterial flora colonies in younger age groups, causing a higher risk of longer wound healing than adults, longer hospital stays, and susceptibility to comorbidities.[9,22]

Etiology of hydrocephalus

IVH of prematurity as the cause of hydrocephalus showed a major significance in this study. Newborns with very low birth weight who survive the critical phase will have a high risk of IVH, including germinal matrix hemorrhage.[16] Very low birth weight is generally associated with prematurity, resulting in a vulnerable immune condition.[17] Infants born before 32 weeks of gestational age are prone to develop hypogammaglobulinemia due to the lack of transplacental maternal IgG transport, which generally occurs after 32 weeks of gestation. This hypogammaglobulinemia condition can result in susceptibility to infection.[8] These conditions concomitantly occurred with IVH in prematurity could increase the risk of infection from a CSF shunt.

CNS tumors, as the etiology of hydrocephalus, have been identified as a significant risk factor for CSF shunt infections. Hydrocephalus associated with malignancies is frequently observed in pediatric patients with primary brain tumors. Studies indicate that hydrocephalus is present in approximately 55–60% of cases, including 50% where it is diagnosed concurrently with the tumor itself.[23] This

underscores the necessity of shunt placement in pediatric patients with CNS tumors complicated by hydrocephalus. While these associations have been well documented in previous cohort studies, the specific mechanisms linking individual risk factors to CSF shunt infections remain unelucidated.[5]

Presence of gastrostomy status

Placement of a CSF shunt is associated with a 2.49-fold increase in the risk of infection in patients undergoing gastrostomy. This increased risk is attributed to an incomplete skin barrier, which facilitates pathogen colonization around the CSF shunt.[4] In addition, the direct manipulation of the gastrointestinal tract during gastrostomy creates a connection between the peritoneal cavity and enteric microorganisms, potentially contributing to CSF shunt infections. A retrospective analysis of 208 gastrostomies performed using the image-guided retrograde percutaneous technique reported significant complications, including peritonitis, in 3% of cases.[7] Investigating whether the distance between the gastrostomy tube insertion site and the VP shunt tip influences the risk of shunt infections is a pertinent research question. Gassas *et al.* recommend delaying gastrostomy tube insertion in pediatric patients with brain tumors until after the VP shunt has fully healed, as early gastrostomy-related complications may increase the risk of ascending infections involving the VP shunt.[6]

Comorbid diseases

A meta-analysis of comorbid conditions associated with CSF shunt placement revealed heterogeneous findings. However, hydrocephalus with comorbid respiratory diseases significantly increases the risk of CSF shunt infection. Other comorbidities, including respiratory, cardiological, congenital, gastrointestinal, hematological, metabolic, and renal conditions, may elevate infection risk due to prolonged hospitalization, repeated surgeries, or immune deficiency.[11] At present, no studies have elucidated the mechanisms linking these comorbidities to CSF shunt infections, aside from the hypothesis that CNS tumors contribute to most pediatric hydrocephalus cases.[23] Severe comorbidities may also impair nutritional status, compromising immune function and increasing infection susceptibility. Malnutrition weakens the skin barrier through thinning of the dermis, reduces stratum corneum hydration, decreases epidermal cell proliferation, and lowers collagen levels, facilitating pathogen entry.[15]

Race and ethnicity

The meta-analysis included participants of Caucasian, African–American, and Latino ethnicities. Significant associations with CSF shunt infections were observed in Caucasians and African–Americans, while no significant link was found in Latinos. The reasons for the higher risk in Caucasians and lower risk in African–Americans remain unclear, and no literature currently explains this disparity. The predominance of Caucasian participants (55.2%) may have influenced the results.

Limitation

The authors did not review ongoing randomized trials because no literature or research reports analyzed risk factors for CSF shunt infection until this study was conducted. The amount of literature that meets the eligibility screening in this meta-analysis is limited, and the population of studies that meet the eligibility screening only comes from the United States, so it does not reflect the world's global population.

CONCLUSION

Several risk factors, such as younger age during the shunt placement procedure, IVH of prematurity, presence of gastrostomy, African–American race, and respiratory comorbidities, have a significant tendency in the incidence of CSF shunt infection in pediatrics. This meta-analysis provides a foundation for future research with higher levels of evidence, as prior studies primarily relied on cohort designs. Future investigations involving larger, multicenter populations across diverse countries are recommended to achieve a more comprehensive global understanding of these risk factors.

