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Determinants of regional differences in the incidence of impetigo ☆

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Abstract

Background and objective: Impetigo is a common contagious skin infection, mostly seen in children and caused by *Staphylococcus aureus* and/or group A B-hemolytic Streptococcus. Two surveys performed in general practice showed a strong geographical gradient in the incidence rates among children in the Netherlands. The incidence in the south was approximately twice as high as in the rest of the Netherlands. We hypothesized that this difference could be explained by differences in the presence of animal farms and differences in temperature. This study examined whether there is a relationship with the numbers of bovines, pigs, sheep, and poultry per km^2, and temperature, which could explain the observed regional gradient in the incidence of impetigo.

Design and setting: In this ecological study, data on the incidence of impetigo in children 0–17 years of age from the second Dutch national survey were linked to data on the density of farm animals from Statistics Netherlands and temperature data from the Dutch Metereological Service. Using logistic regression allowing for overdispersion, we tested the significance of the effect of bovines, pigs, sheep, and poultry per km^2, and temperature on the incidence of impetigo, correcting for known risk factors.

Results: Only the number of sheep at the (COROP) regional level was significant; however, this effect could not explain the regional differences.

Conclusion: The regional differences in the incidence of impetigo in children cannot be explained by the variation in the presence of farm animals or differences in temperature.

1. Introduction

Impetigo is a common contagious skin infection, mostly seen in children and caused by *Staphylococcus aureus* and/or group A B-hemolytic Streptococcus (Hay and Adriaans, 2004). It is generally believed that several risk factors in humans are associated with the occurrence of impetigo, including poor hygiene and crowding. In developed countries, although the incidence of impetigo has been declining for decades, recently there has been an increase ([Koning et al., 2006a] and [Koning and Jabaaij, 2006b]). Impetigo occurrences are higher in hot humid environments and exhibit seasonal variation. A peak incidence of impetigo has been reported in summer and autumn (Kristensen, 1991; Elliot et al., 2006; Rogers et al., 1987); this may be related to closer unprotected skin contact, or to extra skin injuries due to cuts or insect bites in summer. Significant resistance rates of *S. aureus* against commonly used topical treatments have recently emerged in several countries (Howden and Grayson, 2006; Deshpande, 2002).

In the Netherlands, impetigo is the third most common skin disorder in children presented to the general practitioner (GP) (Koning et al., 2006a). Two surveys performed in Dutch general practice showed a geographical gradient in the incidence of impetigo (Koning et al., 2006a). The twofold higher incidence in the south compared with the north was striking, especially for a small country like the Netherlands, although the difference in flowering of fruit trees between south and north is considerable. Other authors found a north–south gradient for the occurrence of MRSA infections in Ireland (Mc Donald et al., 2002).

We hypothesized that temperature differences between north and south may be one explanation. An earlier study showed a relationship between impetigo and temperature with insect bites as a potential intermediate factor (Elliot et al., 2006).

Another explanation may be the distribution of farm animals in the Netherlands, as pig farms are predominantly located in the south. A study among pig farmers in France showed that they were more frequently nasal carriers of *S. aureus* than matched non-farmers, and that isolated samples of *S. aureus* were more frequently macrolide resistant (Aubry-Damon et al., 2004). It is also reported that pyogenic skin infection in humans can be caused by *S. aureus* of animal host origin (Rao et al., 1987).

The aims of the present study were to investigate regional differences in the occurrence of impetigo in the Netherlands, and the relationship between this regional gradient, and the presence of animal farming, climatological circumstances and demographic characteristics.

2. Materials and methods

2.1. Study population and data sources

To study the incidence of impetigo in children in the Netherlands we used data from the Second Dutch National Survey of General Practice (Westert et al., 2005). A total of 195 GPs in 104 practices registered data on all physician–patient contacts during 12 months in the years 2000–2002. Of these 104 practices, 8 were excluded because of insufficient data quality. Because we limited the study to the incidence in children, only data from patients aged 0–17 years were analyzed. We also restricted ourselves to the data collected in the year 2001, to have a common timeframe for all practices. This amounted to 87% of the person-years that were observed during the survey period.

To test our hypotheses, we chose an ecological design, by linking geographically aggregated data from the patients’ GP records to meteorological data and to data on geographical distribution of both humans and livestock.

2.2. Outcome

The outcome variable in this study was the incidence of impetigo during 12 months. Impetigo was diagnosed by GPs at a patient consultation and coded with the International Classification for Primary Care (ICPC) as S84 (Lamberts and Wood, 1987). To determine the incidence, we checked whether or not a patient had an episode of impetigo in 2001, i.e. every impetigo patient counted once, irrespective of the number of episodes.

2.3. Independent variables

The independent variables related to the study hypotheses are number of bovines, pigs, sheep, and poultry per km^2, and day temperature. Other variables were taken into account that could potentially influence the relation between the variables of interest and impetigo. These variables, which were adjusted for when we tested our hypotheses, are region, population density, proportion of people working in the agricultural sector, the patient's age and gender, family size, and socioeconomic class.

