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RESEARCH REPORT

Epidemiology of Guillain-Barré syndrome in Finland 2004–2014

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Abstract At total mean incidence of 0.84–1.1/100,000 the occurrence of Guillain-Barré syndrome (GBS) is reported to be low in Finland compared to other Caucasian populations. However, a recent study from Southwestern Finland reported an incidence of 1.82/100,000 which is comparable to other Caucasian populations. We analyzed discharge data covering the years 2004 through 2014 on all neurological admissions in all Finnish university and central hospitals with a primary diagnosis of GBS. A total of 989 admissions due to GBS (917 individuals) were identified. The standardized (European population) annual incidence rate was 1.70/100,000 person-years (95% confidence interval 1.60–1.81). GBS incidence had an increasing trend with age. The likelihood of GBS was higher among girls and adolescent women than boys and men of same age (male:female incidence rate ratio [IRR] 0.56), while in the older age groups (>19 years) the occurrence of GBS was higher among males than females (male:female IRR 1.59). The incidence of GBS remained stable during the study period. There was no seasonal variation in GBS admission frequencies (p = 0.28). No significant effect of the 2009–2010 H1N1 influenza or vaccination against it for GBS occurrence was observed. We suggest that GBS is as common, and has similar age-distribution in Finland as in other European countries. Sex-associated susceptibility for GBS appears to be different in children-adolescents and adults.

Key words: acute autoimmune neuropathy, acute inflammatory polyradiculoneuropathy, epidemiology, Guillain-Barré syndrome, incidence

Introduction

The incidence of Guillain-Barré syndrome (GBS) in Europe and North America is 0.38–2.66/100,000 person-years and it usually rises with increasing age until 80 years, after which it declines *(McGrogan et al., 2009; Sejvar et al., 2011; Hense et al., 2014; Delannoy et al., 2017)*. The incidence among children is highest at age 2 years *(Sejvar et al., 2011; Hense et al., 2014; Delannoy et al., 2017)*. GBS affects men more often than women *(McGrogan et al., 2009; Sejvar et al., 2011)*. Earlier studies have reported that the mean annual incidence of GBS in Europe is lowest in Finland: 0.84–1.1/100,000 for the total population and 0.38/100,000 for those under 15 years of age *(Färkkilä et al., 1991; Rantala et al., 1991; Kinnunen et al., 1998; McGrogan et al., 2009)*. However, we have recently reported an annual incidence of no less than 1.82/100,000 in Southwestern Finland *(Sipilä and Soilu-Hänninen, 2015)*. Therefore, we

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Table 1. Number and incidence rate of Guillain-Barré syndrome by age group.

Age (years)	Frequency			Incidence rate (per 100,000)		
	Total	Men	Women	Total	Men	Women
0–4	16	7	9	0.49	0.43	0.59
5–9	14	5	9	0.44	0.29	0.57
10–15	34	13	21	0.84	0.60	1.06
16–49	335	188	147	1.32	1.42	1.18
50–79	544	327	217	2.72	4.09	2.08
more than 80	46	19	27	1.72	6.08	1.47
All*	989	559	430	1.70	2.46	1.44

*Overall incidence rates standardized.

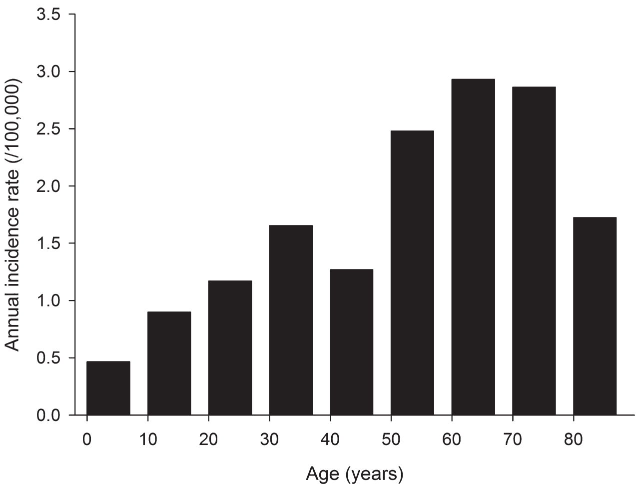

Figure 1. Age-dependent annual incidence rate of Guillain-Barré syndrome in the Finnish population.

