



Evaluation of Antibiotic Use in Dengue Fever Patients Using the ATC/DDD Method at HKBP Hospital

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ABSTRACT

Infectious diseases are diseases caused by the entry and growth of microorganisms, one of which is pathogenic bacteria (Novard et al., 2019). High use of antibiotics for infectious diseases increases the risk of irrational antibiotic use which can result in the therapeutic goal not being achieved. This study aims to determine based on patient characteristics, the profile of antibiotic use in hospitalized patients at RSU. HKBP Balige and the quantity of antibiotic use in DDD units. This study is observational (non-experimental) which was conducted retrospectively using data obtained from the Hospital Information System (SIRS) for the period January-April 2024 in the form of drug names, dosage forms, dosage strengths, quantity of use, number of hospitalized patients per month, length of hospitalization. Data analysis in this study used the quantitative Anatomical Therapeutic Chemical (ATC) / Defined Daily Dose (DDD) and Drug Utilization 90% (DU90%) methods. The results of the study showed that there were 2 types of antibiotics used in dengue fever patients during 2024 with an average total usage value of 280.07 DDD/100 HR. The most widely used types of antibiotics were cefixime (66.70%) and cefotaxime (33.30%), and the most common route of antibiotic administration was intravenous, and the most frequent duration of antibiotic therapy was <3 days (85.71%).

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1. INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is an infectious disease caused by the dengue virus (DENV). The dengue virus is transmitted to humans through the bite of infected female mosquito vectors, especially mosquitoes of the *Aedes aegypti* and *Aedes albopictus* species (Dehghani & Kassiri, 2021). The incubation period of the dengue virus in the human body until symptoms appear ranges from 3-10 days after a mosquito bite, with an average incubation period of 5-7 days. Common symptoms experienced by dengue sufferers are fever for 2-7 days, accompanied by several signs of severe headache, pain behind the eyes, muscle and joint pain, rash, nausea, vomiting, and minor hemorrhagic manifestations or positive tourniquet test results (Sudarmaja et al., 2022).

Dengue fever can develop into a severe condition that causes complications and even has the potential to cause death. The incidence of dengue fever cases continues to experience a sudden high

increase, even resulting in major outbreaks (Wang et al., 2020). This has led to dengue fever being considered a severe public health emergency. CDC explains that around 40% of the world's population lives in areas endemic for dengue fever. Every year there are 390 million dengue virus infections, 96 million of which are clinically manifested. The highest cases globally were in 2019. Dengue cases occurred in all regions and transmission occurred for the first time in Afghanistan. The incidence of dengue fever is endemic in more than 100 tropical and subtropical countries (Wang et al., 2020). The impact is more severe in the Americas, Southeast Asia, and the Western Pacific. Asia represents up to 70% of the global disease burden.

A major dengue fever outbreak occurred in Southeast Asia and China in 2014 and in America in 2016. In 2020, there was an increase in the number of dengue fever cases in several Asian countries such as Bangladesh, India, Nepal, Yemen, Maldives, Sri Lanka, Singapore, Thailand, Timor Leste, and Indonesia (Mohsina et al., 2022). Reported from The Asean post, the highest number of dengue fever cases in the ASEAN region in 2019 was in the Philippines with 414,532 cases, Indonesia with 110,000 cases, and Laos with 38,000 cases. According to the North Sumatra Provincial Health Office, cumulatively from January to September 2022 the number of dengue fever (DBD) sufferers in this area reached 5,270 cases. Head of the North Sumatra Health Office Ismail Lubis said that of the 5,270 dengue fever sufferers, 24 of them died (Krishna et al., 2024).

Hospitals are health service institutions for the community with the aim of improving services that are more qualified and affordable for the community, in order to realize the highest level of health. Hospital Pharmacy Installation (IFRS) is a functional implementing unit that organizes all pharmaceutical service activities in hospitals. Pharmaceutical services in hospitals are an inseparable part of the hospital health service system that is oriented towards the management of pharmaceutical supplies, medical devices, and disposable medical materials that are quality and affordable for all levels of society including clinical pharmacy services (Krishna et al., 2024).

High antibiotic use for infectious diseases increases the risk of irrational antibiotic use which can result in the therapeutic goal not being achieved. Another study found that around 40-62% of antibiotics are used irrationally, including for diseases that do not actually require antibiotics. One of the consequences of irrational antibiotic administration is that it can cause bacteria to become resistant to antibiotics. Resistance causes an increase in the number of deaths and economic burden, due to the extension of the length of hospitalization, the use of antibiotics is more expensive and longer. Deaths due to resistance are estimated to reach around 700,000 people (Zerfu et al., 2023).

