

## Prevalence of *Toxoplasma gondii* specific immunoglobulin G antibodies among pregnant women in Norway

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### SUMMARY

During one year from June 1992 serum IgG antibodies to *Toxoplasma gondii* among 35940 pregnant women were measured in a cross-sectional study conducted in Norway. The overall prevalence was 10·9%. The lowest prevalences were detected in the north (6·7%) and in the inland counties (8·2%). A significantly higher prevalence was detected in the southern counties (13·4%) where a mild, coastal climate prevails. Women with foreign names had a higher prevalence (22·6%) than women with Norwegian names (10·0%). The high prevalence among women living in the capital city (Oslo) as compared to other cities and rural areas (13·2% vs. 10·1% and 10·2% respectively), was explained by the higher proportion of foreign women in Oslo. Prevalence significantly increased with age in women over 34 years old. This increase was only detected among women with Norwegian names. An increase in prevalence according to number of children was detected. Women without children had a prevalence of 8·8% while women with three children or more had a prevalence of 14·9%. Multivariate analyses showed that being seropositive was independently associated with county of residence, age, nationality and number of children.

### INTRODUCTION

Primary infection with *Toxoplasma gondii* in pregnancy may be transmitted to the foetus causing foetal infection and damage [1]. The clinical consequences include intrauterine death, brain damage with physical or mental retardation and chorioretinitis with impaired vision or hearing defects [1]. The outcome depends on gestational age at infection. Many congenitally infected children do not show symptoms of the disease until later in life [2].

Maternal infection may be prevented by informing pregnant women, not previously infected with *T. gondii*, about how to avoid infection [3, 4]. Antiparasitic treatment given to infected mothers, and newborn infants has been shown to reduce the risk of intrauterine transmission and the development of disease [5, 6]. Some European countries have introduced a serological screening programme aimed at early detection and treatment of women infected during pregnancy, together with health education to prevent maternal infection [7–9].

In Norway, a nationwide, prospective study of toxoplasmosis in pregnancy was launched in December 1991 [10]. This article presents the results obtained

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from a cross-sectional study associated with the prospective study, measuring the prevalence of *Toxoplasma*-specific immunoglobulin G (IgG) antibodies among pregnant women in Norway.

## MATERIAL AND METHODS

*Study population.* From June 1992 to May 1993, pregnant women in 11 of Norway's 19 counties, attending their first antenatal health care visit, were invited to participate in the study. An information leaflet about the study was available to all women. A total of 35940 women agreed to be included. In the study area 35343 live births were notified in 1993, representing 59.2% of all live births in Norway that year [11].

*Serum analyses.* A serum sample from each woman was sent to the *Toxoplasma* Reference Laboratory at the National Institute of Public Health through local collaborating laboratories.† The samples were examined for *Toxoplasma*-specific IgG antibodies using an enzyme-immunoassay (EIA) (Platelia Toxo-IgG, Sanofi Diagnostics Pasteur, Marnes la Coquette, France) [12]. The results were expressed in international units per ml (IU/ml). A result of  $\geq 6$  IU/ml was regarded as positive, indicating previous *T. gondii* infection, while  $< 6$  IU/ml was regarded as negative, indicating that the woman was at risk of infection.

*Independent variables.* Information on age, gestational age, number of children, county of residence, type of area of residence (urban or rural, based on postal code) and nationality was requested on the forms accompanying the serum samples. The form was completed by the woman's health care provider. However, nationality was reported for only 1% of the participants. The women were therefore classified into two groups: women with known foreign nationality and women with first and/or family names that were obviously not Norwegian, were classified as 'foreigners'. The remaining women were grouped as Norwegians. By this method any Danish or Swedish women were probably classified as Norwegians.

*Statistical analyses.* Univariate analyses were carried out using the computer programme Epi Info (Epi 6.0; Centers for Disease Control and Prevention, Atlanta, Georgia, US). Age was analysed both as a categorical (5-years interval) and as a continuous variable. The association with number of children was analysed as a continuous, dichotomous (0 vs.  $\geq 1$ )

and categorical variable. The significance of differences between groups was assessed using the  $\chi^2$  test. 95% confidence intervals (CI) around the estimates of proportions were calculated by normal approximation to the binomial distribution. Multivariate analysis with multiple logistic regression was done using the computer programme SPSSW (release 6.1; SPSS Inc., Chicago, Illinois, US). The results are expressed as odds ratios (OR) with 95% CIs and two-tailed *P* values.

