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Original Article

Infantile hypertrophic pyloric stenosis in Bosnia and Herzegovina: A retrospective cohort study from the largest tertiary care facility

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ABSTRACT

Background: Infantile hypertrophic pyloric stenosis (IHPS) is the most common condition requiring surgery in infancy, but the etiology of IHPS is still unclear. The study aimed to analyze the epidemiological and clinical features of the infants with IHPS in our setting and determine the yearly trends in IHPS incidence in the Sarajevo Canton between 2007 and 2016.

Methods: We retrospectively analyzed epidemiologic, clinical, and operative data of all infants undergoing pyloromyotomy for IHPS over ten years in the largest tertiary care facility in Bosnia and Herzegovina.

Results: Fifty-three IHPS patients were diagnosed, yielding an overall incidence of 1.17 per 1000 live births (1.25 and 1.09 cases in 2007–2011 and 2012–2016, respectively). IHPS was more prevalent among male infants (ratio 6.6:1, $p < 0.001$). The mean age at onset of symptoms was 39.6 days (range, 17–107 days). The estimated median time from symptoms onset to hospitalization was 11 days (range, 1–17 days). The mean age at diagnosis was significantly longer in premature infants compared with term infants ($p = 0.003$). Both first-born rank and bottle-feeding were significantly associated with IHPS ($p = 0.001$ and $p = 0.04$, respectively). No seasonal variation associated with IHPS was detected ($p = 0.25$). No evidence was found of differences in the incidence of IHPS related to maternal age ($p = 0.24$) and smoking ($p = 0.59$).

Conclusion: Our data indicate a declining trend and provide insights into the clinical characteristics of IHPS in Bosnia and Herzegovina. Most of the obtained results are in line with the published data and could improve the quality of local pediatric services.

1. Introduction

Infantile hypertrophic pyloric stenosis (IHPS) is the most common acquired pathological condition requiring surgical treatment during early infancy.[1] Its prevalence is ~2–3.5 infants per 1000 live-born infants, with a clear male predominance (4:1 to 6:1).[2,3] IHPS usually presents at 2–12 weeks after birth, with a peak incidence occurring during the fifth week of age.[4] The main characteristic of this condition is pyloric muscle hypertrophy, which progressively blocks the gastric outlet and causes explosive non-bilious vomiting after feeding. Consequently, dehydration followed by hypochloremic, hypokalemic metabolic alkalosis occurs. Although extramucosal splitting of the hypertrophic pyloric muscle proved to be an adequate surgical treatment and has not been changed since 1916,[5]

Abbreviations: ICD, International Classification of Diseases; IHPS, Infantile hypertrophic pyloric stenosis; LB, Live births; SIDS, Sudden infant death syndrome; US, Ultrasonography.

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the etiology of IHPS is still unclear. However, it is believed to be multifactorial, involving genetic predisposition and environmental factors.[2] Several studies have recently explored the various possible factors related to the development of IHPS and analyzed epidemiological and clinical features of infants with IHPS in different countries.[6–9] The status of IHPS in Bosnia and Herzegovina has not been reported yet.

The study aimed to analyze the epidemiological and clinical features of the infants with IHPS in our setting and to determine the yearly trends in IHPS incidence in the Sarajevo Canton between 2007 and 2016.

2. Methods

2.1. Patients

We conducted a retrospective, hospital-based study using a cohort of pediatric patients with a surgically confirmed diagnosis of IHPS born in the Sarajevo Canton over a 10-year between January 1, 2007, and December 31, 2016. The data were analyzed in two 5-year cohorts. All patients with IHPS had a residential address within the Sarajevo Canton. Our center is a tertiary referral hospital in the Sarajevo Canton, located in the central part of Bosnia and Herzegovina, with 413 593 inhabitants (323 inhabitants/km^2). 15.3% of Canton's population are youth up to 14 years of age, 70.7% are between 15 and 64 years of age, and 14% are over 65.

