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MODELING OF DENGUE HEMORRHAGIC FEVER CASES IN AWS HOSPITAL SAMARINDA USING BI-RESPONSES NONPARAMETRIC REGRESSION WITH ESTIMATOR SPLINE TRUNCATED

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Abstract: Research on innovations in the field of statistics implemented in the health sector. This research is the development of birespon nonparametric regression model with spline truncated approach. The purpose of this research is to model and determine the factors affecting the Dengue Hemorrhagic Fever Cases in AWS Hospital Samarinda using Bi-responses Nonparametric Regression with estimator Spline Truncated. The data used in this study were data

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on the platelet count of dengue fever patients when they first checked blood and after three days of treatment in 2022 as well as factors that were thought to have an effect. From the research results, the best model was biresponse nonparametric regression with three knot points where the minimum GCV value was 97.77 and R^2 value of 89.88%. Based on the test results, the factors affecting the response variable were the number of hematocrit and the level of hemoglobin in DHF patients.

Keywords: nonparametric regression; spline truncated; biresponse; dengue hemorrhagic fever; GCV.

2020 AMS Subject Classification: 92C60.

1. INTRODUCTION

Dengue Hemorrhagic Fever (DHF) is one of the diseases in Indonesia that has attracted the attention of the government. According to the World Health Organization [1] dengue is still a health problem for people around the world, especially people in tropical and sub-tropical areas. Indonesia as one of the tropical countries in the world with high humidity is the main trigger for people affected by dengue.

The number of dengue cases itself continues to increase from year to year, recorded in [1],[2] the number of dengue cases in Southeast Asia reached 2.4 million and increased in 2019 to 4.2 million cases. According to the Indonesian experienced a significant increase to 112,954 cases compared to 2018 as many as 53,075 cases [3]. The number of cases of dengue fever in Indonesia can be seen from the number of Incidence Rates [3],[4]. Incidence Rate (IR) is the number of new cases of a disease that appear in a period of time. It is known that the IR of DHF cases in 2019 was 51.48 per 100,000 population. This shows an increase compared to previous years. In 2019 East Kalimantan was included in the highest IR category compared to 34 other provinces [3].

Dengue fever is characterized by fever for 2-7 days with a temperature of 39°C, headache, back pain and heartburn, in addition to children usually characterized by vomiting, bone and muscle pain, accompanied by bleeding, decreased platelet count <100,000 mm3, the presence of plasma leakage is marked by an increase in hematocrit 20% of the normal value [3]. According to WHO, the criteria for a person to be declared affected by dengue can be seen from the results of a complete blood examination. So that medical officers determine only based on clinical signs and symptoms on the examination of platelets, hematocrit, and hemoglobin. The platelet count itself is most often used in Indonesia as a reference to determine whether a person has dengue or not.

There are several studies that use nonparametric spline regression, among others, conducted a multivariable spline regression analysis for modeling the mortality of patients with Dengue Hemorrhagic Fever (DHF) in East Java [5]. Modeled the factors that influence the percentage of the poor and food expenditure per capita in East Java using nonparametric biresponse spline regression [6]. Performs nonparametric spline biresponse regression modeling on the percentage of poor people and the poverty depth index in East Kalimantan [7]. This research will find Modeling of Dengue Hemorrhagic Fever Cases In AWS Hospital Samarinda Using Bi-responses Nonparametric Regression with estimator Spline Truncated.

2. METHODS

2.1. Data Source

The data used in this study were obtained from Abdul Wahab Syahrani (AWS) Hospital in 2022. The research variables used in this study are given in Table 1.

TABLE 1 Research Variables

Variable	Definition	Measure	Data Type
Platelet count of DHF patients at first blood check (Y_1)	Platelet count of DHF patients when they first do a blood check	μl	Continue
Platelet count of DHF patients after 3 days of treatment (Y_2)	The platelet count of DHF patients after 3 days of being treated and then having their blood checked again	μl	Continue
Hematocrit Level (X_1)	The amount of hematocrit found in patients with DHF	%	Continue
Hemoglobin Level (X_2)	The amount of hemoglobin cells found in patients with DHF	g/dL	Continue

2.2. Stage of Analysis

The data analysis technique in this study used the help of R software. The analysis carried out in this study are described in the following stages.

