The Dutch Incidence of Infantile Hypertrophic Pyloric Stenosis and the Influence of Seasons

Fenne A. I. M. van den Bunder1 Jan Hein Allema2 Marc A. Benninga3 Ivo de Blaauw4 Tim van de Brug5 Marcel den Dulk6 Jan B. F. Hulscher7 Claudia M. G. Keyzer-Dekker8 Marieke J. Witvliet9 Ernest L. W. van Heurn1 Joep P. M. Derikx1

1 Department of Pediatric Surgery, University of Amsterdam and Vrije Universiteit, Emma Children's Hospital, Amsterdam UMC, Amsterdam, The Netherlands
2 Department of Pediatric Surgery, Juliana Children's Hospital, HAGA Hospital, The Hague, The Netherlands
3 Department of Pediatric Gastroenterology, University of Amsterdam and Vrije Universiteit, Emma Children's Hospital, Amsterdam UMC, Amsterdam, The Netherlands
4 Department of Pediatric Surgery, Radboud University, Amalia Children's Hospital, Radboud UMC, Nijmegen, The Netherlands
5 Department of Epidemiology and Biostatistics, Vrije Universiteit Amsterdam, Amsterdam UMC, The Netherlands
6 Department of Surgery, MUMC+, Maastricht University, Maastricht, The Netherlands
7 Department of Pediatric Surgery, University of Groningen, Beatrix Children's Hospital, UMC Groningen, Groningen, The Netherlands
8 Department of Pediatric Surgery, Erasmus Medical Center, Erasmus University, Sophia Children's Hospital, Rotterdam, The Netherlands
9 Department of Pediatric Surgery, University of Utrecht, Wilhelmina Children's Hospital, UMC Utrecht, Utrecht, The Netherlands

Address for correspondence Fenne A. I. M. van den Bunder, MD, University of Amsterdam and Vrije Universiteit Amsterdam, Emma Children's Hospital, Amsterdam UMC, PO Box 22660, 1100DD Amsterdam, The Netherlands (e-mail: f.a.vandenbunder@amsterdamumc.nl).

Abstract

Introduction Studies report contradicting results on the incidence of infantile hypertrophic pyloric stenosis (IHPS) and its association with seasons. We aim to assess the IHPS incidence in the Netherlands and to determine whether seasonal variation is present in a nationwide cohort.

Materials and Methods All infants with IHPS hospitalized in the Netherlands between 2007 and 2017 were included in this retrospective cohort study. Incidence rates per 1,000 livebirths (LB) were calculated using total number of LB during the matched month, season, or year, respectively. Seasonal variation based on month of birth and month of surgery was analyzed using linear mixed model and one-way ANOVA, respectively.

Results A total of 2,479 infants were included, of which the majority was male (75.9%). Median (interquartile range) age at surgery was 34 (18) days. The average IHPS incidence rate was 1.28 per 1,000 LB (variation: 1.09–1.47 per 1,000 LB). We did not find a conclusive trend over time in IHPS incidence. Differences in incidence between season of birth and season of surgery were not significant (p = 0.677 and p = 0.206, respectively).

Conclusion We found an average IHPS incidence of 1.28 per 1,000 LB in the Netherlands. Our results showed no changing trend in incidence and no seasonal variation.
Introduction

Infantile hypertrophic pyloric stenosis (IHPS) is characterized by projectile vomiting after feeding. Although many risk factors have been described, including male sex, preterm birth, bottle feeding, delivery by cesarean section, and use of (macrolide) antibiotics, the etiology of IHPS remains unknown.\(^1\)–\(^5\) Incidence rates of IHPS vary from 0.18 to 12.3 per 1,000 livebirths (LB), with higher incidence in Western Europe and North America compared with other parts of the world as Asia and Africa.\(^6\)–\(^11\) It has been observed that the incidence of IHPS is decreasing and that there is a seasonal variation in the occurrence of IHPS, which appears to confirm the role of extrinsic factors in the pathophysiology of IHPS.\(^6\),\(^12\)–\(^18\)

Previous studies reported a decline of the IHPS incidence of 38% in Germany, a 47% decline in New Zealand, and even an 80% decline in Sweden.\(^12\)–\(^14\) Pedersen et al. presented epidemiological data on IHPS from seven European regions and found an overall incidence of 2.0 per 1,000 LB, ranging from 0.86 to 3.96 per 1,000 LB in the different regions.\(^15\) In contrast to others, they described both significant decreases and increases in incidence in the different countries and thus no uniform pattern of change of incidence.

