Decline in the Rate of Infantile Hypertrophic Pyloric Stenosis in Breast Fed Infants

Anne Sütü ile Beslenen Bebeklerde Hipertrofik Pilor Stenozu Oranındaki Azalma

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ABSTRACT Objective: Infantile hypertrophic pyloric stenosis (IHPS) is an important cause of gastric outlet obstruction secondary to hypertrophy and hyperplasia of circular pyloric muscle. Recently, a decline in rates of IHPS has been reported in a number of countries. In our study, we aimed to describe the prevalence of IHPS, associated risk factors and to investigate the association between IHPS incidence and infants feeding practices. **Material and Methods:** Children with IHPS born in Konya Dr. Faruk Sukan Maternity & Children Hospital and Umraniye Education & Research Hospital, from 1995 to 2009 were recruited for the study. Diagnosis of IHPS was confirmed by surgically examination and ultrasonography in all cases. **Results:** The prevalence of IHPS from 1995 to 2009 was 0.22 per 1000 live births. The rate of IHPS declined from 0.88 per 1000 live births in 1995 to 0.09 in 2009. It was seen that 25.6% of 39 infants were breastfed. A statistically significant difference between breast fed and not breast fed cases ($p= 0.002$, $p< 0.01$) was found. **Conclusion:** Our findings showed the decline in the incidence of IHPS. With relevance to these findings, we suggested that exclusive breastfeeding plays an important role in decrease rates of IHPS. Further studies are required in order to identify the association between genetic and environmental factors in pathogenesis of IHPS.

Key Words: Pyloric stenosis, hypertrophic; infant; infant formula; milk, human; breast feeding

ÖZET Amaç: İnfantil hipertrofik pilor stenozu (IHPS), pilor kasının hipertrofisi ve hiperplazisi sonucu olarak gelişen mide çıkışı tıkanıklığının önemli bir nedenidir. Son yıllarda, birçok ülkede IHPS oranlarında azalma bildirilmektedir. Çalışmamızda, IHPS prevalansını ve bununla ilişkili risk faktörlerini tanımlamayı, IHPS insidansı ve bebeklerin beslenme uygulamaları arasındaki ilişkiyi araştırmayı amaçladık. **Gereç ve Yöntemler:** 1995-2009 arasında Konya Dr. Faruk Sükan Doğum ve Çocuk Hastanesi ve Ümraniye Eğitim ve Araştırma Hastanesinde doğan bebekler çalışmaya dâhil edildi. IHPS tanısı cerrahi muayene ve ultrasonografi ile doğrulandı. **Bulgular:** IHPS prevalansı 1000 canlı doğumda 0.22 olarak saptandı. IHPS oranında 1995 yılı ile 2009 yılı arasında 1000 canlı doğumda 0.88'den 0.09'a azalma tespit edildi. IHPS olan 39 bebekten %25.6'sı anne sütü ile beslenirken, %74.4'ü anne sütü almamaktaydı. Anne sütü ile beslenen ve anne sütü almayan bebekler arasında istatistiksel olarak anlamlı farklılık saptandı ($p= 0.002$, $p< 0.01$). **Sonuç:** Bulgularımız IHPS insidansında azalma göstermekte. Bu bulguların doğrultusunda, sadece anne sütü ile beslenmenin IHPS oranlarının azalmasında önemli rol oynadığını öne sürdük. IHPS patogenezinde genetik ve çevresel faktörler arasındaki ilişkiyi tanımlamak için ileri çalışmalar gerekmektedir.

Anahtar Kelimeler: Pilor stenozu, hipertrofik; bebek; bebek maması; süt, insan; emzirme

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Infantile hypertrophic pyloric stenosis (IHPS), is the most common cause of intestinal obstruction in infancy, it accounts for 30% of patients who present with non bilious vomiting.