1. Defining the response variables and the predicted predictor variables.

2. Descriptive statistical analysis of response variables and predictor variables consists of:
   a. Calculating the average value
   b. Calculating the value of the standard deviation and variance
   c. Calculating the maximum and minimum values of data
3. Calculating the correlation test between the two response variables
4. Building scatter plot between each response variable to each predictor variable.
5. Finding a model of the platelet count of DHF patients with linear spline truncated approach for 1 knot, 2 knots and 3 knots.
6. Selecting the optimal knot point using Generalized Cross Validation (GCV) method
7. Calculating the minimum MSE value of the model with the resulting optimal knot point
8. Calculating the R^2 value of the model with each knot point
9. Modeling the platelet count of DHF patients with spline truncated approach for optimal knot points.
10. Performing model interpretation and drawing conclusions

3. RESULT AND DISCUSSION

3.1. Descriptive Statistics on Platelet Count, Hematocrit Level and Hemoglobin Level of DHF Patients at AWS Hospital in Samarinda

Descriptive statistics used in this study are the average value, minimum value, maximum value, and standard deviation.

TABLE 2 Descriptive Statistics

Variable	Measure	Minimum	Maximum	Mean	Standard Deviation
Platelet count of DHF patients at first blood check (Y_1)	μl	24000	248000	83422.41	40193.69
Platelet count of DHF patients after 3 days of treatment (Y_2)	μl	29000	170000	80215.52	32370.09
Hematocrit Level (X_1)	%	25	60.4	41.78	5.64
Hemoglobin level (X_2)	*g/dL*	7.9	19.5	14.32	1.98

Table 2 shows that the platelet count of DHF patients at first blood check (Y_1) is the lowest at 24000 μl and the highest at 248000 μl, with an average value of 83422.41μl. The platelet count of DHF patients after three days of treatment (Y_2) is the lowest at 29000 μl and the highest at 170000 μl, with an average value of 80215.52 l. The lowest level of hematocrit (X_1) is 25% and the highest is 60.4%, with an average value of 41.78%. The lowest level of hemoglobin (X_2) is 7.9 g/dL and the highest level is 19.5 g/dL, with an average value of 14.32 g/dL.

3.2. Scatter Plot on Platelet Count, Hematocrit Level and Hemoglobin Level of DHF Patients At AWS Hospital in Samarinda

Figure 1 shows that the data pattern between the response variable and the predictor variable does not form a certain pattern, hence the right solution to be used in this case is to use a nonparametric approach.

