Neonatal conjunctivitis (NC) or ophthalmia neonatorum refers to any conjunctivitis occurring in the first 28 days of life. NC is the most common infection of any kind in neonates, occurring in up to 10% of live births. NC is identified as a specific entity distinct from conjunctivitis in older infants because it is often the result of infection transmitted from the mother to the infant during delivery.

Specific sexually transmitted infections (STIs) include *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and the herpes simplex virus. These may be associated with severe ocular or systemic complications. Indeed, prior to the introduction of prophylaxis with silver nitrate in 1880, NC caused by *Neisseria gonorrhoeae* (GON) was a significant cause of corneal perforation and neonatal blindness. NC caused by *Chlamydia trachomatis* (CON) has a low risk of blindness. However, *Chlamydia trachomatis* is still an important cause of NC as it may lead to corneal and conjunctival scarring if left untreated, is resistant to usual topical treatments and may be associated with pneumonitis. In mothers who have proven STIs, the transmission to infants developing conjunctivitis is estimated to be around 15% for chlamydia and 30–50% for gonorrhea. But the rate of transmission is unknown for those who have been treated.

Since 2010, two district health boards (DHBs), Lakes and Tairāwhiti have consistently had the highest chlamydia rates in New Zealand. In those aged 15–29 years the highest estimated chlamydia rates were reported for Māori and Pacific ethnic groups. The highest rate of gonorrhoea was reported in Tairāwhiti DHB, with 316 cases/100,000 population—more than four and a half times the estimated national rate (see Table 1 for further breakdown of DHBs).

By comparison, 2016 rates of chlamydial and gonorrhoeal infections in England were 354.7/100,000 and 59.6/100,000, respectively, and in the US, 497.3/100,000 and 145.8/100,000, respectively.
Reported rates of NC around the developed world are sparse. The UK rates of CON and GON in 2003 were 6.9 and 3.7/100,000 births, respectively, while in Ontario, Canada, 2004 combined rates of GON and CON were 4.5/100,000 births. In the US, 2002 combined rates were 8.5/100,000 births and 2015 rates were 2.1 and 0.2/100,000 births for CON and GON respectively.

Prophylactic eye drops have never been formally used in New Zealand. Internationally, including North America and most of Europe, eye drops with a one and two percent silver nitrate solution have been installed into the infant’s eyes at birth. Recently, topical povidone-iodine and antibiotics including tetracyclines and erythromycin ointment have been used, due to lower rates of chemical conjunctivitis and perceived increased efficacy against CON.

There is however a recent trend away from prophylaxis in the developed world.

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There is however a recent trend away from prophylaxis in the developed world.

Given this background, the publicly reported “high rates” of chlamydia and gonorrhoea infections in New Zealand and the recent availability of more sensitive diagnostic swabs, we aimed to characterise rates of NC in a New Zealand setting. Specific aims were to estimate the rates of CON and GON and to compare rates relative to ethnicity and deprivation.

Study methods

The Midland region of New Zealand is comprised of five district health boards: Bay of Plenty (BOP), Lakes, Tairāwhiti, Taranaki and Waikato. Waikato, Pathlab and Midlab Central Laboratories provide for four of the five DHBs in the Midland region (Taranaki excluded) as well as Whanganui and Midcentral DHBs (Figure 1). These DHBs are included in the study as these three laboratories provide complete coverage of these DHBs. As CON and GON are relatively uncommon all six DHBs have been included to allow the most accurate rates to be calculated.

These six DHBs are notable in that they have a higher proportion of Māori, and a higher number of people living in high deprivation compared to New Zealand as a whole. Demographics are reported in Table 1.

Part 1: incidence of NC

A dual infection Nucleic Acid Amplification Technique (NAAT) test, a more sensitive one swab test for chlamydia and gonorrhoea replaced culture in New Zealand in late 2012/early 2013.

A data search for all positive NAAT eye swabs for *Chlamydia trachomatis* and NAAT and bacterial culture eye swabs for *Neisseria gonorrhoeae* for infants younger than one year of age (this allows capture of all relevant results as although infants may develop conjunctivitis before 28 days, it may be some time before the correct swab is taken which identifies the correct organism) were retrieved from the Waikato Hospital.

Table 1: Demographics of DHBs included in this study.

