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# SOCIO-ECONOMIC CHARACTERISTICS IN NOTIFIED ERYTHEMA MIGRANS PATIENTS

## SOCIALNO-EKONOMSKE ZNAČILNOSTI PRIJAVLJENIH BOLNIKOV Z ERYTHEMO MIGRANS

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**ABSTRACT**

**Background.** Lyme borreliosis disease results from infection by members of the Borrelia burgdorferi sensu lato complex. The most common clinical presentation of Lyme borreliosis is erythema migrans (EM). To gain knowledge of the epidemiological parameters and the risk factors of EM in Slovenia, a survey has been carried out in 2010.

**Methods.** A short anonymous and self-administrated questionnaire was sent to 4917 notified EM patients in 2010, aiming to collect epidemiological data and assess socio-economic determinants in patients with EM.

**Results.** Three thousand and five (61%) patients with EM returned completed questionnaires. One thousand and nine hundred twenty-nine (74%) patients noted the tick where the EM developed. The tick bite was most often located on the legs in adults and in the head/neck area in children. The time that elapsed before the tick has been removed increased significantly with age. The attached tick was most frequently overlooked in preschool children. Nearly 70% of patients believed that they contracted the infection with borrelia near home. Infection away from their permanent residence was more often the case in those with a higher level of education and in 15-49 age groups. Compared to the Slovenian general population over 14 years of age, those with a higher level of education, the unemployed and farmers were overrepresented among the EM patients.

**Conclusions.** The risk of Lyme borreliosis is widespread in Slovenia, with some areas more affected then others. Determinants of exposure to infected ticks are different, and depend on the socio-economic status and demographic characteristics.

**Keywords:**
erythema migrans, Lyme borreliosis, tick bite, surveillance, survey

***IZVLEČEK***

***Izhodišče**. Lymska borelioza je posledica okužbe z bakterijami kompleksa Borrelia burgdorferi sensu lato. Erythema migrans (EM) je najpogostejša klinična oblika lymske borelioze. Namen raziskave je bil pridobiti epidemiološke podatke in preučiti socialno-ekonomske značilnosti prijavljenih bolnikov z EM v Sloveniji.*

***Metode**. Kratek anonimni vprašalnik je bil poslan vsem 4917 bolnikom, prijavljenih z diagnozo EM v letu 2010, da bi se zbrali epidemiološki podatki in ocenile socialno-ekonomske determinante.*

***Rezultati**. 3005 (61%) bolnikov z EM je vrnilo popolno ali delno izpolnjene vprašalnike. 1929 bolnikov (74%) je navedlo, da se je EM pojavil na mestu predhodnega vboda klopa. Vbod klopa je bil največkrat na nogah pri odraslih in v predelu glave ali vratu pri otrocih. Čas od vboda klopa do njegove odstranitve je bil značilno daljši pri starejših, pogosteje pa so ga spregledali pri predšolskih otrocih kot pri odraslih bolnikih. Približno 70% bolnikov z EM je menilo, da so se z borelijo okužili v bližini doma. Okužba zunaj kraja stalnega prebivališča je bila pogostejša pri tistih z višjo stopnjo izobrazbe in v starostni skupini 15-49 let. V primerjavi s strukturo slovenskega prebivalstva nad 14 let je bilo med bolniki z EM več tistih z višjo stopnjo izobrazbe, brezposelnih in kmetov.*

***Zaključek**. Lymska borelioza je v Sloveniji zelo razširjena, pri čemer je primerov več v nekaterih predelih. Determinante izpostavljenosti okuženim klopom so različne in odvisne od socialno-ekonomskega statusa in demografskih značilnosti.*

***Ključne besede:***
*erythema migrans, lymska borelioza, klopi, spremljanje, ankete*

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## 1 INTRODUCTION

Lyme borreliosis (LB) is the most frequently reported vector-borne disease in Slovenia (1, 2). The main vector of the causative microorganism, the spirochete *Borrelia burgdorferi*, is *Ixodes ricinus* (3). The appearance and distribution of LB is determined by the natural environment, climatic factors and dynamic interactions between the natural landscape and human activities in the appropriate habitats (4-7). The main reservoir of *B. burgdorferi* is small and medium-sized mammals, birds (especially passerine birds), reptiles and insectivores. Ungulates support the tick population and can be infected with *Borrelia*. They are not a competent reservoir, as the ticks are not capable of acquiring *Borrelia* during their blood meal (8). The landscape structure and climatic factors have an effect on the number of ticks, hosts and the composition of the host community (9). The relationship is complex, depending on factors not yet fully quantified (6).