IHPS occurs secondary to hypertrophy and hyperplasia of the muscular layers of the pylorus leading to narrowing of the gastric antrum.[1]

The causes of IHPS are multifactorial; various environmental and hereditary factors have been implicated. Possible etiologic factors include a deficiency of nitric oxide synthase containing neurons, abnormal myenteric plexus innervation, infantile hypergastrinemia, cow's milk protein allergy and exposure to macrolide antibiotics.[2-4] Recent studies investigated the role of neuronal nitric oxide synthase (NOS) in pathogenesis of IHPS and reported decreased nNOS activity in the muscle layers in IHPS. Diminished nNOS activity due to reduced expression of the nNOS gene, may be responsible for the contracted, hypertrophied pylori.[5,6] IHPS has been associated with chromosomal abnormalities and genetic syndromes, such as Smith Lemli Opitz syndrome, trisomy 21 and Robin sequence.[7]

Epidemiological studies for IHPS report distinct racial and ethnic differences. Incidence of IHPS is greatest in Whites, intermediate in Hispanics and lowest in Black and Asian.[7-9] In all racial and ethnic groups, male infants are affected more often than females, in 4:1 ratio. First born infants have a higher incidence of IHPS than those of birth ranks two to four. The incidence of IHPS is highest among infants of mothers aged 20-24 years and decline with increasing maternal age (> 25 years). Symptoms develop usually in a healthy infant between the third and eighth weeks after birth. Premature infants are diagnosed at a later age after birth, the mean age of diagnosis is reported as 53.5 days for infants with a gestational age (GA) of <34 weeks, 40.1 days for infants with a gestational age of 34-36 weeks and 37.6 days for those with GA ≥37 weeks.[5]

Ultrasonography (US) is the method of choice for the diagnosis of IHPS. US confirms IHPS when the pyloric muscle thickness (MT) is greater than 4 mm and the pyloric channel length (CL) is greater than 15 mm.[10] This modality has a sensitivity and specificity of approximately 100%.[11] Umbilical pyloromyotomy is the definitive treatment for IHPS.[12] Classical right upper quadrant (RUQ) incision is used by a minority of surgeons.[13] Recently, a decline in rates of IHPS has been reported in a number of countries.[14-16] Authors hypothesize that risk factors for pyloric stenosis, and SIDS (Sudden Infant Death Syndrome) are similar, sleeping in the supine position may be at decreased risk for SIDS and IHPS.[17,18] In this study, we aimed to describe the prevalence of IHPS, associated risk factors and to investigate the association between IHPS incidence and infants feeding practices.

MATERIAL AND METHODS

Children with IHPS identified from the population of liveborn infants born in 2 hospital of Turkey (Konya Dr. Faruk Sukan Maternity &Children Hospital and Umraniye Education & Research Hospital) from 1995 to 2009 were recruited for the study. Diagnosis of IHPS was confirmed by surgically examination and ultrasonography in all cases. Demographic characteristics of patients included the maternal age, maternal smoking, and maternal use of Erythromycin, mean gestational age, mean age at diagnosis, gender and nutritional status of infants (breast feeding, cow's milk and formula feeding). Patients with IHPS were evaluated for additional chromosome abnormalities, syndromes, and urinary tract anomalies.

STATISTICAL ANALYSIS

NCSS 2007&PASS 2008 Statistical Software (Utah, USA) package has been used for the statistical analyses when the results were being evaluated. During the evaluation of the study data, along with the descriptive statistical methods, the chi squared test for categorical variables was used. Significance was accepted at $p< 0.05$ level.

RESULTS

IHPS was determined at 39 of 175 314 liveborn infants between 1995 and 2009 years. The distribution of the cases with IHPS by year was shown on Table 1.

Between 2001-2003 IHPS cases were not seen at all, between 2004-2006 it was seen only in 2 cases, and until 2009 it was determined only once. The incidence of IHPS from 1995 to 2009 was

TABLE 1: Distribution of infantile hypertrophic pyloric stenosis (IHPS) cases according to years (1995-2009).

Year	Total number of live birth	Number of cases with IHPS	Incidence per 1000 live births
1995	10220	9	0.88
1996	11300	7	0.62
1997	10469	7	0.67
1998	10453	6	0.57
1999	10569	4	0.38
2000	11367	3	0.26
2001	11756	0	0
2002	11039	0	0
2003	9336	0	0
2004	12860	1	0.08
2005	14579	1	0.07
2006	13322	0	0
2007	13499	0	0
2008	13122	0	0
2009	11423	1	0.09
Total	175314	39	0.22

0.022%. The rate of IHPS declined from 0.88 per 1000 live births in 1995 to 0.09 in 2009 (Figure 1).

