Toxoplasma prevalence among pregnant women in Norway: a cross-sectional study

GRY FINDAL,1,2 REGINE BARLINN,1,2 IRENE SANDVEN,4 BABILL STRAY-PEDERSEN,1,2 SVEIN A. NORDBO,5 HELVI H. SAMDAL,4 KIRSTI VAINIO,3 SUSANNE G. DUDMAN3 and PÅL A. JENUM1,2

1Institute of Clinical Medicine, University of Oslo, Oslo; 2Division of Women and Children, Oslo University Hospital, Oslo; 3Department of Virology, Norwegian Institute of Public Health, Oslo; 4Oslo Centre for Biostatistics and Epidemiology, Research Support Services, Oslo University Hospital, Oslo; 5Department of Medical Microbiology St.Olavs Hospital, Trondheim; 6Department of Microbiology, Oslo University Hospital, Oslo; and 7Department of Medical Microbiology, Vestre Viken Health Trust, Drammen, Norway


Infection by Toxoplasma gondii may lead to complications in the foetus if the mother suffers from primary infection during pregnancy. Previously infected women have produced toxoplasma-specific IgG antibodies. The most recent study on prevalence of toxoplasma IgG in the Norwegian pregnant population was conducted 20 years ago. The present study is part of a research programme initiated by the Norwegian Institute of Public Health. We aimed to update the knowledge regarding the prevalence of toxoplasma IgG among pregnant women in Norway. In this cross-sectional study, sera from 1922 pregnant women in Buskerud (982) and Sor-Trøndelag counties (930) in Norway were collected consecutively. The presence of toxoplasma IgG was identified by values ≥8 IU/mL using an ELISA test. The overall prevalence of toxoplasma IgG seropositivity was 9.3% (95% CI 8.1–10.7); Sor-Trøndelag 10.4% (95% CI 8.6–12.6) and Buskerud 8.3% (95% CI 6.7–10.2). There was no difference between the counties (p = 0.13), and the result did not differ from prevalences found in 1974 (12.1%) and 1994 (10.7%). We found a higher prevalence among women ≥40 years (OR 2.65, 95% CI 1.30–5.42). The prevalence of toxoplasma IgG among pregnant women in Norway is low and has been stable during the last decades.

Key words: Toxoplasma gondii; pregnancy; prevalence; IgG antibody; cross-sectional.

Gry Findal, Division of Women and Children, Oslo University Hospital, Rikshospitalet, PO Box 4950 Nydalen, 0424 Oslo, Norway. E-mail: gryf@medisin.uio.no

Infection with the parasite Toxoplasma gondii represents a hazard to immunocompromised individuals and to the foetuses of mothers suffering from primary infection during pregnancy. Humans are most commonly infected through ingestion of contaminated food or water, but in pregnant women, infection may be transferred to the foetus through the placenta (1).

For the foetus, the risk of transmission and the severity of the disease depend on the gestational age at the time of infection (1–4). Foetal infection may cause a wide spectrum of clinical manifestations, ranging from asymptomatic or mild visual impairment to severe brain damage and foetal death (1). Maternal infection acquired before pregnancy does not affect the foetus (5).

Primary infection is usually followed by persistent toxoplasma-specific immunoglobulin G (IgG) antibodies.

The reported prevalence of toxoplasma seropositivity among pregnant women in Norway and Sweden has been considerably lower than in other parts of the world: 11% in Norway (6) and 18% in Sweden (7) compared to 44% in France (8) and >60% in Indonesia (9). The prevalence in Europe appears to decline, and this reduction has been attributed to the installation of home freezers, improved meat control, education of pregnant women and long-lasting antenatal screening programmes (8, 10).

New data on the prevalence of toxoplasma-specific IgG antibody in pregnant women in Norway

Received 1 October 2014, Accepted 9 November 2014
are lacking because the most recent study in this field was conducted 20 years ago (6).

The present cross-sectional study is part of a larger project initiated by the Norwegian Institute of Public Health, 'Immunity in the Norwegian population', where prevalence of rubella, cytomegalovirus and parvovirus B19 in the pregnant population are studied (11).

Our aims are to examine the toxoplasma IgG prevalence among pregnant women in Norway and to compare the result with prevalence found in Norwegian studies conducted in 1974 (12) and 1994 (6).

MATERIAL AND METHODS

During the period from August 2010 to May 2011, 2000 individual serum samples were collected consecutively from pregnant women in Buskerud county in Southeast Norway (999 samples) and in Sor-Trøndelag county in Mid-Norway (1001 samples) during the first antenatal visit to a primary health care facility. The samples were sent to the local laboratories as part of the routine voluntary screening programme for HIV, rubella and syphilis.

