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MODELING DENGUE DISEASE TRANSMISSION FOR JUVENILE IN BANDUNG, INDONESIA

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Abstract. Dengue disease is the most common mosquito-borne viral diseases in the world, especially in Bandung, Indonesia. Juvenile age group is important to be considered in dengue management since the number of cases in this age group is significantly increasing year by year especially in Bandung, West Java, Indonesia. Another concern to pay special attention to this age group is because dengue infection among juveniles shall hinder their growing process and influence their academic achievement at schools. Apart from that, it will lower parents' productivity as they have to be absent from work, and they have to spend expenses for medication. One of the effective and efficient strategies to prevent the transmission is by analysing the spatial and temporal distribution of dengue disease incidence and its trend. In this study, the random effect Generalized Linear Mixed Model (GLMM) is applied and numerical Bayesian method through Integrated Nested Laplace Approximation (INLA) is used. The models are applied to dengue disease incidence in year 2013 for the juvenile group in Bandung.

Keywords: dengue disease; disease mapping; spatiotemporal model; Bayesian; posterior.

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1. INTRODUCTION

According to [1], dengue disease is a mosquito tropical disease which most rapidly spreading in the world. It can cause death if it is not treated properly. It is estimated that 50 million dengue incidences occur annually. This disease is transmitted by Aedes mosquitoes when they bite human bodies for their blood meal. The habitat of the mosquitoes is in the tropics having warm temperatures, in the regions below 1,000 meters sea level Indonesia. Bandung, especially, lies in the region having such suitable criteria for the mosquitoes to live and breed. In addition to this, the risk of dengue disease in Bandung becomes higher by the fact that Bandung has high population density. From Bandung Health Department, the number of dengue incidences has increased dramatically over the last four years. In 2010, there were 3,434 cases and in 2013, it increased to 5,735 cases.

Dengue disease is one of the major public health problems in Bandung, Indonesia, mainly because there are a lot of dengue disease infecting juvenile age group in Bandung. In 2011, there were 1,758 juveniles infected with dengue disease; in 2012, the number increased to 2,284; and in 2013, it rose up to 2,890 cases. The disease certainly becomes a concern because it disrupts the school time and influences the quality of the youth in Indonesia. It also causes financial loss because parents cannot work well and there will be cost for medication and treatment. Further loss is on productivity due to the unpaid time of caregiver. Therefore, it is important to pay more attention to prevent the transmission of the disease within the juvenile age group.

The spatiotemporal model is indispensable in order to know the stability of the relative risk which cannot be evaluated only by the spatial model [2]. Monitoring the spatial spread of a disease, particularly for a disease such as dengue disease with a very high diffusion rate, is required to identify regions that have great potential to become endemic. Hence, mapping the high-low risk distribution of dengue disease cases may help reduce the number of incidences in the future. Spatiotemporal disease mapping have been used extensively to determine the temporal change of the geographical pattern of mortality/morbidity rate [3,4]. Discrete-space stochastic Susceptible-Infective-Removed (SIR) is the other alternative method that also usually used for modeling and

mapping disease transmission [5].

Some studies have worked on the analysis of age group related to dengue cases. Several publications discussed dengue mapping, concentrating on age group, but none has applied the Bayesian [5-8]. Some researches discussing dengue mapping in Bandung region used Bayesian approach and focused on age group, however, they used MCMC algorithm [9, 10].

The main aim of this study is to estimate the dengue relative risk in Bandung by means Bayesian Spatiotemporal model, focus on juvenile age group. The basic model used is Generalized Linear Mixed Model (GLMM) dealing with count data and assuming the number of cases that follow a Poisson distribution. In this research, the estimated parameter of Spatiotemporal model has used the Bayesian method with a new method called Integrated Nested Laplace Approximations (INLA). INLA has been used to solve marginal posterior distribution in estimating posterior distribution. The computing time of Bayesian Inference is faster than MCMC algorithms [3, 11].