Evaluation of antibiotic use is one of the indicators of the quality of the irrationality control program. Evaluation of antibiotic use can be carried out using qualitative methods to assess the rationality of antibiotic use (Bhatt & Pandey, 2023). One of the evaluation methods that can be used is the Gyssens method, which can assess the rational use of antibiotics (category 0) and irrational antibiotic users (categories I-IV). Based on a preliminary study that has been conducted according to data taken from the HKBP Balige Hospital, dengue fever is a disease that is mostly found in the HKBP Balige Hospital. From the data taken from the period January-April 2024, there were 50 cases of dengue fever patients who had been treated at the HKBP Balige Hospital Inpatient Installation. Based on these data, researchers are interested in conducting a study entitled Evaluation of Antibiotic Use in Dengue Hemorrhagic Fever (DHF) Patients Using the ATC/DDD Method in the HKBP Balige Hospital Inpatient Installation for the Period January-April 2024 (Bhalerao et al., 2023).

2. RESEARCH METHOD

This study is observational (non-experimental) with a quantitative approach, namely by knowing the characteristics of patient profiles of antibiotic use, calculating the quantity of antibiotic use using the DDD (Defined Daily Dose) method (Garbe et al., 2023). The design used in this study is cross-sectional with retrospective data collection taken from inpatient prescriptions at the HKBP Balige General Hospital for the period January-April 2024. The sampling technique used in this study was to use stratified random sampling, which is a technique for obtaining a population in the same stratum. In the results of this study, the number of research samples obtained in January to April was 35 medical

records, this was because after the study, not all patients with dengue fever used antibiotics in January to April and many prescriptions were not read (Garbe et al., 2023).

3. RESULTS AND DISCUSSIONS

Evaluation of antibiotic use in terms of quantity is done by calculating using the DDD (Defined Daily Dose) value with the unit DDD/100 days of care (100 HR) (Leowattana & Leowattana, 2021). Antibiotics used in hospitalized patients are classified based on the ATC code, then the amount of strength is calculated by multiplying the quantity of drug use by the strength of the preparation in grams. Furthermore, the DDD of use is calculated by dividing the total amount of strength by the definitive DDD set by WHO. After that, the total DDD of use is divided by the number of days of patient care per month to obtain DDD/100 HR, which is the unit used in hospitalized patients (Parveen et al., 2023). The data in this study were obtained from the medical records room at the HKBP Balige General Hospital.

The data obtained are in the form of drug names, dosage forms, dosage strengths, number of antibiotic uses each month, number of inpatients in January - April, average length of stay for patients each month January - April 2024. Based on the results of the medical record data search, it is known that the number of inpatients with dengue fever at the HKBP Balige General Hospital for the period January - April 2024 was 50 patients (Murugesan & Manoharan, 2020). Dengue fever patients who received single and combination antibiotics were 35 patients and the rest were patients who did not receive antibiotic therapy, so the research sample that could be evaluated was 35 patients. The total length of hospitalization for all patients was 105 days. The characteristics of dengue fever patients who received antibiotics in the inpatient room of the HKBP Balige General Hospital can be seen in table I.

3.1 Characteristics of DHF patients receiving antibiotics

Table 1. Characteristics of dengue fever patients who received antibiotics in the inpatient room of HKBP Balige Hospital for the period January-April 2024.

Characteristics	Number of Patients	Percentage (%)
Age (Years)		
≤ 1	1	2,8
2-6	10	28,6
7-12	10	28,6
13-18	14	40
Total	35	100
Gender		
Laki-Laki	18	51,43
Perempuan	17	48,57
Total	35	100
Lama Rawat Inap (Hari)		
≤ 3	30	85,71
4 - 6	5	14,29
≥ 7	0	0
Total	35	100
Jenis Antibiotik		
Cefixime 50 mg	3	7,32
Cefixime 120 mg	1	2,43

Cefixime 200 mg	7	17,1
Cefixime 400 mg	1	2,43
Cefixime 450 mg	1	2,43
Cefotaxime 250 mg inj	2	4,88
Cefotaxime 300 mg inj	3	7,32
Cefotaxime 400 mg inj	3	7,32
Cefotaxime 500 mg inj	8	19,51
Cefotaxime 600 mg inj	2	4,88
Cefotaxime 1000 mg inj	10	24,39
Total	41	100

