Identifying the Characteristics of Pregnant Women with Inflammation/Infection in Indonesia

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ABSTRACT

Infection in pregnant women is common and one of the highest causes of death in Indonesia. Reducing infection conditions through early infection prevention needs to be done, one of which is by knowing the characteristics that contribute to the incidence of infection in pregnant women in Indonesia. This study used the Classification and Regression Tree (CART) method to determine the pregnant women with infections and not infections characteristics and classify them. The results of the CART analysis found that seven variables contributed to separating infected and not-infected status in pregnant women, they are nutritional status based on Body Mass Index (BMI), history of anemia, pregnancy distance, Chronic Energy Deficiency (CED) status, ages, socioeconomic and gestational age. Characteristics of the highest incidence of infection, namely 79%, occurred in the group of pregnant women with overweight – obese (BMI>25.0), anemia and pregnancy distance <3 years. The classification analysis of the CART method in this study resulted in the accuracy of identification performance which was still not good, with an accuracy value of 52.78%. It is necessary analysis with other classification methods such as the Chi-square Automatic Interaction Detection (CHAID) in the future.

Keywords: anemia, body mass index, CART, infection, pregnant women

INTRODUCTION

Infection is the entry of viral, bacterial, parasitic, or fungal microorganisms into the body. According to Sinaga and Hasanah (2019), pregnant women are most vulnerable to infection. Based on the Indonesia Health Profile 2020, the number of deaths of pregnant women in 2020 has increased from the previous year, from 4,221 to 4,627 deaths, and one of the highest causes of death is infection. Inflammation /Infection ranks the fourth highest cause of death in pregnant women after bleeding, hypertension, and circulatory system disorders (MoH RI 2021).

The laboratory analysis measured level of C-Reactive Protein (CRP) in serum using Enzyme-Linked Immunosorbent Assays (ELISA). This method was an analysis that can be used as an early marker of infection or inflammation. C-reactive protein is an acute phase protein that increases rapidly in the first 6 to 8 hours after infection and reaches a peak after 48 hours (WHO 2014). Dewi *et al.* (2013) have used this CRP analysis to determine the inflammation/infections status in dyslipidemia patients. However, detection of infection with CRP analisys is still relatively expensive, and not all of hospitals or regional laboratories in Indonesia able to do this analisys, especially for remote areas. However, cases of inflammation/infection in pregnant women in Indonesia must be minimized, so that cases of death or disability in pregnant women and babies born can be suppressed. One effort that can be done to reduce infection cases in pregnant women in Indonesia is to find out what factors are at risk as a cause of inflammation/infection in pregnant women.

Several factors can increase the risk of infection in pregnant women. The increasing infection risk factors are: socioeconomic status (Mohamed *et al.* 2017; Oechsle *et al.* 2020); child spacing of fewer than two years or pregnancy distance of fewer than three years (Mohamed *et al.* 2017); anemia (Sulistyawati & Khanifah 2015; Mohamed *et al.* 2017); nutritional based on Body Mass Index or BMI (Dewi *et al.* 2013; Fakhriadi

et al. 2018); Chronic Energy Deficiency or CED (Fitrianingtyas *et al.* 2018); age when the woman was pregnant (Fitriyah *et al.* 2019); gestational age and number of children (Ginting *et al.* 2019) and young marital age and low education (Surapathi *et al.* 2021) .

Sinaga and Hasanah (2019) stated that most pregnant women are unaware of their infection condition and do not know until the baby with a disability birth. This condition will not only reduce the quality of Indonesian Human Resources (HR) but will also seriously endanger the health and safety of the mother and fetus. Therefore, characteristics contribute to infection incidence need to know of reducing and preventing infections in pregnant women in the future.