*Ethics.* This study was part of the National Norwegian study on Prevention of Congenital Toxoplasmosis approved by the Regional Committee for Ethics and Research (S-92039) and the Data Inspectorate (No. 92/540-2).

## RESULTS

The 35940 women enrolled in the study had a median age of 28 years (range 14–48). The average length of pregnancy was 10.1 weeks (median 10 weeks, range 1–40) at the time when the sample was collected.

*Toxoplasma*-specific IgG antibodies were detected in 3907 of women (10.9%, CI: 10.6–11.2). The prevalence was about 10% in women under 35 years of age, with no clear trend with increasing age (Table 1). Women  $\geq 35$  years had a significantly higher prevalence than younger women (14.7% vs. 10.4%,  $P < 0.001$ ).

Women classified as foreigners had a prevalence of *Toxoplasma* antibodies (24.2%) more than twice that of Norwegians (10.3%) (Table 1). This difference was significant for all age groups ( $P < 0.005$ ) except for  $\geq 40$  years ( $P = 0.066$ ), where a low number of foreigners ( $n = 62$ ) resulted in a broad confidence interval (25.8%, CI: 14.9–36.7) (Fig. 1). The increase in prevalence after 34 years of age was significant for the Norwegian women only. No significant difference according to age was detected among the foreigners.

The highest prevalence (13.4%) was found in the southern part of Norway, characterized by coastal climate with humid summers and relatively mild winters. The lowest prevalence (6.7%) was found in Northern Norway (Table 1). A low prevalence was also found in the inland counties (8.2%) where there is a dry climate with cold winters and warm summers.

In the capital city of Oslo, the most urbanized area in Norway, the prevalence was 13.2% (CI: 12.5–13.9). This was significantly higher than among women living in other cities (10.1%, CI: 9.6–10.7) or in rural areas (10.2%, CI: 9.8–10.7) ( $P < 0.001$ ) (Fig. 2).

† See p. 91.

Table 1. Prevalence of IgG antibodies to *T. gondii* among pregnant women in Norway (1992–4) according to place of residence, age, number of children and nationality, and logistic regression analysis of these risk factors for being seropositive

| Variable/risk factor | Total* | Sero-positive | Sero-negative | Prevalence (%) | 95% CI    | Odds ratio | 95% CI    | P-value |
|----------------------|--------|---------------|---------------|----------------|-----------|------------|-----------|---------|
| Total                | 35940  | 3907          | 32033         | 10.9           | 10.6–11.2 | —          | —         | —       |
| Age group (years)    |        |               |               |                |           |            |           |         |
| < 20                 | 1272   | 123           | 1149          | 9.7            | 8.0–11.3  | 1.00†      | —         | —       |
| 20–24                | 8079   | 826           | 7253          | 10.2           | 9.6–10.9  | 1.02       | 0.77–1.36 | 0.89    |
| 25–29                | 13387  | 1352          | 12035         | 10.1           | 9.6–10.6  | 0.98       | 0.74–1.30 | 0.87    |
| 30–34                | 9074   | 1001          | 8073          | 11.0           | 10.4–11.7 | 1.00       | 0.75–1.34 | 0.98    |
| 35–39                | 3501   | 500           | 3001          | 14.3           | 13.1–15.4 | 1.29       | 0.96–1.75 | 0.096   |
| ≥ 40                 | 627    | 105           | 522           | 16.7           | 13.8–19.7 | 1.53       | 1.05–2.23 | 0.028   |
| Nationality          |        |               |               |                |           |            |           |         |
| Norwegian            | 33386  | 3330          | 30056         | 10.0           | 9.7–10.3  | 1.00†      | —         | —       |
| Foreign              | 2554   | 577           | 1977          | 22.6           | 21.0–24.2 | 2.42       | 2.14–2.74 | < 0.001 |
| Region               |        |               |               |                |           |            |           |         |
| Northern Norway      | 3229   | 215           | 3014          | 6.7            | 5.8–7.5   | 1.00†      | —         | —       |
| Mid Norway           | 9141   | 885           | 8256          | 9.7            | 9.1–10.3  | 3.45       | 2.37–5.01 | < 0.001 |
| Inland               | 6434   | 526           | 5908          | 8.2            | 7.5–8.8   | 2.88       | 1.97–4.22 | < 0.001 |
| Southern Norway      | 8887   | 1193          | 7694          | 13.4           | 12.7–14.1 | 5.38       | 3.72–7.79 | < 0.001 |
| Capital city         | 8249   | 1088          | 7161          | 13.2           | 12.5–13.9 | 4.65       | 3.21–6.75 | < 0.001 |
| Number of children‡  |        |               |               |                |           |            |           |         |
| None                 | 8279   | 732           | 7547          | 8.8            | 8.2–9.5   | 1.00†      | —         | —       |
| 1                    | 10227  | 1046          | 9181          | 10.2           | 9.6–10.8  | 1.17       | 1.05–1.30 | 0.003   |
| 2                    | 4685   | 578           | 4107          | 12.3           | 11.4–13.3 | 1.40       | 1.24–1.59 | < 0.001 |
| ≥ 3                  | 2122   | 317           | 1805          | 14.9           | 13.4–16.5 | 1.54       | 1.31–1.80 | < 0.001 |