The effect of the weather and changes in climate were recognized as an important determinant of LB incidence (10). LB incidence usually increases after mild winters and during warm, humid summers (11). Entomologic risk is not the only critical driver of human vector-borne infections. In addition, weather conditions have an influence on human behaviour as well as on tick abundance and tick infection rate. It was suggested that the recent increases in vector-borne diseases in some Central European countries and the Baltic States may have arisen largely from changes in human behaviour that have brought more people into contact with infected ticks (6). The socio-economic transition that started in the early nineties, the current economic recession and the consequential increase in the unemployment rate affected the utilization of tick-infested forests and increased the incidence of tick-borne encephalitis in the Baltic States and Poland, as well as LB (7). Living in spatially dispersed houses, in wealthy suburban areas, and spending free time doing outdoor activities were found to be the driving forces behind LB in a Belgian study (12).

Lyme borreliosis has been an obligatory reportable communicable disease in Slovenia from 1986 onwards. The reported incidence rates are one of the highest in Europe (from 200/100,000 to 250/100,000) (10). To gain knowledge of the epidemiological parameters of the disease in Slovenia, a survey was begun in 2010. The principal aims of the survey were to assess socio-economic determinants in the notified erythema migrans (EM) patients in 2010 in Slovenia, and their geographic distribution.

## 2 METHODS

### 2. 1 Notification System

A patient diagnosed with LB clinically and microbiologically, or on clinical grounds alone (for EM patients) has to be notified to regional public health authorities, using the standard notification form. In principle, the notification includes the following data: the name, surname, date of birth, permanent address, time of the onset of symptoms/signs, notification date, hospitalization, outcome data and information on whether or not the diagnosis was confirmed by microbiological tests. At regional public health institutes, the notified cases are recorded in the electronic Database for Notifiable Communicable Diseases. The notifications collected regionally are sent to the National Institute of Public Health on a weekly basis, and the data (including personal identifiers and address) is merged at the national level.

According to the International Classification of Diseases (ICD-10), patients with acute or chronic LB are coded by the treating physician as erythema migrans (A69.2), Lyme meningitis (G01.0), Lyme polyneuropathia (G63.0) or Lyme arthritis (M01.2). Patients with EM (representing 97% of all notified LB patients) are typically treated by primary care physicians (general practitioners, family doctors or by paediatricians). Most of the EM patients were diagnosed on clinical grounds alone. Exceptionally, the diagnosis was confirmed by PCR or the culture of a skin biopsy specimen. Patients with other clinical entities, i.e. Lyme meningitis, polyneuropathia or arthritis, are typically referred to the secondary level and the diagnosis is confirmed microbiologically.

### 2.2 The Survey

A short (two page) anonymous and self-administrated questionnaire was sent to all the notified patients coded as EM, together with an invitation letter no later than 30 days after the notification. The patients with late manifestations of a *Borrelia* infection were not invited to participate, as the recall bias would probably distort the results of the survey.

The patients were requested to disclose their gender and age (in years), without a name or any other identifier, education level and employment status (employed, unemployed, retired or student). The patients were asked if they were at risk of tick-borne diseases because of the work they do for a living (farmers, forest workers, professional hunters or working on constructions in natural environments, e.g. building roads through forests, etc.). The feedback forms contained questions on the tick bite at the site of the EM, the location of the tick bite (head, neck, arms, legs or torso) and the estimated duration of the tick attachment. The patients were asked to pinpoint, if possible, the most probable geographic location (at

the county level) where they judged the infection with *Borrelia* occurred. We were interested in whether or not the infection took place in close proximity to where they lived. Near-home infection was defined as a *Borrelia* infection within a 5 kilometre radius of a permanent residence.