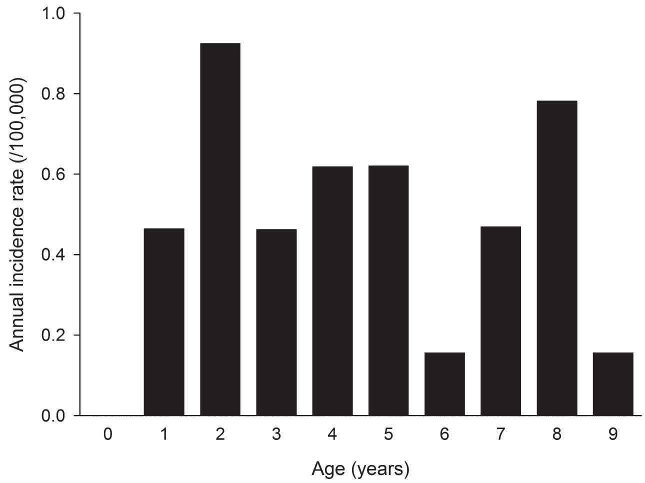

Figure 2. Annual incidence rate of Guillain-Barré syndrome among children aged 0–9 years in Finland in 2004–2014.

investigated the nationwide epidemiology of GBS in Finland.

Materials and Methods

We studied all patients with a primary discharge diagnosis of GBS (ICD-10 code G61.0) during 2004–2014. In order to capture only new GBS admissions, patients with a diagnosis of rehabilitation (ICD-10 code Z50.X) were excluded. The data included all hospitals in mainland Finland that provide care for acute GBS (5 university and 16 central hospitals). The patients were identified from the Finnish Care Register for Health Care (CRHC), which is a legally binding, compulsory, nationwide, and automatically collected database for collecting hospital patient data. The register covers virtually all new GBS admissions in Finland, the population of which grew from 5.2 to 5.4 million during the study period. Age groups were defined as in previous studies *(McGrogan et al., 2009; Sejvar et al., 2011)*. For each patient, one GBS admission per study year was counted, except when modeling seasonality when only the first GBS admission during the study period was included in the analysis.

The H1N1 influenza pandemic began to spread in Finland in October 2009 and lasted until the beginning of March 2010. It was paralleled by a vaccination campaign against the virus. Considering the discussion concerning vaccines as a suggested cause of autoimmune disease, we also specially investigated the incidence of GBS during this period.

Anonymized patient data were collected retrospectively from patient records with the approval of the National Institute of Health and Welfare (permission THL/143/5.05.00/2015).

Incidence rate of GBS was modeled using Poisson's regression with logarithm of the corresponding population as an offset parameter. Annual incidence rates were standardized to the European 2013 and World Health Organization (WHO) standard populations (total incidence) by using a direct standardization method. The seasonality of GBS occurrence was analyzed with Poisson's regression modeling. December, January and February were defined as winter, March,