Ethical approval: Institutional Review Board approval is not required as it is a meta -analysis study.
Declaration of patient consent: Patient's consent is not required as there are no patients in this study.
Financial support and sponsorship: Nil.
Conflicts of interest: There are no conflicts of interest.
Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

REFERENCES

1. Alvi MA, Bhandarkar AR, Daniels DJ, Miller KJ, Ahn ES. Factors associated with early shunt revision within 30 days: Analyses from the National Surgical Quality Improvement Program. J Neurosurg Pediatr 2022;29:21-30.
2. Beckman JM, Amankwah EK, Tetreault LL, Tuite GF. Reduction in CSF shunt infection over a 10-year period associated with the application of concentrated topical antibiotic powder directly to surgical wounds prior to closure. J Neurosurg Pediatr 2015;16:648-61.
3. Capasso L, Borrelli A, Cerullo J, Pisanti R, Figliuolo C, Izzo F, *et al.* Role of immunoglobulins in neonatal sepsis. Transl Med UniSa 2015;11:28-33.

4. Champeaux-Depond C, Ramasy Razafindratovo RM, Chevret S. Gastrostomy and internal cerebrospinal fluid shunt in adults. A systematic review and meta-analysis of the risk of infection. Neurochirurgie 2022;68:e75-83.
5. El Rahal A, Cipriani D, Fung C, Hohenhaus M, Sveikata L, Straehle J, *et al.* Hydrocephalus shunting in supratentorial glioblastoma: functional outcomes and management. Front Oncol 2022;12:796105.
6. Gassas A, Kennedy J, Green G, Connolly B, Cohen J, Dag-Ellams U, *et al.* Risk of ventriculoperitoneal shunt infections due to gastrostomy feeding tube insertion in pediatric patients with brain tumors. Pediatr Neurosurg 2006;42:95-9.
7. Grant JP. Percutaneous endoscopic gastrostomy. Ann Surg 1993;217:168-74.
8. Justiz-Vaillant AA, Hoyte T, Davis N, Deonarinesingh C, De Silva A, Dhanpaul D, *et al.* A systematic review of the clinical diagnosis of transient hypogammaglobulinemia of infancy. Children 2023;10:1358.
9. Kalia YN, Nonato LB, Lund CH, Guy RH. Development of skin barrier function in premature infants. J Invest Dermatol 1998;111:320-6.
10. Kestle JR, Riva-Cambrin J, Wellons JC, Kulkarni AV, Whitehead WE, Walker ML, *et al.* A standardized protocol to reduce cerebrospinal fluid shunt infection: The hydrocephalus clinical research network quality improvement initiative. J Neurosurg Pediatr 2011;8:22-9.
11. Kreutmair S, Kauffmann M, Unger S, Ingelfinger F, Núñez NG, Alberti C, *et al.* Preexisting comorbidities shape the immune response associated with severe COVID-19. J Allergy Clin Immunol 2022;150:312-24.
12. Kulkarni AV, Drake JM, Lamberti-Pasculli M. Cerebrospinal fluid shunt infection: A prospective study of risk factors. J Neurosurg 2001;94:195-201.
13. Langel SN, Blasi M, Permar SR. Maternal immune protection against infectious diseases. Cell Host Microbe 2022;30:660-74.
14. Mallucci CL, Jenkinson MD, Conroy EJ, Hartley JC, Brown M, Dalton J, *et al.* Antibiotic or silver versus standard ventriculoperitoneal shunts (BASICS): A multicentre, single-blinded, randomised trial and economic evaluation. Lancet 2019;394:1530-9.
15. Parke MA, Perez-Sanchez A, Zamil DH, Katta R. Diet and skin barrier: The role of dietary interventions on skin barrier function. Dermatol Pract Concept 2021;e2021132.
16. Ramenghi LA, Fumagalli M, Groppo M, Consonni D, Gatti L, Bertazzi PA, *et al.* Germinal matrix hemorrhage: Intraventricular hemorrhage in very-low-birth-weight infants. Stroke 2011;42:1889-93.
17. Raqib R, Alam DS, Sarker P, Ahmad SM, Ara G, Yunus M, *et al.* Low birth weight is associated with altered immune function in rural Bangladeshi children: A birth cohort study. Am J Clin Nutr 2007;85:845-52.
18. Simon TD, Butler J, Whitlock KB, Browd SR, Holubkov R, Kestle JR, *et al.* Risk factors for first cerebrospinal fluid shunt infection: Findings from a multi-center prospective cohort study. J Pediatr 2014;164:1462-8.e2.
19. Simon TD, Hall M, Riva-Cambrin J, Albert JE, Jeffries HE, LaFleur B, *et al.* Infection rates following initial cerebrospinal fluid shunt placement across pediatric hospitals in the United States. J Neurosurg Pediatr 2009;4:156-65.
20. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, *et al.* ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
21. Stone JJ, Walker CT, Jacobson M, Phillips V, Silberstein HJ. Revision rate of pediatric ventriculoperitoneal shunts after 15 years. J Neurosurg Pediatr 2013;11:15-9.
22. Widia Y, Rosdiana BI. Review article: Skin condition and skin care in premature infants. Berkala Ilmu Kesehatan Kulit Kelamin 2023;35:67-73.
23. Wong TT, Liang ML, Chen HH, Chang FC. Hydrocephalus with brain tumors in children. Childs Nerv Syst 2011;27:1723-34.

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