Studies of seasonal variation in the occurrence of IHPS also show contradictory results. Kwok and Avery described seasonal variation for the first time in 1967, but both incidence peaks occurred 1 to 2 months later than the major peaks in birthrate, suggesting that fluctuation was a reflection of the normal birth pattern.\(^20\),\(^21\) However, others showed a significant difference in seasonal variation as well.\(^6\),\(^15\)–\(^18\) A peak incidence was found in late July in an Oxford (United Kingdom) cohort study \((n = 220)\).\(^16\) In a large population-based cohort \((n = 1,777)\) in Ontario, Canada, a higher incidence of IHPS was found during summer compared with other seasons.\(^15\) While the authors describe the lowest rate of IHPS during winter season, others found a peak incidence in winter in Belfast, Ireland \((n = 289\) patients).\(^6\) Contrary, many studies could not find any significant difference in seasonal variation.\(^11\),\(^22\)–\(^24\) One of these is a large demographic study in Taiwanese children \((n = 1,077)\), in which the authors analyzed for both admission month and birth month.\(^23\) There were also no differences in incidence between seasons in an American \((n = 11,003)\) and a Canadian \((n = 813)\) cohort, respectively.\(^11\),\(^24\)

The aim of this study is to assess the incidence of IHPS in the Netherlands and to determine whether seasonal variation is present in a large nationwide cohort.

Materials and Methods

Inclusion and Exclusion Criteria

In the Netherlands, pyloromyotomy is routinely performed in one of the seven pediatric surgical centers (Emma Children’s Hospital, Amsterdam; Juliana Children’s Hospital, The Hague; Amalia Children’s Hospital, Nijmegen; Maastricht UMC +, Maastricht; Beatrice Children’s Hospital, Groningen; Sophia Children’s Hospital, Rotterdam, and Wilhelmina Children’s Hospital, Utrecht). All Dutch pediatric surgical centers participated in this retrospective study. We included all consecutive infants younger than 6 months, hospitalized, and operated for IHPS between January 2007 and December 2017. Cases were selected based on diagnosis and treatment codes for IHPS and pyloromyotomy in accordance to the National Health Insurance claims (code 125, 126). We excluded patients who did not undergo pyloromyotomy because of misdiagnosis and infants with anatomic malformations. Infants transferred between two attending hospitals were identified and counted only once. Infants undergoing pyloromyotomy in general hospitals were excluded because detailed data were not available.

Data Extraction

Hospital files were retrospectively reviewed in reference to month and year of birth, sex, gestational age, birthweight, type of labor, multiple birth, type of feeding, and month and year of pyloromyotomy. Data were extracted by one of the authors (F.V.D.B.) and verified by a 5% random sample check. Information of national birthrate in all Dutch infants was obtained from CBS StatLine, Statistics Netherlands.\(^25\) The Medical Ethics Review Committee of VU University Medical Center Amsterdam reviewed this study (reference number 2018.210) and confirmed that the Medical Research Involving Human Subjects Act (WMO) does not apply and an official approval of this study was not required. All methods were performed in accordance with the relevant guidelines and regulations.

Definition of Seasons

Seasons were defined by means of the meteorological classification system: Winter (December, January, February), spring (March, April, May), summer (June, July, August) and autumn (September, October, November).

Statistical Analysis

Statistical analyses were performed using SPSS version 26. Incidence rates per 1,000 LB were calculated by dividing the number of infants with IHPS by the total number of LB during the matched month, season, or year, respectively. Incidence over time was analyzed by using linear regression analysis. Patient characteristics were summarized as median with interquartile range or as frequency with percentage. Because the exact etiology of IHPS is still unknown, we tested seasonal variation based on month of birth and surgery to study possible influences of season of birth and surgery. Seasonal variation based on month of birth was analyzed using a linear mixed model, with incidence rate as outcome, month or season as fixed effect and year as random effect. Seasonal variation based on month of surgery was analyzed using ANOVA, with as outcome the number of infants with IHPS per month or season divided by the number of pyloromyotomies per year. A p-value <0.05 was considered as statistically significant.

Results

Patient Characteristics

Between January 2007 and December 2017, a total of 2,568 infants younger than 6 months underwent pyloromyotomy.
A total of 89 infants were excluded because of misdiagnosis (n = 48), anatomic malformations of the gastrointestinal tract and/or prior surgery of the gastrointestinal tract (n = 31), duplicates (n = 4), and primary surgery elsewhere (n = 6). Of 2,479 infants who were included for analysis, the majority was male (n = 1,882; 75.9%). Patient characteristics are shown in Table 1. A total of 625 infants were treated by open approach and 1,855 infants underwent laparoscopic pyloromyotomy.