The structure of the paper is structured as follows: in Section 2, Spatiotemporal model is estimated with INLA are discussed. A brief review of the INLA method and the resulting analysis of dengue disease data in Bandung City are elaborated in Section 3. The paper is closed with a conclusion in Section 4.

2. METHOD

In this Section, the Spatiotemporal models are elaborated and parameters of the model are estimated using Bayesian method. INLA technique is explained and applied in Bayesian method to estimate the posterior distribution [5].

2.1. Spatiotemporal Modeling

This study proposes a Spatiotemporal GLMM involving spatially correlated and temporally auto-correlated random effects [12]. Let $\{y_{it}: i = 1, \dots, \text{and } t = 1, \dots, T\}$ be the number of dengue disease data collected from district *i* at time point *t*. Next, E_{it} is defined as the expected number of case for district *i* at time point *t*. In this case, E_{it} is computed using indirect standardization

with total population as the reference. y_{it} is modelled as conditional to E_{it} and θ_{it} as a standard Poisson distribution [5]:

$$y_{it}|E_{it}, \theta_{it} \sim Poisson(E_{it}\theta_{it}), \quad (1)$$

and,

$$\theta_{it} = \exp(X'_{it}\beta_{it} + f(z_{it})), \quad (2)$$

where θ_{it} is the parameter of the relative risk at region *i* and time *t* and $X'_{it} = (1, X_{it1}, \dots, X_{itP})'$ denotes the design vector of *P* covariates including vector one of district *i* at time *t,* $\boldsymbol{\beta}_{it} = (\beta_{it0}, \beta_{it1}, \dots, \beta_{itP})'$ denotes the corresponding coefficient vector and $f(z_{it})$ denotes the latent function that accommodates the Spatiotemporal dependencies, with z_{it} describes the unobserved latent variable.

Spatiotemporal disease mapping models have been introduced in the literature, most of them based on Conditional Autoregressive (CAR) and combined with convolution prior which well-known as BYM model [3]. Several models can be defined, depending on the specification of $\eta_{it} = \log(\theta_{it})$.

2.2. Linear Time Trend Model

The most common way to estimate the relative risk of disease mapping which has a temporal dimension is to account a number of cases of disease within small regions available for a sequence of T time periods. The some models have been developed to accommodate the spatial and time effects simultaneously in which both region specific intercept and temporal trend are modeled as a random effect [13]. The model is developed from the BYM spatial model with an additional nonparametric dynamic time trend for each small region. The extension of standard disease mapping model which accommodates the temporal component as [4],

$$\eta_{it} = b_0 + u_i + v_i + Temporal, t = 1, \dots, T, \quad (3)$$

where b_0 accounts the log of the global risk, u_i is structured spatial effect in region *i*. The model usually used to present the structured spatial effect is BYM model ([14]):

$$\pi(u|\kappa_u) \propto \kappa_u^{\frac{n-1}{2}} \exp\left(-\frac{\kappa_u}{2}\sum_{i\sim j}(u_i - u_j)^2\right), \quad (4)$$

where κ_u is called precision parameter. Two districts i and j are defined to be neighbours, and $i\sim j$, if they are neighbouring. Further, $\boldsymbol{u}$ are independent zero mean normal with unknown

precision parameter κ_v. The component v_i describes the unstructured one, where $v_i \sim N(0,1/\kappa_v)$. Temporal term accommodates the parametric or nonparametric structure which is enumerated below.

(1) **Model 1**: Parametric Trend

In this model, the temporal component in Equation (3) accommodates the parametric trend with the linear predictor [13]:

$$\eta_{it} = b_0 + u_i + v_i + (\beta + \delta_i) \times t. \quad (5)$$

where β denotes an overall linear time trend and δ_i accounts the interaction between the linear time trend and spatial effect u_i.