All data were collected from medical records and operating room information systems and extracted according to the International Classification of Diseases, Ninth Revision [ICD-9], International Classification of Diseases, 10th Revision [ICD-10], diagnostic codes 750.5 and Q40.0, respectively. Data related to sex, gestational age, birth weight, birth order, associated anomalies, onset age, feeding practice, onset seasonality, age at diagnosis, clinical presentation, treatment and outcomes of treatment (postoperative complications), maternal age, maternal use of macrolides during pregnancy, maternal use after birth, and use in infants after birth, and maternal smoking during pregnancy were analyzed.

Prematurity was defined as a gestational age of <37 weeks. Diagnosis of IHPS was based on clinical and radiological findings. Ultrasonography (US) diagnostic criteria of infantile hypertrophic included the pyloric muscle thickness of ≥4 mm and length of ≥15 mm.[10] Diagnosis of IHPS in all cases was confirmed intraoperatively.

All medical records were de-identified and anonymized for the current study. Ethical approval for the study was obtained by the local institutional review board (Ethical Committee of the Clinical Center, University of Sarajevo, approval number: 0901-2-150/17). The requirement for informed consent was waived due to its retrospective nature.

2.2. Statistical analysis

Mean and median were used to measure central tendency and standard deviation and range as measures of dispersion for continuous variables. The values of categorical variables were presented as numbers or percentages. Student T-test (continuous variables) was used to compare means. The significance of the difference in continuous variables among the study groups was tested by the Mann–Whitney U test because the data was not normally distributed. The Chi-square test was used for testing continuous and categorical variables within contingency tables. All statistical assays were performed using the Statistical Package for the Social Sciences (SPSS) IBM Version 26 (SPSS) (UNICOM Systems, Inc.). Statistical significance was accepted at the $p < 0.05$ levels.

3. Results

3.1. Epidemiologic and clinical characteristics of the IHPS cohort

There were 45.464 births in the Sarajevo Canton, Bosnia and Herzegovina, during the study period. We identified 53 cases of IHPS for an overall incidence of 1.17 per 1000 live births (Table 1). The incidence of IHPS slightly decreased over time from 1.25/1000 in the first five-year period (2007–2011) to 1.09/1000 in the second five-year period (2012–2016). Among all IHPS cases, 46 (86.8%) were males, and seven (13.2%) were females, resulting in of 6.6/1 male/female ratio (Table 1).

Prematurity was recorded in 11.3% of all IHPS (Table 1). Due to incomplete data and loss to follow-up, five patients were excluded (90.6% retrieval rate), and 48 patients were selected for further analysis. Out of those, 41 (85.4%) were males and seven (14.6%) females with a male to female ratio of 5.8:1. Six (five boys, one girl) were preterm (12.5%). The preterm infants were born at 34 and 36 gestational week but had no complications associated with their prematurity. The birth weight was 3330.2 ± 12.1 g (range, 2100–4300 g). The mean age at onset of symptoms was 39.6 days (range, 17–107 days). The estimated median time from symptoms onset to hospitalization was 11 days (range, 1–17 days) (Table 1). Congenital heart defects associated with IHPS were documented in two infants (4.2%) and cleft palate in one infant (2.1%). Seven patients (14.6%) had a documented positive family history of IHPS, all in first-degree relatives. Thirty-nine patients (81.3%) were first-born (82.9% in males and 71.4% in females), seven (14.6%) were second, and two (2.1%) were third born. Thirty-four (70.8%) were bottle-fed before the onset of symptoms, while fourteen (29.2%) were breastfed. Both birth rank (first-born babies) and feeding practice (bottle-feeding) were significantly more often associated with IHPS ($p = 0.001$ and $p = 0.04$, respectively). The association between maternal prenatal ($n = 8$, 16.7%) and postnatal (0%) macrolide use and subsequent occurrence of IHPS was not found, but our results were based on small numbers of exposed individuals. Most babies with IHPS were born in the winter (13 patients, 31.3%), and the fewest were born in the spring (10 patients, 20.8%), but seasonal variations were not significant ($p = 0.25$).