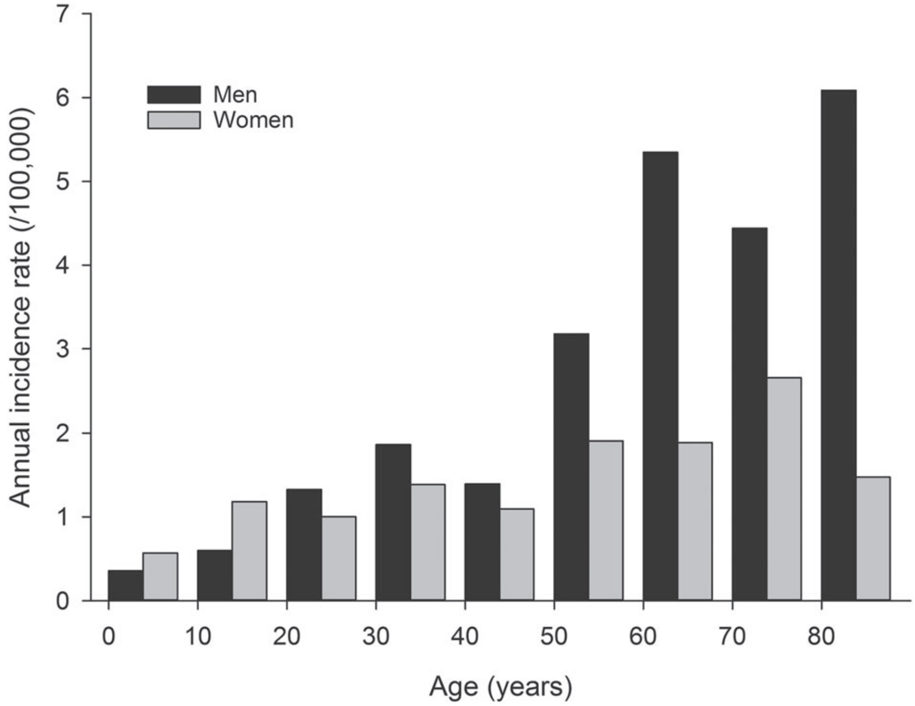

Figure 3. Age- and gender-dependent annual incidence rate of Guillain-Barré syndrome in the Finnish population.

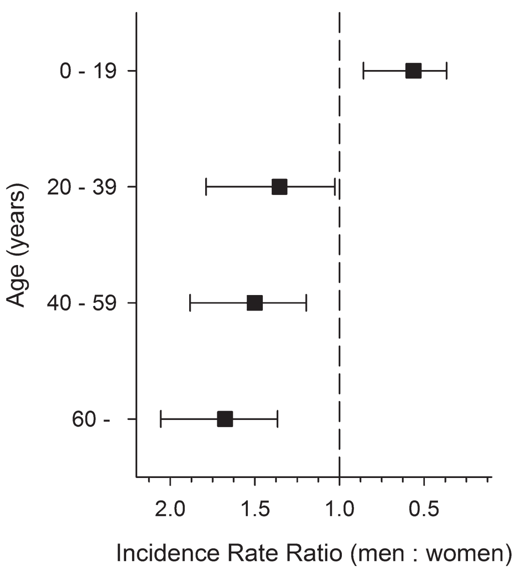

Figure 4. Gender-associated incidence rate ratio of Guillain-Barré syndrome by age in the Finnish population. Error bars represent 95% confidence intervals. P < 0.01 for age group 0–19 years, <0.05 for 20–39 years and <0.0005 for over 40 years.

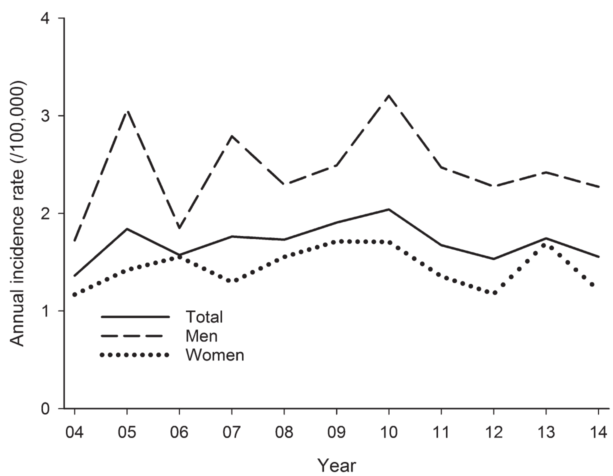

Figure 5. Trends of Guillain-Barré syndrome incidence rate in Finland 2004–2014. Values standardized for the European 2013 standard population.

April and May as spring, June, July and August as summer and September, October and November as autumn. The difference in the number of days of the months was taken into account by using the logarithm of the number of days in the respective month as an offset parameter. Bonferroni's correction for multiple comparisons was used, as appropriate. The results are presented as relative risk or incidence rate ratio with 95% confidence intervals (CIs). Statistical significance was inferred at a p-value <0.05. All analyses were run on the SAS System for Windows, version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

We identified 989 hospital admissions among 917 individuals (7.3% recurrences), yielding a crude annual

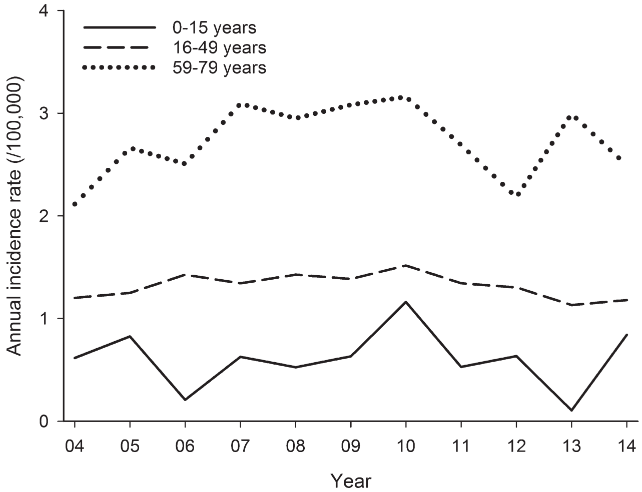

Figure 6. Age-dependent trends of Guillain-Barré syndrome incidence rate in Finland 2004–2014.