Based on Table I. it is known that dengue fever patients in the inpatient room of HKBP Balige Hospital in the period January-April 2024 who received the most antibiotics were in the age range of 13-18 years (40%). Dengue fever patients who received antibiotics in the inpatient room of HKBP Balige Hospital in the period January-April 2024 were mostly male (51.43%) (Czapla et al., 2022). The age of 13-18 years or referred to as teenagers is a stage of child development that already has more activities (Ministry of Health of the Republic of Indonesia, 2014). This is because adolescence is a period when they already have the freedom to choose the food they like and have activities outside the home, so that the nutritional status of teenagers can be disrupted due to children having difficulty eating (NUGROHO, 2018) (Gupta et al., 2020).

The length of hospitalization for most patients (85.71%) was ≤ 3 days and the average length of hospitalization was 3 days. The most widely used type of antibiotic is Cefotaxime Injection 1000 mg (24.39%)(Ann et al., 2020). Cefotaxime is widely used as empirical therapy because it is a broad-spectrum antibiotic that is active against gram-positive and negative bacteria, as well as anaerobic bacteria (Rachmawati et al., 2020). Cefotaxime has a relatively cheap price and relatively lower toxicity for pediatric patients compared to other types of antibiotics (Suyal et al., 2024).

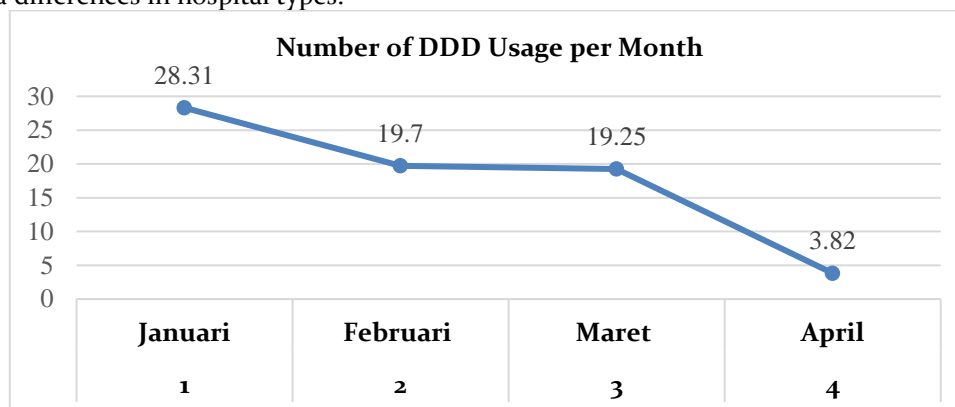
3.2 Antibiotic usage profile

Table II. List of Antibiotics Used in Dengue Fever Patients in the Inpatient Room of HKBP Balige General Hospital in 2024.

Pharmacology Major Group Code	Antibiotic Classes	Generic Name	ATC Code	definitive DDD (g)
J01D	Sefalosporin	Cefixime 50 mg	J01DD08	0,4
		Cefixime 120 mg	J01DD08	0,4
		Cefixime 200 mg	J01DD08	0,4
		Cefixime 400 mg	J01DD08	0,4
		Cefixime 450 mg	J01DD08	0,4
		Cefotaxime 250 mg inj	J01DD01	4
		Cefotaxime 300 mg inj	J01DD01	4
		Cefotaxime 400 mg inj	J01DD01	4
		Cefotaxime 500 mg inj	J01DD01	4
		Cefotaxime 600 mg inj	J01DD01	4
		Cefotaxime 1000 mg inj	J01DD01	4

Based on Table II, it shows that the number of antibiotics used in dengue fever patients at RSU. HKBP Balige in 2024 was 2 types of antibiotics included in the ATC code classification 'J', namely Antiinfectives for systemic use, including cefixime and cefotaxime. The ATC code listed in the table is used to group antibiotics with DDD values in grams (g). Table II also shows that the use of antibiotics in the Inpatient Room of HKBP Balige General Hospital is in accordance with the list of antibiotics listed in the 2024 National Formulary at level 3 health facilities.

A larger DDD/100 HR value illustrates a higher quantity of antibiotic use in 100 days of care (Hanifah et al., 2022). Conversely, a smaller DDD/100 HR value illustrates a lower quantity of antibiotic use, which means that doctors are more selective in prescribing antibiotics so that they can approach the principle of rational antibiotic use. The results obtained by researchers cannot be used to compare the level of selectivity of antibiotic use with other hospitals. This is due to differences in the time span used and differences in hospital types.