### Incidence Over Time

In our cohort, the incidence varied from 1.09 per 1,000 LB per year to 1.47 per 1,000 LB per year, with an average incidence of 1.28 per 1,000 LB. The highest incidence was found in 2012 (Table 2). The incidence over time is shown in Fig. 1. From 2007 to 2012, there seemed to be an increasing trend, while in the period 2012 to 2016 the incidence seemed to decrease. We did not find a significant trend over time in the incidence of IHPS per 1,000 LB during the overall study period (R square 0.004; p = 0.863).

### Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>1,882/2,479 (75.9)</td>
<td></td>
</tr>
<tr>
<td>Age at pyloromyotomy (d)</td>
<td>34 (18)</td>
<td></td>
</tr>
<tr>
<td>Gestational age (d)</td>
<td>275 (17)</td>
<td></td>
</tr>
<tr>
<td>Birthweighta (g)</td>
<td>3,440 (756)</td>
<td></td>
</tr>
<tr>
<td>Pretermb (&lt;37 wk)</td>
<td>242/2,138 (11.3)</td>
<td></td>
</tr>
<tr>
<td>Formula fedc</td>
<td>1,604/2,011 (79.8)</td>
<td></td>
</tr>
<tr>
<td>Delivery by cesarean sectiond</td>
<td>403/1,263 (31.9)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>120/2,479 (4.8)</td>
<td></td>
</tr>
</tbody>
</table>

*Values missing. |

Abbreviations: IHPS, infantile hypertrophic pyloric stenosis; LB, livebirths. 

### Incidence of IHPS and the Influence of Seasons

The incidence of IHPS in European countries varies widely from 0.6 to 8.8 per 1,000 LB, with a most commonly listed incidence of 2 to 5 per 1,000 LB. Since 1990, a decline in incidence of IHPS has been reported in several countries. Most recent incidence rates of IHPS in Europe are 0.6 per 1,000 LB in Sweden (2014) and 2.02 per 1,000 LB in Germany (2012). In the United States and Israel,
Incidence of IHPS and the Influence of Seasons
van den Bunder et al.

Comparative rates were found of 2.29 per 1,000 LB (2015) and 2.1 per 1,000 LB (2019), respectively. We found a lower incidence of IHPS in the Netherlands of 1.28 per 1,000 LB compared with other countries. It is unknown why this difference in incidence exists.

In contrast to earlier studies showing a declining trend, we found no uniform trend in incidence over time. A couple of studies have investigated different potential causes of the declining IHPS incidence, such as changes in sleeping position and folic acid consumption, but no association was found. Known risk factors for IHPS are male sex, formula feeding, birth by cesarean section, preterm birth, multiple birth, macrolide exposure, and maternal smoking. We have missed a few infants who were, despite this was possible that we have missed data through coding errors and therefore, none of the risk factors seemed to exclusively explain the changes in incidence, supporting the idea that the etiology of IHPS is multifactorial.

Several studies have shown seasonal variation in the incidence of IHPS. However, the findings of the current study do not support these findings. We found that most infants who developed IHPS were born in August and/or summer and the lowest number in December and/or winter. Consistently, provided that the majority of the infants with IHPS present around the age of 5 weeks, most infants underwent pyloromyotomy in September. However, none of the differences in month or season were significant.

The most important limitation of this study was that we were, in regard to the analysis of seasonal variation, not able to correct for risk factors such as formula feeding and birth by cesarean section because these data were not available for individuals in the national birth registry. Furthermore, it is possible that we have missed data through coding errors and that we have missed a few infants who were, despite this was a deviation of the standard, not treated in a pediatric surgical center. However, we showed nationwide data and had a large sample size, so the few missed infants would probably have a minimal effect on the results. A major strength of this study is that we performed data verification by analyzing all files of infants with IHPS and did not use a national database which is more error prone. Furthermore, our results are based on a large nationwide series during 10 consecutive years. Further studies on the incidence of IHPS should be performed in different countries and continents to seek out why incidence rates differ and if incidence rates show any pattern.

In conclusion, we found an average incidence of 1.28 of IHPS per 1,000 LB in our nationwide, large cohort without trends of changing incidence over time. The current incidence of IHPS is 1.09 per 1,000 LB. Furthermore, we did not find any evidence for seasonal variation or peak incidence in specific months. Therefore, IHPS appeared to occur at any point in the year.

Conflict of Interest
None declared.

References


