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Cost-effectiveness analysis of clinical pathways for dengue hemorrhagic fever treatments in pediatric cases at PKU Muhammadiyah Hospital, Yogyakarta

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ABSTRACT

Dengue Hemorrhagic Fever (DHF) remains a concerning global problem, especially in Indonesia. This issue particularly deals with the current practice of therapeutic management for pediatric DHF inpatients that does not follow the standard clinical pathway, resulting in increased treatment costs. On this account, a clinical pathway is expected to minimize these costs and reduce patient's length of stay (LoS). However, a cost-effectiveness analysis prior to its implementation in DHF treatments for pediatric patients at PKU Muhammadiyah Hospital, Yogyakarta, is necessary. A retrospective cohort study and cost-effectiveness analysis were carried out from the hospital's (provider) perspective. The research involved two groups based on the adherence of the treatments to the clinical pathway, namely the conformity group and non-conformity group, and collected data on direct medical costs of the pediatric DHF treatment and LoS of both groups from 2016 to 2017. The Incremental Cost-Effectiveness Ratio (ICER) of both groups and the Risk Ratio (RR) were calculated as the outcome. The results confirmed that from the 200 patients involved, 138 of which (69%) received treatments conforming to the clinical pathway, while the therapies given to the remaining 62 patients (31%) deviated from it, with a *p*-value of 0.000 and RR of 1.58. The average calculated costs for these two groups were IDR 1,144,024 $\pm$ 556.372 and IDR 1,989,723 $\pm$ 1,296,899, respectively, while the ICER was IDR 826,917. In conclusion, when implemented on pediatric DHF treatments at PKU Muhammadiyah Hospital, Yogyakarta, clinical pathways can shrink LoS by up to 1.58 times and, consequently, save the cost by IDR 919,238 per one-day reduction off of the average LoS.

Keywords: clinical pathway, child DHF, cost-effectiveness

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INTRODUCTION

Dengue Hemorrhagic Fever (DHF) has been a worldwide concern, including in Indonesia. Specifically, in the City of Yogyakarta, DHF made the top 10 inpatient diseases at the Regional General Hospital (Dinas Kesehatan DIY, 2016). Its severity increased as the number of cases moved up from the seventh (in 2014) to the second rank (2015) at the same hospital (Dinas Kesehatan DIY, 2015). In 2014, 418 cases of DHF in the city were recorded, with the majority of the patients were in the age range of children (Dinas Kesehatan DIY, 2015).

The high incidence of DHF requires that the handling of children with DHF in the hospital be carried out appropriately per the management of pediatric DHF therapy. However, the current management in question still conforms to neither the standards nor the indications (Ni Wayan *et al*., 2014), leading to high treatment costs. For instance, the recorded DHF cases in Indonesia in 2016 caused economic losses in the community by approximately IDR 986 billion (Kementrian Kesehatan RI, 2017). With the implementation of the JKN (National Health Insurance), the government has required the payment for health services to be completed through the BPJS (Social Security Agency) insurance scheme that uses the Indonesia Case-Based Groups (INA-CBGs) system (Kemenkes RI, 2013). This newly adopted system demands that all hospitals optimize their financial management so as not to exceed the predefined rates (Kepmenkes RI, 2012).

Multidisciplinary patient management tools have been proposed as one of the strategies to streamline costs. These tools contain standardized steps to handle a patient from the admission process to discharge or known as clinical pathways. If implemented accordingly to the standards, a clinical pathway can accelerate patient recovery. Previous studies have found that clinical pathways can accelerate patient recovery from 3% to 46% (Schmidt *et al*., 2016) and have a significant role in shaping the effectiveness of the treatment costs (Olsson *et al*., 2009). In addition to reducing medical costs, they also play a part in shortening patient's length of stay (Sylvester and George, 2014). In another study at the KPJ Penang Specialist Hospital, clinical pathways have been reported to improve physicians' compliance with dengue fever management and reduce related mortality in 2015 (Rahman, 2017).

Combined with the high incidence of DHF in children in Indonesia, especially in the City of Yogyakarta, the cost-effectiveness issues in current clinical pathways warrant the need for research that evaluates to what extent the clinical pathways conform to the standards and how much cost of treatment they can potentially save.

