New Zealand national incidence of bronchiectasis – “too high” in a developed country

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Abstract

Aims: To prospectively estimate the incidence of bronchiectasis amongst New Zealand (NZ) children; to consider aetiology and severity; and to evaluate regional and ethnic variation.

Methodology: NZ paediatricians were surveyed monthly for new cases of bronchiectasis during 2001 and 2002 via the NZ paediatric surveillance unit (with coverage of > 94% of NZ paediatricians). All computer tomography scans were reviewed for diagnosis and scored for severity. Confirmed cases were followed up by postal questionnaire one year after diagnosis. Demographic, aetiological and severity data was collected.

Results: Ninety nine notifications were received. Sixty five cases were confirmed. An overall incidence of 3.7 diagnoses per 100,000 under 15 year old children per year was estimated. Incidence was highest in Pacific children, 17.8 compared with 4.8 in Maori, 1.5 in NZ European and 2.4 other per 100,000 per year. Incidence varied significantly by region. The median age at diagnosis was 5.2 years. The majority had symptoms for more than 2 years. Eighty three percent had bilateral disease, with a median of 3 lobes affected. The mean FEV1 of 77% predicted and mean modified Bhalla HRCT score was 18.

Conclusions: The incidence of bronchiectasis is high in NZ children, nearly twice the rate for cystic fibrosis and 7 times the only other country reporting a childhood national rate, Finland. Incidence varied substantially between ethnicities. Most cases developed disease in early childhood and had delayed diagnosis.
Introduction

Bronchiectasis is a morphological diagnosis based on dilatation of bronchial airways and is associated with recurrent lower respiratory tract infection, significant morbidity and mortality. The incidence of bronchiectasis (BE), not due to cystic fibrosis, may have fallen in the 20th century with the advent of improved living conditions, vaccination and antibiotics. However recent reports of high prevalence, morbidity and mortality within certain communities raises concern.1-6 The limited population data that does exist is hard to compare due to the use of varying denominators, case definitions and methodologies. Good data is needed to make informed decisions on population health measures, as well as determining the need and direction of future research.

Two national bronchiectasis estimates have recently been reported. In Finland the incidence has been estimated at 0.5 per 100,000 under 15 year old children per year and 3.9 per 100,000 per year overall.7 In the United States the prevalence has been estimated at 52:100,000 overall and results in an additional 1.1 billion US dollars of health care expenditure per annum.6 Much higher prevalences have been reported in some communities - 16:1,000 Southwest Alaskan Native children and 15:1,000 central Australian Aborigine children.4,8 The impact of BE in New Zealand (NZ) has caused concern for some time but data has largely been limited to hospitalisation and mortality data – reported at 50 deaths per 100,000 in Maori and Pacific People.9,10 Compared with asthma, a far more common respiratory disease, BE causes one tenth the hospital admissions and half the number of deaths.11,12 It results in 75% more admissions and nearly five times as many deaths as CF.11,12 Significant BE mortality doesn’t begin until adulthood in NZ, however it is likely that in many cases the disease began in childhood.13 A recent report of high prevalence in children living NZ’s largest city (1:6,000 overall with 1:1,900 Pacific Island children) increases concern.2

The aim of this study is to prospectively estimate the national incidence of BE diagnoses over a 2 year period in the 0.85 million NZ children. The study will also identify regional variation, aetiology and severity.

Methods

New cases of BE were identified through the NZ Paediatric Surveillance Unit (NZPSU). Each month participating clinicians are sent either a reply paid card or an email (as self nominated) to report new cases of conditions under surveillance. BE was included on the NZPSU Report Card for 2001 and 2002.

Case definition:

• a high resolution computer tomography (HRCT) consistent with bronchiectasis,
• ≤15 years of age at HRCT diagnosis,
• productive cough daily for >6 weeks or for 3 months per year for 2 consecutive years,
• persistent chest x-ray abnormalities and
• not due to cystic fibrosis.