<table>
<thead>
<tr>
<th>Region</th>
<th>Population 2016/17 +/- 500</th>
<th>Māori %</th>
<th>NZ Dep Q 5* %</th>
<th>2014 adult STI rates per 100,000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bay of Plenty</td>
<td>227,000</td>
<td>25.1</td>
<td>25</td>
<td>689</td>
</tr>
<tr>
<td>Lakes</td>
<td>105,000</td>
<td>35.2</td>
<td>35</td>
<td>1,144</td>
</tr>
<tr>
<td>Midcentral</td>
<td>174,000</td>
<td>19.9</td>
<td>26</td>
<td>695</td>
</tr>
<tr>
<td>Tairāwhiti</td>
<td>48,000</td>
<td>50.2</td>
<td>48</td>
<td>1,143</td>
</tr>
<tr>
<td>Waikato</td>
<td>401,000</td>
<td>22.9</td>
<td>25</td>
<td>661</td>
</tr>
<tr>
<td>Whanganui</td>
<td>62,000</td>
<td>26.5</td>
<td>37</td>
<td>702</td>
</tr>
<tr>
<td>Subtotal</td>
<td>1,017,000</td>
<td>25.6</td>
<td>28</td>
<td>748</td>
</tr>
<tr>
<td>Total NZ population</td>
<td>4,794,000</td>
<td>15.8</td>
<td>20</td>
<td>629</td>
</tr>
</tbody>
</table>

*Percentage of population in New Zealand Deprivation Quintile 5, the most deprived quintile.
laboratory, Pathlab and Medlab Central from 1 January 2013 to 31 December 2016 (Medlab Central started NAAT testing in February 2013). The following variables were collected: Date of birth, Date swab taken, Chlamydia swab positive yes/no, Gonorrhoea swab positive yes/no. The National Health Identifier number (NHI) was collected to ensure no duplication of results.

The annual birth rate, from Statistics New Zealand, was taken for each DHB—1 January to 31 December, available as total live births and live births Māori child.
Part 2: subgroup analysis

To collect ethnicity, domicile and maternal information, positive swabs from Waikato and Tairāwhiti DHBs were further evaluated using each DHBs intranet health record, Clinical Workstation. If the patient had their NHI anonymised no other data was collected.

The following data was collected: From the infant; total number of eye swabs taken, and organisms tested for (initial misdiagnosis), ethnicity of the infant (using prioritised output), domicile at birth. From the mother (if recorded from DHB clinical intranet); maternal age at birth, if maternal STI investigations during pregnancy and, if diagnosed with an STI during pregnancy, date of subsequent tests occurring during or after pregnancy.

The domicile (as recorded for the infant) was used to link the NZDep2013 index of deprivation score for each infant (ordinal scale ranges from 1 to 10, where 1 represents the areas with the least deprived scores and 10 the areas with the most deprived scores). This score is independent of ethnicity.

To compare the incidence between Māori and non-Māori births, birth rates from Statistics New Zealand were used; this is the ethnicity reported by the parents at the time of birth. To align with the collected ethnicity of the case series, using prioritised output we subtracted Māori births from total births to calculate non-Māori births.

This study is registered with Waikato DHB. Ethics approval was obtained in October 2017 by the Northern B Health and Disability ethics committee full review pathway; an amendment to include Part 2 was approved in November 2017. Māori consultation has occurred.

Statistical methods

Incidence was calculated per 100,000 births per annum based on four years of observations and is reported with Poisson 95% confidence intervals calculated using the mid-p method. Incidence rates were compared between regions and ethnic groups with rate ratios with mid-p exact 95% confidence intervals calculated using the epitools package, while for continuous variables (deprivation index and time) linear regression with 95% confidence and prediction intervals were calculated, population means were compared using students t-test assuming unequal variance. All analysis was conducted in R 3.4.3 (Vienna, Austria) with two-sided statistical tests considered significant at 5%.

Results

Chlamydial neonatal conjunctivitis

The mean incidence for the six DHBs is shown in Table 2. There was no evidence of a change in rate over time (P=0.8, linear regression).

Figure 2 shows the rates of CON for each DHB based on their percentage in the most deprived quintile. No DHBs fall outside the prediction interval, the variation in CON rates by DHB is most likely stochastic, that is we have observed no evidence of over or under performance by DHB after accounting for deprivation. However, there was no statistically significant linear relationship between incidence and deprivation (P=0.15).

Table 2: Incidence of CON.