Demographic characteristics of infants with IHPS were shown on Table 2.

Six cases (15.4%) were girls and 33 (84.6%) were boys. We found a significant male predominance in our study. The ratio of males to females was 5.5:1. The age at diagnosis of IHPS vary from 4 to 12 weeks. The mean age was 6.39 ± 1.93 weeks. The mean age at diagnosis for boys was 5.8 ± 2.2 weeks, and 4.8 ± 0.96 weeks for girls with IHPS. The mean maternal age was 22.25 ± 3.47 years (17-31 years). Maternal smoking and history of erythromycin use during pregnancy or lactation were not reported. Positive family history of IHPS was reported only in one patient. We found that the number of breast fed infants increased year by year over the last 15 years (Table 3).

When IHPS cases were analyzed according to their feeding practices, it was seen that 25.6% of 39 infants were breast fed and 74.4% were not breast fed (Table 4).

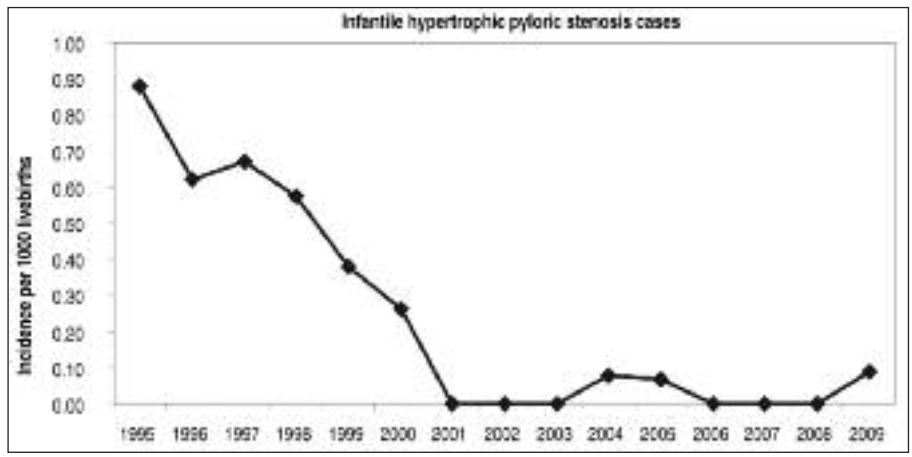

FIGURE 1: Distribution of infantile hypertrophic pyloric stenosis (IHPS) cases according to years (1995-2009).
Legend to the Figure 1: The figure shows the decline of IHPS cases from 0.88 in 1995 to 0.09 in 2009.

TABLE 2: Demographic characteristics of infants with infantile hypertrophic pyloric stenosis.

	Mean ± SD	
Age at diagnosis (weeks)	6.39 ± 1.93	
Maternal age (years)	22.25 ± 3.47	
Gender	**n**	**%**
Female	6	15.4
Male	33	84.6

TABLE 3: The annual prevalence of the different types of infant feeding.

Year	Breast fed	Not breast fed	Total
1995	2759	7461	**10220**
1996	3164	8136	**11300**
1997	2984	7485	**10469**
1998	3031	7422	**10453**
1999	3276	7293	**10569**
2000	3774	7593	**11367**
2001	4115	7641	**11756**
2002	4029	7010	**11039**
2003	3790	5546	**9336**
2004	5967	6893	**12860**
2005	7406	7173	**14579**
2006	7061	6261	**13322**
2007	7532	5967	**13499**
2008	7348	5774	**13122**
2009	6854	4569	**11423**
Total	**73091**	**102223**	**175314**

There was a statistically significant difference between breast fed cases and not breast fed cases ($p= 0.002$, $p< 0.01$). Not breast feeding during 1995-99 years was statistically significant higher than breast feeding. The higher incidence of pyloric stenosis was determined during 1995-99. After 2005, a significant decrease in not breast feeding and increase in breast feeding was observed. We found a statistically significant decline in IHPS incidence during 2005-09 (Table 5).

