JOURNAL LA MEDIHEALTICO

VOL. 05, ISSUE 04 (848-856), 2024
DOI: 10.37899/journallamedihealtico.v5i4.1542

The Relationship between the Classic Triad of Meningitis and Types of Meningitis

Selma Nissa Budi Iftiyastuti[1], Leonny Dwi Rizkita[2], Nuni Ihsana[3], Andrianto Selohandono[4]

[1]*Faculty of Medicine, Ahmad Dahlan University Yogyakarta, Indonesia*
[2]*Department of Pharmacology, Faculty of Medicine, Ahmad Dahlan University, Yogyakarta*
[3]*Department of Physiology, Faculty of Medicine, Ahmad Dahlan University, Yogyakarta*
[4]*Department of Neurology, Faculty of Medicine, Ahmad Dahlan University, Yogyakarta*

**Corresponding Author: Selma Nissa Budi Iftiyastuti*
E-mail: selma.iftiyastuti@gmail.com

Article Info

Article history:
Received 3 August 2024
Received in revised form 9 August 2024
Accepted 23 September 2024

Keywords:
Classic Triad
Fever
Headache
Meningitis
Neck Stiffness

Abstract

Meningitis is an inflammatory disease of the meninges caused by infection and non-infection. Based on WHO data for 2023, the CFR (Case Fatality Rate) for meningitis is 5.88%. In 2016 at the Southeast Asian level, Indonesia became the country with the highest mortality rate caused by meningitis. The classic triad of meningitis can assist in the early diagnosis of meningitis so that early management can be carried out to reduce mortality and morbidity if a cerebrospinal fluid examination is not possible immediately. Therefore, a study was conducted to determine the characteristics of meningitis patients, prevalence, and the relationship between the classic triad of meningitis and the incidence of infectious and non-infectious meningitis at Dr. Sardjito General Hospital Yogyakarta in 2017-2021. This study uses a cross-sectional method. The data taken is secondary data from 118 medical records of patients who have been treated. From the results, it was obtained that the highest characteristics and distribution were the age category 0-5 years (27.1%), male sex (51.7%), the most domicile outside DIY (54.2%), no/not yet school (36.4%) not/not yet working (38.1%), bacterial meningitis (39.0%), fever (89.8%), neck stiffness (78.8%). There is a significant relationship between the classic triad of meningitis and the type of meningitis (p-value 0.000). Among the three triads, it turned out that there was a solid relationship between the classic triad of meningitis and the type of infectious meningitis as indicated p-value by neck stiffness 0.000, fever 0.000, and headache 0.000.

Introduction

Meningitis is an infectious disease that causes inflammation of the meninges (Dawod et al., 2019). Although there has been progress in terms of prevention and treatment. However, meningitis still contributes to significant morbidity and mortality rates (Waghdhare et al., 2019). In 2018 WHO recorded more than 1 million cases with 6,613 cases and 485 deaths due to meningitis with a CFR rate of 7.9%. It is estimated that around a quarter of adults experience bacterial meningitis and one third of patients who experience tuberculous meningitis die (Gahlot, 2021; Boubour et al., 2020). Most experience sequelae of temporary or permanent neurological disability (Wall et al., 2021). In Southeast Asia, the distribution of meningitis cases cannot be said to be low. Indonesia became the country in Southeast Asia with the highest mortality rate in 2016 with a death incidence reaching 4,314 out of 78,018 cases (Kemenkes RI, 2019).

ISSN 2721-1215 (Print), ISSN 2721-1231 (Online)

Meningitis can be caused by infection or non-infection which is influenced by the body's immune system, predisposing factors such as age, gender, history of infection and history of injury head (Kemenkes RI, 2019; Maisuri, 2021). The clinical picture of meningitis in the early stages is often nonspecific. However, after these clinical symptoms and signs appear, they show a classic triad that is easily recognized (Juwita et al., 2022). Fever arises as an inflammatory response to the meninges. blood brain barrier resulting in accumulation of monocytes, macrophages and other inflammatory agents (Juwita et al., 2022; Yau et al., 2018). The triggering of the inflammatory response in the meninges causes edema, an increase in intracranial pressure which stimulates nociceptors and is transmitted by type C fibers to the spinal cord so that it is perceived as pain. The other is a stiff neck (Akaishi et al., 2019; Maisuri, 2021). The classic meningitis triad, especially meningeal excitatory signs, can help in the early diagnosis of meningitis (Maisuri, 2021; Bautista et al., 2024; McMillan et al., 2024).