Data on the numbers of the four types of livestock (bovines, pigs, sheep, and poultry) were obtained from the Statline database of Statistics Netherlands [www.cbs.nl/statline]. In order to incorporate both local and regional influences, both the number of animals at municipal level in which the practice of the GP was located and the number of animals at a regional level (COROP) were included in our analysis. The COROP classification divides the Netherlands into 40 regions following a nodal principle, with a central nucleus (often a city) surrounded by the adherent region. Six of these regions did not contain participating GPs. The information on temperature was obtained from the Royal Netherlands Meteorological Institute. The data are for the year 2001, measured by 10 weather stations, throughout the country. To obtain temperature data for each practice location, piecewise linear interpolations were performed between adjacent weather stations. Since the highest prevalence of impetigo in the Netherlands has been observed in August, September, and October (unpublished data), we used the mean day temperature for these three months.

The age and gender of the patient were taken from the registration data in the second Dutch national survey. Family size and occupation of family members were taken from the mailed questionnaires used in the second Dutch national survey. Occupation was used to derive the proportion of people working in the agricultural sector at practice level. Unfortunately, it was not possible to distinguish between animal husbandry, which we expect to be a risk factor for impetigo, and agronomy and horticulture, which we do not think are risk factors. Occupation was also used to derive the socioeconomic class of a family (missing for one-third of the population due to nonresponse).

The population size and area of the municipalities with participating practices were also derived from the Statline database of Statistics Netherlands. Population density was calculated as the number of inhabitants per km^2. Similar to our previous analysis (Bruijnzeels et al., 1993), we divided the Netherlands into three regions (north, middle, and south), with 16, 58, and 22 participating practices in each part, respectively.

2.4. Statistical analysis

To test differences between the characteristics of impetigo patients and other people registered with the GPs, χ^2-tests were used for categorical variables and Mann–Whitney *U*-tests for continuous variables. To test whether impetigo and its determinants were distributed evenly among the north, middle, and south of the country, the Kruskal–Wallis test was used.

Logistic regression models were used to calculate the association between each of the variables denoting the density of farm animals or temperature and the occurrence of impetigo while adjusting for region, population density, proportion of people working in the agricultural sector, the patient's age and gender, family size, and the socioeconomic class.

We used generalized estimating equations (GEE) to take into account possible clustering of incident cases at the level of the practices (Liang and Zeger, 1989).

A logarithmic transformation with base 2 was applied to the numbers of animals and people per km^2 before carrying out the significance test. For computational reasons a small number was added before transformation. The reason for applying this transformation is that it is more logical for the effect of these densities on the odds ratio (OR) to be proportional rather than exponential. The temperature was measured in tenths of a degree Celsius; hence the effect estimates for temperature and density are more or less of the same order of magnitude. Statistical analyses were carried out with the statistical packages R, SAS, and SPSS.

3. RESULTS

Table 1 shows the baseline characteristics of the study population. The overall incidence of impetigo was 16.5 per 1000 patients aged 0–17 years. Table 2 shows the association between the incidence of impetigo and possible determinants in the north, middle, and south of the Netherlands. The numbers of animals per km^2 measured at the municipal and COROP level differ significantly between regions, except for sheep at the municipal level and bovines at the COROP level; the differences within each region are relatively large.

[TABLE 1]

[TABLE 2].

Table 3 shows the results of the multivariate analysis to test our study hypotheses. Note that, because of the logarithmic transformation applied, the ORs of the densities of the animals indicate the effect of a doubling of the density on the log odds of the incidence. Of the variables that we hypothesized to have an influence on the incidence of impetigo, only the number of sheep at the COROP level is significant; this relationship cannot explain the previously observed regional gradient. In all of the estimated regression equations, the OR of living in the southern part of the Netherlands is approximately two, which is significant at the 5% level (data not shown).

[TABLE 3]

4. Discussion

We could not confirm that the higher incidence in the south of the Netherlands is explained by selected climate and animal farming characteristics, and only small effect sizes were found. In the univariable comparison of north, middle, and south of the Netherlands, although several factors showed significant differences between the regions, most of these did not show a clear north–south gradient. In the logistic regression model adjusted for known risk factors, only sheep farming at the COROP level showed a significant effect on the incidence of impetigo, although it could not explain regional differences.

The fact that sheep are the only type of farm animal to show an effect on the incidence rate seems remarkable, because the intensity of sheep farming in the Netherlands is relatively low. One would expect more infections in case of high-intensity farms where more animals live closer together (van Loo et al., 2007). On the other hand, children may have easier contact with sheep than with animals that are kept in closed quarters.

The observed lack of an effect of our selected variables may be because we also included region in the analysis, which is highly correlated with many of the animal densities and with temperature (Table 2). When region was removed from the analyses, however, the ORs remained small and the temperature was the only remaining variable that had a significant effect on the incidence of impetigo.