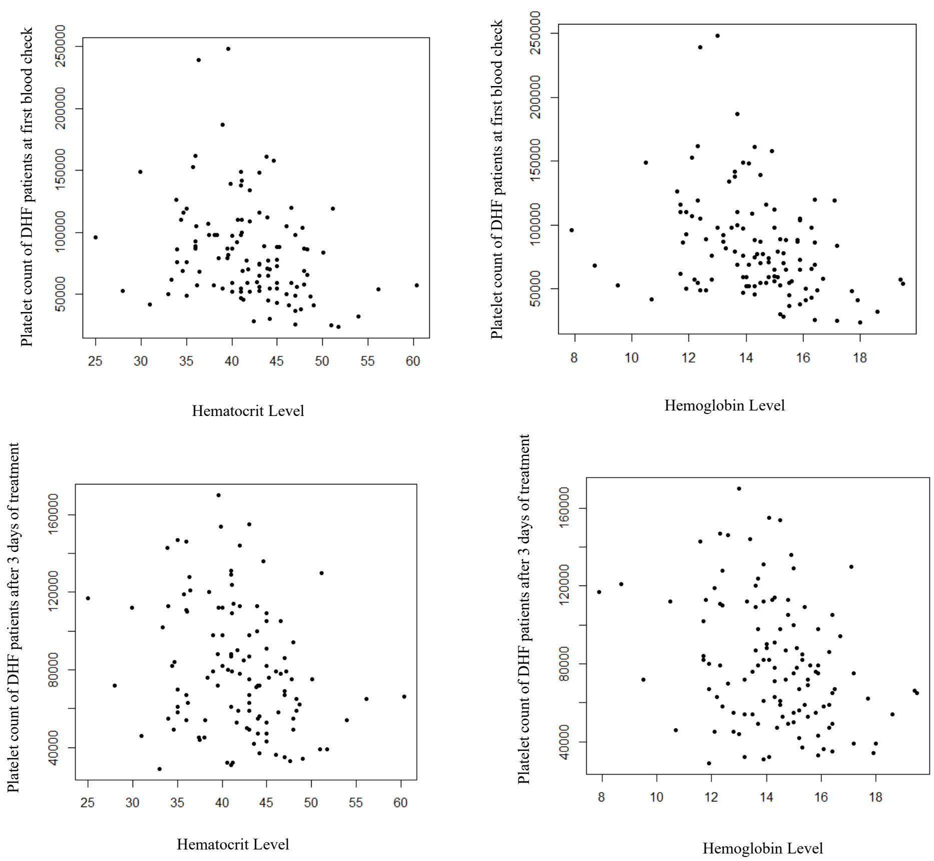

FIGURE 1. Scatter Plot Between Response Variable and Predictor Variable.

3.3. Biresponse Nonparametric Regression Model with Truncated Spline

Nonparametric regression is a statistical method to determine the relationship pattern between predictor variables and response variables which form of function is unknown [8], [9], [10]. This is different from parametric regression which forces the regression curve to follow a certain model such as a linear model. The advantages of nonparametric regression, the regression curve is determined by the observational data itself without having to be forced to adjust a certain function [11], [12], [13]. In view of nonparametric regression, the data seeks its own form of estimation of the regression curve without having to be influenced by the subjectivity of the researcher, this means that the nonparametric regression model approach is very flexible and very objective [14], [15], [16].

Identification of the pattern of relationship between the two response variables and the predictor variable does not form a linear, quadratic or other relationship pattern, so the approach that can be used is nonparametric regression. The biresponse nonparametric regression models with spline truncated using two predictor variables are given in Equation (1) and Equation (2)

$$\begin{aligned} y_{1i} &= \sum_{j=1}^{2}\sum_{h=1}^{m}\theta_{hj}x_{ij}^{h} + \sum_{j=1}^{l}\sum_{k=1}^{r}\emptyset_{m+k;j}\left(x_{ij}-k_{kj}\right)_{+}^{m} \\ &= \theta_{11}x_{i1} + \emptyset_{21}(x_{i1}-k_{11})_{+} \end{aligned} \tag{1}$$

$$\begin{aligned} y_{2i} &= \sum_{j=1}^{2}\sum_{h=1}^{m}\psi_{hj}x_{ij}^{h} + \sum_{j=1}^{l}\sum_{k=1}^{r}\tau_{m+k;j}\left(x_{ij}-\lambda_{kj}\right)_{+}^{m} \\ &= \psi_{11}x_{i1} + \tau_{21}(x_{i1}-\lambda_{11})_{+} \end{aligned} \tag{2}$$

Biresponse nonparametric regression models with linear splines using two predictor variables and one knot point are given in Equation (3) and Equation (4)

$$y_1 = \theta_{11}x_{i1} + \emptyset_{21}(x_{i1}-k_{11})_{+} + \theta_{12}x_{i2} + \emptyset_{22}(x_{i2}-k_{12})_{+} \tag{3}$$

$$y_2 = \psi_{11}x_{i1} + \tau_{21}(x_{i1}-\lambda_{11})_{+} + \psi_{12}x_{i2} + \tau_{22}(x_{i2}-\lambda_{12})_{+} \tag{4}$$

