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ORIGINAL ARTICLE

RISK FACTORS OF DENGUE MORTALITY IN PAMEKASAN DISTRICT (2018-2020)

Faktor Risiko Kematian Akibat Demam Berdarah Di Kabupaten Pamekasan Pada Tahun 2018-2020

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ABSTRACT

Background: The incidence of Dengue Haemoragic Fever (DHF) in the Pamekasan District is still high. Mortality of DHF was always happening in Pamekasan District from 2016 to 2020. **Purpose:** This study aims to analyze the risk factors of DHF mortality in the Pamekasan District (2018-2020). **Methods:** The study was conducted from October 2020-June 2021 with a case-control study. Total population was 293 cases. The sample was 54 respondents (1:2) with proportional random sampling. The inclusion criteria were families living under the same roof for a minimum of 17 years. The variables were dengue mortality, age, sex, education, history of DHF, comorbidities, access to health services, delay in treatment, family income, residence, and family knowledge. Data were collected through interviews and documentation study. The analysis in this study used univariate (frequency) and bivariate (crosstabs use OR). **Results:** Risk factors of DHF mortality in Pamekasan District are children (OR = 2.05; 95% CI=0.59-7.04), low education (OR=1.16; 95% CI=0.30-4.46), history of dengue (OR=3.57;95%CI=1.09-11.66), comorbidities(OR=17.50; 95% CI=4.25-72.05), difficult access to health services (OR=3.10; 95% CI=0.79-12.09), delay in treatment (OR=5.20;95% CI=1.50-18.0), low income family (OR=1.16; 95% CI = 0.30-4.46) and low of family knowledge about dengue (OR = 7.00; 95% CI = 1.99-24.58). Meanwhile, protective factors are female (OR = 0.70; 95% CI = 0.22-2.23) and rural (OR = 0.48 ; 95% CI = 0.13-1.73). **Conclusion:** Risk factors of DHF mortality in Pamekasan District (2018-2020) are the history of DHF, comorbidities, delay in treatment, and low family knowledge about

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DHF.

ABSTRAK

Pendahuluan: *Angka kasus Demam Berdarah Dengue (DBD) di Kabupaten Pamekasan masih cenderung tinggi. Semenjak tahun (2016-2020) kematian akibat DBD di Kabupaten Pamekasan selalu terjadi.* ***Tujuan:*** *Menganalisis faktor risiko kematian akibat DBD di Kabupaten Pamekasan Pada Tahun 2018-2020.* ***Metode:*** *Penelitian dilakukan sejak Oktober 2020-Juni 2021 dengan desain Case-Control. Populasi berjumlah 293 kasus. Sampel penelitian yaitu 54 responden (1:2). Teknik pengambilan sampel menggunakan proportional random sampling. Kriteria inklusi penelitian merupakan keluarga yang bertempat tinggal satu atap yang sama dengan usia minimal 17 tahun. Variabel penelitian yaitu: kematian DBD, usia, jenis kelamin, pendidikan, riwayat DBD, penyakit penyerta, akses pelayanan kesehatan, keterlambatan pengobatan, pendapatan keluarga, wilayah tempat tinggal dan pengetahuan keluarga. Pengumpulan data menggunakan wawancara dan studi dokumentasi. Analisis data menggunakan uji uinvariat (frekuensi) serta uji bivariat (uji tabulasi silang dengan nilai OR).* ***Hasil:*** *Faktor risiko kematian akibat DBD di Kabupaten Pamekasan terdiri atas: usia anak (OR = 2,05;CI95%=0,59-7,04), pendidikan rendah (OR=1,16; CI 95%=0,30-4,46), memiliki riwayat DBD (OR=3,57; CI 95%=1,09-11,66), penyakit penyerta (OR=17,50;CI 95%=4,25-72,05), akses pelayanan kesehatan sulit (OR=3,10; CI 95% = 0,79-12,09), keterlambatan pengobatan (OR = 5,20; CI 95% = 1,50-18,0), pendapatan keluarga rendah (OR = 1,16; CI 95% = 0,30-4,46) dan pengetahuan keluarga kurang terkait DBD (OR = 7,00; CI 95% = 1,99-24,58) sedangkan faktor protektif yaitu:jenis kelamin perempuan (OR=0,70; CI 95% = 0,22-2,23) serta wilayah pedesaan (OR=0,48; CI 95% = 0,13-1,73).* ***Kesimpulan:*** *Riwayat DBD, penyakit penyerta, keterlambatan pengobatan serta pengetahuan keluarga kurang terkait DBD merupakan faktor risiko kematian akibat DBD di Kabupaten Pamekasan pada tahun (2018-2020).*