\* There were no missing values except where indicated.

† Baseline level for comparison.

‡ Missing value for 10627 women (29.6%) (1234 seropositive and 9393 seronegative).

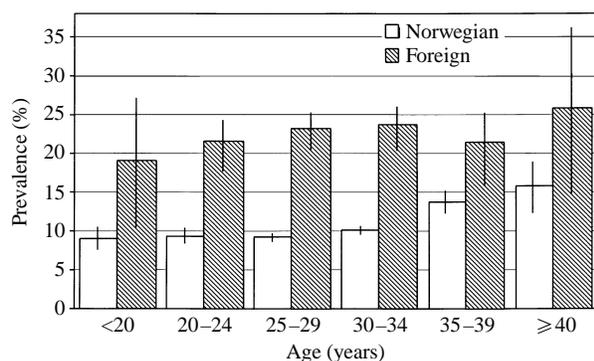


Fig. 1. Prevalence of *Toxoplasma*-specific IgG for Norwegians and foreigners among 35940 pregnant women in Norway (1992–3). Vertical bars: 95% CI.

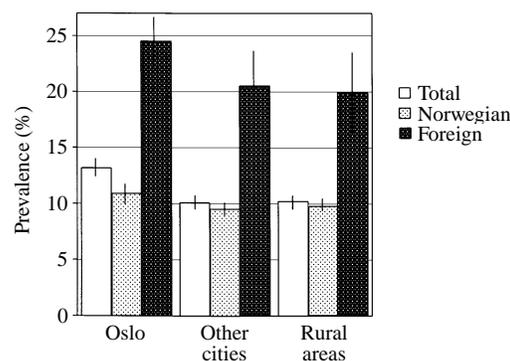


Fig. 2. Prevalence of *Toxoplasma*-specific IgG according to living in an urban or rural area among 35940 pregnant women in Norway (1992–3). Vertical bars: 95% CI.

55.1% of all pregnant women in the study classified as foreigners, lived in Oslo, where 17.2% of the women had foreign names. Outside Oslo the proportion of foreigners was only 4.3%. When comparing Norwegians only, there was no significant difference in prevalence between pregnant women living in Oslo and those living in other urban or rural areas (Fig. 2).

Information on the number of children was available for 70.4% of the women. The prevalence was higher for women with children, and increased with increasing numbers of children (Table 1).

Logistic regression analysis confirmed that the risk of being previously infected with *T. gondii* increased for pregnant women living in the southern part of the

country as compared to women living in the north (Table 1).

Having a foreign name was also independently related to an increased risk of previous infection.

The association of increasing prevalence and age was weakened by the regression analysis. The risk of being seropositive was significantly higher only for women  $\geq 40$  years of age, compared to women  $< 20$  years (OR = 1.53,  $P = 0.028$ ). However, the positive association between prevalence and number of children remained significant (Table 1).

No significant first order interactions among the variables were observed.

## DISCUSSION

The prevalence of IgG antibodies against *T. gondii* among pregnant women in Norway is low compared to pregnant women from other European countries [13]. Recent studies from the neighbouring countries of Denmark [14] and Finland [15] reported prevalences of 27.4% and 20.3% respectively. In general, a higher prevalence has been found in southern countries than in northern countries [13]. This difference may be explained by the influence of the climate on the survival of *Toxoplasma* oocysts in the environment [16, 17]. In addition different eating habits and differences in husbandry of domestic animals may influence exposure to infection.