(2) **Model 2**: Nonparametric Dynamic Trend

In Knorr-Held (2000) [15], the temporal component in Equation (3) is elaborated as,

$$\eta_{it} = b_0 + u_i + v_i + \gamma_t + \phi_t, \quad (6)$$

with $\gamma_t|\gamma_{t-1},\gamma_{t-2} \sim Normal(2\gamma_{t-1} + \gamma_{t-2}, \sigma^2)$. γ_t is the temporally structured effect and ϕ_t is means of a Gaussian exchangeable prior and distributed $Normal(0, {}^{1}/_{\kappa_\phi})$.

(3) **Model Interaction**: Space-Time Interaction

In this model, expanded Model 2 to consider the space-time interaction accommodated in δ_{it} term as below [15],

$$\eta_{it} = b_0 + u_i + v_i + \gamma_t + \phi_t + \delta_{it}. \quad (7)$$

where δ_{it} in Equation (7) can be extended to define the structure matrix, elaborated in [4] as figured out in Table 1.

Table 1. Interaction types

Model	Parameter Interacting	Rank
Model 3	v_i and ϕ_t	nT
Model 4	v_i and γ_t	$n(T-2) for\ RW2$
Model 5	ϕ_t and u_i	$(n-1)T$
Model 6	u_i and γ_t	$(n-1)(T-2) for\ RW2$

For Models (4) and (6), this study only considers the random walk of order 2 (RW 2). In this research, those six models are compared to find the best model for the analysis.

2.3. Integrated Nested Laplace Approximation (INLA)

INLA is designed as the alternative of MCMC approaches of the Bayesian inference to solve marginal posterior distribution in estimating posterior distribution. This method is applicable in spatial, Spatiotemporal models, epidemiology, ecology, and environmental risk assessment [3, 5, 11].

A Bayesian hierarchical with three stages is used to estimate the Spatiotemporal models. The first stage is the likelihood model $\boldsymbol{\pi}(\boldsymbol{y}|\boldsymbol{\Phi})$; the second stage is the latent Gaussian Markov Random field (GMRF), $\boldsymbol{\pi}(\boldsymbol{\Phi}|\boldsymbol{\psi}) \sim N\left(\boldsymbol{\mu}_{\boldsymbol{\psi}}, \boldsymbol{Q}_{\boldsymbol{\psi}}^{-1}\right)$, and the third stage is the hyperparameter $\boldsymbol{\pi}(\boldsymbol{\psi})$ controlling parameters model. Here, **y** denotes the number of dengue disease incidence and $\boldsymbol{\Phi} = (\alpha, \boldsymbol{f})'$ denotes the random vector consisting of all terms of the structured additive predictors which have Gaussian priors; and $\boldsymbol{Q}_{\boldsymbol{\psi}} = \boldsymbol{\Sigma}^{-1}$ denotes the precision matrix. To complete the Bayesian model, the following prior distributions are specified as under [5]:

$$b_0 \sim N(0, 10^6)$$

$$\kappa_i, \kappa_u, \kappa_v, \kappa_\gamma, \kappa_\phi, \kappa_\delta \sim \text{Gamma } (1, 0.0005)$$

The prior distributions defined on those parameters are weakly informative and independent so that the estimation and inference for these parameters are based mainly on the data. Gamma distribution is used for hyperparameter due to Gamma distribution is a conjugate hyperprior. The advantage of conjugate distribution the advantage of conjugate prior is speeding up computational time and relatively narrow credible intervals. Hal-Cauchy, Penalized Complexity, and Uniform priors are the other priors that can be a good alternative for Gamma distribution in case to avoid the sensitivity problem of Gamma hyperprior.

Finally, the relative risk ($\hat{\theta}_{it}$) estimates are calculated from the exponent of $\hat{\eta}_{it}$ with $\hat{\eta}_{it}$ obtained from one of the Equations (5) - (7) depending on model selection. Generally, it can be written as the following [5]:

$$\hat{\theta}_{it} = \exp(\hat{\eta}_{it}) ; i = 1,..,N, t = 1,2,\dots,T. \quad (8)$$

2.4. Model Selection

There are several criteria of the model selections, Deviance Information Criterion (DIC) and coefficient determination R^2. $DIC = \overline{D} + p_D$ where $\overline{D}$ is the posterior of the mean deviance and measure model fit; and p_D is the effective number of model parameters and measures model complexity [5]. The coefficient determination $R^2 = \frac{\sum_{j=1}^{m}(\hat{y}_j - \bar{y})^2}{\sum_{j=1}^{m}(y_j - \bar{y})^2}$ for j=1,2,..,m denotes the index of the observation. The best model has smallest DIC and highest R^2 [16-19].