One of analyzes to identify characteristics able to use is a classification analysis. This classification analysis had widely applied in everyday life and was used to diagnose a disease in the health field (Suwardika 2017). Analysis of data patterns with this supervised learning approach will produce grouped outputs, so the new data classification from the separator function between one label and another can be searched by studying the available data classes

According to Setiawaty *et al.* (2021), one method for classification without assumptions of statistics is the Classification and Regression Tree (CART) method. This method can see the relationship between the response variable and one or more explanatory variables (Hartati *et al.* 2012). This binary recursive partitioning method will divide the parent node into two child nodes, and then from each child node, it will be divided into two new child nodes. This repeated process until all nodes cannot divide again. Furthermore Nazar (2018) stated advantages of the CART method are: the ability to use both categorical and numerical data types, is not affected by outliers, collinearities, and heteroscedasticity from explanatory variables, and produces easy-to-understand decision trees. Suwardika (2017) used this CART method to classify hepatitis data with a high accuracy value of 83.2%.

In this study, we used the CART method to identify characteristics to determine pregnant women with infection and not infection and classify them. Our hope with knowing the characteristic pregnant women with infection condition will be to use for early detection of pregnant women with infections, and further avoid the causes of infection to reduce infection rates in pregnant women in the future

METHODS

Design, location, and time

The design of this research was secondary data analysis from Riskesdas 2013 data. Riskesdas was a national-scale survey with a cross-sectional and non-interventional design. The research location for Riskesdas 2013 was in 33 provinces in Indonesia, meanwhile the data analysis of this research was conducted in Bogor on February-July 2022.

Sampling

The data used in the research is especially the pregnant women in four age groups: early teens (12–16 years), late teens (17–25 years), early adulthood (26–35 years), and late adulthood (36–45 years). The inclusion criteria for this study are individual data had been complete data for all variables used (Table 1). Exclusion criteria if an individual's data is not a link between the Public Health block data and the Biomedical Block Data in 2013, and Biochemical Biological Materials (BBT) analysis data in 2016 from Biomedical Block samples. The available data includes 360 data on pregnant women respondents from all provinces in Indonesia, both urban and rural. The variables used in the study can be seen and presented in Table 1.

Data collection

The secondary data used in this research consisted of three sets of Riskesdas 2013 data, namely: the Community Health Data RISKESDAS 2013, the Biomedical Data RISKESDAS 2013 and laboratory analysis data from Biochemical Biological Materials (BBT) in 2016. All secondary data RISKESDAS 2013 were obtained from the National Institute of Health Research and Development (NIHRD), Ministry of Health of Republic Indonesia (MoH RI).

Data analysis

The CART method was developed by Leo Breiman, Jerome H. Freidman, Richard A. Olshen, and Charles J. Stone. The CART method is one nonparametric method used to see the relationship between variable response with

Table 1. Research Variables

Notation	Variables	Description	Source
Y	Infection status	0= Inflammation/Infection (if serum CRP>5 mg/l) 1= Not inflammation/Infection/normal (if serum CRP<5 mg/l)	WHO (2014); Mahapatra *et al.* (2021)
X1	Age	1= Early teens (12–16 years old) 2= Late teens (17–25 years old) 3= Early adulthood (26–35 years old) 4= Late adulthood (36–45 years old)	MoH RI (2019)
X2	Nutritional status based on BMI	1= Very thin (BMI is <17.0) 2= Thin (BMI is 17.0-<18.5) 3= Normal (BMI is 18.5–25.0) 4= Fat (Overweight) (BMI is >25.0–27.0) 5= Obese (BMI is >27.0)	MoH RI (2014)
X3	Gestational age	1st trimester (0–13 weeks) 2nd trimester (14–26 weeks) 3rd trimester (27–40 weeks)	Ginting *et al.* (2019)
X4	Pregnancydistance	1= <3 years 2= ≥3 years	Mohamed *et al.* (2017)
X5	Number of children	1= ≤3 children 2= >3 children	Ginting *et al.* (2019)
X6	CED status	0= Not CED (Upper arm circumference >=23.5 cm) 1= CED (Upper arm circumference <23.5 cm)	Fitrianingtyas *et al.* (2018)
X7	Anemia History	0= Normal (not anemia) (Hb≥11 g/dl) 1= Snemia (Hb<11 g/dl)	Sulistyawati & Khanifah (2015)
X8	Socio-economic status	1= Poor 2= Middle 3= Upper	Mohamed *et al.* (2017); Oechsle *et al.* (2020)