Biresponse nonparametric regression models with linear splines using two predictor variables and two knot points are given in Equation (5) and Equation (6)

$$\begin{aligned} y_1 = {} & \theta_{11}x_{i1} + \emptyset_{21}(x_{i1}-k_{11})_{+} + \emptyset_{31}(x_{i1}-k_{21})_{+} + \\ & \theta_{12}x_{i2} + \emptyset_{22}(x_{i2}-k_{12})_{+} + \emptyset_{32}(x_{i2}-k_{22})_{+} \end{aligned} \tag{5}$$

$$\begin{aligned} y_2 = {} & \psi_{11}x_{i1} + \tau_{21}(x_{i1}-\lambda_{11})_{+} + \tau_{31}(x_{i1}-\lambda_{21})_{+} + \\ & \psi_{12}x_{i2} + \tau_{22}(x_{i2}-\lambda_{12})_{+} + \tau_{32}(x_{i2}-\lambda_{22})_{+} \end{aligned} \tag{6}$$

Biresponse nonparametric regression models with linear splines using two predictor variables and three knot points are given in Equation (7) and Equation (8)

$$\begin{aligned} y_1 = {} & \theta_{11}x_{i1} + \emptyset_{21}(x_{i1} - k_{11})_+ + \emptyset_{31}(x_{i1} - k_{21})_+ + \emptyset_{41}(x_{i1} - k_{31})_+ \\ & \theta_{12}x_{i2} + \emptyset_{22}(x_{i2} - k_{12})_+ + \emptyset_{32}(x_{i2} - k_{22})_+ + \emptyset_{42}(t_{i2} - k_{32})_+ \end{aligned} \quad (7)$$

$$\begin{aligned} y_2 = {} & \psi_{11}x_{i1} + \tau_{21}(x_{i1} - \lambda_{11})_+ + \tau_{31}(x_{i1} - \lambda_{21})_+ + \tau_{41}(x_{i1} - \lambda_{31})_+ \\ & \psi_{12}x_{i2} + \tau_{22}(x_{i2} - \lambda_{12})_+ + \tau_{32}(x_{i2} - \lambda_{22})_+ + \tau_{42}(x_{i2} - \lambda_{32})_+ \end{aligned} \quad (8)$$

3.4. Selection of Optimum Knot Point

The selection of the best model from the spline biresponse regression can be seen from the minimum GCV [17] value and the maximum R^2 value. Table 2 shows the GCV value and R^2 value for each knot point.

TABLE 2 Minimum GCV Value and R^2 Value of Each Knot Point

Knot Points	GCV Value	MSE	$\boldsymbol{R^2}$
1 Knot Point	99.71	0,1347	85.64%
2 Knot Points	97.92	0,0642	87.69%
3 Knot Points	97.77	0,0402	89.88%

Table 2 shows that the modeling that produces the smallest GCV value and the largest R^2 value is at three knot points with an R^2 value of 89.88%. Therefore, it was decided that the best model to be chosen was a nonparametric regression model with spline truncated using three knot points. So that the results of the knot point position for each variable and the parameter values of the three knot point linear model are obtained in Table 3 and Table 4.

TABLE 3 Optimal Knot Point Position with Three Knot Points

Predictor Variable	Y_1	Y_2
	26.22	35.98
X_1	32.32	37.20
	33.54	38.42
	8.3	11.5
X_2	10.3	11.9
	10.7	12.3

TABLE 4 Parameter Estimation of Models with Three Knot Points

Predictor Variable	Y_1		Y_2	
	$\hat{\theta}$	$\hat{\emptyset}$	$\hat{\theta}$	$\hat{\emptyset}$
X_1	1727.307	−6362.79 12001.96 6749.22	6752.98	−40006.22 5054.67 4251.51
X_2	−7766.68	8507.38 −78549.72 5507.34	−5279.42	5073.92 −48861.56 37080.24