Knowing whether there is always the classic triad of meningitis, especially fever, headache and neck stiffness, in the presence of infectious and non-infectious meningitis, is expected to be useful for clinicians. It is hoped that earlier treatment can be carried out to reduce mortality and morbidity if cerebrospinal fluid examination is not possible immediately. This research was conducted to detect the presence of symptoms and clinical signs of the classic triad of meningitis types at Dr. Sardjito General Hospital, Yogyakarta.

Methods

This research is an analytical research approach cross-sectional to find the relationship between the classic triad of meningitis and the type of meningitis at RSUP Dr. Sardjito Yogyakarta 2017-2021. The population in this study were all meningitis sufferers at RSUP Dr. Sardjito from 2017-2021 as recorded in the medical records. Inclusion criteria in this study were complete medical record data, patients diagnosed with infectious and non-infectious meningitis, showing one of the clinical manifestations of fever, headache and signs of meningeal stimulation. The exclusion criteria in this study were incomplete medical records, patients diagnosed with chronic meningitis or patients with follow up after treatment, patients diagnosed with meningitis due to malignancy. The sampling technique uses non-probability sampling by consecutive sampling.

This research uses data sourced from secondary data in the form of medical records at RSUP Dr. Sardjito Yogyakarta. The variables in this study were the classic triad (fever, headache and neck stiffness) as the independent variable and type of meningitis as the dependent variable, while pain threshold and previous medication administration were variables. Confounding. Data were analyzed with the SPSS program (Statistical Program for Social Science) version 26. Univariate analysis is displayed in the form of a frequency distribution table. In bivariate analysis, data is analyzed using chi-square tests. Multivariate analysis was carried out with a contingency test and logistic regression. A relationship is said to be significant if p-value<0,05.

Result and Discussion

During the study in November–December 2022, the number of subjects who met the inclusion and exclusion criteria was 118 patients. The characteristics of meningitis patients can be seen in table 1 which shows the frequency distribution of characteristics of meningitis patients at RSUP Dr. Sardjito Yogyakarta.

Table 1. Frequency Distribution of Sociodemographic Characteristics of Respondents

Variable	F (118)	% (100%)
Age		
0-5	32	27,1
6-11	16	13,6
12-16	10	8,5

17-25	11	9,3
26-35	18	15,3
36-45	8	6,8
46-55	13	11,0
56-65	6	5,1
> 65	4	3,4
Gender		
Man	61	51,7
Woman	57	48,3
Domicile		
Sleman	34	28,8
Bantul	12	10,2
Kulon Progo	3	2,5
Gunung Kidul	5	4,2
Outside DIY	64	54,2
Education		
No/not yet at school	43	36,4
Elmentary	30	25,4
Junior	16	13,6
Senior	16	13,6
Diploma, Bachelor, Master	13	11,0
Type of work		
No/Not yet working	45	38,1
Student/college student	27	22,9
civil servants	16	13,6
Self-employed	7	5,9
Farmers, Laborers, Fishermen, Traders	12	10,2
House Wife	6	5,1
Other professions	5	4,2

The sociodemographic characteristics of meningitis patients in this study included gender, domicile, education and type of work. Data on meningitis patients (n=118) underwent univariate analysis and showed that the age of the most 32 patients (27.1%) was 0-5 years old and the age of the least 4 patients (3.4%) was >65 years old. Most patients are male is as many as 61 (51.7%) while there were 57 (48.3%) female patients. Patients whose domicile comes from outside the Special Region of Yogyakarta are the most meningitis patients who come to Dr. The majority of patients with a diagnosis of meningitis were dominated by no education level, 43 (36.4%) while the least number of patients had a D3, S1, Masters education level, 13 (11.0%) (13). Most types of work are not yet working at 45 (38.1%) while the lowest were teachers, doctors, TNI and Polri at 5 (4.2%).

This research is in line with research conducted by (Maisuri, 2021) that meningitis can occur in all age groups but is more common in people aged <18 years because this age group has a low immune system so they are vulnerable to the risk of disease and environmental influences (Maisuri, 2021). The greatest risk occurs in babies aged between 1-12 months with 95% of cases occurring between the ages of 1 month – 5 years. Research conducted by (Abelina, 2019) states that meningitis occurs 2-10 times more often in those aged less than 10 years than in other age groups.