The serum samples were marked with collecting day, year of birth and county, and anonymized and forwarded to the Norwegian Institute of Public Health where the samples were stored at −20 °C according to national research bio-bank regulation.

In the present study, the participants were included if the serum sample had sufficient volume for analysis (1922 out of 2000).

Serum analyses

The sera were examined for toxoplasma-specific IgG antibodies using an indirect ELISA test (Bio-Rad, Marnes la Coquette, France); the same method was used in the national prevalence study in 1993–94 (6, 13). The analyses were performed on the BEST 2000™ analysing instrument (Werfen Group, Bilbao, Barcelona, Spain) at the Department of Medical Microbiology, Vestre Viken Health Trust, during autumn 2012 and winter 2013. The results of the analyses were validated against independent controls included in each run.

The results were expressed in international units per mL (IU/mL) and interpreted according to the manufacturer's recommendations: A value of ≤4 IU/mL was regarded as negative, reflecting susceptibility for infection during pregnancy, 4 to <8 IU/mL was interpreted as borderline and ≥8 IU/mL was regarded as positive, indicating previous or ongoing T. gondii infection.

Statistical analysis

IgG status was analysed both as a continuous variable (IU/mL) and as a categorical variable. The presence of toxoplasma IgG seropositivity was estimated by a period prevalence from August 2010 to May 2011 with 95% confidence interval (14). Continuous variables were described by the median with its quartiles and ranges. Maternal age was polymized into six 5-year interval categories. The frequency of toxoplasma IgG seropositivity was studied along county and the six age groups. Univariate analysis was performed using contingency tables.

Data were analysed using IBM SPSS statistics version 20 (version 20.0.1; IBM corp. New York).

Sample size and power estimation

The power estimate was done before the start of the study. In Norway, the prevalence of toxoplasma IgG seropositivity in pregnant women was estimated to be 10.9% (6).

Considering a total population of approximately 133 000 women of fertile age in Buskerud and Sor-Trøndelag (www.ssb.no), a type-I error = 5%, power = 80% and precision = 2% (which means accepting a variability in the range of prevalence between 8.9–12.9%), it was estimated that sera from 926 subjects would be needed.

Ethics

The research programme 'Immunity in the Norwegian population', initiated by the National Institute of Public Health, was approved by the Regional Committee for Ethics and Research (2009/1322-2). The present study, considered a part of the main study (2012/203), was performed without consent from the patients, according to the 'Act relating to control of communicable diseases' (Ssmittevernloven) § 3–7 concerning use of anonymized sera (15).

RESULTS

In total, 1922 (96%) of 2000 serum samples were available for analysis. The overall prevalence of toxoplasma IgG seropositivity was 9.3% (95% CI 8.1–10.7). As shown in Table 1, there was a difference in prevalence between Buskerud and Sor-Trøndelag counties, but the difference was not statistically significant ($\chi^2 = 2.263, df = 1, p = 0.13$).

<table>
<thead>
<tr>
<th>County</th>
<th>Women tested No</th>
<th>Toxoplasma IgG ≥8 IU/mL No</th>
<th>Prevalence % (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buskerud</td>
<td>992</td>
<td>82</td>
<td>8.3 (6.7–10.2)</td>
<td>0.133*</td>
</tr>
<tr>
<td>Sor-Trøndelag</td>
<td>930</td>
<td>97</td>
<td>10.4 (8.6–12.6)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1922</td>
<td>179</td>
<td>9.3 (8.1–10.7)</td>
<td></td>
</tr>
</tbody>
</table>

*Difference in Toxoplasma IgG between Buskerud and Sor-Trøndelag = 2.1% (95% CI: −0.6 to 4.8), $\chi^2 = 2.263, df = 1$
Borderline toxoplasma antibody result was detected in 18 women (0.9%, 95% CI 0.57–1.5). Median maternal age was 29 years (range 15–46, quartile25 = 26, quartile75 = 33) with no clinically significant difference in age profile between Buskerud and Sør-Trøndelag counties, median = 30 and median = 29, respectively. No gradient increase in frequency of toxoplasma IgG seropositivity was observed over the five youngest age categories, but in the oldest age group, the prevalence was higher (Table 2). The odds of being toxoplasma IgG seropositive were 2.65 times higher in pregnant females 40 years or older than in the younger age groups combined (OR = 2.65, 95% CI 1.30–5.42). The mean IgG value in the subgroup of seropositive women was 58.2 IU/mL (median 26.5 IU/mL). Median IgG value was highest in the youngest age group, age ≤19 years (85.3, IU/mL), and lowest in the oldest age group, age ≥40 years (19.2 IU/mL) (Table 3).

