

Parallel Incidences of Sudden Infant Death Syndrome and Infantile Hypertrophic Pyloric Stenosis: A Common Cause?

Sofia Persson, MD*; Anders Ekblom, MD, PhD§; Fredrik Granath, PhD‡; and Agneta Nordenskjöld, MD, PhD*||

ABSTRACT. *Objective.* To determine whether there was a correlation between the incidence of infantile hypertrophic pyloric stenosis (IHPS) and the incidence of sudden infant death syndrome (SIDS) during the period 1970 to 1997 and to discuss different causative factors that could be influencing the changing trend in incidence.

Methods. We compared the incidence of IHPS in the Stockholm Health Care Region with the incidence of SIDS in Sweden each year between 1970 and 1997. First, the relation was assessed by calculation of a correlation coefficient; second, the relative linear decrease was estimated for the time period 1990 to 1997.

Results. The incidence of IHPS increased steadily during the 1970s, from 0.5 per 1000 live births in 1970 to 2.7 in 1979. During the 1980s, the average incidence was 2.8. During the 1990s, there was a significant decrease in the number of IHPS cases in Stockholm. The incidence rate of IHPS parallels the incidence of SIDS during the study period ($r = 0.58$). The incidence of SIDS dropped after the risk-reduction campaign in the beginning of the 1990s, which recommended that infants sleep on their back. We could not identify any other changes of behavioral risk factors in early exposures that could explain the temporal trends.

Conclusions. The statistical findings suggest that IHPS and SIDS have causative factors in common. We suggest that prone sleeping is one of those factors. *Pediatrics* 2001;108(4). URL: <http://www.pediatrics.org/cgi/content/full/108/4/e70>; infantile hypertrophic pyloric stenosis, sudden infant death syndrome, epidemiology.

ABBREVIATIONS. IHPS, infantile hypertrophic pyloric stenosis; SIDS, sudden infant death syndrome; CI, confidence interval.

Infantile hypertrophic pyloric stenosis (IHPS) is a hypertrophy of the pyloric circular muscle sphincter of unknown cause. IHPS is categorized as a congenital malformation, but most often the muscular hypertrophy is absent at birth.¹ The hypertrophy develops gradually until it obstructs the gastric outlet, resulting in postprandial nonbilious projectile vomiting. The onset of clinical symptoms usually occurs at 2 to 4 weeks of age. IHPS is effec-

tively treated with surgical pyloromyotomy, which permanently relieves the obstruction.

The prevalence of a family history of IHPS is 13% to 14%, and the sex ratio (male:female) is 4 to 4.5:1.¹⁻⁷ The increased risk among relatives and the sex distribution strongly suggest that genetic factors are important. The inheritance pattern cannot be explained by Mendelian genetics; instead, IHPS has served as a prototype for the multifactorial threshold model of inheritance.⁸

IHPS has been reported to be associated with a number of different exposures. Apart from male sex and white ethnicity, the results from different studies have been contradictory.⁶ Feeding habits, maternal stress, high birth weight, and primogeniture are some exposures that have been implicated.⁹⁻¹³ A recent report suggested oral erythromycin intake as a possible risk factor for IHPS.¹⁴ Erythromycin induces strong nonpropagated gastric contractions when distributed in high doses, which may lead to hypertrophy of the pylorus.^{15,16} In addition, several biochemical markers in the hypertrophied pyloric muscle have been studied, such as the neuronal nitric oxide.¹⁷

The reported incidence figures of IHPS vary between 1.5 and 3.0 per 1000 live births. Changing trends in incidence of IHPS occasionally have been seen in some populations. Four independent studies from geographically diverse areas of the United Kingdom reported an increasing incidence of IHPS during the 1970s: from 1.7 to 3.6 and from 1.5 to 8.8 between 1970 and 1979, respectively, and from 3.3 to 6.8 and from 2.1 to 3.5 between 1974 and 1980, respectively.^{12,18-20} Another study from the United Kingdom compared the incidence rates in 1976 and 1978 with those in 1986 and 1988 and found an increased incidence from 1.54 to 2.22.²¹ A significantly increasing trend also was evident in Ireland between 1981 and 1990, when the incidence rose from 0.87 to 5.10.²² However, this increasing trend is not universal; for instance, in Denmark during the period 1950 to 1984 and in Atlanta during the period 1968 to 1982, there were no significant changes in the incidence rates.^{6,7} The underlying reasons for these differences are unknown.

