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

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Eur J Pediatr Surg

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.

Keywords

- ▶ hypertrophic pyloric stenosis
- ▶ infantile hypertrophic pyloric stenosis
- ▶ incidence
- ▶ seasonal variation
- ▶ epidemiology

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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.¹⁹ 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; Beatrix 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.

Table 1 Baseline characteristics

Male	1,882/2,479 (75.9)
Age at pyloromyotomy (d)	34 (18)
Gestational age (d)	275 (17)
Birthweight ^a (g)	3,440 (756)
Preterm ^a (<37 wk)	242/2,138 (11.3)
Formula fed ^a	1,604/2,011 (79.8)
Delivery by cesarean section ^a	403/1,263 (31.9)
Multiple	120/2,479 (4.8)

Abbreviations: IHPS, infantile hypertrophic pyloric stenosis; IQR, interquartile range.

Note: Legend values are number/ total number (valid percent) or median (IQR).

^aValues missing.

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%; ▶Table 1). 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 2 Incidence of infantile hypertrophic pyloric stenosis

Year	No. of infants with IHPS	No. of LB	Incidence per 1,000 LB
2007	224	181,336	1.24
2008	206	184,634	1.12
2009	241	184,915	1.30
2010	253	184,397	1.37
2011	230	180,060	1.28
2012	259	175,959	1.47
2013	249	171,341	1.45
2014	241	175,181	1.38
2015	191	170,510	1.12
2016	188	172,520	1.09

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

Fig. 1 Incidence of infantile hypertrophic pyloric stenosis 2007 to 2016.

Seasonal Variation based on Date of Birth

Most infants with IHPS were born in August (1.39 per 1,000 LB; 95% confidence interval [CI]: 1.18–1.59) and the least in December (1.19 per 1,000 LB; 95% CI: 0.98–1.40). In accordance to the months, we found that the incidence rate was highest in infants who were born in summer (1.33 per 1,000 LB; 95% CI: 1.18–1.48) and lowest in infants born in winter (1.22 per 1,000 LB; 95% CI: 1.06–1.37). Incidence rates of all months and seasons were shown in Supplementary data (▶Supplementary Table S1 and ▶Supplementary Table S2 [available in the online version]). When adjusted for year-to-year differences by using a linear mixed model, we found no significant differences between months and seasons of birth respectively ($p = 0.98$ and $p = 0.68$).

Seasonal Variation based on Date of Surgery

When adjusted for the number of cases per year, September had the highest average of IHPS cases per month (9.2%; 95% CI: 7.9–10.5) and February the lowest average of IHPS cases (7.6%; 95% CI: 6.3–8.9). Other values were shown in the Supplementary data (▶Supplementary Table S3 and ▶Supplementary Table S4 [available in the online version]). No significant differences between months were present ($p = 0.692$). Correspondingly, the highest mean incidence was seen in autumn (26.5%; 95% CI: 24.4–28.6), without significant differences between seasons ($p = 0.206$).

Discussion

This study shows an incidence of IHPS of 1.28 per 1,000 LB in the past 10 years in the Netherlands, without any trend in incidence over time. The majority of infants diagnosed with IHPS are born in the summer, but differences in incidence between season of birth or season of surgery were not significant.

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.^{3,13,14} Since 1990, a decline in incidence of IHPS has been reported in several countries.^{12–14,26–30} 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).^{12,14} In the United States and Israel,

comparable rates were found of 2.29 per 1,000 LB (2015) and 2.1 per 1,000 LB (2019), respectively.^{30,31} 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.^{12–14,19,26–30} 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.^{9,27,30} Known risk factors for IHPS are male sex, formula feeding, birth by cesarean section, preterm birth, multiple birth, macrolide exposure, and maternal smoking.^{3–5,14,31–33} McAteer et al showed a decrease in incidence of IHPS from 1.4 per 1,000 LB in 2003 to 0.9 per 1,000 LB in 2009, while the prevalence of breastfeeding at birth discharge increased from 80 to 94%.³³ During the same time period, the prevalence of other risk factors remained stable, suggesting type of feeding could be an explanatory factor for the declining incidence of IHPS. This inverse correlation between breastfeeding and IHPS incidence was also seen in a Taiwanese cohort, but was nonsignificant.²³ The trend in breastfeeding over time in the Netherlands seemed not fully comparable with the increase and decrease of incidence of IHPS in our cohort.³⁴ Unfortunately, we were not able to analyze the exact correlation because we could not obtain the type of feeding for all individuals in the national birth registry. The Dutch annual trends of other risk factors as birth by cesarean section, preterm birth, and multiple birth also did not seem to be in accordance with the trend in incidence of IHPS in the Netherlands.²⁵ 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.^{6,15–18,20} 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.

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