3. RESULT AND DISCUSSION

3.1. Data Description

The dengue disease data used in this study were 2013's data provided by seven reputable hospitals in Bandung. The number of juvenile cases is observed weekly since the incubation time of dengue disease is 4 – 8 days. Therefore, we have 52 observations from 30 sub-districts and the total number of observations is 1,560 observations while the total number of juvenile dengue cases is 2,768 cases.

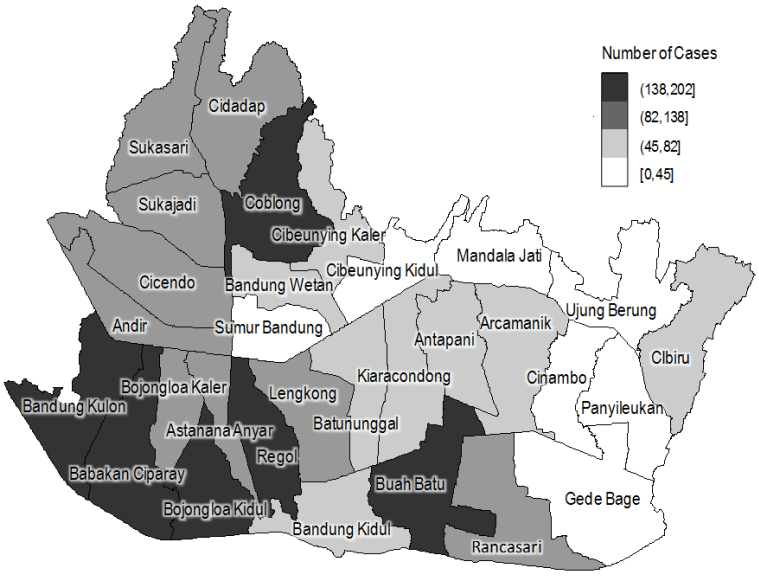

Figure 1. Distribution the number of dengue cases for Juvenile in Bandung City in 2013

Figure 1 shows the distribution of the total number of dengue cases for Juvenile in a year. Dengue cases for juvenile are mostly found in sub-districts located in the south-west region of Bandung (e.g., Bandung Kidul, Babakan Ciparay, Bojongloa Kidul); on the other hand, the eastern regions usually have a small number of cases (e.g., Gede Bage, Penyileukan, Cinambo, and Ujung Berung).

In epidemiology study, the standardized morbidity ratio (SMR) has been commonly applied. SMR is an unbiased estimate of the relative risk but it is unreliable if it is applied to a small region as discussed in Tango (2010). The heterogeneity and autocorrelation problems detected in previous studies can be accommodated by the spatial and temporal risk information and autocorrelation to give a reliable estimate of the risk. Therefore, we propose the Spatiotemporal models, i.e. Model 1 – Model 6 mentioned in the previous section to model and estimate the relative risk of dengue disease. We propose six different models for estimating the relative risk of dengue disease for the juvenile at 30 sub-districts of Bandung City.