We observed a significant decrease of IHPS cases during the 1990s within the catchment area of the Stockholm Health Care Region, Sweden, that parallel the decrease of sudden infant death syndrome (SIDS) during the same time period. This prompted us to

From the Departments of *Molecular Medicine and ‡Medical Epidemiology, Karolinska Institutet; and §Department of Medicine, Unit of Clinical Epidemiology, and ||Department of Women and Child Health, Astrid Lindgrens Children Hospital, Karolinska Hospital, Stockholm, Sweden.

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Reprint requests to (A.N.) Karolinska Institutet, Department of Molecular Medicine, CMM: 02, Karolinska Hospital, Stockholm, Sweden, SE-171 76.
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compare in detail the incidence of IHPS and SIDS from 1970 to 1999 to generate a hypothesis on the cause of IHPS.

METHODS

The Swedish Health Care System, which delivers emergency surgical care, is entirely public and financed by local taxes. The majority of patients are provided care within their county of residence, and no emergency surgical care is offered outside the public health care system. The Stockholm Health Care Region encompasses approximately 1.8 million (approximately 20 000 infants born per year); during the period 1970 to 1999, only 2 hospitals within the Stockholm Health Care Region provided emergency pediatric surgery: the Karolinska Hospital (1970–1982 and 1998–1999) and St Görans Children's Hospital (1970–1998). These were the only hospitals that performed pyloromyotomy on infants, and they served the entire Stockholm Health Care Region.

We conducted a review of the pediatric hospital records for children who received a diagnosis of IHPS at these 2 hospitals between 1970 and 1999 using a discharge diagnosis of pyloric stenosis (*International Classification of Diseases, Eighth, Ninth, and Tenth Revisions*, codes 750.10 [1970–1986], 750F [1987–1996], and Q40.0 [1997–1999], respectively). Only patients who required pyloromyotomy were included. Information on the number of live births in the region was obtained from yearly official statistics in Sweden. We calculated the number of IHPS cases per 1000 live births for each year during the period 1970 to 1999.

Data of SIDS incidence for the entire Swedish population between 1970 and 1997 were obtained from the Swedish Causes of Death Registry. In addition, we obtained exposure data, such as smoking, breastfeeding, and sleeping position, during the study period from the Nordic Epidemiologic SIDS study.

The relation between the incidence of IHPS and SIDS first was assessed by calculating the correlation coefficient. In a second approach, the relative linear decrease in incidence of both IHPS and SIDS was estimated for the time period 1990 to 1997, ie, the

time period after the first reports that sleeping position is a risk factor for SIDS. Furthermore, a shift-point model with a constant rate from 1984 followed by a log-linear decrease at an estimated year was fitted to the incidence of SIDS and IHPS. The most likely years when the rates started to decrease were estimated by the maximum likelihood method, and the corresponding test-based confidence intervals (CI) were calculated. The statistical analyses were based on the assumption of Poisson distribution of number of events.

RESULTS

During the 30-year study period, a total of 1184 cases of IHPS were registered in the pediatric surgery records. In 1970 to 1974, there was an average of 1.3 cases of IHPS per 1000 live births to be compared with an incidence of 2.8 in the 1980s. Thereafter, there was a decrease and the mean annual incidence during the period 1996 to 1999 was 0.7 per 1000 live births. A similar pattern is present over time for SIDS, with an increase from 0.2 per 1000 in 1970 to 1974 to an incidence of 0.9 in the 1980s, followed by a decrease during the 1990s (Fig 1).