CRP: C-Reactive Protein; CED: Chronic Energy Deficiency; BMI: Body Mass Index

one or more explanatory variables (Hartati *et al.* 2012). this method consists of two analyses, namely classification tree and regression tree. When variable the response is categorical data, a classification tree will be generated, but if the response variable is a continuous variable then it will generated regression tree (Breiman *et al.* 1993). Therefore, on research This will produce a classification tree because the response variables used are of type categorical. CART generally works by partitioning or sorting the parent node into two child nodes left and right. Then from each node the child will be the new parent node which will be partitioned again later into two new child nodes. This process takes place continuously until the vertices can no longer be sorted. Therefore, Lewis (2000) mentions that CART is a binary analysis method recursive partitioning. The term "binary" means that each node will be split into two child nodes. The term "recursive" refers to a binary partitioning process done repeatedly. The term "partitioning" describes that dataset divided into sections or partitioned. The process of forming a CART tree This is in line with the

CART method algorithm developed by Breiman *et al.* (1993). The stages in the formation of a CART classification tree includes four things, namely: 1) Sorter Selection: At this stage, the separator of each node will be determined resulted in a decrease in the highest level of heterogeneity. To measure The degree of heterogeneity of a particular node in the classification tree is known with the term impurity measure or improvement. Impurity is a level the variety, randomness or dirtiness of a node. As for those who were chosen to be the best sorter is the one with the highest impurity reduction value. Score High impurity indicates that the node is not yet homogeneous, while a node that has a low impurity value indicates a node it is homogeneous. There are several types of impurity functions, one of which will used is the Gini index. The Gini index is a function of impurities The calculation process is quite simple. As for the equation of the Gini index, that is $i(t)=1-\sum_{j=1}^{j} p^2 (j \mid t)$, where, $p(j \mid t)=\frac{N_j(t)}{N(t)}$, $i(t)$=Gini index Heterogeneity Function, $p(j \mid t)$=Probability of observing category j at node t, $N_j(t)$=Number of categories j at node t, $N(t)$=Number of observations at node t. The heterogeneity reduction of the s selector at the t-th node can be determined based on the goodness of split criteria with the equation: $\Delta i(s,t)=i(t)=P_L$ $i(t_L)–P_R$ $i(t_R)$, where $c\Delta i(s,t)$=Derivation of impurity class to the t-th node, $I(t)$=Heterogeneity function, P_L = Left node observation probability, $i(t_L)$=Impurity value of the left t-node, P_R=Right-node observation probability, $i(t_R)$= Right t-node impurity value. The separator with the highest goodness of split value is the separator the best because it can reduce the highest heterogeneity; 2) Terminal Node Determination: A node t will become a terminal node if at node t it is there was no significant decrease in heterogeneity in the sorting, with In other words, the vertices are homogeneous or because of the minimum limit of cases that are occur. According to Breiman *et al.* (1993), generally the minimum number of cases in a terminal node is 5 cases and if it is met then growth tree will be stopped; 3) Class Marking: According to (Breiman *et al.* 1993), assigning class labels to terminal nodes based on the rule of greatest number, namely: p(j0|t)=jmax p(j|t), where j0=class label for terminal node p(j|t)=probability of observation in the jth category of node t; 4) Classification Tree Pruning: After the classification tree is formed,

the next step is pruning trees to prevent the formation of large trees. A large classification tree will result in a high complexity value (Breiman *et al.* 1993). Therefore, it is necessary to make pruning efforts to obtain a feasible tree size based on cost complexity. Here's the equation: $R\alpha(T)=R(Tk) + |\hat{T}k|$, where is $R\alpha$ (T)=A measure of the complexity of sub-tree T_k at complexity α, R(Tk)=Size of misclassification in sub tree T_k, A=complexity cost parameter, $|\hat{T}k|$=number of tree terminal nodes T_k. Cost complexity can determine the sub-tree T_k that minimizes R(T) for each value of α. The results of pruning are several trees T_k classification and with cross-validation a classification tree can be determined optimal, namely the T_{k0} subtree which has the smallest error value, namely: $R^{Cv}(T_{ku})=\min_k R^{cv}(T_k)$.
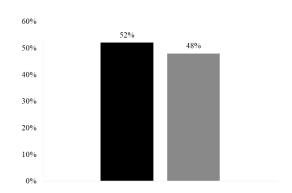
Stages of data analysis procedure

To complete the research, the stages of the data analysis procedure are as follows: 1) Pre-processing data is in the form of labeling data according to the expected variable categories in Table 1; 2) Data exploration using descriptive statistics to find out the percentage of infection and not infection for each categories of independent variables; 3) Divide the data into 80% training data and 20% test data; 4) Classify the status of infection and not infection using the CART method; 5) Interpretation of results, and 6) Assessing the performance of the classification results of the CART method.