There are more meningitis patients than women. This is in accordance with research conducted by (Tsai et al., 2019) that meningitis tends to occur more often in men than women 12. This happens because men tend to have more comorbidities and conditions. *immunosuppressive*

from women, history of the condition *immunosuppression* significantly more common in men at 30% compared to women at 22% (Lestari et al., 2021). Research conducted by (Tsai et al., 2019) states that the male hormone testosterone dampens the immune response, the female hormone estrogen increases the number of immune cells and the intensity of the response 14. This is also because men tend to have more strenuous activities and various exposures such as alcohol, cigarettes, stress, and unhealthy lifestyles cause men to be more susceptible to infection 13.

Meningitis patients who live from outside the Special Region of Yogyakarta tend to have more cases because Dr. Sardjito Hospital is a referral hospital in Yogyakarta. The education level of meningitis patients tends to be higher in patients who do not/have not attended school. This is in line with the highest proportion of people infected with meningitis who are aged 0-5 years. Where in this age group their immune system is still low and they have not received an education. This is not a risk factor for meningitis, but only indicates that there are more meningitis sufferers in sufferers who have not/don't go to school 7. Meningitis patients who have the most types of work are not/not yet working. This is in line with the highest proportion of people infected with meningitis who are aged 0-5 years. This is also in line with research conducted by (Maisuri, 2021) that at this age patients are not yet working and their immune system is still low (Maisuri, 2021). Work is closely related to the environmental conditions in which one lives and a person's nutritional status (Herlina et al., 2021).

Table 2. Frequency Distribution of Meningitis Characteristics based on Type, Clinical Manifestations, and Neurological Signs

Variable	f	% (n=118)
Meningitis Type		
Bacterial meningitis	46	39,0
Aseptic Meningitis	9	7,6
Fungal Meningitis	0	0
Meningitis TB	40	33,9
Non-Infectious Meningitis	23	19,5
Clinical Manifestations		
Fever	106	89,8
Headache	83	70,3
Seizures	61	51,7
Nauseous vomit	68	57,6
Loss of consciousness	49	41,5
Neurological Signs		
Stiff neck	93	78,8
Kernig sign	62	52,5
Brudzinski Sign	62	52,5

Univariate analysis of meningitis patient data based on type characteristics and clinical symptoms (n=118) showed that the highest type of meningitis was bacterial meningitis at 46 patients (39.0%) and the lowest type of meningitis was fungal meningitis at 0 (0%). The most common clinical manifestation was fever in 106 patients (89.8%) while the lowest manifestation was decreased consciousness in 49 patients (41.5%). The most common neurological sign shown by meningitis patients was neck stiffness in 93 patients (78.8%) while the lowest was *pithy sign* and *brudzinski sign* 62 patients each (52.5%).

Characteristics of the most common types of meningitis at Dr. Sardjito Yogyakarta is bacterial meningitis. This is in line with research by (Sindise et al., 2019) at Dr. Sardjito General Hospital Yogyakarta in 2011 which found that the proportion of patients diagnosed with bacterial meningitis was 39 patients. This is different from research conducted by (Abelina, 2019) at

RSUD Dr. Pirngadi Medan in 2014 - 2018 also found that the highest proportion of meningitis classification was meningitis *serious* as many as 59 patients (55.1%) (Abelina, 2019). Research conducted by Lestari (2021) at Sanglah General Hospital Denpasar in January 2018-2019 stated that the most common meningitis was tuberculous meningitis with 30 patients (42.9%) and the second highest was bacterial meningitis with 29 patients (41.4%) with the number the difference is not very significant (Lestari et al., 2021).

The distribution of the proportion of clinical manifestations in this study was fever. This is in line with (Sindise et al., 2019) research at RSUP Dr. Sardjito Yogyakarta who found that the highest clinical manifestation was fever in 31 patients and the lowest was decreased consciousness in 15 patients. Research conducted by (Lestari et al., 2021) at Sanglah General Hospital Denpasar January 2018-September 2019 showed similar results, namely the clinical manifestation of the most patients, namely fever in 60 patients (85.7%) followed by headache in 53 patients (75.7%) (Lestari et al., 2021). The results of this study are quite different from the results of research conducted by (Maisuri, 2021) which found that the highest proportion of clinical manifestations of meningitis sufferers at Labuang Baji Hospital, Makassar and Wahidin Sudirohusodo Hospital, Makassar in 2018-2021 was decreased consciousness with a total of 27 patients (77.1%) (Maisuri, 2021).