The three knot points spline model can be written in the form of the following equation (9) and (10):

$$\hat{y}_1 = 317942{,}28 + 1727{,}307x_1 - 6362{,}79(x_1 - 26{,}22)_+ + 12001{,}96(x_1 - 32{,}32)_+ + 6749{,}22(x_1 - 33{,}54)_+ - 7766{,}68x_2 + 8507{,}38(x_2 - 8{,}3)_+ - 78549{,}72(x_2 - 10{,}3)_+ + 5507{,}34(x_2 - 10{,}7)_+ \quad (9)$$

$$\hat{y}_2 = 1438667{,}46 + 6752{,}98x_1 - 40006{,}22(x_1 - 35{,}98)_+ + 5054{,}67(x_1 - 37{,}20)_+ + 4251{,}51(x_1 - 38{,}42)_+ - 5279{,}42x_2 + 5073{,}92(x_2 - 11{,}5)_+ - 48861{,}56(x_2 - 11{,}9)_+ + 37080{,}24(x_2 - 12{,}3)_+ \quad (10)$$

3.5. Interpretation of the Birespon Spline Nonparametric Regression Model

The best model for data on platelet counts of DHF patients at first check blood and after three days of treatment is birespon spline nonparametric regression model with three knot points. The interpretation for the first response variable spline model is explained as follows:

1. If the variable of hemoglobin level in DHF patients is considered constant, then the influence of the hematocrit level on the platelet count of DHF patients at first blood check is given in Equation (11).

   $$\hat{y}_1 = 1.72x_1 + 1.43(x_1 - 26.22)_+ - 0.06(x_1 - 32.32)_+ - 0.36(x_1 - 33.54)_+ \quad (11)$$

   The truncated function is given in Equation (12)

   $$\begin{cases} 1.72x_1 & ;\ x_1 < 26{,}22 \\ 3.15x_1 - 37.4946 & ; 26.22 \le x_1 \le 32.32 \\ 1.66x_1 - 1.9392 & ; 32.32 \le x_1 \le 33.54 \\ 1.36x_1 + 12.077 & ;\ x_1 \ge 33.54 \end{cases} \quad (12)$$

Equation (12) explains that if the hematocrit level of a DHF patient is less than 26.22%, then every 1% addition of hematocrit in a DHF patient will increase the platelet count of a DHF patient at the first blood check by 1.72%. If the hematocrit level of a DHF patient is 26.22% to less than 32.32%, then every 1% addition of hematocrit in a DHF patient will increase the platelet count of a DHF patient at the first blood check by 3.15%.

2. If the variable of hematocrit level in DHF patients is considered constant, then the influence of the hemoglobin level on the platelet count of DHF patients at first blood check is given in Equation (13).

$$\hat{y}_1 = 1.03x_2 - 0.31(x_2 - 8.3)_+ - 0.81(x_2 - 10.3)_+ - 0.90(x_2 - 10.7)_+ \tag{13}$$

The truncated function is given in Equation (14)

$$\begin{cases} 1.03x_2 & ;\ x_2 < 8.03 \\ 0.72x_2 + 2.573 & ; 8.3 \leq x_2 \leq 10.3 \\ 0.22x_2 + 8.343 & ; 10.3 \leq x_2 \leq 10.7 \\ 0.13x_2 + 9.63 & ;\ x_2 \geq 10.7 \end{cases} \tag{14}$$

Equation (14) explains that if the hemoglobin level of a DHF patient is less than 8.03 g/dL, then every 1 g/dL addition to the hemoglobin level in a DHF patient will increase the platelet count of a DHF patient at the first blood check by 1.03 g/dL. If the hemoglobin level of a DHF patient is from 8.3 g/dL to less than 10.3 g/dL, then every 1 g/dL addition to the hemoglobin level in a DHF patient will increase the platelet count of a DHF patient at the first blood check by 0.72 g/dL.