INTRODUCTION

One of the main contributing factors to the world's mortality rate with CFR 1-5% is Dengue Hemorrhagic Fever (DHF). The incidence of dengue fever causes the deaths of 25,000 people every year. 40% of the world's population, or 390 million people, was at risk of dengue fever infection. Globally, the number of dengue fever has increased significantly.The number of cases was recorded from 2,4 million people in 2010 to 4,2 million people in 2019 (WHO, 2019). Indonesia is a DHF endemic country with the highest DHF incidence in Asia. The incidence of DHF in Indonesia has increased significantly. In 2017, there were 68,407 cases of DHF with 467 deaths (CFR=0.72%) and there were 65,602 cases with 467 deaths (CFR=0.71%) in 2018. Dengue fever cases in Indonesia increased doubled in 2018, with a total of 138,127 cases and 919 deaths (CFR 0.67%). East Java is in the top of 10 regions with the highest number of dengue mortality and the second ranks as the highest incidence of dengue fever in Indonesia The case fatality rate(CFR) due to dengue fever in East Java until 2019 was still not available to reach the minimum target (CFR ≤ 1%). The Indonesian Health Profile report shows that the CFR of dengue mortality in

East Java was (CFR=1.01%) from 18,327 cases in 2019 (Dinas Kesehatan Provinsi Jawa Timur, 2020).

Based on East Java Health Profile report in 2019, Pamekasan was the second highest number of dengue mortality in East Java (Dinas Kesehatan Provinsi Jawa Timur, 2020). Since 2016, dengue mortality cases have always happened in Pamekasan District. Based on the annual report of the Pamekasan Health Office District, the case fatality rate of dengue fever increased (from 2016-2018). Total of CFR in 2018 was recorded at (4.50%). This number has increased from 2016 (CFR 1.60%) to 2017 (CFR 2.60%). In 2019, the CFR of dengue fever reached 3.20% of 281 cases, and in 2020 the CFR of dengue fever reached 0.75% of 135 cases (Dinkes Pamekasan, 2020).

Various factors influence the cases of dengue mortality. The research shows that factors significantly associated with death from dengue fever were age, gender, the occurrence of shock, and bleeding (Liew et al., 2016). Comorbidities also increase the risk factors of dengue mortality (Trisasri, Arguni, & Ahmad, 2017). Delays in treatment and knowing the symptoms of fever also increase the risk of shock and death from dengue mortality (Lestari, 2018). The background of this research is the high incidence of dengue fever and the occurrence of deaths every year in Pamekasan District since 2016. This study aims to know the risk factors of dengue mortality in the Pamekasan District (2018-2020). The results of this study are expected to be a source of improvement and evaluation programs to prevent dengue mortality so that similar incidents do not occur again.

METHODS

This research was quantitative research with a case-control type. The study was conducted from October 2020 to June 2021 in 9 primary health care. There were recorded deaths due to dengue fever from 2018 to 2020. The total population was 293 cases. The sample included 54 respondents with case-control (1:2), 18 respondents in the case group (total of dengue mortality), and 36 respondents in the control group. The sampling technique in this study was random propionate sampling for controls. The sample was unmatching. Respondents in this research were families who lived in the same place with controls or cases for a minimum of 17 years. The dependent variable in this study was dengue mortality. In contrast, independent variables in this research consisted of age, gender, education, history of dengue, comorbidities, access to health services, delay in treatment, family income, area of residence, and family of knowledge about dengue. Sources of research data were primary and secondary. Data were collected by documentation and interviews. The analysis of this study used univariate (frequency) and bivariate (crosstabs use OR).