<table>
<thead>
<tr>
<th>Region</th>
<th>Cases</th>
<th>Births</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>4 years</td>
<td>4 years</td>
</tr>
<tr>
<td>Bay of Plenty</td>
<td>16</td>
<td>11,000</td>
<td>143.0</td>
</tr>
<tr>
<td>Lakes</td>
<td>5</td>
<td>6,000</td>
<td>86.3</td>
</tr>
<tr>
<td>Midcentral</td>
<td>9</td>
<td>8,500</td>
<td>107.0</td>
</tr>
<tr>
<td>Tairāwhiti</td>
<td>7</td>
<td>3,000</td>
<td>248.8</td>
</tr>
<tr>
<td>Waikato</td>
<td>34</td>
<td>21,000</td>
<td>160.1</td>
</tr>
<tr>
<td>Whanganui</td>
<td>6</td>
<td>3,500</td>
<td>180.3</td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td>53,000</td>
<td>145.9</td>
</tr>
</tbody>
</table>
The regions studied all have greater deprivation than New Zealand as a whole, with minimum 25% Q5 deprivation.

**Part 2 results from case series Waikato and Tairāwhiti**

The specific ethnicity rates for Māori and non-Māori births for Waikato and Tairāwhiti DHBs is shown in Table 3. Non-Māori were predominantly New Zealand European and Pacifica. The incidence of CON is 2.5 times greater in Māori than non-Māori (1.3,5.1, P<0.01).

The mean number of swabs performed to gain correct diagnosis was 1.35 (median 1, maximum 3). The mean age of the infant at time of the correct swab was 16 days (median 14, minimum 1, maximum 57). The mean NZDep13 score was 8.00 (CI 7.10–8.90), median 9. There was no significant difference in mean NZDep13 for Māori vs non-Māori.

The median maternal age was 20 (minimum 16, maximum 36), (National median age of birth 30 years). There was

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**Table 3: Specific ethnicity rates for Tairāwhiti and Waikato DHBs.**

<table>
<thead>
<tr>
<th>Location</th>
<th>Ethnicity</th>
<th>Cases</th>
<th>Births</th>
<th>Incidence</th>
<th>Rate ratio</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>±500</td>
<td>Cases/births (95% CI)</td>
<td>Māori/non-Māori (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Tairāwhiti</td>
<td>Māori</td>
<td>5</td>
<td>2,000</td>
<td>255.2 (93.5, 565.7)</td>
<td>1.04 (0.22, 8.12)</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>Non-Māori</td>
<td>2</td>
<td>1,000</td>
<td>233.9 (39.2, 772.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waikato</td>
<td>Māori</td>
<td>19</td>
<td>8,500</td>
<td>230.2 (142.7, 352.9)</td>
<td>2.70 (1.30, 5.91)</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Non-Māori</td>
<td>11</td>
<td>13,000</td>
<td>84.8 (44.6, 147.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>Māori</td>
<td>24</td>
<td>10,000</td>
<td>235.0 (154.1, 344.4)</td>
<td>2.49 (1.28, 5.06)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>Non-Māori</td>
<td>13</td>
<td>14,000</td>
<td>94.0 (52.3, 156.7)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
no significant age difference between Māori and non-Māori. Eleven women (30%) had STI screening investigations in pregnancy, of those only one result was negative, and no repeat tests of cure were carried out on the other positive samples. Fifty-four percent (n=20) of women had no STI investigations in pregnancy. It was unknown if a further 16% (n=6) of women were investigated or not.

Gonorrhoeal neonatal conjunctivitis

Two infants had a positive eye swab for gonorrhoea, giving a total incidence density rate for the study population of 3.8/100,000 births/year (CI 0.5, 12.5).

Discussion

Our calculated rates for the greater New Zealand Midland region are CON, 146 per 100,000 births/year (CI 116, 181) and GON, 3.8 per 100,000 births/year (CI 0.5, 12.5). For combined Tairāwhiti and Waikato DHBs the incidence of CON is 2.5 times greater in Māori than non-Māori (CI 1.28, 5.06). Mean NZDep13 score was 8.00, there was no significant difference in mean NZDep13 for Māori vs non-Māori. Median maternal age at birth was 20. The mean number of swabs in the case series taken to gain the correct diagnosis was 1.35. This highlights incorrect testing by medical practitioners for NC in infants as some infants did not have the initial correct swab taken for NAAT testing.

Rates from the greater New Zealand Midland region are 21x higher for CON and similar for GON compared to the UK 2003 rates and are 69x higher for CON and 19x higher than US 2015 rates.