The most probable geographic location of the infection was entered on the map of Slovenia. The population by county was extracted from the web pages of the Statistical Office of the Republic of Slovenia (http://www.stat.si/tema_demografsko.asp) and the incidence rates of EM cases were calculated on a county level.

### 2.3 Statistical Analysis

The data collected was entered into Microsoft Excel and subsequently analysed using the R statistical software package (13). The descriptive statistics included frequency analyses (percentages) for categorical variables. The denominator used to calculate all the percentages was the number of patients with available (non-missing) data for each specific variable. A chi-square test was used to test the differences between sample and general population demographic distributions. Bivariate logistic regression was used to assess the effect of each independent variable on the odds of one outcome vs. the other for every dependent variable. P values of $<0.05$ were considered statistically significant (using Bonferroni correction for multiple comparisons).

As the age and gender structure of the responders differed from the structure of the notified EM patients, the raking procedure was applied. Raking is a procedure for adjusting the sample weights in a survey, so that the adjusted weights match known population totals for the post-stratified classifications, when only the marginal population totals are known. The resulting adjusted sample weights provide a closer match between the sample and the population (14). In general, this weighting procedure uses auxiliary data from a supplementary source, such as a larger survey or census. The advantages of this method are to reduce the bias and variance of the estimates, force the totals to match external totals and adjust for sources of error (15).

The raking procedure was repeated until the values converged (i.e. yielding the same age/gender structure as among the notified EM patients). The weighted data of the responders was compared to the general population data retrieved from the web pages of the Statistical Office of Republic of Slovenia (SORS, http://www.stat.si/).

## 3 RESULTS

The questionnaire was sent to 4917 notified EM patients in 2010. 3005 (61%) returned completed or partially completed questionnaires. The age/gender structure of the responders differed from the age/gender structure of the notified EM patients, with the elderly and females being significantly over-represented ($p<0.0001$ and $p=0.001$, respectively). The results throughout this paper are presented as weighted data.

### 3.1 Education Level and Employment Status

To allow comparison of EM patients' demographic distribution to general Slovenian population, only data for the responders above 14 years of age was used. 556 (22.1%) responders had finished primary school, 1328 (52.8%) secondary school/gymnasium and 562 (22.3%) college/faculty. There were a higher percentage of those with a higher level of education and less of those without any accomplished education (without finishing the eight-year primary education programme) in comparison to the Slovenian general population over 14 years of age (Table 1).

More than one third of the respondents were employed (1226, 37.8%) and approximately a third were retired (986, 33.1%). There were 571 (19.2%) students and 101 (3.4%) housewives. 197 (6.6%) respondents with EM declared that they were unemployed. Unemployment has been associated with higher odds for infection with Borrelia compared to employed responders (Table 1).

Roughly, one fifth of the respondents were professionally at risk of tick-bites. According to official statistics, there were 3% of registered farmers in Slovenia in 2010. Being a farmer was associated with three times higher odds of EM than among the adult Slovenian working and unemployed population (Table 1).

**Table 1.** Notified EM patients compared to general Slovenian population in terms of the level of education, employment status being a farmer (CI= confidence interval).