Gambar 1. Total Kuantitas Penggunaan Antibiotik Per Bulan dalam Satuan DDD Tahun 2024

Based on Figure 3, it shows that the highest use of antibiotics in DDD units was in January at 28.31. This is directly proportional to the number of inpatients and the average length of hospitalization of patients in January when compared to other months.

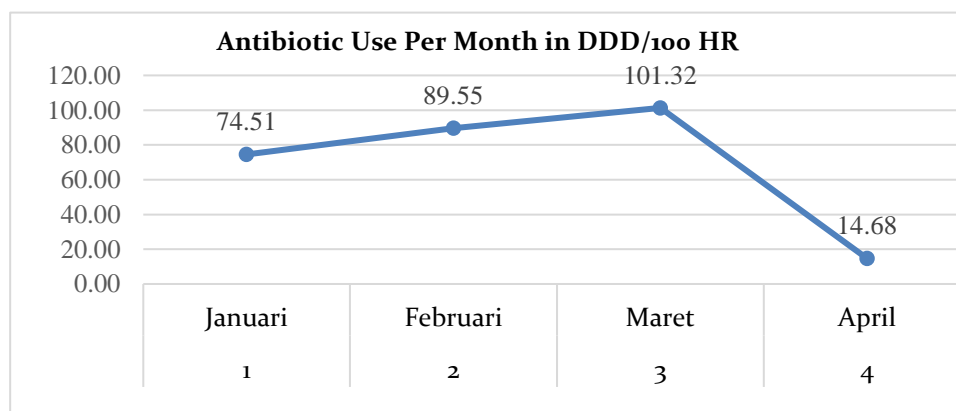


Figure 2. Total Quantity of Antibiotic Use Per Month in DDD/100 HR Units in 2024

In Figure 2, the highest antibiotic use in DDD/100 HR units was in March at 101.32. These results differ when compared to the highest DDD units in January. This difference may occur because the DDD value of January usage was higher and the number of inpatients was greater than in March. The DDD units do not yet reflect the average maintenance dose per day in 100 days of hospitalization.

3.3 Total quantity of antibiotic use by antibiotic type in 2023

The data obtained from the medical records of the HKBP Balige General Hospital, namely a list of the names of antibiotics used, the strength of the preparation, the form of the preparation, and the quantity of drug use in January - April 2023, were recorded and classified based on the ATC code obtained from the ATC/DDD system established by WHO.

Table 3. Quantity of Antibiotic Use Per Month in the Inpatient Room of HKBP Balige General Hospital in 2024

Drug Name	Route of Administration	DDD/100 HR				Final Amount Total
		Januari	Februari	Maret	April	

Cefixime 50 mg	Oral	6,58	5,68	0,00	0,00	12,26	
Cefixime 120 mg	Oral	6,32	0,00	0,00	0,00	6,32	
Cefixime 200 mg	Oral	15,79	72,73	94,74	0,00	183,26	237,04
Cefixime 400 mg	Oral	26,32	0,00	0,00	0,00	26,32	
Cefixime 450 mg	Oral	8,88	0,00	0,00	0,00	8,88	
Cefotaxime 250 mg inj	Parenteral	2,47	0,00	0,00	0,96	3,43	
Cefotaxime 300 mg inj	Parenteral	1,38	0,00	0,00	0,00	1,38	
Cefotaxime 400 mg inj	Parenteral	0,53	0,00	1,05	1,54	3,12	
Cefotaxime 500 mg inj	Parenteral	4,93	0,00	1,32	2,56	8,81	43,03
Cefotaxime 600 mg inj	Parenteral	0,00	2,05	1,58	0,00	3,63	
Cefotaxime 1000 mg inj	Parenteral	1,32	9,09	2,63	9,62	22,66	
		74,52	89,55	101,32	14,68	280,07	280,07

Based on table 3, it is known that there are 2 types of antibiotics with different strengths used by dengue fever patients at HKBP Balige General Hospital during the period January - April 2024, with an average total DDD value / 100 patient-days of 280.07. These results are higher when compared to research conducted at Dr. Moewardi Hospital during the period of 2017, which was 111.87 DDD / 100 HR and research conducted on surgical patients at Dr. Slamet Martodirjo Pamekasan Hospital (Syafitri & Yerlina, 2024) which was 72.12 DDD / 100 HR.

