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ORIGINAL PAPER

Changes in infectious disease mortality among children in the Netherlands

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Abstract In this study we examine the changes in mortality due to infectious diseases in childhood over recent decades. We analysed mortality data among children due to infectious diseases from 1969 until 2006. This study shows a steep decline of infectious disease mortality in the 1970s, followed by a relative stabilisation thereafter. This was caused by an isolated decline in infectious disease mortality in children younger than 5 years. In children over 5 years of age the infectious disease mortality remained stable during the entire study period. Analysis of mortality data of our paediatric intensive care unit (PICU) shows an increasing trend in mortality due to infections in children with underlying illnesses. Infections in childhood have remained a stable burden of mortality over recent decades.

Keywords Mortality · Infection · Children

Abbreviations

CBS	Central Bureau of Statistics (the Netherlands)
PICU	Paediatric intensive care unit
PICE	Paediatric intensive care evaluation

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Introduction

Infectious diseases are common in childhood. Although they are mostly harmless and self-limiting, we regularly admit children with life threatening infections to our paediatric intensive care unit (PICU). In this study we examine the changes in mortality due to infectious diseases in childhood during recent decades.

Materials and methods

We obtained the Dutch population data from the website of the Central Bureau of Statistics (CBS) in the Netherlands [7]. This information included the total number of alive children in different age groups from 1969 to 2006, the total number of deaths in each age group, deaths due to infections in each age group, and the mortality due to meningococcal disease. The different age groups were infants, children between 1 and 5 years of age, children between 5 and 10 years, children between 10 and 15 years, and adolescents between 15 and 20 years of age. All data were collected in an Excel file. We then calculated mortality rates due to infections for different age groups from 1969 to 2006.

To find a possible explanation for the results and to estimate if the CBS data were complete, we examined the PICU mortality secondary to infections in the second part of this study.

First we obtained data from the Dutch National Paediatric Intensive Care Evaluation (PICE) database for the year 2005 only. This is a relatively new database in which all eight PICUs in the Netherlands register their admissions (epidemiological data, severity of illness score, diagnosis, outcome). We checked this database for the total

PICU mortality rate in the Netherlands in 2005, as well as the mortality due to infections.

We also performed a detailed analysis of all fatal cases admitted to the PICU of the University Medical Centre Utrecht (14 beds tertiary PICU) over the last 10 years. All patients who died were identified in our admission book, which contains information regarding the patient, date of admission, discharge date, and outcome. All medical notes of patients who died were reviewed. We specifically looked at causes of death and underlying medical conditions. The causes of death were divided into three groups. The first group was a proven infectious cause of death, which we defined as being a proven infection by culture, polymerase chain reaction, or the typical clinical picture of meningococcal disease. The second group was a possible infectious cause of death. In this group the infectious cause was not proven, but infectious cause was clinically suspected, like viral myocarditis or cardiomyopathy. The last group consisted of all other causes of death except infectious causes.

Results

Infectious disease mortality in children in the Netherlands

A steep decline in mortality due to infectious diseases in children was seen in the 1970s, followed by a relative stabilisation in the years thereafter. The mortality rate due to infections in childhood decreased from 4.3 fatal cases per year per 100,000 children in 1969 to 2.2 fatal cases per year per 100,000 children in 1978. From 1979 onwards the mortality varied around a mean of 1.5 fatal cases per year per 100,000 children (range, 0.8–2.3) (Fig. 1). Over the whole period the relative infectious disease mortality compared to the total childhood mortality remained constant around 3.0% (range, 1.38–4.96%).

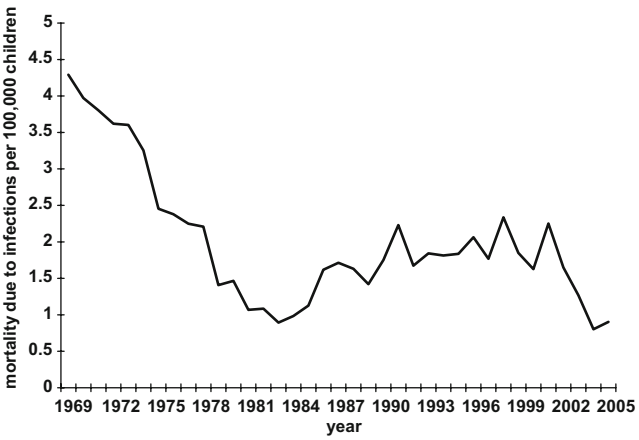

Fig. 1 Annual number of deaths in the Netherlands per 100,000 children due to infections [7]