MATERIALS AND METHODS

The study employed a retrospective cohort design from the perspective of the hospital observed (care provider). The collected data consisted of age, sex, financial situation, length of stay (LoS), and the suitability of the treatment that the DHF inpatients received at PKU Muhammadiyah Hospital, Yogyakarta, from 2016 to 2017 with the standard clinical pathways.

The inclusion criteria were patients aged <15 years old and hospitalized between 2016 and 2017 with the primary diagnosis of DHF (ICD 10-A91, 2017). The exclusion criteria were incomplete medical records, infectious (typhoid, pneumonia, specific diarrhea) and non-infectious diseases (asthma, bronchitis, and COPD), DSS (Dengue Shock Syndrome), and admission to the ICU/ICCU.

The research subjects were divided into two groups: the group receiving treatments that conformed to the clinical pathway ("conformity group") and another group receiving treatments that did not conform to the clinical pathway ("non-conformity group"). The implemented clinical pathways were analyzed for its cost-effectiveness using the Incremental Cost-Effectiveness Ratio (ICER). In the cohort study, the Risk Ratio (RR) was observed as a parameter. Meanwhile, the effectiveness analysis was focused on the parameter LoS and followed by sensitivity analysis based on the maximum and minimum variations in LoS. Differences in age, sex, the suitability of treatments to clinical pathways, average LoS, and costs between the two groups were determined statistically by the chi-square and the Mann-Whitney tests.

RESULTS AND DISCUSSION

The research population who met the inclusion criteria consisted of 277 pediatric DHF patients. These 277 patients were further screened using the exclusion criteria into 200 patients. The cost-effectiveness and suitability of treatments to the clinical pathway of these 200 patients were then analyzed in the research.

Patient characteristics

Based on the characteristics presented in Table I, more than one-third of the research samples (68 patients or 34.0%) were at the age of 6-10 years, with an average of 7 years old in each group. This finding is in line with the research carried out in South India from 2015 through 2016 (Nagaram *et al*., 2017), in which most pediatric DHF patients were in the age range of 6-10 years old. The chi-square test results showed no significant difference in the number of pediatric DHF patients between the age groups ($p = 0.689>0.05$).

Table I also shows that male patients were found higher in number (71 patients or 51.5%) than their female counterparts. Although both have a nearly equal chance of contracting dengue virus (Achmadi *et al*., 2010), boys are generally more susceptible to infections because their immunoglobulin and antibody productions are genetically and hormonally less efficient than that of girls (Soedarmo *et al*., 2010). The chi-square test revealed that the numbers of male and female pediatric DHF patients were not significantly different ($p = 0.065>0.05$).

There are four types of wards (or classes or care) at PKU Muhammadiyah Hospital in Yogyakarta, namely Class 1, Class 2, Class 3, and VIP Class. The results showed that Class 3 wards had the most number of pediatric DHF patients belonging to the two clinical pathway groups (conformity and non-conformity). Based on the chi-square test results, there was no statistically significant difference in the number of patients between the types of wards ($p = 0.170>0.05$).

In terms of severity, Grade II patients accounted for about half of the total research samples each in the conformity group (76 patients or 55.1%) and non-conformity group (31 patients or 50%). This finding is consistent with the results of several previous studies (Cecilia *et al*., 2019 and Ikrima *et al.*, 2017) (e.g., that the largest share of DHF patients is at Grade II. This fact is most likely attributable to the less understood severity of DHF by the patients' family; hence, by the time they are admitted to hospitals or health care facilities, their DHF has developed from Grades I to II (Sumirah *et al.*, 2014). The statistical test results found no significant differences in the number of patients between the Grades I, II, and III DHF ($p = 0.802>0.05$).

In terms of health insurance, the patients were classified into two groups, namely the BPJS and non-BPJS user groups. The results showed that the BPJS and non-BPJS users were nearly equal in number ($p = 0.924>0.05$), indicating no statistically significant differences between the two groups.