The most common neurological sign is stiff neck. This is in line with research conducted by (Maisuri, 2021) at Labuang Baji Hospital Makassar and Wahidin Sudirohusodo Hospital Makassar in 2018-2021 that patients with positive neck stiffness were the highest proportion, namely 19 patients (54.3%) (Maisuri, 2021). Research conducted by (Lestari et al., 2021) at Sanglah General Hospital Denpasar January 2018-September 2019 showed similar results, namely that the most neurological sign shown was stiff neck in 53 patients (75.5%) while other neurological symptoms were only present in 21 patients (30 .0%) (Lestari et al., 2021).

Table 3. Correlation of Classic Triad and Non-Triass Meningitis with Infectious and Non-Infectious Meningitis Types

Clinical Symptoms	**Meningitis**		***P-value***	**CI (95%)**
	Infection	**Non-Infectious**		
Trias	59 (50,0%)	4 (3,4%)	0,000	7,785
Non-Trias	36 (30,5%)	19 (16,1%)		

Bivariate analysis was carried out to determine whether there was a relationship between the clinical symptoms of the classic triad and non-classical triad of meningitis with the types of infectious and non-infectious meningitis. The clinical symptoms of meningitis are said to be triad if the patient complains of all three symptoms of meningitis, namely fever, headache and stiff neck, while it is said to be non-triad if they only complain of one or two of these classic symptoms. From this analysis, the results showed that infectious meningitis patients with triad symptoms were 50.0%, while those who did not show classic meningitis triad symptoms had infectious meningitis at 30.5%. The result of non-infectious meningitis patients with triad symptoms was 3.4%, while those who did not show classic meningitis triad symptoms in infectious meningitis was 16.1%. Mark *p-value* <0.05 so the data is said to be significant.

Table 4. Correlation of the Classic Triad of Meningitis (fever, neck stiffness and headache) with the type of meningitis at RSUP Dr. Sardjito Yogyakarta 2017-2021

Classical Triassic	**Meningitis Type**									
	Bacterial		**Aseptic**		**Mold**		**TB**		**Non-Infectious**	
	f	**%**	**f**	**%**	**f**	**%**	**f**	**%**	**f**	**%**
Stiff neck	43	6,4	7	5,9	0	0	5	9,7	8	6,8
Fever	44	7,3	8	6,8	0	0	7	1,4	1	7,8
Headache	3	9,5	2	1,7	0	0	39	3,1	9	6,1

Based on the clinical symptoms of the classic triad of stiff neck meningitis, 43 patients (36.4%) had bacterial meningitis, 7 patients (5.9%) had aseptic meningitis, 0 patients (0%) had fungal meningitis, 35 patients (29 .7%) with TB meningitis type and 8 (6.8%) with non-infectious meningitis type. Clinical manifestations of fever showed 44 patients (37.3%) with bacterial meningitis type, 8 patients (6.8%) with aseptic meningitis type, 0 patients (0%) with fungal meningitis type, 37 patients (31.4%) with TB meningitis type and 21 patients (17.8%) with non-infectious meningitis type. Clinical manifestations of headache showed that 23 patients (19.5%) had bacterial meningitis type, 2 patients (1.7%) had aseptic meningitis type, 0 patients (0%) had fungal meningitis type, 39 patients (33.1%) with TB meningitis type and 19 (16.1%) with non-infectious meningitis type. From this study it can be seen that the classic triad of meningitis is often seen in bacterial meningitis types.

This is similar to research conducted by (Lestari et al., 2021) at Sanglah Hospital, Denpasar, January 2018-September 2019, showing appropriate results, namely that the most clinical manifestation shown was fever in 60 people (85.7%) (Lestari et al., 2021). Research conducted by (Maisuri, 2021) found that the second most common clinical picture found in meningitis sufferers at Labuang Baji Hospital, Makassar and Wahidin Sudirohusodo Hospital, Makassar in 2018-2021 was fever, 25 people (71.4%) (Maisuri, 2021).