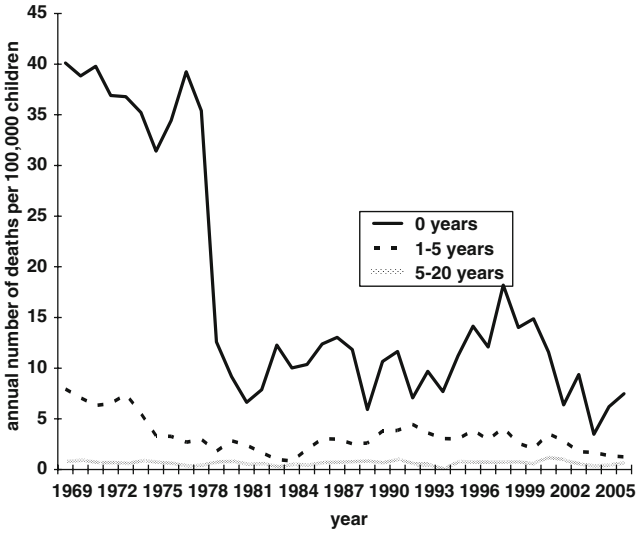

Fig. 2 Infectious disease mortality in the Netherlands in different age groups [7]

A decline in mortality due to infections was seen in infants (40 deaths per 100,000 infants per year to ten deaths per 100,000 infants per year) and to a lesser extent in children between 1 and 5 years of age (7.9 deaths per 100,000 children per year to a mean of 2.6 deaths per 100,000 children per year). The mortality rate in children over 5 years remained relatively constant over the whole study period with a mean of 0.66 deaths per 100,000 children per year (Fig. 2).

From 1987 until 2002 childhood mortality secondary to meningococcal disease and overall infectious disease mortality were associated, with about half the infectious disease mortality being caused by meningococcal disease (Fig. 3). Data on causes of infectious disease mortality were available from 1996 onwards. From that time more than

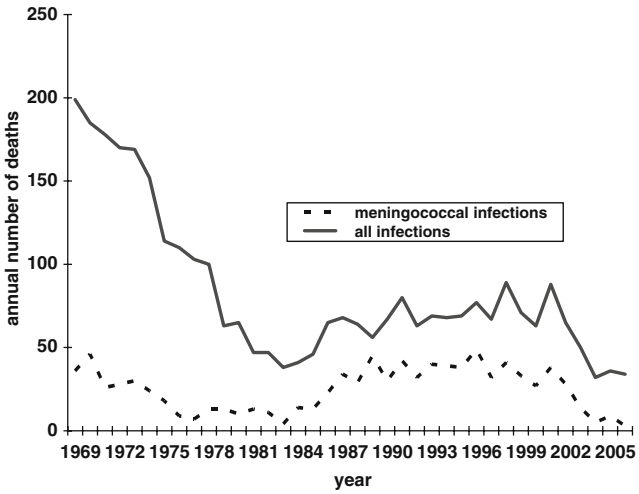

Fig. 3 Infectious disease mortality compared to meningococcal disease mortality in childhood [7]

50% of the infectious disease mortality was caused by sepsis.

Infectious disease mortality in children admitted to Dutch PICUs (PICE database)

In 2005 in the Netherlands, 4,639 children were admitted to a PICU. Of these admissions 218 children did not survive (mortality rate 4.7%). Twenty-three percent (n = 52) of these 218 children died due to an infection, most commonly sepsis. The CBS reported a fewer number of deaths (36 children) due to infections in 2005, as compared to the PICE database.

Infectious disease mortality in children admitted to PICU University Medical Centre Utrecht

We analysed the mortality data of the PICU in Utrecht for the past 10 years. This 14-bed PICU admits about 600 patients per year. The mortality rate was 5.9% of all children admitted during this period. Proven infections caused 10.5 (range, 6–15) deaths per year (29.6% of total deaths). Possible infections accounted for another 2.8 (range, 0–6) deaths per year (8.2%). Pathogens responsible for infectious disease mortality were bacteria in 66% of cases, viruses in 25%, and yeasts or moulds in 9%.

More than half of the children admitted to our PICU with a fatal infection suffered from an underlying medical condition known to increase the risk of a severe infection, like immune deficiencies, congenital heart diseases, and neuromuscular disorders. We noticed an increasing number of children with underlying illnesses among those who died due to infectious diseases over the last 10 years (Fig. 4).

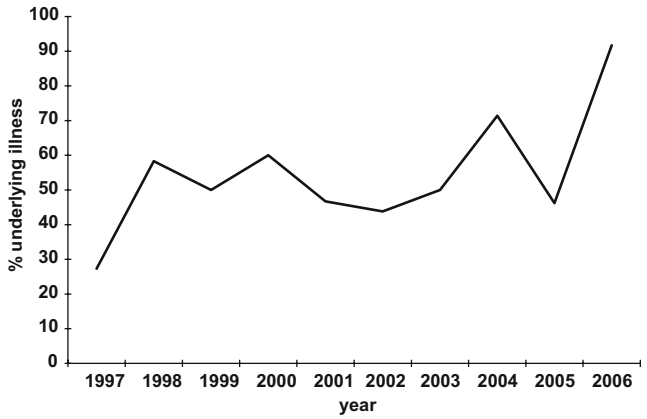

Fig. 4 Underlying illnesses in children admitted to PICU Utrecht with a fatal infection

Discussion

This study showed a steep decline of mortality due to infectious diseases in the 1970s, with a stabilisation thereafter. This can be explained by an isolated decline in mortality in children between 0 and 5 years of age. In children over 5 years of age the infectious disease mortality remained stable over the whole study period.