Table I. The characteristics of the pediatric dhf inpatients observed

Characteristics	Conforming to the Clinical Pathway	Not conforming to the Clinical Pathway	Total	*p*-values
Age				
< 1 y.o.	10 (7.2 %)	6 (9.7 %)	16 (8 %)	
1-5 y.o.	42 (30.4 %)	14 (22.6 %)	56 (28 %)	0.689
6-10 y.o.	46 (33.3 %)	22 (35.5 %)	68 (34 %)	
11-15 y.o.	40 (29.0 %)	20 (32.3 %)	60 (30 %)	
Total	138 (100 %)	62 (100 %)	200 (100 %)	
Mean ± SD	7.22 ± 4.23 y.o.	7.65 ± 4. 14 y.o.		0.493
Gender				
Male	71 (51.5 %)	41 (66.1 %)	112 (56 %)	0.065
Female	67 (48.5 %)	21 (33.9 %)	88 (44 %)	
Total	138 (100 %)	62 (100 %)	200 (100 %)	
Types of Wards				
Class 1	38 (27.5%)	12 (19.4%)	50 (25%)	
Class 2	33 (24.0%)	13 (21.0%)	46 (23%)	0.170
Class 3	45 (32.6%)	19 (30.6%)	64 (32%)	
VIP Class	22 (15.9%)	18 (29.0%)	40 (20%)	
Total	138 (100%)	62 (100%)	200 (100%)	
Severity of DHF				
Grade I	42 (30.4%)	21 (33.9%)	63 (31.5%)	
Grade II	76 (55.1%)	31 (50%)	107 (53.5%)	0.802
Grade III	20 (14.5%)	10 (16.1%)	30 (15%)	
Total	138 (100%)	62 (100%)	200 (100%)	
Health Insurance				
BPJS	70 (50.7%)	31 (50%)	101 (50.5%)	0.924
Non-BPJS	68 (49.3%)	31 (50%)	99 (49.5%)	
Total	138 (100%)	62 (100%)	200 (100%)	

Conformity of pediatric dhf treatments to the clinical pathway

The conformity analysis revealed that there more than half of the patients observed, amounting to 138 patients or (69%), were in the conformity group. In other words, the clinical pathway of the pediatric DHF treatment in the studied hospital was fairly well-implemented. This result corresponds to previous research (Bryan *et al*., 2017), which confirmed that the number of patients who receive treatments adhering to clinical pathways is significantly higher than in the opposite group.

As seen in Table II, 62 patients (31%) belonged to the non-conformity group due to possible reasons summarized in Table IV. The statistical chi-square test results (Table III) proved that there was a significant relationship between the conformity of treatment to clinical pathways and LoS (p = 0.000). As for the strength of the relationship, it was determined from the RR (Risk Ratio) value, which was 1.58. These results imply that the conformity group has a possibility of shorter LoS by up to 1.58 times that in the non-conformity group.

Table II. The conformity of current pediatric DHF treatments to the clinical pathway based on number of patients at PKU Muhammadiyah Hospital from 2016 to 2017

	Conforming to the Clinical Pathway	Not conforming to the Clinical Pathway	Total
Number of patients	138 (69 %)	62 (31 %)	200 (100 %)

Table III. The conformity of current pediatric DHF treatments to the clinical pathway based on length of stay at PKU Muhammadiyah Hospital from 2016 to 2017

	Conforming to the Clinical Pathway (patients)	Not conforming to the Clinical Pathway (patients)	*p*-values
LoS ≤ 4 days	113 (81.9 %)	32 (51.6 %)	0.000
LoS > 4 days	25 (18.1 %)	30 (48.4 %)	
Total	138 (69 %)	62 (31 %)	
RR (CI 95 %)	1.58 (1.23-2.04)		