An analysis of the pair-wise correlation showed $r = 0.58$ ($P = .0013$) for the whole study period. Restricting this analysis to the period from 1990 to 1997 (ie, from the time of the clarifying of the association between sleeping position and SIDS) increased this correlation to $r = 0.82$ ($P = .01$). The estimated yearly decrease in incidence from 1990 was 18% (95% CI: 12–23) for IHPS and 19% (95% CI: 16–22) for SIDS. Finally, the estimated years for the start of decrease in incidences were 1989 (95% CI:

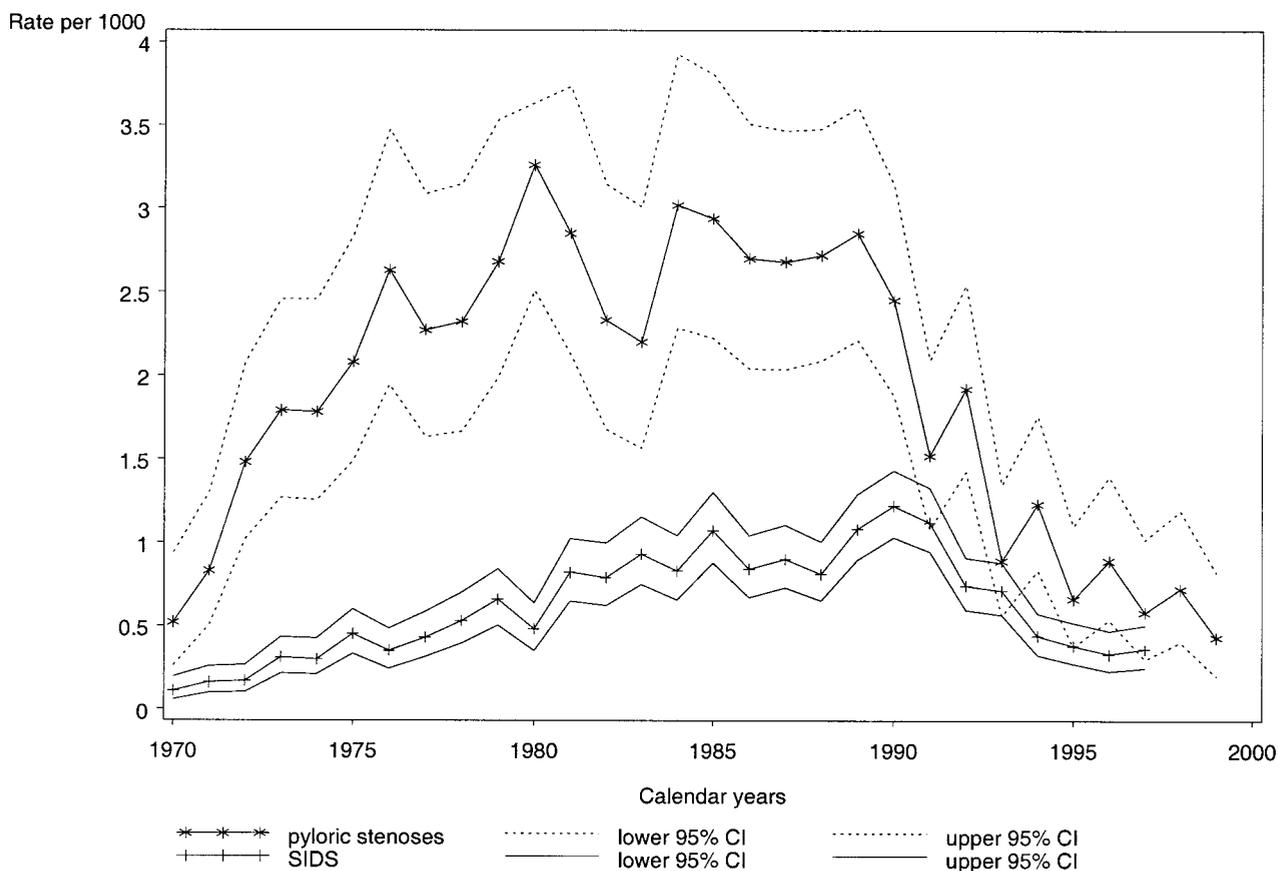


Fig 1. Yearly incidence of IHPS in the Stockholm area in 1970 to 1999 and of SIDS in Sweden in 1970 to 1997. Dashed lines represent the 95% CI for each observation.

1987–1990) and 1991 (95% CI: 1990–1992) for IHPS and SIDS, respectively.