RESULTS AND DISCUSSION

Data exploration

Exploration of C-Reactive Protein (CRP) levels data found 188 from 360 pregnant women have inflammation/infections condition and 172 pregnant women without inflammation/infections (Figure 1). The pregnant women with inflammation/infection status are slightly higher than pregnant women without inflammation/infections are 52% vs. 48%. This data includes balanced data because the difference in the percentage of data obtained is not too different. According to Sun *et al.* in Achmad *et al.* (2022), the data with binary classes is unbalanced if the comparison of minor and mayor are 1:100, 1:1,000, or more. Percentage of inflammation/infection and not inflammation/infection status for all explanatory variables is show in Table 2.

Figure 1. Percentage of inflammation/infection and not inflammation/infection status in pregnant women

Table 2 shows that infection status during pregnancy has different percentages each group. Inflammation/Infection status during pregnancy for each age group, gestational age, the number of children, nutritional status based on BMI, CED status, and history of anemia are different. Shown that age, gestational age, number of children, nutritional status based on BMI, CED status, and history of anemia affect the inflammation/infection status of pregnant women, and this followed the research of Fitriyah *et al.* (2019); Mohamed *et al.* (2017); Fakhriadi *et al.* (2018); Fitrianingtyas *et al.* (2018); Sulistyawati and Khanifah (2015), as well as socioeconomic status (Mohamed *et al.* 2017)

Based on the age variable (Table 2), the pregnant women who experience inflammation/infection dominated by the early adult age group (26–35 years), followed by late adolescence and late adulthood. While in the early adolescent group, there were no infected pregnant women, this is likely because the number of women in the early adolescent age group who became pregnant was only one respondent. The age group of early adolescents is still very young, namely 12–17 years (MoH RI 2019), so they are still too young to get pregnant and generally do not have a family. So the number of respondents in this early adolescent group is minimal in this study

Table 2. Shows inflammation/infection status on nutritional status dominated by the obese group or BMI>27 kg, while gestational age dominated in the 3rd trimester of pregnancy. Child spacing of fewer than two years or pregnancy distance of fewer than three years (<3 years) is

Table 2. Percentage of inflammation/infections and not inflammation/infections itatus based on groups of explanatory variables

Explanatory Variables	Number of cases (%)	
	Inflammation/ Infections	Not inflammation/ Infections
Age		
Early teens	0.00	100.00
Late teens	51.33	48.67
Early adulthood	55.15	48.85
Late adulthood	45.10	54.09
Nutritional status based on BMI		
Very thin–thin	42.86	31.82
Normal	42.22	41.03
Overweight	58.97	57.78
Obese	68.18	57.14
Gestational age		
Ist trimester	43.66	45.03
2nd trimester	53.62	46.38
3rd trimester	54.97	56.34
Pregnancy distance		
<3 years	59,26	40.74
>=3 years	50.98	49.02
Number of children		
<=3 Children	52.07	47.93
>3 children	52.45	47.55
CED Status		
Normal (Not CED)	57.71	66.67
CED	33.33	42.29
Anemia history		
Normal (Not anemia)	55.46	44.54
Anemia	45.56	53.44
Socio-economic status		
Poor	55.56	44.44
Middle	48.96	51.04
Upper	57.14	42.86

BMI: Body Mass Index; CED: Chronic Energy Deficiency

also the group with the highest inflammation/ infection cases than the other groups, the same for women with more than three children (Table 2). This condition follows the opinion of Dewi *et al.* (2013); Fakhriadi *et al.* (2018); Fitriyah *et al.* (2019); and Ginting *et al.* (2019).