Table 2. The relative risk interval

Model	Interval			Mean	Standard deviation
SMR	0.000	-	17.493	1.244	1.696
Model 1	0.154	-	5.592	1.239	1.117
Model 2	0.180	-	4.381	1.232	1.076
Model 3	0.179	-	4.386	1.232	1.077
Model 4	0.161	-	8.206	1.251	1.180
Model 5	0.187	-	4.460	1.237	1.077
Model 6	0.092	-	9.112	1.254	1.222

Table 2 presents the interval, mean and standard deviation of weekly relative risk estimates based on SMR and six different models. SMR estimates the relative risk with high variability of

the relative risk estimations from zero to 17.493. This indicates that the SMR provides crude estimates due to heterogeneity and autocorrelation problems and this condition is in accordance with the elaboration about SMR drawbacks in [20]. The estimates of the relative risk based on SMR estimation needs to be smoothed using the Spatiotemporal model by introducing the random effect model to overcome the heterogeneity and autocorrelation problems. We used INLA numerical Bayesian approach with R-INLA package to estimate the Spatiotemporal model with six different characteristics. Models (1) – (6) present the estimates of the relative risk for Juvenile based on Spatiotemporal models. We use R^2 and DIC criteria to select the best model for Juvenile.

Table 3. Model selection based on R^2 and DIC

Model	R^2	DIC
Model 1	0.48	4601.39
Model 2	0.49	4621.04
Model 3	0.49	4621.04
Model 4	0.51	4607.51
Model 5	0.45	4718.40
Model 6	0.52	4595.84

The criteria of the best model are the models with the largest R^2 value and the smallest DIC. Based on these criteria [16, 17], Model (6) can be concluded as the best model.

3.3. Model Interpretation

In this section, the relative risks of dengue transmission among juveniles in Bandung are estimated. It is important to consider the local estimator of the relative risk of each sub-district in this region. There are five random effect parameters which influence the local estimator in this case, i.e.: spatial heterogeneity (v_i), spatial autocorrelation (u_i), temporal heterogeneity (ϕ_t), temporal autocorrelation (γ_t) and spatio temporal interaction (δ_{it}) which are explained in Equation (7). The posterior mean of the standard deviation of the hyperparameters displayed in Table 4.

Table 4. The posterior mean of the standard deviation of the hyperparameters of the random effect components[a]

Random Effect Parameter	Posterior Mean	Fraction variance (%)
SD of the Spatial Heterogeneity(σ_v^2)	0.0221	44.654
SD of the Spatial Autocorrelation (σ_u^2)	0.0219	43.994
SD of the Temporal Heterogeneity (σ_ϕ^2)	0.0049	2.172
SD of the Temporal Autocorrelation (σ_γ^2)	0.0065	3.853
SD of the Spatiotemporal Interaction (σ_δ^2)	0.0076	5.326

[a]SD: Standard deviation

Table 4 shows that the spatial heterogeneity and spatial autocorrelation has the largest fraction variance followed by spatiotemporal interaction. It means beside of spatial heterogeneity and spatial autocorrelation, the spatiotemporal interaction is the most important random effect of Model (6). It indicates that the spread of dengue cases in a juvenile age group in Bandung is affected by the interaction between spatial and temporal effect. The analysis of these effects is discussed later after the weekly relative risks of each sub-district are determined.

Further, the weekly relative risks of each sub-district are estimated using SMR model and the most suitable model, i.e.: Bayesian Spatiotemporal Model (Model 6). Six selected Sub-districts are displayed in Figure 2 (the other sub-districts are provided upon by request). The red colour line is the relative risk based on SMR and the black colour line is the relative risk based on Bayesian Spatiotemporal Model (BST).