Based on the operational definition, age was the length of time a person with DHF lived from birth until the time of research. Age in this study was categorized into children (< 15 years), adults (15-59) years, and the elderly (≥60 years). Gender was a person's biological status related to physical appearance characteristics present since birth with male and female categories. Education was categorized into low education (no education-junior high school) and higher education (Senior high school-bachelor). A history of dengue fever was a condition where a person had dengue fever before being re-infected. Comorbidities were conditions in which a person simultaneously has two or more disease disorders. Access to health services was an effort to seek or obtain health services to get the treatment which is categorized as difficult and easy.

Difficult conditions included requirements for distance > 10 km, travel time > 15 minutes, and there were obstacles to access to health services. The delay in treatment in this study means that the patient's condition when he entered the health facility got the experience of delay in treatment with a marked condition including shock, unconsciousness, and decreased platelets. This study was categorized into rural and urban areas based on the residence. The economic level was based on the average monthly family income according to the regional minimum wage in Pamekasan District in 2020. It was categorized into low (< IDR 1,913,321.00) and high (≥IDR 1,913 .321.00). Family knowledge was an understanding of dengue fever obtained from the results of information through a person's sensing process using a research questionnaire with a total of 18 questions related to DHF. Family knowledge was categorized into poor knowledge (score 0-9) and good knowledge (score 10-18). This research has passed the ethical test and was approved by the Health Research Ethics Committee Faculty Of Public Health University Of Jember (No.02/KEPK/FKM-UNEJ/II/2021).

RESULTS

Based on the result of the study, it was known that the majority of respondents in this study were adults (51.90%), female (68.50%), education ≤ 9 years (53.70%), and status as parents (79.60%) (Table 1).

Table 1.
Distribution Characteristics of Respondents

Variable	requency ı)	Percentag e (%)
Age (Years)		
Children(<15 years)	0.00	0.00
Adults (15-59 years)	51	94.40
Elderly (≥60 years)	3	5.60
Sex		
Male	17	31.50
Female	37	68.50
Education		
Low (≤ 9 years)	29	53.70
High (> 9 years)	25	46.30
Kinship Status		
Parents	43	79.60
Brothers/Sisters	3	5.60
Children	1	1.90
Husband/ Wife	3	5.60
Others	4	7.40
Total	54	100.00

The description of dengue mortality in the Pamekasan district (2018-2020) mostly occurs in children <15 years (24.10%), female (30.30%), with low education (34.10%) and has a history of dengue (50%) and comorbidities (70%). Also, most cases of dengue mortality were found in patients who had easy access to health services (31.90%), delays in treatment (52%), people coming from low-income families(34.10%), people in rural areas (29.30%) and patients with less family knowledge about dengue (60%) (Table 2).

Based on the results of bivariate analysis using the tabulation test of OR value, it was known the variables that are proven to be a risk factor (OR>1) of dengue mortality in the Pamekasan District (2018-2020) include the age of children, low education, history of dengue, comorbidities, delays in treatment, difficult access to health services, low family income and less family knowledge about dengue. While, the variables that proved to be a protective factor (OR <1) to dengue mortality in the Pamekasan district (2018-2020) were the female gender and rural areas. Based on these variables, the risk factors believed to be the cause of death from dengue mortality in the population with a confidence level of 95% CI in Pamekasan District (2018-2020) were history of dengue, comorbidities, delays in treatments, and low knowledge of dengue (Table 2).

DISCUSSION

Age

This research shows that children were a risk factor for dengue mortality in the Pamekasan District (2018-2020), with a risk of 2,053 times that of elderly. The results of this study are similar to the research of Nunes et al. (2019), which states that more than 53% of fatal cases of death occur in children. Theoretically, the cause of death is due to hypovolemic shock, which can increase the risk of dengue shock syndrome due to increased permeability of blood vessels in the child's body. (Idris, Tjeng, & Sudarso, 2017).

Sex

The results show that females were proven protective of dengue mortality in Pamekasan District (2018-2020). Female has 0,70 times lower risk of dying from dengue fever than male. This study was different from several studies that have been conducted previously. Liew et al (2016) stated that women were 1,53 times greater risk than men. It relates to biological components in the body and behavioral factors in women who tend not to get treatment. Women tend to experience dengue shock syndrome more than men because a stronger immune response causes inflammation to increase capillary permeability of blood vessels. Therefore, the risk of plasma leakage in women is higher, increasing dengue shock syndrome and mortality (Naeem, Pari, Gulzar, Yousaf, & Akhtar, 2018). The different conditions in this study resulted in females having a protective factor of dengue mortality in the Pamekasan District (2018-2020) due to the differences in samples and their characteristics. In this study, the results also show that the number of females is more than males. Besides that, the age of females was also mostly in adulthood, so it will be possible to allow good conditions for immunity.

