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ORIGINAL ARTICLE

Are There Spatial and Temporal Correlations in the Incidence Distribution of Scrub Typhus in Korea?

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Abstract
Objectives: A hierarchical generalized linear model (HGLM) was applied to estimate the transmission pattern of scrub typhus from 2001 to 2011 in the Republic of Korea, based on spatial and temporal correlation.
Methods: Based on the descriptive statistics of scrub typhus incidence from 2001 to 2011 reported to the Korean Centers for Disease Control and Prevention, the spatial and temporal correlations were estimated by HGLM. Incidences according to age, sex, and year were also estimated by the best-fit model out of nine HGLMs. A disease map was drawn to view the annual regional spread of the disease.
Results: The total number of scrub typhus cases reported from 2001 to 2011 was 51,136: male, 18,628 (36.4%); female, 32,508 (63.6%). The best-fi;t model selected was a combination of the spatial model (Markov random-field model) and temporal model (first order autoregressive model) of scrub typhus transmission. The peak incidence was 28.80 per 100,000 persons in early October and the peak incidence was 40.17 per 100,000 persons in those aged 63.3 years old by the best-fit HGLM. The disease map showed the spread of disease from the southern central area to a nationwide area, excepting Gangwon-do (province), Gyeongsangbuk-do (province), and Seoul.
Conclusion: In the transmission of scrub typhus in Korea, there was a correlation to the incidence of adjacent areas, as well as that of the previous year. According to the disease map, we are unlikely to see any decrease in the incidence in the near future, unless ongoing aggressive measures to prevent the exposure to the vector, chigger mites, in rural areas, are put into place.

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1. Introduction

Scrub typhus is one of the major febrile diseases occurring in autumn in the Republic of Korea (hereafter, "Korea"). Its causative organism, *Orientia tsutsugamushi* is transmitted by chigger mites such as *Leptotrombidium pallidum* and *Leptotrombidium scutellare* [1]. Chigger mites are carried by wild rodents. *Apodemus agrarius, Mus musculus, Microtus fortis, Micromys minutus, Tscherskia triton,* and *Rattus norvegicus* have been known to be serologically positive for *O. tsutsugamushi* in Korea [2]. Reports of the incidence of scrub typhus in Korea have been increasing [3]. To identify the annual pattern of scrub typhus incidence according to age and sex in Korea from 2001 to 2011, we propose the use of a hierarchical generalized linear model (HGLM), which has been used to identify the annual pattern of malaria in Korea [4]. In this paper, using a variety of combinations of spatial and temporal correlation models, we aim to address the following questions: (1) What is the annual changing pattern of incidence? (2) What is the geographical pattern of incidence? (3) Are there spatial or temporal correlations of the scrub typhus incidence pattern?

The HGLM is applied to understand how the incidence of scrub typhus has spread spatially over consecutive years, which helps in control and prevention of scrub typhus transmission in Korea.

2. Materials and Methods

2.1. Data collection and management

Data were collected by the Korean Centers for Disease Control and Prevention from 2001 to 2011 from medical clinics and hospitals, as well as health centers, based on the "Law on the prevention and control of infectious diseases" in Korea. Scrub typhus is one of the communicable diseases that should be reported to a health center, by law. Age, sex, city or county of resident, and month and year of occurrence, were obtained from the reporting system. Data manipulation was performed in the same way as in our previous work on *Plasmodium vivax* malaria [4]. Data are grouped according to sex, address, and year. The age of each group is the mean age of infected persons. Also, the month of infection was a mean of the number of months (period of time) each person was reported to be infected. The incidence in each city or county was standardized, based on the number of infections per 100,000 persons in the population. Populations in each city or county were obtained from the website of Statistics Korea, available from: http://kostat.go.kr. In this analysis, we used the same R script as in our previous work and the same dhglmfit() function in the R package dhglm from the Comprehensive R Archive Network (CRAN) [5].

2.2. Statistical model

$$y_{itk}|u_i, v_{it} \sim Poisson(\mu_{itk})$$

$$\eta_{itk} = \log\left(\mu_{itk}\right) = \log\left(\frac{N_{itk}}{100,000}\right) + \beta_0 + \beta_1 I\left(k=2\right) + b\left(age_{ik}\right) + c\left(month_i\right) + u_i + v_{it}$$

where, η_{itk} is the linear predictor, μ_{itk} is the conditional expected numbers of cases, N_{itk} is the population of group (city or county) acquainted from Statistics Korea according to sex and year, age_{ik} is the mean age of infection occurrence between year 2001 and 2011 out of i^{th} city or county, month$_i$ is the mean month of infection occurrence between year 2001 and 2011 out of i^{th} city or county, $b(age_{ik})$ is the smoothing spline on the mean age of infection occurrence, $c(month_i)$ is the smoothing spline on the mean month of infection occurrence, u_i is the random effects for temporal model and v_{it} is the random effects for spatial model.

We considered 3 spatial models for u_i and 3 temporal models for v_{it}, which were the same as in our previous work [4]. Spatial Model 1 is the independent model, where the incidence of a region is assumed to be independent of adjacent regions, $u_i \sim i.i.d.\ N(0, \lambda_1)$

Spatial model 2 and 3 assume spatial effects where the incidence of a region is affected through adjacent regions. Spatial model 2 is the intrinsic autoregressive model, $u_i \sim IAR$ with kernel $\sum_{i\sim j}(u_i - u_j)^2/\lambda_1$. Spatial model 3 is the Markov random-field model, $u_i \sim MRF$ with $\mathrm{var}(u)^{-1} = (I - \rho N)/\lambda_1$

Table 1. Value of conditional Akaike information criterion of each combination model for the estimation of three spatial and three temporal correlations of scrub typhus in Korea from 2001 to 2011, according to the cases reported to the Korea Centers for Disease Control and Prevention.

		Temporal model		
		1	2	3
Spatial model	1	113,692.1	113,236.6	109,421.0
	2	113,578.8	113,116.4	109,368.2
	3	113,530.2	113,074.7	109,253.0