Based on the predetermined criteria of conformity, some patient treatments do not comply with the clinical pathway because of the therapeutic criteria/medical advice. The majority of the patients (46 out of 75 patients) took an additional therapy, that is, any therapies that are not listed in the clinical pathway and are taken or prescribed without a preceding secondary diagnosis. The most incompatible adjunct therapy is the provision of antibiotics and dexamethasone. Such provision deviates from the standardized management of pediatric DHF therapy, which mainly applies fluid resuscitation without the administration of antibiotics unless secondary infections are diagnosed (WHO, 2012). Furthermore, the administration of oral paracetamol as needed is another treatment that does not conform to the clinical pathway, and this practice was found in 16 cases. Thirteen (13) patients who should have been given oral paracetamol received paracetamol infusion therapy instead, and the other three (3) patients should not have received fever medications like ibuprofen and metamizole other than paracetamol. In these cases, despite the non-conformity to the clinical pathway, the administration of paracetamol infusion is still tolerable because it did not harm the patient, and there might be certain conditions that require patients to receive intravenous administration (Kassir *et al*., 2011).

Apart from antibiotics, dexamethasone, and paracetamols, the injections of ondansetron, domperidone, and dimenhydrinate are also noncompliant with the clinical pathway. However, the administrations of dimenhydrinate are categorically safe for pediatric patients (Enarson *et al*., 2011), and the same case applies to domperidone when administered at a dose of 0.25 mg/kg body weight three times a day (HPRA, 2014). Therefore, both therapies are allowed even though they are not adherent to the clinical pathway. In addition to these three medicines, therapies involving ranitidine injections, pantoprazole, and antacids also deviate from the clinical pathway. Despite this non-conformity, the administrations of pantoprazole and antacids in pediatric patients are classified as safe and tolerable (Ward *et al*., 2010; Bhatia, 2012). The overall discrepancies in the therapeutic/medical criteria are most likely caused by doctors disobeying the established clinical pathway in prescribing drugs or determining therapies (Zheng *et al*., 2014).

Table IV. The components of non-conformity of current pediatric DHF treatments to the clinical pathway

Treatments	Number of cases = 75 (100%)
Therapy/medical advice	
Oral Paracetamol if necessary	16 (21.4%)
Ondansetron injection if necessary	7 (9.3%)
Ranitidine injection if necessary	6 (8%)
Additional therapies	46 (61.3%)
- Antibiotics	30
- Dexamethasone	16
As prescribed by doctors	
IVFD RL/ASERING/D5-1/2NS	0
As provided by nurses	
Monitoring of vital signs	0
Monitoring of AT & HMT per 12 hours	0
Monitoring of liquid balance	0
Laboratory tests	
AT	0
HMT	0

Notes:
IVFD RL : Intravenous Fluid Drip
RL : Ringer Lactate
AT : Thrombocyte Level
HMT : Hematocrit
D5-1/2NS : Dextrose 5%- ½ Normal Saline

The effectiveness of the clinical pathway

The analysis found that the application of clinical pathways was effective in the conformity group with an average LoS of less than four days, specifically 3.66 ± 1.11 days, as seen in Table V. This result is consistent with the previous study stating that clinical pathways play a crucial role in shortening the length of stay in a hospital (LoS) (Rotter *et al*., 2012). The Mann-Whitney test produced a *p*-value of 0.000, which means that the average LoS of the group who conformed to the clinical pathway is significantly different from that of the opposite group.

Table V. The average Length of Stay (LoS) of pediatric DHF patients at PKU Muhammadiyah Hospital from 2016 to 2017 based on conformity to clinical pathways

	Conforming to the Clinical Pathway (n= 138)	Not Conforming to the Clinical Pathway (n = 62)	*p*-value
Average LoS	3.66 ± 1.11 days	4.58 ± 1.46 days	0.000

The cost-effectiveness of the clinical pathway

The cost of applying the clinical pathway can be represented by direct medical costs, which include the costs for drugs (and medical supplies), the services of pediatrician/poly physicians, nursing

services, laboratory tests, radiology, physiotherapy, ultrasound, and administration as seen from the perspective of a care provider or hospital. In this study, the costs of inpatient treatments and medical visits during hospitalization were not included in the calculation because they depended on the type or class of wards where the sampled patients stayed. Each of these wards has different prices that may lead to biased results.

Table VI shows that the average direct medical costs for patients in the conformity group were smaller than in the non-conformity group. The statistical Mann-Whitney test yielded a *p*-value of <0.05, which means that there is a significant difference between the average direct medical costs of the two groups. In other words, if implemented correctly and according to the included dimensions/criteria, clinical pathways can substantially reduce the cost of care. These results are consistent with the previous research highlighting how adherence to clinical pathways can lower treatment costs in hospitals (Bryan *et al.*, 2017).