Table.2
Analysis of the Relationship between Risk Factors to Dengue Mortality in the Pamekasan District (2018-2020).

Variables	Incidence of Dengue Mortality				Total		OR	(95% CI)
	Yes		No					
	n	%	n	%	n	%		
Age								
Children(< 15 Years)	13	24.10	19	35.20	32	100	2.05	0.59-7.04
Adult (15-59 Years)	5	9.30	15	20.00	20	100	0.59	0.44-0.79
Elderly (≥ 60 Years)	0	0.00	2	3.70	2	100		1.00
Sex								
Female	10	30.30	23	69.70	33	100	0.70	0.22-2.23
Male	8	38.10	13	61.90	21	100		1.00
Education								
≤ 9 Years	14	34.10	27	65.90	41	100	1.16	0.30-4.46
> 9 Years	4	30.80	9	69.20	13	100		1.00
History Of Dengue								
Yes	11	50.00	11	50.00	22	100	3.57	1.09-11.66
No	7	21.90	25	78.10	32	100		1.00
Comorbidities								
Yes	14	70.00	6	30.00	20	100	17.50	4.25-72.05
No	4	11.80	30	88.20	34	100		1.00
Access to health services								
Difficult	6	54.50	5	45.50	11	100	3.10	0.79-12.09
Easy	12	27.90	31	72.10	43	100		1.00
Delays of treatment								
Yes	13	52.00	12	48.00	25	100	5.20	1.50-18.01
No	5	17.20	24	82.80	29	100		1.00
Family Income								
Low	14	34.10	27	65.90	41	100	1.16	0.30-4.46
High	4	30.80	9	65.90	13	100		1.00
Area of residence								
Rural area	12	29.30	29	70.70	41	100	0.48	0.13-1.73

Urban area	6	46.20	7	53.80	13	100		1.00
Family of Knowledge About Dengue								
Low	12	60.0	8	40.00	20	100	7.00	1.99-24.58
High	6	17.6	28	82.40	34	100		1.00

Education

Education in this study is the last highest education that has been successfully taken by cases or controls. The results show that low education ≤ 9 years was a risk factor for dengue mortality in Pamekasan District (2018-2020). Low education has a risk of a 1,167 times greater risk of dying than higher education.

In this study, most cases of dengue mortality occurred in patients with low education (34.10%), with most cases of dengue mortality deaths not attending school, namely in the category of child age (toddlers). Education is one of the important things that can be a source of increasing knowledge and education related to dengue fever (Usman et al., 2018). Theoretically, a lower education affects someone's understanding to act. People with low education generally have low awareness of accessing health and tend not to care about health, so health problems worsen and can have a fatal impact on death (Zajacova & Lawrence, 2018).

History Of Dengue

History of dengue means that the patient has not experienced a fever for the first time or is commonly referred to as a secondary infection. Cases of dengue mortality in this study (50%) had a history of dengue compared to the control group, in which the majority did not have a history of dengue (78.10%). The results showed a history of dengue fever was a risk factor for dengue mortality in Pamekasan District (2018-2020). History of dengue has 3,571 greater times risk of dengue mortality than patients without a history of dengue. The results of this study had smilarity to the research of Hegazi et al. (2020), which stated that a history of dengue infection was a factor that significantly increased the risk of mortality 2,20 greater times.

Theoretically, the occurrence of more than one infection (secondary infection) in the presence of viruses from different serotypes can affect the severity of dengue patients. The Antibody-Dependent Enhancement (ADE) hypothesis theory explains that the presence of immunity due to the first (primary) infection by one serotype of the fever virus does not provide complete protection against other serotypes. The presence of antibodies in the body during the first infection is not effective enough in neutralizing all types of dengue virus serotypes. The occurrence of secondary infection results in a low number of heterotypic antibodies that promote viral access to monocytes in the body. This condition causes an increase in viral load and disease severity (Khetarpal & Khanna, 2016). Secondary infection causes viral antibody complexes in the body to be internalized by receptor carrier cells resulting in increased viral replication so that the severity of the disease can increase and can have a fatal impact on death.(Cáceres Munar, Castellanos Parra, & Rodríguez Panduro, 2019; Aryati, Wardhani, Rochaeni, Akualing, & Hadi, 2017; Arhana, 2016).