Following notification the referring paediatrician was asked to send the HRCT to the study centre. The case’s identity remained anonymous. A single paediatric radiologist (RM), with no clinical data, reviewed HRCT for diagnosis using the criteria of Naidich et al14 and severity using the modified Bhalla score.15-17 This score has been validated in adult and paediatric BE and assigns a value to each lobe and the lingula as follows: BE extent (0-3), bronchial wall dilatation (0-3) and thickness (0-3), presence of mucus in large (0-1) and small
airways (0-1), air trapping (0-4), atelectasis (0-1) and consolidation (0-1) resulting in a worst possible score of 102.\textsuperscript{15,16} Postal questionnaires were sent to the paediatrician one year after notification collecting demographic details, investigation results and ascribed aetiology. The delay was to allow time for investigation without influencing it. Multiple responses were allowed for ethnicity data. Incidences were calculated using under 15 year old cases as numerators and NZ 2001 Census figures for denominators.\textsuperscript{18} Pulmonary function is reported as percentage of predicted (Polgar reference).\textsuperscript{19} Prospective ethical approval was gained. Statistical software package SPSS version 11.5 (SPSS Inc. Chicago, IL, USA) was used. Chi-square, Kruskal-Wallis and Spearman (Rs) were used for non-parametric data, T-test and ANOVA for parametric data.

**Results**

Ninety nine notifications were received over the two years. Thirty-two were excluded due to: duplication / error (10), diagnosis outside the study time period or age range (7), no or non-definitive HRCT (15). Two cases were lost to follow up leaving sixty-five confirmed cases, 63 under 15 years of age. Half of confirmed notifications came from respiratory specialists and one third from general paediatricians. At diagnosis (median age 5.2 years) forty percent of cases had cough for $\geq 2$ years (Table 1.) The median age of reported symptom onset was 2.3 years. Three quarters had prior hospital admission for other respiratory illness at a median 1 year of age. Only 8% had no hospital admissions and 18% were known to have BE during their first respiratory admission. Ninety percent were NZ born and 5% were born outside the Pacific.

<table>
<thead>
<tr>
<th>Male: Female ratio</th>
<th>28:37 (54% female)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>Median 5.2 years (range 0.5-15 years)</td>
</tr>
<tr>
<td>Age at onset of cough</td>
<td>Median 2.3 years (range 0-14 years)</td>
</tr>
<tr>
<td>Duration of symptoms</td>
<td>Median 1.0 years (range 6 weeks to 14 years)</td>
</tr>
<tr>
<td>Age first (non BE) respiratory hospitalisation (74%)</td>
<td>Median 1.0 years (range 1 month to 13 years)</td>
</tr>
<tr>
<td></td>
<td>29% bronchopneumonia</td>
</tr>
<tr>
<td></td>
<td>33% lobar pneumonia</td>
</tr>
<tr>
<td></td>
<td>38% bronchiolitis</td>
</tr>
</tbody>
</table>

Table 1. Age, gender and past history.

**Incidence estimates:**

An overall incidence of 3.7 per 100,000 under 15 year olds per year is estimated. Incidence varied with ethnicity (1.5-17.8 per 100,000 per year, $p<0.001$, Table 2) and by region (0-8.3 per 100,000 per year, $p=0.03$, Figure 1.) More females were reported (37/65 of cases, difference not significant, $p=0.09$).
<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>NZ &lt;15 year old population (multiple choices, 2001 census)</th>
<th>Proportion of study cases</th>
<th>Incidence (per 100,000 &lt;15 year olds per year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pacific Peoples</td>
<td>11%</td>
<td>50%</td>
<td>17.8</td>
</tr>
<tr>
<td>Maori</td>
<td>23%</td>
<td>30%</td>
<td>4.8</td>
</tr>
<tr>
<td>NZ European</td>
<td>73%</td>
<td>28%</td>
<td>1.5</td>
</tr>
<tr>
<td>Other</td>
<td>8%</td>
<td>5%</td>
<td>2.4</td>
</tr>
</tbody>
</table>

Table 2. Ethnic distribution and incidence.