Table VI also shows that the average total direct medical costs for patients in the conformity group were smaller than for those in the opposite group. In terms of treatments, pharmaceuticals and laboratory depots significantly determine the total costs. In the non-conformity group, pharmaceuticals cost higher than in the conformity group because the therapies given or prescribed were outside the clinical pathway and without any prior secondary diagnosis. Also, the non-conformity group needed to pay higher for laboratory services because the Grade III patients belonging to it required cross-transfusion in the first place and were thereby treated with blood transfusion.

Table VI. The average costs of care for pediatric DHF patients at PKU Muhammadiyah Hospital, Yogyakarta, from 2016 to 2017 based on conformity to clinical pathway

Cost Component	Average		*p*-values
	Conforming to the Clinical Pathway (IDR)	Not Conforming to the Clinical Pathway (IDR)	
Pharmacy Depot	304,076 ± 219,082	689,200 ± 716,895	0.000
Laboratory	634,884 ± 429,950	976,471 ± 765,191	0.000
Administration	87,374 ± 24,909	87,747 ± 21,020	0.434
IGD/pediatric polyclinic	166,663 ± 52,883	169,258 ± 66,167	0.795
Physiotherapy	40,000	98,000	-
Radiology	217,000 ± 121,243	168,666 ± 70,776	0.711
Total cost	1,144,024 ± 556,372	1,989,723 ± 1,296,899	0.000

Differences identified between the conformity and non-conformity groups confirm that clinical pathways that are well-implemented and compliant to the predefined criteria can lower patient treatment costs. According to previous research (Rejeki, *et al.*, 2017), clinical pathways in pediatric DHF treatments in hospitals can reduce the cost of care. For this reason, conformity to clinical pathways is more cost-effective than the opposite. The Mann-Whitney test yielded *p*-value = 0.000, meaning that the average direct medical costs of the conformity group are significantly different from the non-conformity group. Based on Table VII, the ICER was estimated at IDR 919,238/day. This figure indicates that, if compliant with the clinical pathway, a reduction of one day off the LoS at the hospital can save IDR 919,238.

Table VII. The Incremental Cost-Effectiveness Ratio (ICER) Calculated for the PKU Muhammadiyah Hospital, Yogyakarta, from 2016 to 2017

	Conforming to the Clinical Pathway	Not Conforming to the Clinical Pathway	Cost Difference	ICER
Average Cost	IDR 1,144,024	IDR 1,989,723	-IDR 845,699	IDR 919,238/day
Average LoS	3.66 days	4.58 days	-0.92 day	

Sensitivity analysis

Sensitivity analysis was performed by recalculating the ICER and creating a variation in LoS according to the minimum and maximum values in the conformity and non-conformity groups. The results of the sensitivity analysis are summarized in Table VIII.

Table VIII. The sensitivity analysis of the groups conforming and not conforming to clinical pathways with variations in Length of Stay (LoS)

	Conforming to the Clinical Pathway	Not Conforming to the Clinical Pathway	ICER
Minimum Cost	IDR 337,000	IDR 536,300	IDR 216,630/day
Minimum LoS	1 day	2 days	IDR 845,699/day
Maximum Cost	IDR 4,242,100	IDR 6,434,875	IDR 2,383,451/day
Maximum LoS	7 days	9 days	IDR 422,849/day
Initial ICER	-	-	IDR 919,238/day

The sensitivity analysis showed that the new ICER values were different from the original ones, indicating that LoS and costs influence the resulted ICER. Compared to LoS, costs have a more considerable influence on ICER.

CONCLUSION

The conformity of the pediatric DHF treatments at PKU Muhammadiyah Hospital, Yogyakarta, to the clinical pathway can reduce the length of stay (LoS), as evidenced by the average LoS that is lower in patients in the conformity group than in the non-conformity group. A briefer LoS by 1.58 times can save up to IDR 919,238 for a one-day reduction off of the LoS.

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