The prevalence in the current sample (9.3%) was similar to prevalence obtained in the previous nationwide studies in 1994 (10.9%) (6) and 1974 (12.6%) (12) (Table 4).

**DISCUSSION**

The aim of our study was to examine the prevalence of *T. gondii*-specific IgG antibodies in pregnant women in two counties of Norway. An IgG seropositivity prevalence of 9.3% indicates that the presence of *T. gondii* antibodies among pregnant women in Norway is still low compared to other European countries. Studies from other northern countries in previous years showed a higher prevalence, 27.4% in Denmark (16) and 18% in Sweden (7).

When compared to previous studies on the prevalence of *T. gondii* IgG seropositivity in Norway, our results show only a small reduction in the prevalence during the last 40 years (Table 4) (6, 12). The previous studies cover a larger geographic area of Norway and therefore may not be compared directly to our results. The prevalence in Sør-Trøndelag county, however, can be compared with the previous results from mid-Norway (6). More and Romsdal counties (12), because these regions represent the same geographical area with demographic similarities. As our results show, there is only a minor change in prevalence in this region. This indicates that the reduction in prevalence among pregnant women observed in other European countries is not found in Norway. The county of Oslo and Buskerud are geographically closely situated; however, Oslo has higher proportion of immigrants than Buskerud, which means that direct comparison is not easily done.

Any change in prevalence over time is the total result of different factors contributing to an alteration in the rate of infected individuals. The following relevant factors may add to the prevalence: *T. gondii* seropositivity increases with age (6, 7), and the mean maternal age of birth has increased significantly from 22 to 29 years in Norway during the last 40 years (17).

During the same period, the overall economy of Norwegian households has improved (www.ssb.no/intekt-og-forbruk/statistiker/ifhus/aar/2013-2013-182013) and this has contributed to increased travel to different parts of the world in the population (18). Travelling outside northern Europe has been found to correlate with increased *T. gondii* IgG seropositivity among fertile women (19).

Ingestion of uncooked or raw meat and unclean vegetables is a well-known risk factor for toxoplasma infection (19). Norwegian dietary habits have changed towards more consumption of meat and vegetables the last 20 years (20).

The prevalence of *T. gondii* IgG is higher among immigrants than in the native population (6, 12, 21, 22). The number of immigrants living in Norway has increased the last 40 years.

Taking these risk factors of toxoplasma infection into account, one would expect an increase in *T. gondii* IgG seropositivity among the fertile population of Norway during recent years. Yet, this is not coherent with our findings. This may have several explanations: although antenatal screening surveillance of toxoplasma infection has been rejected in Norway, midwives and physicians frequently order toxoplasma serology during pregnancy (23, 24). The number of *T. gondii* serology tests performed at the

| Table 2. Prevalence of toxoplasma IgG by age group among 1922 pregnant women in two counties in Norway |
|-------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Age group (years) | Women tested No (%) | Toxoplasma IgG ≥8 IU/mL | Prevalence (95% CI) |
| ≤19 | 43 (2.2) | 5 | 11.6 (3.9–25.1) |
| 20-24 | 281 (14.6) | 30 | 10.7 (7.3–14.9) |
| 25-29 | 651 (33.9) | 59 | 9.1 (7.0–11.6) |
| 30-34 | 616 (32.0) | 52 | 8.4 (6.4–11.0) |
| 35-39 | 283 (14.7) | 23 | 8.1 (5.2–11.9) |
| ≥40 | 48 (2.5) | 10 | 20.8 (10.51–35.0) |
| Total | 1922 | 179 | 9.3 (8.1–10.7) |
Table 3. IgG values (IU/ml) in different age groups among T.gondii seropositive pregnant women in Buskerud and Sør-Trøndelag counties

<table>
<thead>
<tr>
<th>Age groups (years)</th>
<th>Median</th>
<th>Lower quartile</th>
<th>Upper quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤19</td>
<td>85.3</td>
<td>37.3</td>
<td>100.0</td>
</tr>
<tr>
<td>20-24</td>
<td>26.9</td>
<td>14.9</td>
<td>86.0</td>
</tr>
<tr>
<td>25-29</td>
<td>27.9</td>
<td>14.9</td>
<td>65.7</td>
</tr>
<tr>
<td>30-34</td>
<td>27.5</td>
<td>20.3</td>
<td>62.2</td>
</tr>
<tr>
<td>35-39</td>
<td>23.0</td>
<td>14.7</td>
<td>53.3</td>
</tr>
<tr>
<td>≥40</td>
<td>19.2</td>
<td>16.3</td>
<td>27.5</td>
</tr>
</tbody>
</table>