incidence rate of 1.69/100,000 person-years. European standardized incidence rate was 1.70/100,000 person-years (95% CI 1.60–1.81; Table 1) and WHO standardized incidence rate 1.40 (95% CI 1.31–1.50). Slightly over half (57%) of the patients were male. The mean age of the entire population was 51 years (SD 20.1; range 1–89); there was no difference between the genders ($p=0.12$). Total annual GBS incidence increased steadily from birth to 40 years of age, and again from 50 to 70 years (Fig. 1). In the subset of children aged 0–9 years, the annual incidence rate was highest among children aged 2 years (Fig. 2).

There was a significant interaction between gender and age regarding incidence rate ($p<0.0001$, Fig. 3). Among males, the estimated incidence rate of GBS increased by 28% (23%–33%) and among women by 14% (10%–19%) overall for every 10-year increment of age ($p<0.0001$ for both). The likelihood of GBS was 44% higher in girls and adolescent females compared with boys and males of the same age (0–19 years) (Fig. 4), while in older age groups males were progressively more susceptible to GBS with age compared to females (by 35.5%–67.6%).

The incidence rate of GBS remained roughly stable during the study period, and there were no significant overall ($p=0.45$), gender-related ($p=0.67$) or age-related interactions (0.49) (Figs. 5 and 6). GBS incidence did not differ in winter 2009–2010 (H1N1 influenza period) from other winters (Figs. 5 and 6). There was no variation in the occurrence of GBS admissions between seasons ($p=0.28$, Fig. 7).

Discussion

This population-based study on the incidence of GBS over one decade (2004–2014) in Finland shows that GBS is as common in Finland as in other countries with mainly Caucasian populations. Previous studies on the incidence of GBS in Finland have implied a lower incidence, but those studies were restricted to certain age groups or geographical areas *(Färkkilä et al., 1991; Rantala et al., 1991; Kinnunen et al., 1998; Sipilä and Soilu-Hänninen, 2015)*. The current study is the most extensive investigation into the epidemiology of GBS in Finland published, thus far and we found a national mean incidence rate of 1.70/100,000 for all age groups combined, which contrasts to previous reports of incidences of 0.84–1.1/100,000 *(Färkkilä et al., 1991; Rantala et al., 1991; Kinnunen et al., 1998)*. The current result is congruent with a recent report on a mean incidence figure of 1.82/100,000 for adults in Southwestern Finland *(Sipilä and Soilu-Hänninen, 2015)*. Overall, these new results suggest that the incidence of GBS in Finland is similar to other countries with mainly Caucasian populations *(McGrogan et al., 2009)*.

French investigators have recently reported, for the first time in Europe, a childhood incidence peak of GBS around age 2 years *(Delannoy et al., 2017)* and our data shows a similar peak in Finnish children. Comparable findings have, however, previously been reported from outside Europe. Incidence peak of GBS at 2 years has been reported from Brazil *(Dias-Tosta and Kückelhaus, 2002)*. Similar incidence peak at 1–4 years has also been reported from Latin America and the Caribbean *(Landaverde et al., 2010)* and from China *(Tang et al., 2011)*. It will therefore be interesting to see if these novel French and Finnish findings can be observed in other European populations.

We also found a higher standardized incidence rate for females than males in the age group 0–19 years, which contrasts with the previous data from Finland, that reported similar gender incidence *(Rantala et al., 1991)*. Studies from Sweden *(Cheng et al., 2000)*, the Canary Islands *(Aladro-Benito et al., 2002)* and the UK *(Hughes et al., 2006)* have also reported a higher prepubertal incidence of GBS in girls than boys, while a German study *(Hense et al., 2014)* reported no gender difference in the incidence of GBS below 30 years of age. Furthermore, a recent study from the Netherlands reported a female preponderance *(van der Maas et al., 2011)*, another from Switzerland reported an almost equal gender distribution with only slightly more women *(Gensicke et al., 2012)* and one study from Spain showed no gender sex difference *(González-Suárez et al., 2013)*. On the other hand, another recent study from Spain reported a typical male-to-female ratio of 1.5 *(Alcalde-Cabero et al., 2016)*, in line with recent studies from France, Italy, and Germany *(Hense et al., 2014; Benedetti et al., 2015; Delannoy et al., 2017)*. The question about a gender