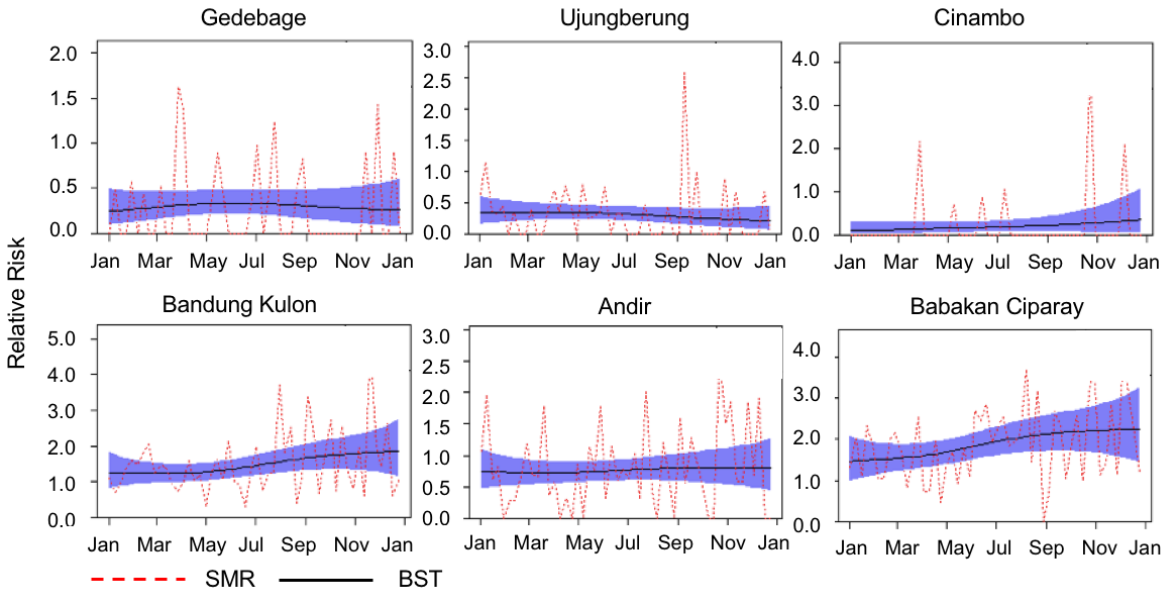

Figure 2. The Relative Risk Estimations for six selected sub-districts in Bandung City

The BST line clearly shows the smoothing temporal pattern of the relative risk for juveniles for six selected sub-districts in Bandung City. This fact is in line with the previous studies which emphasized that Bayesian model is better than SMR model because it is smoother and has the capability to remove the noise by considering spatial and temporal effects [18, 21, 22]. Therefore, it can be concluded that this model is more reliable.

There are five levels of relative risk defined here, i.e. very low $(0,0.5]$, low $(0.5,1]$, medium $(1,1.5]$, high $(1.5,2]$, and very high $(2,\infty]$. From Figure 2, it is obtained from regions which have medium until very high risk that dengue disease is estimated to have risk to spread relatively within the months around the beginning and end of the year: in the beginning of the year is around January – March; while at the end of the year is about October – December. The cause is high rainfall that leaves a lot of puddles of clean water which are the habitat of the mosquitoes. Apart from that, the immunity of juveniles in rainy season is decreasing, hence, juveniles have a higher risk to be infected by dengue This condition is in accordance with the analysis of some previous studies although they were conducted in different regions and used different method [9, 23].

4. CONCLUSION

Juvenile age group is important to be considered in dengue management since the number of cases in this age group is significantly increasing year by year especially in Bandung, West Java, Indonesia. Another concern to pay special attention to this age group is because dengue infection among juveniles shall hinder their growing process and influence their academic achievement at schools. Apart from that, it will lower parents' productivity as they have to be absent from work, and they have to spend expenses for medication. The dynamic temporal trend can be used to develop etiology hypothesis about high-risk sub-districts and it is important information for official health office for developing an early warning system of dengue disease. According to the result of this model, it can be concluded that dengue disease is high potential to spread in sub-districts Coblong, Babakan Ciparay, Bojongloa Kidul; and very high potential to spread in sub-districts Sukasari, Bojongloa Kaler, Regol, Buah Batu and Rancasari. In addition, it can be concluded that juveniles in Bandung are relatively having a high risk to be infected by dengue disease during the rainy season around January – March, and October – December.

For further study, it is suggested to consider other factors, i.e.: the climatology data, environmental, economic aspects and social conditions, elevation, to be included into the models to have a better picture of the disease transmission [24, 25]. The model can be extend by accommodating the varying coefficients for each covariates [26, 27]. Applying the same model to data of the following years is also highly recommended to verify the relevance of this study with the real condition in the following years.

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CONFLICT OF INTERESTS

The author(s) declare that there is no conflict of interests.

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