| | Number (%) - sample | Number (%) - overall population | Odds ratio (95% CI) | p-value (Wald $x^2$) |
|---|---|---|---|---|
| Level of education | | | | |
| Higher level of education | 562 (22.4%) | 562 (22.4%) | 1 | 1 |
| Without finishing primary education | 69 (2.7%) | 69 (2.7%) | 0.52 (0.41-0.67) | 0.52 (0.41-0.67) |
| Primary education | 556 (22.1%) | 556 (22.1%) | 0.85 (0.76-0.96) | 0.85 (0.76-0.96) |
| Secondary school | 1328 (52.8%) | 1328 (52.8%) | 0.76 (0.69-0.84) | 0.76 (0.69-0.84) |
| Employment status | | | | |
| Employed | 1226 (86.3%) | 1226 (86.3%) | 1 | 1 |
| Unemployed | 197 (13.8%) | 197 (13.8%) | 2.04 (1.75-2.37) | 2.04 (1.75-2.37) |
| Farming | | | | |
| All other vocations except farming | 2520 (90.4%) | 2520 (90.4%) | 1 | 1 |
| Being a farmer or working on a farm | 266 (9.6%) | 266 (9.6%) | 3.42 (3.01-3.88) | 3.42 (3.01-3.88) |

### 3.2 Tick Bite

1929 (74%) patients noticed the tick on the site where the EM developed later. There was no statistically significant difference between male and female patients (p=0.578). The tick bite on the EM site was most frequently overlooked in preschool children and most frequently noticed in patients over 65, as shown in Figure 1. The same holds for tick-bites on other locations (the data is not shown).

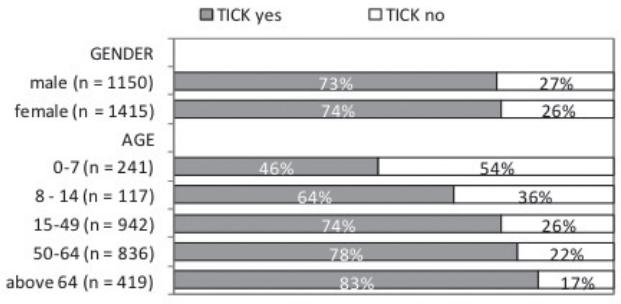


**Figure 1.** The percentage of patients who noticed the tick-bite on the site of the erythema migrans.

The most frequent location of a tick bite was the legs (1362, 45.3%), followed by the torso (948, 31.6%) and arms (529, 17.6%). Patients with EM were bitten least frequently on the head or neck. Age and gender influenced the location of the tick bite. Significantly higher numbers of females claimed to have the tick on the lower extremities (p=0.001) than the male patients. No differences were noticed for other locations. The torso was the most frequent location in the 50-64 age group, and the head or neck in preschool children.

The patients were asked for their opinion on how long the tick has been attached to the skin before it was found and removed. 444 (14.8%), 639 (21.3%) and 510 (17.0%) estimated that the tick was attached for <6, 6-12 and 12-24 hours, respectively. 336 (11.2%) were less specific and judged that the tick was attacked for ≥24 hours, or the responders were not able to assess the duration of the tick attachment, or left the question unanswered. The time that elapsed before the attached tick was noticed and removed increased with age (p<0.0001). Ticks located on the head/neck area were noticed more quickly than those attached to the torso, legs or arms (p<0.0001). Within the estimated 6-12 hours interval of the tick attachment, the ticks were most frequently noticed on the arms (p<0.0001) and on the legs after 12 hours (p<0.0001). Patients with more than one tick attached tended to notice the ticks later than with those who had only one bite (p=0.007).

2093 (69.7%) patients believed that they contracted the infection near the place they lived, and 596 (19.8%) believed they became infected with *Borrelia* away from their permanent residence. 316 (10.5%) left this question unanswered. A near-home infection was less likely (OR=0.54, CI: 0.38-0.76, p=0.0003) in the 15-49 age group, compared to preschool children (age group 0-7). Being a pensioner or housewife predisposed infection in the vicinity of home. In comparison to working population, housewives have 2.47 (CI: 1.33-4.61, p=0.002) and pensioners 1.76 (CI: 1.41-2.21, p<0.0001) fold greater odds for getting infected near home. Odds ratio for infection in another district was 2.63 (CI: 1.73-3.23, p<0.0001) for respondents with a higher education level in comparison to respondents with no formal education.

Forests, meadows or pastures and gardens were the most probable location of infection in 55%, 30% and 15% of the responders, respectively. Male responders claimed to get the tick bite in woods more often than female responders (OR 1.64, CI 1.42-1.90, p<0.0001). On the other hand, males were less frequently bitten in the garden then females (OR 0.44, CI 0.35-0.54, p<0.0001).