These other international studies do not state the methods of testing, collection and reporting rates of CON and GON, so it is unknown if this is the first study to calculate rates of NC using NAAT testing. Comparison of the rates in our study with these other studies should be treated with reservation. Bacterial STI epidemiology often reflects social determinants of health, including access to quality preventative and screening/treatment services. STI rates are generally higher in areas of greater deprivation and in more rural isolated areas of New Zealand. In 2014, the highest rates of genital chlamydia infections by age and sex-specific rate occurred in the 15–19 years age group in females in the Māori ethnic group (11,246 per 100,000). Rates among females were consistently higher than those of their male counterparts. The female Māori rates were two to three times greater than the estimated national rate in all three age groups. STIs also frequently co-exist, with dual infection of gonorrhoea and chlamydia present in up to 39% of cases. It is estimated that one in five women aged under 25 years will be re-infected with chlamydia within six months.

These higher rates of genital chlamydia in young Māori women may explain why rates of CON are higher in Māori infants and why the median maternal age of mothers affected by CON is lower than the national median birth age.

The mean NZDep13 score for the infants in the case series is eight (range 0 to 10). This indicates that the infants in this case series reside in areas of high deprivation. This is not a direct measurement of the deprivation of the infant or representative of all the infants included in this study. However, this score is consistent with the higher deprivation indices of the DHBs included in this study. Māori are more likely to reside in areas of greater deprivation in New Zealand compared to non-Māori. As there is no statistical difference in NZDep13 scores between Māori and non-Māori this suggests that deprivation rather than ethnicity is accounting for higher rates among Māori in this case series.

Strengths of this study are that rates have been observed over four years and over 53,000 births. Conjunctivitis in a newborn infant creates worry in parents, and so they are likely to seek medical advice. As GON and CON are generally resistant to the usual topical treatments, it is likely that most cases will present for eye swabs until a NAAT test is undertaken, and as NAAT is a more sensitive test, it is likely that most cases over the duration of this study have been identified. Weaknesses of this study are in the fact of its retrospective, observational nature. The regions included in this study are of a higher deprivation than the national average, so data from areas of different demographic regions with less Māori, greater migration, or the major urban area around Auckland is needed to infer national rates. Total birth number ethnicity was recorded from Statistics New Zealand, whereas for identified cases from...
DHB records, only two cases of GON were identified. A larger population or longer duration study is needed to calculate more accurate rates. It should be noted that NAAT was introduced in Medlab Central in February 2013 and so cases could have been missed while uptake of the test occurred.

New Zealand guidelines recommend antenatal screening for genital chlamydia and gonorrhoea for those that may be at increased risk of infection due to local prevalence, but don’t define increased risk. New Zealand studies have shown variable rates of uptake of antenatal screening (24–61%). Newer evidence also points to the importance of re-infection or persistent infection within three months. It is unknown how much, if any, repeat testing occurs in pregnancy in New Zealand. We feel this study highlights the essential importance of antenatal STI screening. Some revision of the New Zealand guidelines may be needed to better define this.

If NC is suspected in an infant, both a NAAT swab and a bacterial swab are indicated to ensure timely identification of the correct organism and to allow appropriate treatment. This is especially so with the increased prevalence of drug resistant strains of *N. Gonorrhoeae*.

In our study, CON and GON rates are higher than the US and similar to rates of GON in the UK, where prophylaxis has been abandoned. Prophylaxis is generally only effective against GON, with only marginal benefit against CON. Larger studies with broader demographic coverage are necessary to make estimates for the entire population of New Zealand and to enable valid recommendations on the role of ocular prophylaxis.

Greater Midland region rates of CON and GON are higher compared to other international reported rates. For Tairāwhiti and Waikato, rates of CON are significantly higher in Māori than non-Māori, although there is no difference in mean NZDep13 scores between Māori and non-Māori. CON appears to be a condition of babies of young mothers with higher deprivation. Practitioners should be aware of this. Current guidelines suggest antenatal screening for STIs only if there is perceived increased risk. We suggest that antenatal STI screening should be routinely advised, especially for those of higher deprivation. If an infant does present with conjunctivitis, practitioners should be aware that taking a NAAT swab to test for chlamydia and gonorrhoea is of essential importance in their evaluation of the infant.

Competing interests: Nil.

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samuelnewlands@gmail.com

URL:
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10. Table 1. Sexually Transmitted Diseases — Reported Cases and Rates of Reported Cases per 100,000 Population, United States, 1941–2016 Atlanta, USA Centers for Disease Control and Prevention; 2017 [Updated September 26, 2017. Available from: https://www.cdc.gov/std/stats16/tables/1.htm.]


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