**Aetiology**

Notifiers reported aetiology to be unknown in 54% of cases, post infectious in 22%, sequelae of oncological disease or treatment in 11%, aspiration in 6% and primary immunodeficiency in 6% (Table 3.)

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Percent (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown / Idiopathic</td>
<td>54% (35)</td>
</tr>
<tr>
<td>Post infectious</td>
<td>22% (6 Adenovirus, 3 Pertussis, 1 Tuberculosis, 4 Other)</td>
</tr>
<tr>
<td>Post oncology</td>
<td>11% (5 leukaemia, 2 lymphoma; 1 had bone marrow transplant)</td>
</tr>
<tr>
<td>Aspiration</td>
<td>6% (3 chronic aspiration, 1 retained peanut)</td>
</tr>
<tr>
<td>Primary</td>
<td>6% (4, all humoral deficiencies)</td>
</tr>
</tbody>
</table>

Table 3. Aetiology of confirmed cases.

Those of unknown aetiology were older (median 8.3 versus 3.6 years, \( p=0.02 \)), had a longer duration of cough (3.0 versus 1.0 years, \( p=0.002 \)) and a trend to milder disease (median CT score 14 vs 21, \( p=0.11 \)). Co-morbidities were volunteered (not requested) in 10 cases - prematurity (8%), trisomy 21 (5%), congenital heart disease (2%) and progressive neuromuscular disease (2%).

**Pulmonary function**

Ninety percent (28/31) of children aged over 6 years had spirometry. The mean forced vital capacity was 85% predicted, mean forced expiratory volume in one second (FEV1) was 77% predicted and mean forced expiratory flow 25-75% was 76% predicted. Half had an FEV1 <80% and a quarter <60%. No difference in lung function was found between gender (\( p=0.13 \)), ethnicities (\( p=0.72 \)) or aetiologies (\( p=0.62 \)).

**Radiology**

Eighty three percent of cases had bilateral bronchiectasis, 61% had \( \geq 3 \) of the 5 lobes involved and only 16% had unilobular disease. Lower lobes were most frequently and most severely affected (Figure 2). The median modified Bhalla score was 18 (range 4-65) with no significant differences between gender (\( p=0.67 \)), ethnicities (\( p=0.93 \)), aetiologies (\( p=0.47 \)) or by age (\( R_s=-0.15 \)). The median scores (ranges) for CT score components (sum of lobes) were: bronchiectasis extent 5 (2-16), bronchial dilatation 4 (1-16), wall thickness 2 (0-7),
centrilobular mucus 0 (0-4), large airway mucus 0 (0-3), atelectasis 2 (0-6) and consolidation 0 (0-5). FEV1 correlated modestly with HRCT score (Rs= -0.38, p=0.04).

Investigations
A full blood count was reported in 97%, quantitative immunoglobulins in 88% (30% elevated, 2% low), specific antibody responses in 46%, immunoglobulin subclasses in 26%, complement in 25% and nitroblue test in 14% of cases. Cilia were assessed in 8% (all normal). Reflux / aspiration was assessed in 28% of cases (45% abnormal). Bacterial respiratory cultures grew *Haemophilus influenzae* in 48%, *Streptococcus pneumoniae* in 14%, *Moraxella catarrhalis* in 8%, *Staphylococcus aureus* in 8%, *Pseudomonas aeruginosa* in 3% and were negative / not done in 25%. CF was not excluded in 27% of cases; 65% of these had a definitive aetiology and the remaining were non-European with neither *Pseudomonas aeruginosa* nor *Staphylococcus aureus*.