The following graph illustrates the total quantity of use of each antibiotic used in the Irna Anak Inpatient Room, Porsea Regional General Hospital in 2023 in DDD / 100 HR units which is shown in Figure 3.

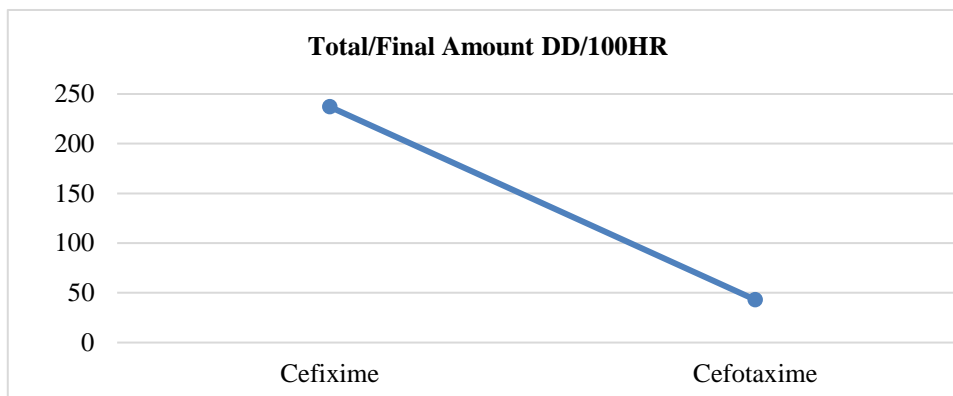


Figure 5. Total Quantity of Antibiotic Use in 2024

Based on Figure 3, cefixime is the antibiotic with the highest DDD/100 HR value during 2024, which is 237.04. This can be interpreted that on average in 100 days of hospitalization at HKBP Balige General Hospital during 2024, there were around 13 patients who received cefixime therapy according to the WHO standard DDD, which is 0.6 grams per day.

The DDD/100 HR value of cefixime is lower when compared to a study conducted on surgical patients at Dr. H. Slamet Martodirjo Pamekasan Hospital during the period January-March 2020 which showed the largest DDD/100 HR value, namely cefixime, of 34.50 (Syafitri & Yerlina, 2024). Cefixime is widely used as empirical therapy because it is a third-generation cephalosporin antibiotic that has a broad spectrum against gram-positive and negative bacteria and anaerobic bacteria (Rachmawati et al., 2020).

3.4 DU90% Profile

The DU90% profile is obtained from the calculation of the percentage of use of each antibiotic in the Inpatient Room of HKBP Balige General Hospital in 2024. The antibiotic percentage data is then sorted from the highest percentage to the lowest percentage. The percentage is calculated quantitatively by adding it to the cumulative percentage to determine the accumulation of antibiotic use up to 90%. The DU90% profile is a list of the names of the most widely used antibiotics in hospitals in an accumulation of 90% and can be used for the purpose of quantitative analysis of antibiotic use used at HKBP Balige General Hospital during the period January-April 2024.

Table IV. DU90% Profile in 2024.

Drug Name	% Usage	% Cumulative
Cefixime	66,70	66,70
Cefotaxime	33,30	100,00

Based on table IV, with the blue block, antibiotics included in the DU90% segment include cefixime and cefotaxime. which means that the drug is used for the treatment of dengue fever patients at RSU. HKBP Balige, there are only 2 types of antibiotics included in the DU90% segment. The fewer variations of antibiotics included in the DU90% segment, the smaller the risk of resistance.

4. CONCLUSION

Based on the antibiotic evaluation study using the ATC/DDD method that has been carried out, it can be concluded that the characteristics of patients using antibiotics in the inpatient care of the Balige HKBP Hospital for the period January - April 2024 based on gender and age are male patients (51.43%) aged 13-18 years (40%). The antibiotic use profile shows that the most widely used antibiotic groups and types of antibiotics are respectively Cefotaxime Injection 1000 mg (24.39%), and the most commonly given route of antibiotic administration is intravenous, and the most frequent duration of antibiotic therapy is <3 days (85.71%). The evaluation of the quantity of antibiotic use using the ATC/DDD method shows that the antibiotic with the highest DDD/100 patient-days value is cefixime at 237.04 DDD/100 patient-days. The type of antibiotic that exceeds the standard value set by WHO is cefixime. Antibiotics included in the DU90% segment are cefixime, cefotaxime.