The body will experience an infection and an inflammatory process occurs in the membrane covering the brain, this causes the body to stimulate monocytes and macrophages to produce *Endogenous pyrogens* such as IL-1, IL-6, TNF-α, and IFN-γ (Kuswanto et al., 2019). Pyogenic cytokines will act on the preoptic anterior hypothalamus to induce the production of prostaglandin E2 and an increase in *set point* body temperature that causes the patient to have a fever. Prostaglandin E2 also increases *blood brain barrier permeability* which will cause vasogenic edema and result in increased pressure *intracranial* in the brain (Kuswanto et al., 2019; Ratnasari et al., 2021).

This study shows that the clinical manifestation of neck stiffness is most often seen in bacterial type infectious meningitis. This research is similar to research conducted by Ashwini in 2019 in an Indian hospital which stated that neck stiffness had a sufficient level of sensitivity to be considered (sensitivity 39.4; 95%, CI 29.7, 49.7%)10. In Indonesia, research conducted by Lestari (2021) at Sanglah General Hospital Denpasar January 2018-September 2019 showed similar results, namely that the most neurological sign shown was neck stiffness in 53 people (75.5%)13.

Stimulation of the lining of the brain is a symptom that arises due to inflammation of the lining of the brain (meningitis) or the presence of a foreign object in the lining of the brain. *subarachnoid 18*. The process of irritation of the meninges that causes the picture *meningismus* (stiff neck) occurs due to reflex spasm of the paravertebral muscles 18,19. Because the brain stem is relatively fixed, it causes only the inflamed spinal cord and meninges to be pulled upwards. This stimulation produces a tonic impulse that causes muscle spasm *extensor* as a protective mechanism 19. The clinical manifestation of muscle spasm is called stiff neck. This is in line with the classic triad of meningitis, namely fever, headache and stiff neck 19,20.

This study shows that the clinical manifestation of headache is most often seen in bacterial meningitis infections. This is similar to research conducted by Abeline in 2019 at RSUD Dr. Pirngadi Medan in 2014-2018 which found that the highest proportion of meningitis sufferers based on subjective symptoms was headache with a total of 40 cases (37.4%)11. This is also supported by research conducted by (Lestari et al., 2021) at Sanglah General Hospital Denpasar January 2018-September 2019 showing similar results, namely that the most common clinical manifestation shown by meningitis patients was headache at 75.7% (Lestari et al., 2021).

Headaches arise as a result of stimulation, one of which is caused by infection of the lining of the brain in the structures in the head and neck area that are sensitive to pain (Maisuri, 2021).

Changes to *Blood brain barrier* (BBB) due to increased permeability causes elements of albumin, ions, metals, chemicals, viruses to easily pass through the structure of nerve fibers so that in a short time it will result in the formation of *micro edema*, inflammation which then causes symptoms in the form of headaches. If this continues continuously it can cause cerebral edema, increased pressure *intracranial* and irreversible brain damage (Jain, 2021; Gu et al., 2022)).

Table 5. Correlation of neck stiffness, fever and headache to infectious and non-infectious meningitis at Dr. Sardjito 2017-2021

Clinical Symptoms	**Infectious Meningitis**		***value***	**Non-infectious meningitis**		***value***	***Nagelkerke R Square***
	Of	**No**		**Of**	**No**		
Stiff neck	84 (71,2%)	10 (8,5%)	0,000	9 (7,6%)	15 (12,7%)	0,994	0,530
Fever	93 (78,8%)	2 (1,7%)	0,000	17 (14,4%)	6 (1,6%)	0,994	
Headache	63 (53,4%)	32 (28,2%)	0,039	20 (16,9%)	3 (2,5%)	0,995	