DISCUSSION

There is a significant correlation between the incidence of IHPS and SIDS during the years 1970 to 1997. Furthermore, there is an overlap regarding the estimated shift point where the incidences went from stable incidence to a decrease, and the rate of decrease for both diseases is very similar thereafter. These findings strongly suggest common causative factors. Neither IHPS nor SIDS is congenital; in the case of IHPS, 95% of cases are diagnosed between 3 and 12 weeks after birth, and SIDS occurs during the first year.⁴ Thus, early environmental factors such as the child's sleeping position, feeding practice, and exposure to other environmental factors such as smoking could be of importance.

The habit of putting infants to sleep on their front gained popularity during the early 1970s, especially in the European setting after the international pediatrics congress in Vienna in 1971, where the positive effects of the prone position were strongly advocated.²³ No data are available about the prevalence of the prone sleeping position in Swedish infants in the 1970s. There were no recommendations to put infants to sleep in the prone position, but it was part of informal health advice given from physicians and nurses at different child care centers throughout the country starting in the 1970s.²⁴

Epidemiologic studies from the United Kingdom, New Zealand, and the Netherlands in the early 1990s indicated that a prone sleeping position in infants was associated with a substantially increased risk of SIDS.^{25–27} These reports were followed by other studies from Scandinavia with similar results.^{28,29} After the results of these studies were reported, a risk-reduction campaign to change the sleeping practice was launched in Norway in 1990, followed by Denmark in 1991 and Sweden in 1992. These campaigns were reinforced in 1994 in both Sweden and Denmark. The result of the campaign was a reduction of the prevalence of the prone sleeping position. In Sweden, it was reduced from 42% in 1991 to 29% in 1993 and 15% in 1994 to 1995.²⁹ A similar trend of decreasing incidence of IHPS recently was reported independently from Denmark.³⁰ The Danish group observed that the decline of IHPS coincides with the timing of changed recommendations concerning infants' positioning during sleep. The authors suggested a theoretical possibility of a causative link between sleeping position and IHPS.

During the study period, there also were changes concerning feeding practice in Sweden. Around 1972, the frequency of breastfeeding reached the lowest level ever reported. A committee was appointed in 1973 by the National Board of Health and Welfare to promote breastfeeding. In 1976 to 1977, 62% of infants were breastfed at 2 months of age compared with 31% in 1972.^{31,32} The proportion of children being breastfed was constant until the beginning of the 1990s. Because the risk-reduction campaign also focused on breastfeeding, there was a further increase to 74.5% in 1995, and in 1997 90% of all infants

at 2 months of age were at least partly breastfed.³³ This makes the breastfeeding frequency in Sweden one of the highest in Europe. No studies of feeding practices and IHPS have been able to conclude that there exists a correlation between breastfeeding and pyloric stenosis, however.

Smoking habits also have changed, but these changes are much less pronounced. In 1991 to 1992, 25.5% reported smoking during pregnancy compared with 21.6% during the period 1994 to 1995. There also has been a reduction in maternal smoking after pregnancy, from 33.5% in 1991 to 1992 to 21.8% during the period 1994 to 1995.²⁹

Of behavioral risk factors associated with SIDS, sleeping position is most closely correlated with the decrease in both SIDS and IHPS during the 1990s. The emptying process of the stomach gives further credence to this hypothesis. Figure 2 shows the radiograph of a stomach after a meal in a 12-week-old infant in a prone position. In this position, the major part of the meal is localized in the antrum of the stomach. Figure 3 shows the infant in a supine position; the contents of the meal are in the fundus. These pictures show that placing an infant in the prone position after a meal will result in a shift of the gastric contents to the antral parts of the stomach. Hypothetically, this could result in a disproportionate stimulation of the gastric emptying mechanism, and excessive contraction may lead to the pyloric hypertrophy in individuals with a predisposition for IHPS. The exact physiologic role of these radiographic findings must be investigated further, however.