It still remains unclear why an isolated decrease in mortality during the 1970s in young children was seen, without any changes in the older age group.

It is unlikely that the sudden improvement could be explained by better general living conditions and medical facilities. Obviously younger children are more prone to infections in cases of poor hygienic circumstances, but living conditions in the Netherlands did not change dramatically during the 1970s. During the 1970s there was no change in immunization practices in the Netherlands, except for the introduction of a measles vaccination in 1976 and introduction of rubella vaccination in 11 year old girls in 1974. Neither of these infections had previously caused significant mortality. The combined diphtheria, tetanus, and polio immunization was introduced in 1965, but it is doubtful that this could explain our results. It is unlikely that the isolated decline of mortality in younger children is explained by poor registration of mortality data, as the same accuracy of registration in all age groups is expected. The decline of infectious disease mortality could not be explained by a concomitant decline in meningococcal mortality. The question remains if meningococcal mortality was reported well in the 1970s, as this might not have been readily recognized at that time, compared to the end of the 20th century. The decline of infectious disease mortality in infants might be explained by an isolated decline in neonatal infectious disease mortality. An epidemiological study of severe sepsis in the United States shows a high rate of severe sepsis in infants, which was largely due to neonatal severe sepsis (69.7% of infants). Two-thirds of neonates were low birth weight and half were very low birth weight [5]. Because of improved neonatal care more (very) low birth weight neonates might survive the early neonatal period and die because of severe infections. Unfortunately we do not have data on neonatal infectious disease mortality.

Mortality due to infections did not decrease since the end of the 1970s. A changing population in the Netherlands could have contributed to this: in 1972, 1.24% of the Dutch population under 20 years of age was of non-Western background, compared to 15.9% in 2007 [7]. It is possible that ethnicity plays a role in infectious disease mortality.

Moreover, the relatively constant infectious disease mortality rate since the end of the 1970s might be explained by an increase in the number of children with underlying

medical conditions with increased risk of severe infections. Decades ago children with malignancies, for example, used to die because of the malignancy, whereas more recently they often die due to complications of the treatment, like infections. This was confirmed by analysis of our PICU mortality data. In 1997, 27.3% of the children admitted to our PICU with a fatal infection had an underlying medical condition, compared to 91.7% in 2006. A similarly high rate of underlying conditions was described in an epidemiological analysis of severe sepsis in children in seven states in the United States in 1995, which showed that half of the patients had an underlying condition, like neuromuscular, cardiovascular, and respiratory disorders. Chronic lung diseases and congenital heart diseases were common in infants, whereas neuromuscular disorders and malignancies were common in older children [5].

This is the first study describing changes in mortality due to infections in children during recent decades in the Netherlands. Most studies compared the mortality rates during the last century, which showed a decline in mortality rates [1, 2]. Mortality figures from the 1970s, 1980s, and 1990s show mortality due to infections to be between 3% and 13%, depending on the year and the age group [3–6]. In these studies neonates and infants had the highest mortality rates.

The mortality rates in childhood due to infection which we report here might be an underestimation. The use of mortality data to evaluate disease burden has its limitations. Mortality statistics are only as accurate as the data provided by physicians who fill out death certificates. Validation studies have shown that the major ICD disease category (i.e. categories such as infectious diseases, respiratory diseases) listed as the underlying cause of death on death certificates differs from that determined by autopsy in 12–29% of cases [2]. This may lead to inaccurate representation of infectious diseases in mortality data. The underestimation is confirmed by our data. In 2005 only 36 children died due to an infection according to the CBS (data based on mortality statistics) compared to 52 children as noted by the PICE database (data on children admitted to one of the Dutch PICUs). In contrast, we would expect a higher mortality rate based on the CBS database, compared to the PICE database, as some children die without being admitted to PICU. In addition, changes over time in autopsy rates and in diagnostic capabilities may affect trends in mortality statistics [2].

This study confirms that the burden of infections in childhood has remained unchanged over recent decades, despite improvement of therapeutic and preventive measures. The data described here suggest that this might be explained by an increased prevalence of risk factors for a fatal infection. This has important consequences for planning further research in prevention and treatment of infections especially in children with underlying medical conditions and investing in quality care for these children.

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