The mean maternal age was 29.15 years (range, 19–37 years, SD 4.31). The prevalence of maternal smoking during pregnancy was 37.5%. No significant associations were found between maternal age and maternal smoking and the IHPS incidence ($p = 0.24$ and $p = 0.59$, respectively).

3.2. Diagnostics and treatment of the patients with IHPS

The leading IHPS symptom was progressive non-bilious vomiting (48/48, 100%), followed by poor weight gain (25/48, 52.1%), visible gastric peristalsis (15/48, 31.3%), palpable abdominal mass (8/48, 16.7%), and constipation/infrequent stooling (6/48, 12.5%). Bloodstained vomiting was not reported in any of the patients.

The diagnosis of IHPS was confirmed by US examination in 46 out of 48 infants (95.8%). Both longitudinal and transverse US images showed increased muscle thickness of ≥4 mm in all accurately diagnosed patients, increased pyloric channel length of >16 mm in 41 (85.4%) patients, and increased muscle diameter of >14 mm in 44 (91.7%) patients. In two patients with prolonged symptoms following a false negative US finding (4.2%), the diagnosis of IHPS was established by a barium study (fluoroscopy), revealing a delayed gastric emptying and elongated pyloric channel in both cases.

After adequate resuscitation and vigorous correction of fluids and electrolytes, an open Ramstedt's pyloromyotomy was carried out in all patients. Right upper quadrant transverse incision was

Table 1
Demographic characteristics of infants with IHPS.

	The Sarajevo Canton	*p*-value
Total population	413593	
Total number of live births	45464	
Total percentage of prematurely born live births	7.6%	
Total number of IHPS cases	53	
Incidence of IHPS/1.000 live births	1.17	
% males	86.7	<0.001
% females	13.3	
Median gestational age (days) (48 infants)	264.1	
Number of preterms (%) (48 infants)	11.3	
Median weight at birth (grams) (48 infants)	3330.2 ± 12.1	0.0001
Terms (37–42 weeks) (48 infants)	3463 ± 9.2	
Preterms (<37 weeks)	2400 ± 12.9	
Median age at diagnosis (days) (48 infants)	39.6 (17–107)	0.003
Preterms (<37 weeks)	57.8 (24–107)	
Terms (37–42 weeks)	37 (17–88)	

IHPS – Infantile hypertrophic pyloric stenosis.

used in all cases. Thirty patients (62.5%) received prophylactic antibiotic therapy at the induction of anesthesia. There was one (2.1%) iatrogenic mucosal injury during pyloromyotomy, which was repaired. The most common postoperative complication was wound infection seen in two patients (4.1%). The average duration of hospital stay was 7.2 days. No mortality was reported for any of the patients.

4. Discussion

The current literature indicates that the incidence of IHPS varies among different ethnic groups worldwide,[11,12] with a lower prevalence among African-American and Asian children.[13] We found that the studied population had an IHPS incidence rate of 1.17 per 1000 live births (LB). This finding is in line with the reported overall incidence of IHPS in Europe assessed by EUROCAT (registries of congenital malformations) of 2.0 per 1000 LB, ranging from 0.86 to 3.96 per 1000 LB.[14]

Similar to some other countries,[9,15] IHPS incidence in our setting slightly declined in the studied period. This might be attributed to putative changes in environmental factors, such as decreasing rates of maternal smoking,[16] decreased exposure to bottle feeding,[17] and changes in infant's sleeping positions due to recommendations for the prevention of sudden infant death syndrome (SIDS).[18]

Several studies have suggested an association of IHPS with environmental and familial factors. For example, epidemiologic features of disproportionate gender distribution in favor of males and familial aggregation may indicate a genetic component of the etiology of IHPS.[2,19] However, the fact that IHPS occurs almost exclusively in the first three months of life suggests that perinatal factors may significantly contribute to the development of IHPS.[8,20]

Like other studies,[2] we also observed a strong male predominance in patients with IHPS. However, the reasons for the male predominance are not yet well understood … Previous studies showed strong familial aggregation and heritability in patients with IHPS.[19,21] Such observed genetic predispositions to IHPS could explain the racial differences between IHPS incidence.[19] Krogh et al found that IHPS familial aggregation of 20-fold increased risk among siblings and that the estimated heritability from twins was 87%.[19] We found a positive family history of IHPS in ~15% of patients, which is similar (17%) to the study of Taylor et al[22]