Discussion
The principle outcome is a minimum incidence of non CF bronchiectasis in the NZ under 15 year old population of 3.7 per 100,000 per year. This rate is 7 times higher than the only other comparable national study, 0.49 per 100,000 Finnish under 15 year old children and equates to 1 in 1,700 births being diagnosed with BE before the age of 15 (about twice the CF rate, 1:3,179). If we speculate that the incidence rate is static and that all children with BE survive to 15 years of age, then our figure equates to a prevalence of 1:3,000 children overall and 1:625 Pacific children.

Ethnic differences in disease incidence, morbidity and mortality are phenomena of most developed countries. Grant et al reported the Auckland hospitalisation rate for pneumonia was twice as common in Maori and five times as common in Pacific than in NZ European children. Pacific and Maori children hospitalised also had more severe pneumonia. We found the incidence of BE to be 3 times higher in Maori and 12 times higher in Pacific Peoples compared with those of European ethnicity but with no differences in severity or aetiology. Nearly 90% of Pacific children came from Auckland which holds the largest Polynesian community in the world. Pacific Peoples are not indigenous to NZ but have immigrated in large numbers since World War II. They are a young (median age 21) and rapidly growing population with twice the national unemployment rate. They are seven times as likely to live in a dwelling with more than 2 occupants per bedroom.

Assignment of aetiology was made by the referring doctor (unverifiable by the authors) one year after diagnosis. Published case series have variable aetiological distributions, due to different diagnostic criteria, source populations, and the degree of investigation. Over half the cases in this study were of unknown aetiology. The ‘unknowns’ were older, had a longer duration of symptoms, tended to have more investigations and milder disease (CT score), perhaps a reflection of later presentation and a ‘colder trail’ for causation. Some of ‘unknown aetiology’ might have a cause determined with further investigation. Specific antibody assessment, a key element in humoral immunity evaluation, had not been performed in half of cases. Cilia studies were rarely obtained, due to poor availability. All those without a definitive aetiology and not tested for CF were non-European, had normal growth, and did not grow *Staphylococcus* or *Pseudomonas* species making CF unlikely. While NZ has had universal neonatal CF screening since 1982, clinical suspicion still warrants its exclusion. The significant number of cases in association with oncological disease deserves further review.
This study is limited by its reliance on all cases being diagnosed and then notified. A paediatrician would be expected to be involved in the diagnosis of a child with BE. The NZPSU system includes an estimated 94% of NZ paediatricians. Half the notifications came from respiratory specialists and one third from general paediatricians. There were no significant difference in aetiology, severity or investigations between notifying specialty. Surveillance unit study sensitivity varies by condition but not region or specialty with reported sensitivities of 62-89% in other NZPSU studies. Given respiratory symptoms are common in childhood and BE symptoms are non-specific, a significant proportion of cases are likely to go undiagnosed, particularly in Maori and Pacific Peoples with poorer access to health care. Fifteen notifications were excluded due to not meeting the HRCT criteria (one not having had a CT) – further review and repeat radiology may have confirmed the diagnosis. We believe our incidence figure should be taken as a minimum.

While one third of cases had cough for ≥3 years at diagnosis, children in this study were diagnosed younger and with less delay than reported in the previous Auckland study and in a recent large UK series, perhaps reflecting increasing awareness of the disease and earlier referral. However NZ children have more extensive disease than those in overseas case series and the childhood incidence is high, particularly in Pacific children. A decade ago, a NZ Public Health Commission report of the health of NZ Pacific Peoples identified bronchiectasis as a major cause of hospitalisation and the 7th highest cause of death in women. The Ministry of Health concluded the report provided a baseline for future monitoring and policy development. In the same year the NZ Government established child and Maori health as “priority gain areas”. The results of this study suggest the situation is unlikely to be better. If we are to improve, prevention of childhood BE must be a priority, and early identification and intervention is vital. We hope this study which documents a high minimum incidence figure, will contribute positively towards that goal.

Acknowledgements
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Conflicts of interest
None declared.

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Figure Legends

Figure 1
Regional Incidence

Figure 2
Proportion of cases with each lobe (and lingula) affected.

References


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