Table 2 also shows that the percentage of healthy pregnant women (without CED and anemia status) have a higher inflammation/infection than pregnant women with CED and anemia. It is the same with the upper socioeconomic. In upper socioeconomic, cases inflammation /infection cases are more than among pregnant women with lower socioeconomic status. This situation is different from research by Fitrianingtyas *et al.* (2018); Sulistyawati and Khanifah (2015); and Mohamed *et al.* (2017). They found the incidence of inflammation/infection more in CED conditions, anemia, and low economic status. The percentage analysis in Table 2 is only between the same variables and does not consider the interaction between variables, so the results are not yet a decision. So the research continued with CART analysis.

CART analysis

CART analysis of 8 explanatory variables resulted in 21 nodes arranged by seven explanatory variables. The process of pruning the maximum classification tree after the classification tree is formed is carried out to obtain the optimal tree. The trimming process is based on the Complexity Parameter (CP). The CP with the smallest relative error value was chosen to trim the maximum classification tree. Based on Figure 2, the smallest relative error value is
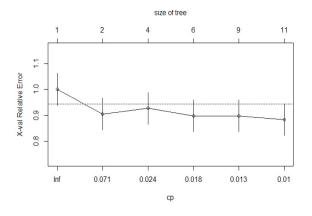

Figure 2. Complexity parameter CART plot

obtained when c=CP is 0.01. Furthermore, the tree is pruned with a value of CP=0.01.

CART analysis after pruning still produced 21 nodes arranged by seven explanatory variables, namely nutritional status based on BMI, history of anemia, pregnancy distance, CED status, ages, socioeconomic and gestational age. The tree of CART analysis results can be seen in Figure 3.

The results of the CART analysis resulted in 11 terminal nodes which were the last nodes of the tree. Terminal nodes showed the classification results of the variables related to the incidence of inflammation/infection. Of the 11 terminal nodes shown dark color area (for pregnant women in the not infected) and the light color area (for pregnant women in the inflammation/infection), there are 5 terminal nodes in the inflammation/ infections category and 6 terminal nodes, not inflammation/infections (Figure 3).

Figure 3 shows that the highest characteristic of infection status in pregnant women is 79% (terminal node 2), followed by terminal node 1, which is 75%, and terminal 7 node at 65%. Interpretation of all of Figure 3 can to reading in Table 3.

Based on the CART method to classify inflammation /infection and not inflammation/ infection status for pregnant women (Figure 3 & Table 3), the highest incidence of inflammation/ infection is 79%. The highest incident occurred in terminal node 2, in the group of pregnant women with BMI>25 kg/m^2 (overweight-obese), who had a history of anemia and with a pregnancy distance <3 years. The result is in line with the research of Fakhriadi *et al.* (2018), which states that a person with a BMI>25 kg/m^2 is more susceptible to infection. The immune system with obese nutritional status (BMI>25 kg/m^2) tends to be poor, so the body does not have an adequate resistance system to fight inflammation/infection.

This study is also in line with Sulistyawati and Khanifah (2015) research, which states that pregnant women with a history of anemia are more susceptible to inflammation /infection because anemia affects the immune system and wound healing process, thereby increasing the infection risks. Our study is also in line with the research of Mohamed *et al.* (2017), which states that the condition of the uterus that has not entirely healed due to postnatal wounds with a pregnancy distance <3 years are more susceptible to inflammation/infection. In addition, women of
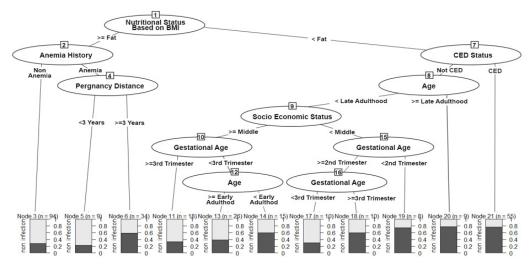
Figure 3. CART analysis classification result tree

Table 3. Classification of inflammation/ infection and not inflammation/infection according to CART analysis