In this study, we used pyloromyotomy (surgical treatment) as the diagnostic criteria for IHPS. During the past decades, this has served as the treatment of choice regarding IHPS; however, a small and unknown number of the affected infants during the first part of the 1970s may have been subjected to non-

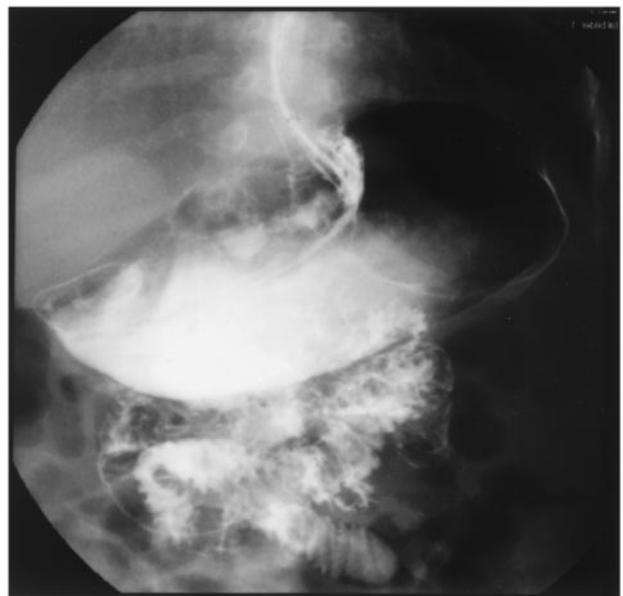


Fig 2. Radiograph of the stomach of a child in the prone position. Most of the contrast fluid is localized in the antral (distal) part of the stomach.

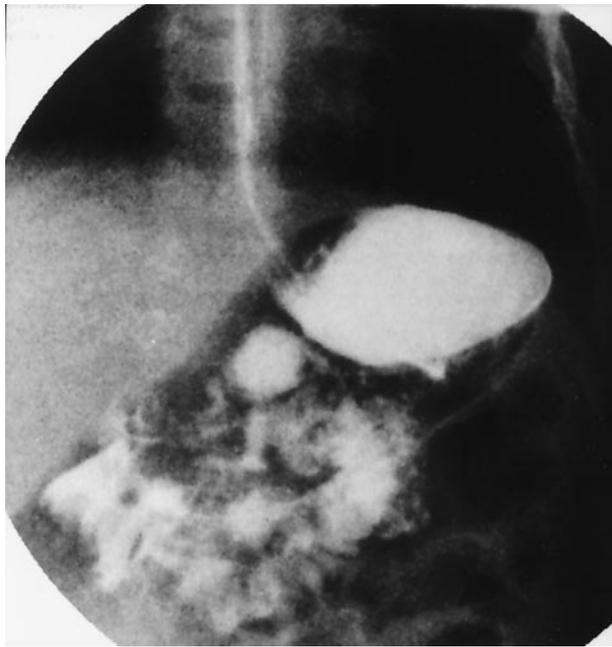


Fig 3. The same child in the supine position. The contrast fluid has moved toward the fundus (proximal part).

surgical treatment. Thus, we cannot quantify the actual number or rule out an underestimation of the incidence of IHPS during the first part of the period. This cannot be the case during the 1990s because there have been no changes in treatment practices. Since the middle of the 1970s, all children with radiographically, ultrasonographically, or clinically confirmed IHPS have been treated surgically. Similar underreporting for SIDS is probable during the 1970s, when the awareness of this condition was not as well spread among physicians as it became during the 1980s. Furthermore, different regions of investigation were used in this study. The IHPS cases were collected from the city of Stockholm, whereas the number of SIDS cases represent the whole country of Sweden. A city often is known to represent an area of fast adapters, taking on new behaviors, such as trends in sleeping position, more quickly, which might be the reason that the curve of the increase of IHPS is steeper than the one for SIDS. However, no such underestimation is likely to have occurred during the 1980s or 1990s, when the underlying reason for this tragic outcome puzzled the medical community.

There is always an inherent danger to infer from ecological data. In the case of SIDS, most observational studies consistently have implicated sleeping position, and the decrease of the incidence after intervention focused on sleeping position strongly indicates a causal association. In the case of IHPS, no observational studies exist, but the proposed biological mechanism together with ecological data presented in this study suggest a causal association.

CONCLUSION

Changes in recommendation of sleeping position in the newborn have led to a decrease in SIDS, and data from the present study strongly suggest that a

decrease in IHPS is an additional gain. Of course, studies like this need to be replicated by others. An interesting factor is that different countries in Europe introduced risk-reduction campaigns at different times, which provides a statistical tool for comparison of data from different regions and time periods.

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