Based on the presence or absence of symptoms of stiff neck, fever and headache in infectious meningitis, the results were obtained, namely that in infectious meningitis it was confirmed that there were symptoms of stiff neck in 84 patients (71.2%), fever in 93 patients (78.8%), headache in 63 patients. (53.4%) while 10 patients (8.5%) did not show symptoms of neck stiffness, 2 patients had fever (1.7%), 32 patients (28.2%) had headaches. In non-infectious meningitis, 9 patients (7.6%) showed symptoms of neck stiffness, 17 patients had fever (14.4%), 20 patients (16.9%) had headaches, while 15 patients did not show symptoms of neck stiffness. (12.7%), fever in 6 patients (1.6%), headache in 3 (2.5%). Results *p-value* 0.000 for the neck stiffness and fever variables and 0.039 for the headache variable, which means the p value is smaller than the significance value, namely 0.05 ($p<0.05$) so it can be stated that There is a significant relationship between the clinical manifestations of neck stiffness, fever and headache in the incidence of meningitis at Dr. Sardjito Hospital in 2017-2021. This shows that simultaneously neck stiffness, fever and headache have a significant effect on meningitis. Mark *nail church R square* of 0.530 or equivalent to 53% so that the dependent variable (neck stiffness, fever and headache) has the ability to explain the independent variable (type of meningitis) of 53% and 47% is explained by other factor variables not examined by the researcher (Julián-Jiménez & Morales-Casado, 2019). The significance value of the clinical symptoms of stiff neck, fever and headache shows <0.05. It can be concluded that the clinical symptoms of stiff neck, fever and headache have an influence on the type of infectious meningitis.

Conclusion

In this study, it can be concluded that there is a significant relationship between the classic triad of meningitis (neck stiffness, fever, headache) and the type of infectious meningitis at Dr. Sardjito Yogyakarta 2017-2021. It is known that meningitis is more common in patients who are male, aged 0 – 5 years, who live outside the Special Region of Yogyakarta, and who have not attended school and have not worked. The most common type of meningitis is bacterial meningitis with the most frequent clinical symptoms being fever, headache and meningeal signs of neck stiffness. Thus, this triad is significant in helping to establish a diagnosis, especially infectious meningitis, as long as a cerebrospinal examination cannot be carried out. Further research needs to be carried out with a larger sample, more diverse data, and a longer period of time in order to increase the level of confidence in the research results and can be used to assist in early management if cerebrospinal fluid examination cannot be carried out.

References

Abelina, A. (2019). *Karakteristik Penderita Meningitis yang Dirawat Inap di Rumah Sakit Umum Daerah Dr. Pirngadi Medan Tahun 2014-2018* (Doctoral dissertation, Universitas Sumatera Utara).

Akaishi, T., Kobayashi, J., Abe, M., Ishizawa, K., Nakashima, I., Aoki, M., & Ishii, T. (2019). Sensitivity and specificity of meningeal signs in patients with meningitis. *Journal of General and Family Medicine, 20*(5), 193–198. https://doi.org/10.1002/jgf2.268

Ashwini, B. G. (2019). *The Prevalnece of Hypothyroidism in Diagnosed Cases of Gall Bladder Stones at KR Hospital* (Master's thesis, Rajiv Gandhi University of Health Sciences (India)).

Bautista, J. M., Morro, I. G., García, P. F., & Herrera, I. H. (2024). FLAIR hyperintensity in the subarachnoid space: Main differentials. *Radiología (English Edition)*, *66*(1), 78-89. https://doi.org/10.1016/j.rxeng.2022.01.003

Boubour, A., Paradkar, M., & Thakur, K. T. (2020). Global and regional burden of tuberculosis and tuberculous meningitis. In *Tuberculous Meningitis* (pp. 1-15). Academic Press. https://doi.org/10.1016/B978-0-12-818825-5.00001-2

Dawod, H., Naguib, A., Amer, S., & Mohamed, L. (2019). The Frequency of Meningitis Cases in Zagazig Fever Hospital: A Cross-sectional Study. *Afro-Egyptian Journal of Infectious and Endemic Diseases, 9*(2), 158–166. https://doi.org/10.21608/aeji.2019.12173.1023

Gahlot, T. (2021). A Cross - Sectional Study of Etiological and Sensitivity Profiling of Meningitis in Under - Five Children. 149–154. https://doi.org/10.4103/ijmy.ijmy

Gu, Y., Zhou, C., Piao, Z., Yuan, H., Jiang, H., Wei, H., ... & Ji, X. (2022). Cerebral edema after ischemic stroke: Pathophysiology and underlying mechanisms. *Frontiers in neuroscience*, *16*, 988283. https://doi.org/10.3389/fnins.2022.988283

Herlina, T., Rahayu, S., Suryani, R. L., & Utami, T. Gambaran Tingkat Pengetahuan Ibu Tentang Stunting Pada Balita Di Desa Kedawung Kecamatan Susukan Kabupaten Banjarnegara. 2021; 4 (1): 10–17.