In the present study, ~81% of affected infants were first-born, which is in line with previous studies.[2,23] However, it is unclear whether these findings suggest a unique position of first birth or increased birth order, generally declining risk for IHPS. Instead, the association between IHPS and first-born order probably reflects differences in the hormonal or nutritional milieu between first-born and later-born infants.[2]

Prematurity was recorded in ~11% of our IHPS patients, which is a higher percentage than that recorded in a study by Stark et al,[7] but in line with Taylor et al[22] Similar to Shaoul et al,[24] all premature patients in our study were ≥35 weeks. Like other studies,[7,8,25] premature infants in the present study were diagnosed with IHPS at a later age after birth than term infants. Although preterm infants may present with milder, atypical symptoms resulting in a delay in diagnosis, a more likely explanation for this possible clinical phenomenon is the impact of exogenous factors after birth combined with a postnatal maturation of the pyloric muscle.[22]

Early infant feeding practice as one of the possible environmental factors has been the subject of several studies.[17] Krogh et al showed that bottle-fed infants experienced a 4.6-fold higher risk of IHPS than infants who were not bottle-fed.[26] In line with the above studies, we also documented a statistically significant association between bottle-feeding and IHPS. Possible mechanisms by which bottle-feeding may increase the risk of IHPS remain unclear. .

The next potential environmental risk factor for IHPS is macrolides (erythromycin), frequently used during the perinatal period.[27] Erythromycin binds to the duodenum and colon's motilin receptor and induces intestinal contractions.[28] When administered at higher doses, erythromycin might cause prolonged antral contraction and hypertrophy.[29] However, we could not confirm any association between macrolide use and the risk of IHPS since none of the infants received erythromycin in the early postnatal period.

Although the definitive diagnosis of IHPS was usually confirmed by typical US findings,[10] a careful clinical examination and typical clinical features enabled the clinical diagnosis of IHPS to be made in most cases in our study. Like other studies, non-bilious vomiting was the most common initial symptom, while other clinical features were less frequent.[30,31]

Krogh et al and Sorensen et al demonstrated that infants born to smoking mothers during pregnancy have a 1.6-2-fold increased risk of being diagnosed with IHPS over infants born to nonsmoking mothers, retrospectively.[2,16] Krogh et al hypothesized that smoking might cause infantile pylorospasm with consequent hypertrophy of the pylorus muscle, but without further data that could substantiate this argument.[2] However, we could not explore this factor due to the limited sample size.

Our study has several important limitations, including its retrospective nature, single-center experience, and small sample size. Moreover, the current study results are limited by the lack of a control group, which made it difficult to deduce whether these factors increase the risk of IHPS. The present study is also limited by

the absence of some disease data such as fluid and electrolyte abnormalities whose values could be correlated with the duration of the disease.

Despite these limitations, the results of the present study provide insights into the clinical characteristics and epidemiology of the disease in Bosnia and Herzegovina. Most of the obtained results are in line with the published data and could be used to improve the quality of local pediatric services.

Authorship

Zlatan Zvizdic: Conception and design of study, Acquisition of data (laboratory or clinical), Data analysis and/or interpretation, Drafting of manuscript and/or critical revision, Approval of final version of manuscript. Tarik Halimic: Acquisition of data (laboratory or clinical), Data analysis and/or interpretation. Emir Milisic: Acquisition of data (laboratory or clinical), Data analysis and/or interpretation. Asmir Jonuzi: Acquisition of data (laboratory or clinical), Data analysis and/or interpretation. Jasmina A. Halimic: Acquisition of data (laboratory or clinical), Data analysis and/or interpretation. Semir Vranic: Conception and design of study, Acquisition of data (laboratory or clinical), Data analysis and/or interpretation, Drafting of manuscript and/or critical revision, Approval of final version of manuscript.

Declaration of competing interest

The authors declare no conflict of interest.

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