The differences in prevalence within Norway strengthen the evidence that differences in climate play a role in the risk of being *Toxoplasma* infected. However, we cannot completely exclude the possibility that minor differences in eating habits and husbandry practices across geographical regions within the country may have contributed to the differences in prevalence observed. Previous studies of pregnant women in Norway [18] and Sweden [19], and of military recruits in Norway [20] and the USA [21], have also found a lower prevalence among individuals living in a cold or dry climate.

The higher prevalence among pregnant women in Oslo city compared to other urban or rural areas in our study, was explained by the high proportion of foreigners in Oslo. Women with foreign names had a much higher prevalence than Norwegians. In Denmark [14] and Sweden [19] no difference in prevalence between urban versus rural areas has been found. However the global prevalence in these studies was higher.

Many studies have found increasing antibody prevalence with age [1, 13, 22–24]. Our study showed only an increase in prevalence for women  $\geq 35$  years of age. A similar prevalence profile was found in the UK [25, 26]. Our results indicate that the risk of infection prior to pregnancy is low in Norway. The increase in prevalence above the age of 40 does not necessarily reflect an increase in risk of infection among the eldest pregnant women. The possibility exists that this finding reflects a cohort effect, caused by a higher risk factor exposure earlier in life for women now above 40 (e.g. before the introduction of household freezers in Norway in the 1960s).

A study among pregnant women in Oslo in the late seventies found a similar prevalence (12%) to that in our study (13.2%) [18]. Thus, a decrease in prevalence over the last decade, as demonstrated in studies from Sweden [29], UK [30] and France [13], seems not to have occurred among pregnant women in the capital city of Norway, not even when only Norwegians are considered.

In the multivariate analysis the risk of being *Toxoplasma* IgG antibody positive was slightly higher for women with children (Table 1), independent of age. To our knowledge, an association between previous *Toxoplasma* infection and number of children, has not previously been demonstrated. How children contribute to an increase in prevalence of *T. gondii*-specific antibodies among pregnant women, is not known. It is possible that women with children are more likely to have contact with cats, or are less careful when preparing food. In a case-control study on risk factors for *T. gondii* infection during pregnancy, children were not identified as representing an independent risk factor [3]. However, since that study comprised only 63 cases and 128 controls, small differences in risk, as observed in the present investigation, would not have been detected.

Our method of classifying women as Norwegian or foreign gave a crude estimate of nationality. In the whole country approximately 5% of the population is classified as first or second generation immigrants [31]. In our study Norwegian women with uncommon names may have been erroneously classified as foreigners, while some women, especially from the other Scandinavian countries and foreign women who have married Norwegians, may have been grouped as Norwegians. However, women with foreign names had a significantly higher prevalence of *Toxoplasma*-specific antibodies than Norwegian women (Table 1). This may be explained by a greater risk of infection

before settling in Norway and by different eating habits. A higher prevalence among women of foreign nationality has also been found in Sweden and in London [29, 32].

Several attempts have been made to estimate incidence of *Toxoplasma* infection on the basis of prevalence data [19, 26–28]. While such estimations seem warranted when based on repeated cross-sectional studies performed over a period of several years [27], the estimates are likely to be inaccurate when only a single investigation has been done. The incidence of primary *T. gondii* infection among pregnant women in Norway was studied in the prospective part of this research project, and the result will be presented separately.

The cut-off used in the specific *Toxoplasma* IgG assay may have had an influence on the proportion of seropositive women. According to the recommendations given by the manufacturer  $\geq 6$  IU/ml was regarded positive in our study. We compared the global prevalence at different cut-off values. The global prevalence was significantly different from 10.9% (cut-off value  $\geq 6$  IU/ml) only when the cut-off value was  $\leq 4$  IU/ml or  $\geq 9$  IU/ml (results not shown).

The total cost of a prenatal antibody screening programme aimed at preventing congenital toxoplasmosis, heavily depends on the number of women susceptible to primary *T. gondii* infection and the number of serum samples collected per woman during pregnancy. In Austria 63.3% of pregnant women have been found to be susceptible to infection and they are examined three times [7]. In France, where examination for specific *Toxoplasma* antibodies is performed routinely every month during pregnancy [9], the proportion of susceptible women varies from 28–64% in different regions [13]. If a nation-wide prenatal antibody screening programme were introduced in Norway, 89.1% of pregnant women would have to be followed serologically until delivery. The number of tests recommended and costs of such a programme, must be weighed against the effectiveness of the programme to prevent congenital infection and damage.

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