Comorbidities

Comorbidities are the condition of a person who has two or more disease disorders at the same time. The results showed comorbidities were a risk factor for dengue mortality in the Pamekasan District (2018-2020). Comorbidities increase the risk 17,50 times greater than patients without comorbidities. In this study, cases of dengue mortality (70%) occurred in patients with comorbidities, while the control group did not have comorbidities (88.20%). The results of this study align with the research of Werneck et al. (2018), which shows that comorbidities have 11 times greater risk of dying from dengue without comorbidities. This result is also in line with the research findings by Mehta & Hotez (2016), which resulted in information that comorbidities increased the risk of death from DHF in the dengue epidemic in Lahore in 2011 with 60% of dengue patients dying having at least one comorbidity.

Comorbidities were found to be an important risk factor for DHF mortality because it allows the severity of the disease for sufferers (Wei, Shu, & Hung, 2016; Macias et al., 2021). In this study, most of the respondents who died from DHF experienced comorbidities, namely obesity (87.50%). Theoretically, obesity is able to increase the presence of adipocytes in white tissue that can

secrete and release the pro-inflammatory cytokine Tumor Necrosis Factor alpha (TNF-α), so it affects the increase in plasma leakage in DHF patients(Trisasri et al., 2017). Based on field facts, this study found another comorbid disease, namely asthma. Asthma plays a role in causing the fever to worsen. It is in line with research by Yu et al. (2019), which stated that patients with asthmatic respiratory disorders also experience an increase in the incidence of dengue shock syndrome.

Access to Health Services

Access to health services is a community effort to find or use available health services in the community. Access to health services can be seen as an indicator of easy or difficult-to-reach health services from the patient's residence, transportation, distance and time to access health facilities (Laksono et al., 2016). Research shows that difficult access to health services is a risk factor for dengue mortality in the Pamekasan District (2018-2020). The risk of death from dengue fever in patients with difficult access to health services is 3.10 times greater than in those with easy access to health services. The results of this study agree with the research by Hikmah & Kasmini H (2015), which states that dengue mortality occurs in people with difficult access to health services (54.80%) with a risk of death 0,24 times than patients with easy access health services.

Based on the facts, the results showed that 6 cases (54.50%) had difficult access to health services. Access to health facilities is difficult related to the distance of > 10 km, travel time of > 15 minutes, and the rocky and unpaved road conditions to get to the health facility. Based on field facts, the difficult locations are in the area of the Tampojung Pregi Primary Health Care and the Kadur Primary Health Care. The locations are rural areas where access to health facilities is more complex than other primary health care (most roads are paved and easy to reach). Difficult conditions in accessing health services can be the reason behind people's reluctance to access health facilities, so there can be delays in treatment. Conditions of delay in treatment can lead to disease severity and fatal impact on death (Casas, Delmelle, & Delmelle, 2017).

Delay in Treatment

Delay in treatment is a condition of patients who are late for treatment at health facilities which can be characterized by shock, bleeding, and the severity of dengue disease when accessing health care facilities (Hikmah & H, 2015). The results showed that delay in treatment was a risk factor for dengue mortality in the Pamekasan District (2018-2020). Delayed treatment had a 5,20 times greater risk of increased mortality than patients without delay in treatment. This research is in line with the results of Mallhi, Khan, Sarriff, Adnan, & Khan (2017), which stated that patients who experience treatment delays have a 2,30 times greater chance of dying.

Based on the facts in the field, most patients died from dengue because when they first accessed health facilities, the patient's condition was in severe condition, with the number of platelets decreasing drastically. This research is in line with the results of Linn et al. (2020), who stated that shock conditions when the patient enters treatment could increase the risk of dengue mortality. The delay in treatment in this study was also evidenced by the information that a case takes a long time to decide to access health facilities for ≥ 4 days (72.70%). This research is in line with the results of Woon et al. (2016), which resulted in information that delays in seeking health services ≥ 4 days, classified as a critical phase of fever, can increase dengue mortality by up to 66.50%.