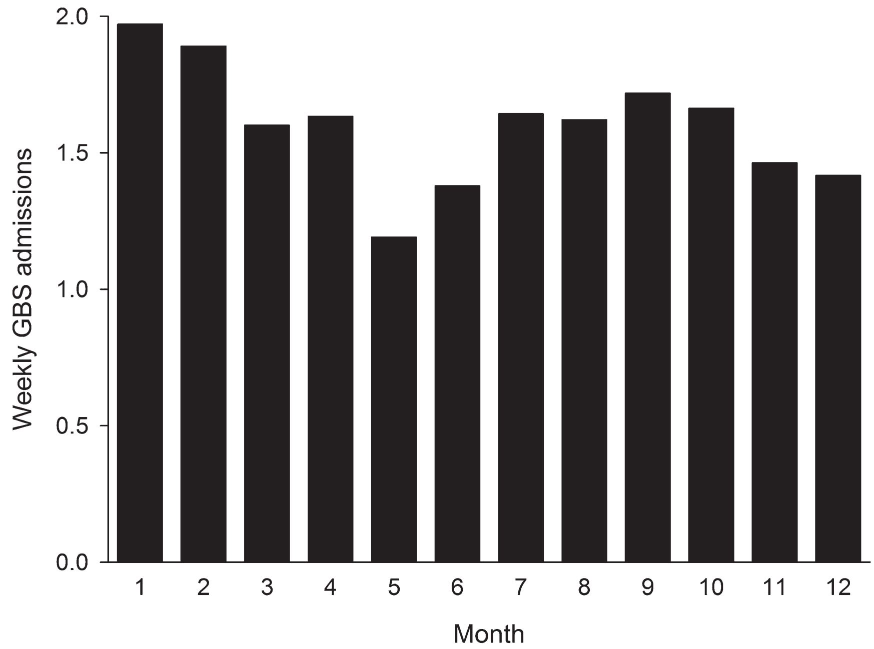

Figure 7. Weekly Guillain-Barré syndrome (GBS) admission rates in Finland 2004–2014 by month.

ratio of GBS incidence therefore remains unsolved. Considering this, it is interesting to note that the incidence of multiple sclerosis, another autoimmune disorder, has increased particularly in women in Northern Finland *(Krökki et al., 2011; Holmberg et al., 2013)* and in the Netherlands *(Kramer et al., 2012)*.

In view of the previous conflicting reports on the seasonality of GBS *(Färkkilä et al., 1991; Kinnunen et al., 1998; Sejvar et al., 2011; Shui et al., 2012; van der Maas et al., 2011; Webb et al., 2015)*, it is not surprising that we observed no variation in the incidence of GBS by season. Also in keeping with most previous reports *(Prestel et al., 2014; Romio et al., 2014; Sipilä and Soilu-Hänninen, 2015; Alcalde-Cabero et al., 2016)*, we observed no effect on the incidence of GBS of the H1N1 influenza pandemic nor the vaccination campaign. Given that 52% of the Finnish population took the vaccine with a coverage of 75% in the population under 15 years of age, an unusual peak in GBS incidence should have been observed for that winter if the vaccine had predisposed its recipient to the syndrome. The GBS incidence figures during the winter 2009–2010 did not differ from that of other winters.

An obvious weakness of this study is its retrospective design and reliance on solely data retrieved from an administrative registry. However, the earlier Finnish study that also used CRHC data (then called the Finnish Hospital Discharge Register or FHDR) found that 87% of the patients entered into the registry with a diagnostic code of GBS did fulfill the diagnostic criteria for GBS of Asbury and Poser *(Kinnunen et al., 1998)*. The current results concur with a recent regional, chart-verified incidence figure *(Sipilä and Soilu-Hänninen, 2015)*. Our data also does not allow us to categorize patients by GBS subtypes and this may influence the results, for instance, concerning seasonal variations. The strengths include that CRHC has been found to be reliable for data collection *(Kinnunen et al., 1998*; *Sund, 2012)*.

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