Earlier studies reported that a history of animal contact increases the risk of impetigo (Rao et al., 1987; van Loo et al., 2007); however, just living close to the animals does not seem enough to substantially increase the risk. A study among infected sheep showed a great variety of *S. aureus* strains (Goñi et al., 2004); the authors suggest that sheep may be a source of dissemination of certain strains to humans.

Some limitations of our study must be addressed. First, the ecological design does not permit further exploration of causal relationships between the determinants and outcome. Second, since we were only able to study 1 year (2001), we cannot extrapolate our findings to other years. Finally, because of the nature of the data (a registration database) we do not know whether any differences observed are due to a real difference in the underlying factor or due to differences in the tendency to contact a GP with a problem (Bruijnzeels et al., 1998).

In conclusion, in this study the striking regional difference in incidence of impetigo in children cannot be explained by differences in climate and animal farming. Further studies are needed to either replicate our study, or to explore other characteristics such as differences in bacterial etiology (Goñi et al., 2004), day-care attendance, handwashing routines ([Luby et al., 2002] and [Luby et al., 2005]), and pet ownership.

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TABLES

Table 1. Characteristics of 1457 impetigo patients compared to the listed population aged 0–17 years (*n*=86,850).

	Impetigo patients	Total listed population	*p*-value
Age (years)[a]	7.0 (4.2)	8.8 (5.2)	<0.001
Female	670 (46%)	42,291(48.7%)	0.04
Family size[a]	4.2 (1.2)	4.1 (1.3)	0.001
Socioeconomic status			
High	392 (37.8%)	22,955 (41.4%)	0.07
Middle	435 (41.9%)	21,702 (39.1%)	<0.001
Low	210 (20.3%)	10,788 (19.5%)	0.02
Agriculture job	83 (6.0%)	3465 (4.3%)	0.008
Population density[a]	1139 (1152)	1327 (1199)	<0.001
Location			
North	138 (9.5%)	12,617 (14.5%)	
Middle	766 (52.6%)	49,929 (57.5%)	<0.001
South	553 (38.0%)	24,304 (28%)	

Table 2. Incidence of impetigo and possible determinants in north, middle, and south of the Netherlands.

	Mean (SD)			p-value
	North	**Middle**	**South**	
Individual level (n=86,850)				
n	12.617	49.929	24.304	
Impetigo incidence (per 1000 children per year)	10.8 (10.7)	15.1 (14.9)	22.2 (21.7)	<0.001
Age (years)	8.2 (5.3)	8.2 (5.2)	8.5 (5.2)	<0.001
Family size (n)	3.9 (1.3)	4.1 (1.4)	4.1 (1.1)	<0.001
High socioeconomic status	0.44 (0.25)	0.40 (0.24)	0.42 (0.24)	<0.001
Middle socioeconomic status	0.37 (0.23)	0.40 (0.24)	0.38 (0.24)	

	Mean (SD)			p-value
	North	Middle	South	
Low socioeconomic status	0.19 (0.15)	0.19 (0.15)	0.20 (0.16)	
Agriculture job (fraction)	0.02 (0.02)	0.04 (0.04)	0.06 (0.06)	<0.001
Municipal level (68 municipalities)				
Number of municipalities	9	43	16	
Population density (n/km2)	733 (671)	1519 (1204)	787 (657)	0.04
Temperature (August–October)	15.02 (0.21)	15.61 (0.40)	15.64 (0.9)	<0.001
Animals (n/km2)				
Bovines	76 (49)	58 (63)	112 (65)	0.001
Pigs	62 (88)	104 (211)	966 (1136)	<0.001
Sheep	30 (17)	31 (38)	15 (10)	0.13
Poultry	2007 (1536)	623 (1387)	5933 (7393)	<0.001
COROP level (34 COROP regions)				
Number of COROP regions	7	20	7	
Animals (n/km2)				
Bovines	122 (62)	97 (59)	116 (47)	0.40
Pigs	77 (49)	185 (264)	968 (657)	0.002
Sheep	44 (35)	49 (28)	18 (3)	0.02
Poultry	2262 (522)	2019 (3280)	6200 (4453)	0.03

Table 3. Candidate determinants of the incidence of impetigo.

	Odds ratioa	95% CIa	p-valuea
Animals (n/km2) at municipal level			
Pigs	1.000	0.959–1.035	0.849
Bovine	1.030	0.934–1.136	0.552
Sheep	1.046	0.970–1.129	0.243
Poultry	1.014	0.986–1.043	0.339
Animals (n/km2) at COROP level			
Pigs	1.007	0.938–1.081	0.850
Bovine	1.103	0.913–1.332	0.311
Sheep	1.300	1.097–1.542	0.003
Poultry	0.981	0.932–1.103	0.456
Temperature (0.1 °C)	1.012	0.973–1.053	0.546