Family of Knowledge about Dengue

The results showed that low family knowledge about dengue was a risk factor for dengue mortality in the Pamekasan District (2018-2020). The risk increased 7 times greater than patients with good family knowledge about dengue. Based on the facts in the field, the family knowledge with less category is more significant in the case (60%) compared to the control (40%). From the results of the knowledge questionnaire, it is known that there are still many people who answer questions incorrectly, respondents cannot answer correctly regarding the transmission of dengue (59.25%), signs and symptoms of the critical phase of dengue (72.22%). They did not know how to give the first care to dengue patients (50%), did not know about the natural history of dengue (38.8%), and the characteristics of the occurrence of shock due to dengue fever (29.63%). The majority of respondents also said that there were no cadres who provided educational socialization related to dengue fever.

Knowledge of families with less category in this study may be related to the low education successfully completed by the research respondents (families who live under the same roof with dengue fever sufferers). Most

respondents' education is in the category of low education (53.70%). According to research by Putri & Naftassa (2018), education is closely related to knowledge. The higher level of education, the higher information of knowledge obtained by a person. Family knowledge is closely related to the perception and early treatment of dengue. The better the family's perception of dengue urgency, the better the early handling of dengue. Therefore, it can prevent dengue mortality. Families with low knowledge generally tend to be normal when there is a fever and give makeshift medicines so that there can be delays in treatment and a fatal impact on death (Permata, 2021).

Family Income

Based on the results of the study, it is known that low family income was a risk factor for dengue mortality in the Pamekasan District (2018-2020). The risk of death increased 1.16 times greater in families with low family incomes than in patients with high family incomes. The results of this study are in line with Hikmah & Kasmini H (2015), which results in information that low family income has a 3.80 times greater risk of dying from dengue when it is compared to high family income.

Based on field facts, it is known that most respondents work as construction workers, farmers, traders, entrepreneurs, and housewives, so the income earned is generally relatively small and uncertain. It causes the family income to be low. Low income makes it difficult to access health services, so there is the potential to experience delays in treatment, which can be fatal if left unchecked to increase the risk of dengue mortality (Napirah, Rahman, & Tony, 2016).

Area of Residence

The residential area in this study is administratively divided into two areas, namely rural areas and urban areas. The results showed that rural areas were a protective factor for dengue fever deaths in the Pamekasan Regency (2018-2020). Protective factors indicate that rural areas can reduce the risk of death from dengue. Based on the OR value, it is known that the risk of dengue mortality decreased by 0.48 times in patients with dengue in rural areas compared to patients living in urban areas.

The results of this study are not the same as previous research. Research by Trisasri et al. (2018) contained information that the area of residence in urban areas is a protective factor of dengue mortality compared to rural areas. Based on this research, it is known that deaths from dengue fever in cities are 18% lower than in rural areas. Rural areas are at risk of dying from DHF due to the low economic condition of the community, so they cannot access health services, and are also related to the lack of concentration on health care and treatment. Residential areas in rural areas may also have inadequate health facilities, long distances to health facilities, a lack of transportation systems, inadequate health workers, and an inability to pay for health services. The difference in the results of this study is possible because there are differences in research design, location, number of samples, and characteristics. Based on field facts, health service facilities are already spread across every sub-district in rural areas. It is also possible that it is related to the high income of rural communities (20.37%) so that it is possible to be able to access health facilities.

RESEARCH LIMITATIONS

The limitations of this study were that recall bias errors may have occurred during the study. The number of samples in this study was limited by using a total sampling of 18 cases of dengue mortality in the Pamekasan District (2018-2020).

CONCLUSION

Variables who proven to be a reliable risk factor (OR>1) with (95% CI) of dengue mortality in the Pamekasan District (2018-2020) are the history of dengue, comorbidities, delay in treatment, and the lack of family knowledge about dengue.

CONFLICT OF INTEREST

In this study, the authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

SMZ, YA, and AME contributed to the conceptualization and final approval of this study. Then, SMZ took part in the background, methodology, data collection, analysis, and writing of the original draft. YA and AME took part in reviewing, editing, checking, and revision.

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