DISCUSSION

Contradictory to many studies, the pathogenesis of IHPS is not clearly understood. IHPS has been associated with genetic factors, gender and race, and environmental factors. Feeding practice is an important environmental factor in the etiology of IHPS. Epidemiological studies for IHPS reported different incidences.

Schechter et al.[7] identified 1963 cases of IHPS born from 1983 to 1988 and recorded in the California Birth Defects Monitoring Programme. The incidence of IHPS per 1000 live births was highest among whites (2.4/1000) and Hispanics infants (1.8/1000), African Americans, and Asians had the lowest incidence at 0.7 and 0.6/1000 respectively. In all racial groups, male (82%) predominance was observed. As in previously reported study, the prevalence of IHPS in our study was 0.22 per 1000 live birth, and a male predominance was determined. Pedersen et al. evaluated infants from seven European regions for the period of 1980 2002 and diagnosed 2534 infants with IHPS. The incidence of IHPS was 2.0 per 1000 live births, ranging from 0.86 per 1000 to 3.96 per 1000, depending on the region. Young maternal age (<20 y) was associated with an increased risk of IHPS, and maternal age of 30 years and older was found to be associated with a decreased risk.[7,15] The mean maternal age in our study was 22.25 ± 3.47 years. The incidence of infantile hypertrophic pyloric stenosis has decreased in developing countries. We found the similar

TABLE 4: Distribution of cases with IHPS according to the feeding practices between 1995 and 2009.

Year	Number of IHPS cases	Breast fed	Not Breast fed
1995	9	3 (33.3%)	6 (66.7%)
1996	7	2 (28.6%)	5 (71.4%)
1997	7	2 (28.6%)	5 (71.4%)
1998	6	1 (16.7%)	5 (83.3%)
1999	4	0	4 (%100)
2000	3	1 (33.3%)	2 (66.7%)
2001	0	0	0
2002	0	0	0
2003	0	0	0
2004	1	0	1 (100%)
2005	1	0	1 (100%)
2006	0	0	0
2007	0	0	0
2008	0	0	0
2009	1	1(100%)	0
Total	**39**	**10 (25.6%)**	**29 (74.4%)**

TABLE 5: Incidence of IHPS according to the feeding practices in five years periods.

Years	Feeding practices		Breast fed		Not breast fed		Total	
	Breast fed	Not breast fed	Normal	Pyloric stenosis	Normal	Pyloric stenosis	Normal	Pyloric stenosis
1995-99	15215 (28.7%)	37796 (71.3%)	15207 (99.9%)	8 (0.1%)	37771 (99.9%)	25 (0.1%)	52978 (99.93)	33 (0.062%)
2000-04	21675 (35.8%)	34683 (61.5%)	21674 (99.995%)	1 (0.005%)	34680 (99.991%)	3 (0.009%)	56354 (99.993%)	4 (0.007%)
2005-09	36201 (54.9%)	29744 (45.1%)	30200 (99.999%)	1 (0.001%)	29743 (99.996%)	1 (0.004%)	65943 (99.997%)	2 (0.003%)
Total	0.001*		0.0001*		0.0001*		0.0001*	

●: Chi Square test, Yates correction

trend in our country. The rate of IHPS declined from 0.88 per 1000 live births in 1995 to 0.09 in 2009.