The model for the second response variable is data on the platelet count of DHF patients after three days of treatment. The interpretation for the second response variable spline model is explained as follows:

1. If the variable of hemoglobin level in DHF patients is considered constant, the effect of hematocrit level on the platelet count of DHF patients after three days of treatment is given in Equation (15):

$$\hat{y}_2 = 2.37x_1 + 0.67(x_1 - 35.98)_+ - \ 0.33(x_1 - 37.20)_+ - 0.005(x_1 - 38.42)_+ \tag{15}$$

The truncated function is given in Equation (16)

$$\begin{cases} 2.37x_1 & ;\ x_1 < 35.98 \\ 1.7x_1 - 24.1066 & ; 35.98 \leq x_1 \leq 37.20 \\ 2.04x_1 + 12.276 & ; 37.20 \leq x_1 \leq 38.42 \\ 2.365x_1 + 0.192 & ;\ x_1 \geq 38.42 \end{cases} \tag{16}$$

Equation (16) explains that if the hematocrit level of DHF patients is less than 35.98%, then every 1% addition of the hematocrit in DHF patients will increase the platelet count of DHF patients after three days of treatment by 2.37%. If the hematocrit of a DHF patient is 35.98% to less than 37.20%, then every 1% addition of the hematocrit in DHF patients will increase the platelet count of DHF patients after three days of treatment 1.7%.

2. If the variable of the hematocrit level in DHF patients is considered constant, the influence of the hemoglobin level on the platelet count of DHF patients after three days of treatment is given in Equation (17)

$$\hat{y}_2 = 1.32x_2 - 0.81(x_2 - 11.5)_+ - 0.92(x_2 - 11.9)_+ - 1.03(x_2 - 12.3)_+ \qquad (17)$$

The truncated function is given in Equation (18)

$$\begin{cases} 1.32x_2 & ;\ x_2 < 11.5 \\ 0.51x_2 + 9.315 & ; 11.5 \le x_2 \le 11.9 \\ 0.4x_2 + 10.948 & ; 11.9 \le x_2 \le 12.3 \\ 0.29x_2 + 12.669 & ;\ x_2 \ge 12.3 \end{cases} \qquad (18)$$

Equation (18) explains that if the hemoglobin level of a DHF patient is less than 11.5 g/dL, then each addition of 1 g/dL to the hemoglobin level in a DHF patient will increase the platelet count of DHF patients after three days of treatment by 1.32 g/dL.

3.6. Model Fit Test

The comparison between the actual and predicted data on the platelet count of DHF patients at the first blood checks is given Figure 2.

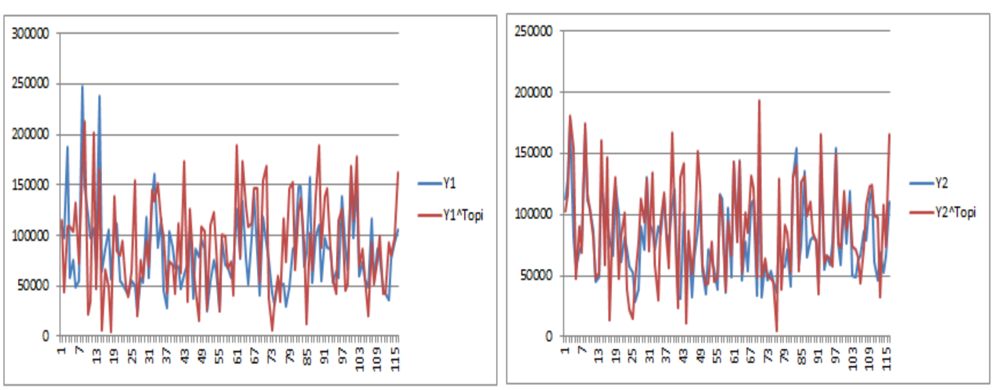

FIGURE 2. Graph of Actual and Predicted Response Variables for Spline Truncated Estimators

The pattern formed from the two lines in Figure 2 does not show a significant difference.

4. CONCLUSION

The best model for data on platelet counts of DHF patients at first check blood and after three days of treatment is birespon spline nonparametric regression model with three knot points. This model gave the smallest GVC value of 97.77 and R^2 of 89.86%. The graph formed by the two lines in Figure 2 does not show a significant difference. The prediction results showed a similar pattern to the actual data. The biresponse nonparametric regression model with spline truncated is generated by Equation (9) dan Equation (10).

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CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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