REFERENCES

- Ann, S. J. S., GANGADHAR, R., & Priyanga, R. (2020). Utilisation Pattern, Safety Profile and Cost Analysis of Antimicrobials Prescribed in an Intensive Care Unit of a Teaching Hospital. *Journal of Clinical & Diagnostic Research*, 14(3).
- Bhalerao, U., Preethi, L., Bhukya, P. L., & Mhaske, S. T. (2023). Dengue Haemorrhagic Fever: A Resurgent Arbovirolosis in Humans. In *Emerging Human Viral Diseases, Volume I: Respiratory and Haemorrhagic Fever* (pp. 315-343). Springer.
- Bhatt, L., & Pandey, D. (2023). Review on Dengue Fever. *International Journal of Multidisciplinary Educational Research*, 12(7), 74-86.
- Czapla, M., Juárez-Vela, R., Łokieć, K., Wleklik, M., Karniej, P., & Smereka, J. (2022). The association between nutritional status and length of hospital stay among patients with hypertension. *International Journal of Environmental Research and Public Health*, 19(10), 5827.
- Dehghani, R., & Kassiri, H. (2021). A review on epidemiology of dengue viral infection as an emerging disease. *Research Journal of Pharmacy and Technology*, 14(4), 2296-2301.
- Garbe, E., Suissa, S., & Douros, A. (2023). Pharmacoepidemiology. In *Handbook of epidemiology* (pp. 1-55). Springer.
- Gupta, N., Ish, P., Kumar, R., Dev, N., Yadav, S. R., Malhotra, N., Agrawal, S., Gaiind, R., Sachdeva, H., & group, S. H. C. 2019 working. (2020). Evaluation of the clinical profile, laboratory parameters and outcome of two hundred COVID-19 patients from a tertiary centre in India. *Monaldi Archives for Chest Disease*, 90(4).
- Krishna, G., Sreedevi, S., & Thrimothi, D. (2024). Dengue Virus Infection: Etiology, Epidemiology, Pathogenesis, Diagnosis, and Prevention. In *Viral Infectious Diseases Annual Volume 2024*. IntechOpen.
- Leowattana, W., & Leowattana, T. (2021). Dengue hemorrhagic fever and the liver. *World Journal of Hepatology*, 13(12), 1968.
- Mohsina, F. P., Faheem, I. P., Mohammad, M., Tabassum, S., Tarkash, S., Shah, I., & Patil, A. (2022). Prevalence, pathogenesis and identification of clinical risk factors associated with dengue virus (DENV). *Indo Global Journal of Pharmaceutical Sciences*, 12, 189-196.
- Murugesan, A., & Manoharan, M. (2020). Dengue virus. In *Emerging and reemerging viral pathogens* (pp. 281-359). Elsevier.
- Parveen, S., Riaz, Z., Saeed, S., Ishaque, U., Sultana, M., Faiz, Z., Shafqat, Z., Shabbir, S., Ashraf, S., & Marium, A. (2023). Dengue hemorrhagic fever: a growing global menace. *Journal of Water and Health*, 21(11), 1632-1650.
- Sudarmaja, I. M., Swastika, I. K., Diarthini, L. P. E., Prasetya, I. P. D., & Wirawan, I. M. A. (2022). Dengue virus transovarial transmission detection in *Aedes aegypti* from dengue hemorrhagic fever patients' residences in Denpasar, Bali. *Veterinary World*, 15(4), 1149.

- Suyal, D. C., Karnwal, A., Kumar, V., & Zhong, Y. (2024). Achhada Ujalkaur Avatsinghi¹, Shilpa Sharma¹, Shilppreet Kouri¹, Yukta Arora¹, Sheetal Sharma¹, Divya Joshi², Prem Prashant Chaudhary³, Kahkashan Perveen⁴, Mohab Amin Kamal⁵ and Nasib Singh ¹. *Hazardous Pollutants in Agricultural Soil and Environment*, 37.
- Wang, W.-H., Urbina, A. N., Chang, M. R., Assavalapsakul, W., Lu, P.-L., Chen, Y.-H., & Wang, S.-F. (2020). Dengue hemorrhagic fever—A systemic literature review of current perspectives on pathogenesis, prevention and control. *Journal of Microbiology, Immunology and Infection*, 53(6), 963–978.
- Zerfu, B., Kassa, T., & Legesse, M. (2023). Epidemiology, biology, pathogenesis, clinical manifestations, and diagnosis of dengue virus infection, and its trend in Ethiopia: a comprehensive literature review. *Tropical Medicine and Health*, 51(1), 11.