### 3.3 Map

The patients were asked about the most probable geographical location of their infection. The county incidence rates are shown in Figure 2.

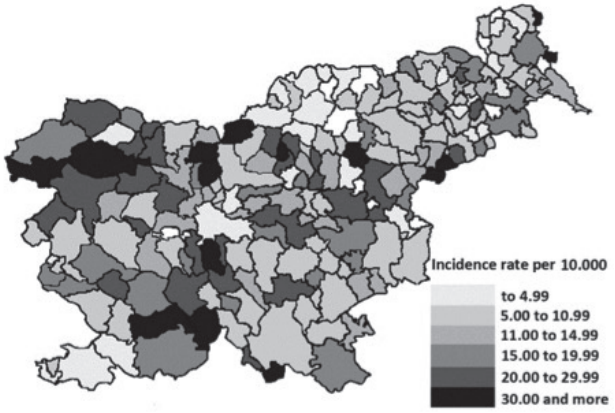


**Figure 2.** The incidence rate (per 10.000 inhabitants) of erythema migrans cases by counties with most probable site of infection, Slovenia 2010.

## 4 DISCUSSION

Lyme borreliosis is the most prevalent arthropod-borne disease in the temperate regions of the northern hemisphere. The real burden of LB is difficult to assess (16). The published data derives from studies limited to the areas where the disease is fairly prevalent, or the data is collected through active or passive public health surveillance systems (10). In case of the latter, the completeness and quality of the data is variable depending on willingness of the physicians to report it (16, 17). The main drawback of the passive notification systems is underreporting and therefore underscoring the incidence of LB by at least 3 times (17). Conversely, there is the possibility of over-diagnosis by the medical community in high risk areas. Local hypersensitivity to tick bites is the most common reasons for the misclassification of patients with erythema (18). In Slovenia, the incidence rate of notified EM cases was 245 per 100,000 inhabitants in 2010, which is one of the highest in the world. Without doubt, not all patients with EM were notified. Conversely, it might be that some patients with erythematous skin lesion after a tick bite were wrongly classified as EM. The validity of EM diagnosis has not been verified after the notification, which is one of the limitations of the present study, along with under-ascertainment and under-reporting. Even so, the true incidence of LB is high, as already shown by clinical studies (19).

The age and gender distribution of notified patients with EM (and survey responders) was comparable with the published data (10). As in most of the studies from Europe, there were more female than male patients, with the peak incidence rates in the 50-64 age groups (Figure 1). There might be some biological reasons for the high incidence rates in these age groups, though the lifestyle of middle agers and seniors is probably the main driving force behind infection with *Borrelia* (10). In 2010, the average age of retirement in Slovenia was 56.2 years – one of the lowest in the European Union (SORS, http://www.stat.si/novica_prikazi.aspx?id=3461). Relatively young and still fit pensioners have time to spend in natural environments for leisure activities. There is also an alternative explanation for the obvious high exposure to risky environments – as the monthly income after retirement is rather low (the monthly income was approximately 700 euros in 2010 on average), growing vegetables in the garden or picking berries and mushrooms in the forests becomes a necessity and not just a hobby for at least some pensioners. The unfavourable socio-economic status of those who had lost their jobs most likely explains the higher probability of EM among the unemployed, compared to employed responders. The impact of poverty on the incidence of tick-borne encephalitis (TBE) has been studied in Baltic States and Eastern European countries (7). It was shown that increased unemployment triggered a sudden increase in the risk for TBE. In Poland, in one of the studies, nearly half of the survey respondents stated that the worse financial status of the family was the main reason for an increased harvest (20).