Terminal code	Characteristics	Status	
		Infection	Non-infection
1	Pregnant women with BMI ≥25 kg/m² (overweight−obese) with an anemia condition	75%	25%
2	Pregnant women with BMI ≥25 kg/m² (overweight−obese) and with anemia condition and pregnancy distance <3 years	79%	21%
3	Pregnant women with BMI ≥25 kg/m² (overweight−obese) and with anemia condition and pregnancy distance ≥3 years	40%	60%
4	Pregnant womon with BMI <25 kg/m2 (very thin−normal), not CED status, age <36 years, upper-middle socioeconomic status, and gestational age 27−40 weeks.	62%	36%
5	Pregnant women with BMI <25 kg/m² (very thin−normal), not CED status, age 26−35 years, middle to upper socioeconomic status, and gestational age <27 weeks	60%	40%
6	Pregnant women with BMI <25 kg/m² (very thin−normal), not CED status, age <26 years, upper-middle socioeconomic status, and gestational age <27 weeks	40%	60%
7	Pregnant women with BMI <25 kg/m² (very thin−normal), not CED status, age <36 years, lower socioeconomic status, and gestational age 14−26 weeks	65%	35%
8	Pregnant women with BMI <25 kg/m² (very thin−normal), not CED status, age <36 years, lower socioeconomic status, and gestational age 27−40 weeks	40%	60%
9	Pregnant women with BMI <25 kg/m² (very thin−normal), not CED status, age <36 years, lower socioeconomic status, and gestational age 1−13 weeks	22%	78%
10	Pregnant women with BMI <25 kg/m² (very thin−normal), status not CED, age 36−45 years	21%	79%
11	Pregnant women with BMI <25 kg/m² (very thin−normal), status CED	21%	79%

BMI: Body Mass Index; CED: Chronic Energy Deficiency

childbearing age who do not practice birth control and experience pregnancy at a close distance can increase the risk of lack of nutrients the body needs. For example, there is a lack of folic acid intake, which functions to form red blood cells. If the information on folic acid is not enough, it will result in reduced red blood cell production and will increase the occurrence of anemia. This anemia condition can also increase the risk of inflammation/infection in the body. This is in line with the study of Liyew *et al.* (2021). They found that anemia, in this case, iron deficiency anemia was an independent factor associated with inflammation/infection among surgical patients studied.

An analytical accuracy test was carried out to assess the accuracy of the classification results. The results of accurate test results of the CART method are presented in Table 4. The accuracy value of the classification results of the CART method for this study is 52.78%, with the sensitivity value or the proportion of positive infections that were classified correctly was 51.35%, and proportion correctly classified of not infections was 54.29%. Difference types of data cause different the results, which means the CART method unsuitable for this data, even though Suwardika (2017) found high accuracy value of 83.2% for groups of hepatitis data. Other classification methods like the Chi-square Automatic Interaction Detection (CHAID) can be used to improve the performance the results. The method can be applied to this data so that the results of identifying characteristics that contribute to the incidence of inflammation/ infection in pregnant women in Indonesia are more accurate.

Table 4. The accuracy of CART classification using test data

Observation	Prediction		Accuracy (%)
	Non-infection	Infection	
Non-infection	19	16	51.35
Infection	18	19	54.29
Accuracy			52.78

CONCLUSION

Seven variables that play a role in separating infection and non-infection in pregnant women based on the results of CART analysis are nutritional status based on Body Mass Index (BMI), history of anemia, pregnancy distance, Chronic Energy Deficiency (CED) status, age, socioeconomic and gestational age. Meanwhile, the highest incidence of inflammation /infection, which is 79%, occurred in the group of pregnant women with overweight-obese (BMI>25.0), anemia, and a pregnancy distance <3 years. CART classification analysis performed poorly in classifying pregnant women with inflammation/ infection, with an accuracy value of 52.78%

This study showed that identification performance accuracy is still not good, with an accuracy value of 52.78%. It is necessary to carry out a classification analysis with other methods, such as the Chi-square Automatic Interaction Detection (CHAID) method so that the results of identifying characteristics that contribute to the incidence of inflammation /infection in pregnant women in Indonesia are more accurate with higher sensitivity.

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DECLARATION OF INTERESTS

All the authors have no conflict of interests.

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