Table 4. The prevalence of toxoplasma IgG among pregnant women in different regions in Norway the last 37 years

<table>
<thead>
<tr>
<th>Year</th>
<th>Study sample No</th>
<th>Mean age years</th>
<th>Total prevalence %</th>
<th>County/ Region</th>
<th>Study sample No</th>
<th>Regional prevalence %</th>
<th>County/ Region</th>
<th>Study sample No</th>
<th>Regional prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>1922</td>
<td>29.1</td>
<td>9.3</td>
<td>Ser-Trøndelag</td>
<td>930</td>
<td>10.4</td>
<td>Buskerud</td>
<td>992</td>
<td>8.3</td>
</tr>
<tr>
<td>1994 (2)</td>
<td>35940</td>
<td>28.0</td>
<td>10.9</td>
<td>Mid-Norway</td>
<td>9141</td>
<td>9.7</td>
<td>Oslo</td>
<td>8249</td>
<td>13.0</td>
</tr>
<tr>
<td>1974 (12)</td>
<td>11736</td>
<td>26.0</td>
<td>12.6</td>
<td>Møre and Romsdal</td>
<td>1007</td>
<td>13.3</td>
<td>Oslo</td>
<td>10729</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Toxoplasmosis Reference Laboratory at Oslo University Hospital, Rikshospitalet, has increased by 37% from 2005 to 2012 (http://www.oslo-universitetssykehus.no/fagfolk_/laboratoriete/jnastjonale-referansefunkjonet/Sider/Nasjonalt-referanselaboratorium-for-toxoplasmose.aspx). There are reasons to believe that this development reflects an increasing awareness of toxoplasma infection among health practitioners and pregnant women.

The prevalence of T. gondii IgG in pigs and sheep in many western countries has declined during the previous years (25). This is most likely also the case in Norway, indicating that the risk of being infected with T. gondii by eating undercooked meat may be reduced.

Thus, better hygiene, meat control and health information, together with more precautious pregnant women, may explain the stable prevalence detected through the last 40 years, despite the overall increased risk factors in the Norwegian population.

The seroprevalence was relatively high in the oldest age group, but this subgroup is small, (n = 10) and the findings must be interpreted with caution. Yet, previous studies from Norway and other countries support this finding (6, 12). This may be attributed to changes in diet and travelling habits in this group or to increased number of children that has been found to be risk factors (6). However, there was a trend towards a decrease in antibody level with increasing age, indicating that for the older women, the primary infection may have occurred at an earlier time than for the younger women. Thus, the increase in prevalence in the oldest age group may represent a cohort effect rather than an increased risk of infection.

The sera were included consecutively until there were 1000 samples per lab; every woman attending their first antenatal control in this period was included. Only 4% were excluded due to insufficient serum volume for testing. This strengthens the validity of the present study.

The definition of the cut-off value used in the toxoplasma IgG assay may have influenced the proportion of seropositive women. Prevalence was calculated with ≥ 6 IU/ml and ≥10 IU/ml as alternative cut-off values, but this did not change the prevalence significantly (data not shown).

The two counties studied represented 10.9% of the total number of births in Norway in 2010 (Buskerud 4.7% and Sør-Trøndelag 6.2%). These regions may reflect Norway in terms of socioeconomics, climate, lifestyle and health parameters (www.norgeshelsa.no). The mean age and the age distribution in this study were equal to what has been recorded in the Medical Birth Registry of Norway for 2010, indicating that the data are representative according to age (26).

We believe that the result of a 9.3% seropositivity of T. gondii IgG antibodies among the study population is representative as a mean for the pregnant population in Norway.

CONCLUSION

Approximately 90% of the Norwegian pregnant population is at risk of being infected with the toxoplasma parasite and transmitting the infection to the offspring.

The prevalence of T. gondii IgG seropositivity among pregnant women in Norway is observed to be stable during the last 40 years, without the decline seen in other western countries.

With such a large proportion of unprotected pregnant women, we recommend thorough information on how to avoid risk factors for toxoplasma
infection. This is especially important when pregnant women travel to countries with a higher toxoplasma prevalence compared to Norway.

CONFLICTS OF INTEREST

None of the authors have any financial interest or other conflicts of interest to disclose.

FUNDING

The study was funded by a grant from the Vestre Viken research foundation.

We thank Therese Bernsten Vestgarden, Mette Andersen-Holthe and Eva Eikum at the Department of Medical Microbiology, Vestre Viken Health Trust for technical assistance.

REFERENCES