The advanced level of education increased the odds for EM (Table 1). There are a few possible explanations. Higher education correlates with a healthier lifestyle, and out-door recreational activities are a part of it. The study from Belgium showed that there was a higher incidence rate of LB in the wealthy peri-urban areas, where living in houses with large gardens favoured human-vector contact (12). A higher income combined with higher education affects the disease awareness as well (12). It is possible that the responders with a higher level of education looked for medical advice earlier and more often than those less knowledgeable. Being a farmer has been recognized as a risk factor for LB by previous studies, and this is confirmed in the present survey (21).

A tick bite on the site of the EM was noticed by 79% patients in a study from Southern Sweden and 71% in a study from France. In the present survey, almost 75% of the responders noted the tick bite at the site of the EM. The tick bite was most commonly overlooked in small children. It seems that children were not inspected by their parents thoroughly for ticks after activities in forests and other natural environments.

The most frequent location of the tick bite were the legs and torso with more female then male patients bitten in the lower extremity – the same distribution found by previous studies (21, 22). The head and neck area was

a frequent location of the tick bite for children – an expected finding as children often crouch or sit on the ground while playing out-doors.

The estimated time of tick attachment was less than a day in more than half of the survey responders. The transmission of borreliae can occur in a few hours if the ticks contain high numbers of bacteria in their salivary glands (10). The transmission is always more likely with longer attachment, but the lag period seems to vary with the genospecies. *B. burgdorferi* sensu stricto is not usually transmitted before the tick has been attached for 48 hours, while *B. afzelii* (the most prevalent species in Slovenia) can be acquired with an attachment period of less than 24 hours (10, 23). Nevertheless, the time of attachment was only assessed and the reliability of this information is impossible to test. Furthermore, the data were collected with a time-lag of at least month duration. The recall bias is therefore one of the limitations of the study, which warrants the caution in interpretation or generalization of the results.

Nearly 70% of the patients claimed to get infected near their permanent residence. The percentage of those who presumably got infected in another region was much lower in the French population based study (10%). The male gender, being young adult or middle-aged and higher educated, correlated with the tick bite away from home. The active, wealthier population probably acquired the infection with borrelia while staying at their weekend houses or spending leisure time out-doors. The natural environments where the infection occurred were different in male and female patients, as expected. Females are usually more engaged in gardening and therefore are at risk of tick bites in their gardens. Timbering is physically demanding and remains a typical male job. There are unrivalled numbers of male members in hunting societies compared to females. Therefore, male responders were more often bitten by the tick then females in forests.

The different incidence rates among the counties (as shown on Figure 3) were probably influenced by the abundance of ticks infected with borrelia and by human-vector interaction in a suitable habitat. The increased fragmentation of deciduous forest has been identified as a natural environment favouring the abundance of the host reservoir (small mammals) and infected ticks (24). Slovenia is the third most forested country in the Europe (http://www.zgs.gov.si/slo/gozdovi-slovenije/index.html). Forests cover approximately 60% of the country with at least 22% of the forests being highly fragmentized (25). Most Slovenian counties (71%) are sparsely inhabited and only two counties are classified as thickly populated according to EUROSTAT's concept of urbanization rate. The dispersion of the population in highly forested countries creates ideal conditions for coming into contact with tick-borne diseases. A Polish study has showed regional differences in LB incidence that correlated with the availability of medical personnel, including physicians (26). In Slovenia, the situation is not comparable – the country is very small and has a relative geographically equal distribution of health-care institutions providing health care for every citizen of the country.

## 5 CONCLUSIONS

Determinants of exposure to infected ticks are different and depend on socio-economic status and demographic characteristics. Infection with borrelia seems to be connected to recreational activities in highly educated middle class individuals and an occupational disease for farmers. The poor economic situation of underprivileged members of society (e.g. the unemployed, pensioners) most likely creates the need for spending more time in risky environments, and becomes a driving force for LB. Whatever the reason for exposure to infected ticks, the high incidence rate in Slovenia demands public health attention and intensive efforts to educate the population about preventive measures and the manifestations of the disease.

## CONFLICTS OF INTEREST

The authors declared that they have no financial, professional or personal conflicting interests related to this article.

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## ETHICAL APPROVAL

National Medical Ethics Committee was not asked for ethical approval.

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