Jain, K. K. (2021). Cerebral edema. *MedLink Neurology. Cerebral edema| MedLink Neurology*.

Julián-Jiménez, A., & Morales-Casado, M. I. (2019). Usefulness of blood and cerebrospinal fluid laboratory testing to predict bacterial meningitis in the emergency department. *Neurología (English Edition), 34*(2), 105–113. https://doi.org/10.1016/j.nrleng.2018.05.005

Juwita, S., Indrawati, A., Damajanti, R., Safika, S., & Mayasari, N. I. L. U. H. P. I. K. A. (2022). Multiple antibiotic resistance and virulence factors of Staphylococcus aureus strains isolated from dairy farms in South Sulawesi, Indonesia. *Biodiversitas Journal of Biological Diversity, 23*(2). https://doi.org/10.13057/biodiv/d230244

Kemenkes RI. (2019). Panduan - Deteksi dan Respon Penyakit - Infeksi Emerging. *Panduan Deteksi Dan Respon Penyakit MENINGITIS MENINGOKOKUS*, 1–100.

Kuswanto, R. A., Rizal, A., & Koesoemadinata, R. R. C. (2019). Association between Fever during Admission and Outcome of Treatment in Tuberculous Meningitis Patients in Hasan Sadikin General Hospital Bandung. *Journal of Medicine and Health, 2*(3). https://doi.org/10.28932/jmh.v2i3.1233

Lestari, Yulinda, N., Suryapraba, AAA, & Tini, K. (2021). Karakteristik pasien meningitis

dewasa di rumah sakit umum pusat sanglah denpasar januari 2018- september 2019. *Jurnal Medika Udayana, 10*(4), 3–5.

Maisuri, N. K. (2021). *Karakteristik Pasien Meningitis Di Rsud. Labuang Baji Dan Rsup. Dr. Wahidin Sudirohusodo Makassar Tahun 2018-2021= Characteristics Of Meningitis Patients In Rsud. Labuang Baji And Rsup. Dr. Wahidin Sudirohusodo Makassar Period 2018-2021* (Doctoral dissertation, Universitas Hasanuddin).

McMillan, K., Shaw, H., Hemesley, A., Zaman, W., & Qazim, N. (2024). Neurological observations in infants, children and young people: part one. *Nursing children and young people*, *36*(1). Https://doi.org/10.7748/ncyp.2023.e1472

Ratnasari, I., Nur, F. T., & Riza, M. (2021). Rasio Neutrofil Limfosit untuk Membedakan Meningitis Bakterial dan Viral pada Anak. *Sari Pediatri, 23*(4), 222–227. http://dx.doi.org/10.14238/sp23.4.2021.222-7

Sindise, I. F., Satiti, S., & Yudiyanta, Y. (2019). Kadar procalcitonin serum abnormal sebagai prediktor mortalitas meningoensefalitis. *Berkala NeuroSains, 18*(1), 38–45. https://doi.org/10.22146/bns.v18i1.55062

Tsai, W.-C., Lien, C.-Y., Lee, J.-J., Hsiao, W.-C., Huang, C.-R., Tsai, N.-W., Chang, C.-C., Lu, C.-H., & Chang, W.-N. (2019). The clinical characteristics and therapeutic outcomes of cryptococcal meningitis in elderly patients: a hospital-based study. *BMC Geriatrics, 19*, 1–6. https://doi.org/10.1186/s12877-019-1108-0

Waghdhare, S., Kalantri, A., Joshi, R., & Kalantri, S. (2019). Accuracy of physical signs for detecting meningitis: A hospital-based diagnostic accuracy study. *Clinical Neurology and Neurosurgery, 112*(9), 752–757. https://doi.org/10.1016/j.clineuro.2010.06.003

Wall, E. C., Chan, J. M., Gil, E., & Heyderman, R. S. (2021). Acute bacterial meningitis. *Current Opinion in Neurology, 35*(3), 386–395. https://doi.org/10.1097/WCO.0000000000000934

Yau, B., Hunt, N. H., Mitchell, A. J., & Too, L. K. (2018). Blood–brain barrier pathology and CNS outcomes in Streptococcus pneumoniae meningitis. *International Journal of Molecular Sciences, 19*(11), 3555. https://doi.org/10.3390/ijms19113555