Applegate and Druschel[8] evaluated infants born to residents of New York State from 1983 to 1990. They reported that the rate of IHPS decline from 2.4 per 1000 live births in 1984 to 1.7 in 1990. White race and male gender were associated with a higher occurrence of IHPS; high birth order, older maternal age, higher maternal education, and low birth weight were associated with lower occurrence. Seven percent of children with IHPS had a major malformation compared with 3.7% of the general population. Three major malformations occurred more frequently in children with IHPS: intestinal malrotation, obstructive defects of the urinary tract, and esophageal atresia. In California study group from 131 complex IHPS cases, only 13% had a specific syndrome or chromosomal abnormality. They found more frequently association with Robin sequence, Smith Lemli Opitz syndrome, trisomy 21 and fetal alcohol syndrome.[7] In our cases additional chromosomal abnormalities or syndromes were not found. Similar findings were reported from Sweden. There was a decline from 2.7/1000 to 0.85/1000 between 1989 and 1996 years. Authors hypothesize that sleeping in prone position may increased the risk for IHPS.[18] We did not determine differences in sleeping position in infants with IHPS. A marked reduction in Scotland's IHPS incidence was observed. IHPS incidence fell from 4.4 to 1.4 per 1000 live births between 1981 and 2004. They suggested that this is unlikely to be a consequence of a change in infant sleeping position.[16] Results from Greater Glasgow area from 1980 to 1996 were similar to that shown in prior studies. The annual incidence of IHPS was calculated. An increasing incidence was observed between 1980 and 1988 but not thereafter. There is a suggestion that environmental factors may play a role in the etiology of this condition.[19]

Several studies reported an increased rate in the 1970s and 1980s.[20,21] The incidence of IHPS increased significantly from 0.87/1000 live births in 1981 to 5.10/1000 in 1990 ($p< 0.001$), peaking in 1989 at 6.8/1000 in the West of Ireland. There was not a correlation between the increasing incidence and feeding habits, birth rank, family history or gender distribution. The reason for this increase was unclear.[20]

The data on the role of infant feeding are not consistent, some studies reported that high rates of IHPS might be related to the increased prevalence of breast fed babies; others found high rates in formula fed babies.[21-25]

A study from Saskatchewan reported a decrease in the incidence of IHPS between 1978 and 1985 as compared with 1970-77. They found that bottle feeding was 2.9 times more among the infants with IHPS than among the control subjects, and suggested that this observed decrease in the incidence of IHPS is due to the decline in bottle feeding.[23]

Between 1978 and 2008, fifty seven children with IHPS were treated in Benin City, Nigeria. Authors reported a significant decrease in incidence of IHPS following the introduction of exclusive breast feeding in late 1980s and early 1990 s in Nigeria, with only one case seen in the past 5 years. They suggested that this decrease in the incidence

of IHPS might be due to exclusive breast feeding.[25] With relevance to their study, we observed an increase of the number of breast fed infants year by year over the last 15 years and a marked decline in IHPS incidence after promotion of exclusive breast feeding in our country after 1998. We found the highest prevalence of IHPS in not breast fed infants than exclusively breast fed infants ($p< 0.01$). Protective effect of breast feeding in IHPS might be explained with lower levels of some hormones in human milk that can prevent pyloric hypertrophy. Insulin like growth factor I (IGF I) is a polypeptide hormone that has influence on cellular growth, replication, and differentiation. Thus IGF I plays an important role in both gastrointestinal (GI) maturation and smooth muscle cell (SMC) hypertrophy. The increased expression of IGF I in hypertrophic pyloric muscle suggests that increased local synthesis of growth factors may play an important role in smooth muscle hypertrophy in IHPS.[26]

Infants receiving breast milk had lower IGF I levels [90 ng/ml] than infants receiving formula [97 ng/ml] or both [94 ng/ml]; $p< 0.001$.[27] In accordance with these findings we speculated that higher protein intake from formula or cow's milk can stimulate IGF I secretion and predispose pyloric hypertrophy. Appropriate for gestational age (AGA) born girl infants had significantly higher IGF binding protein 3 (IGFBP 3) levels compared with male infants. This may play role in male predominance of IHPS. Somatostatin is known to inhibit the actions of inhibitory neurotransmitters in the pylorus and may explain the development of pylorospasm. Somatostatin levels increase in IHPS.[28] Also the increased plasma gastrin concentration in exclusively formula fed[29] might be associated with pyloric hypertrophy. Our study as other published reviews was an observational study. Therefore, it did not give an accurate explanation of the causality based on our findings. Further studies are required in order to identify the association between genetic and environmental factors in pathogenesis of IHPS.

CONCLUSION

Our findings showed the decline in incidence of IHPS and we suggested that exclusive breast feeding plays an important role in decrease rates of IHPS. Further studies on gastrointestinal hormones in breast fed infants are necessary to explain their role in the pathophysiology of IHPS.

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