BIOMEDICAL JOURNAL 45 (2022) 948–956

Available online at www.sciencedirect.com

ScienceDirect

Biomedical Journal

journal homepage: www.elsevier.com/locate/bj

Original Article

Factors associated with pyloric hypertrophy severity and post-operative feeding and nutritional recovery in infantile hypertrophic pyloric stenosis

Yao-Hung Chuang [a], Hsun-Chin Chao [a,b,*], Hung-Yu Yeh [a], Ming-Wei Lai [a,b], Chien-Chang Chen [a,b]

[a] Division of Pediatric Gastroenterology, Department of Pediatrics, Chang Gung Children's Medical Center, Chang Gung Memorial Hospital, Taoyuan, Taiwan

[b] Chang Gung University College of Medicine, Taoyuan, Taiwan

ARTICLE INFO

Article history:
Received 1 September 2020
Accepted 29 December 2021
Available online 4 January 2022

Keywords:
Infantile hypertrophic pyloric stenosis
Ramstedt pyloromyotomy
Nutritional recovery

ABSTRACT

Background: To examine factors that affect the severity of pyloric hypertrophy, post-operative feeding and nutritional recovery in infantile hypertrophic pyloric stenosis (IHPS).
Methods: Medical records of infants diagnosed with IHPS at a single tertiary center between 2009 and 2018 were retrospectively reviewed. Clinical characteristics, biochemistry data and outcome were assessed for their association with the severity of pyloric hypertrophy and post-operative recovery. Nutritional recovery was assessed using weight-for-age status improvement after surgery.
Results: Eighty-five patients were recruited in this study. The mean pre-operative weight-for-age percentile was 18.2. Elevated bicarbonate was positively correlated with symptom duration ($p = 0.007$). Pyloric muscle thickness was significantly correlated with age, weight, and symptom duration ($p = 0.004$, 0.003, 0.008, respectively). The mean weight-for-age percentile increased to 41.6 by post-operative weeks 6–8. Pyloric muscle thickness was negatively correlated with nutritional recovery by post-operative weeks 6–8 ($p = 0.003$). In multivariable analysis, pyloric length related to nutritional recovery at week 1–2 post-operatively (OR = 1.42, $p = 0.030$, 95% CI = 0.03–1.94), and pyloric muscle thickness related to nutritional recovery at week 6–8 postoperatively (OR = 4.08, $p = 0.032$, 95% CI = 1.13–14.7).
Conclusion: Our study indicated that favorable nutritional outcome and successful weight gain was observed 6–8 weeks after surgery in children with IHPS. Pyloric muscle thickness positively correlated with age, weight, symptom duration, and favorable nutritional recovery. Serum bicarbonate showed a positive correlation with symptom duration.

* *Corresponding author*. Chang Gung Children's Medical Center, Chang Gung Memorial Hospital at Linkou, 5 Fusing St., Gueishan, Taoyuan 333, Taiwan.
E-mail address: hcchao1021@gmail.com (H.-C. Chao).
Peer review under responsibility of Chang Gung University.
https://doi.org/10.1016/j.bj.2021.12.011

At a glance of commentary

Scientific background on the subject

The IHPS patients tend to have metabolic alkalosis. Elevated bicarbonate and hypochloremia are two most common biochemical abnormalities in patients with IHPS. Previous reports have indicated that symptom duration affected biochemical imbalances, and found that vomiting duration was longer in higher bicarbonate group as for the lower bicarbonate group.

This study adds to the field

Pyloric muscle thickness positively correlates with age, weight, symptom duration, and favorable nutritional recovery in IHPS patients. Pyloric length positively correlates with early nutritional recovery in IHPS patients. Nutritional outcomes for IHPS patients are good with significant weight gain at 6-8 weeks after surgery.

Infantile hypertrophic pyloric stenosis (IHPS), the most common cause of gastric outlet obstruction in infants, was first described by Hirschsprung in 1888 [1]. Its characteristic symptom is projectile vomiting. The incidence of IHPS varies among ethnic groups and races around the world, with a higher incidence among northern Europeans than Asians and Africans. IHPS occurs in about 2–5 per 1000 live births, with an estimated male:female sex ratio of between 4:1 and 6:1 [2–5]. A study using data from the national insurance program in Taiwan showed the frequency of IHPS was around 0.39 per 1000 live births between 1996 and 2004 [6].

Because vomiting is the most common symptom, diagnosis of IHPS is often considered in young infants with repeated nonbilious vomiting, hypochloremic alkalosis, and rapid clinical improvement after rehydration, even in the absence of projectile vomiting or a palpable “olive-like” mass [7,8]. Pyloromyotomy is an effective and common treatment for IHPS [9]. The timing of surgery depends on the infant's clinical status, and surgery is often delayed when the patient is experiencing dehydration and/or electrolyte imbalance [10].

This study examines the demographic, clinical, pre-operative, and post-operative characteristics of infants with IHPS to evaluate the associations of demographic and clinical parameters with the severity of pyloric hypertrophy, electrolyte imbalance, duration of symptoms, and post-operative feeding and nutritional recovery.

Methods

Study population

Pediatric patients who were diagnosed with IHPS between January 2009 and December 2018 at Chang Gung Memorial Hospital (Linkou branch) were included in this study. Medical records were retrospectively reviewed, and patients meeting the diagnostic criteria of IHPS on ultrasound (US) and final surgical proof of IHPS were enrolled. At this hospital, US was used as the primary method for diagnosing IHPS. The diagnostic criteria for IHPS included pyloric muscle thickening of >3 mm and pyloric length >15 mm on US [11–13].

Treatment protocol

Patients with IHPS were treated by pediatric gastroenterologists and pediatric surgeons. The guidelines for IHPS management were as follows: infants presenting with normal electrolyte values and mild dehydration received maintenance intravenous fluids of 5% dextrose with quarter-normal saline (0.22% NaCl) and 2 mEq KCl per 100 mL, and infants with moderate or severe dehydration received intravenous fluids of half-normal saline (0.45% NaCl) and 2 mEq KCl per 100 mL at higher rates of administration (1.5–2 times maintenance). Renal function was assessed prior to adding potassium to the intravenous fluids in severely dehydrated infants. If the patient had alkalosis, the alkalosis was addressed prior to surgery to reduce the risk of post-operative apnea [14,15]. The criteria for discharge from the hospital were an absence of dehydration, absence of hazardous complications, and adequate dietary intake (feeding volume >100 ml/kg/day in those with bottle feeding or >4 ml/kg/hour of urine output in those with breastfeeding). Surgical complications, feeding condition and nutritional recovery (measured by weight-for-age percentile) were monitored at follow-up. The initial follow-up occurred 5–7 days after hospital discharge and then every 2 weeks within the first 2 months. Patients with persistent vomiting, inadequate feeding, or poor weight gain (no increase in weight-for-age percentile) at follow-up were further evaluated for possible residual IHPS or other conditions (i.e., adhesion ileus). The weight-for-age percentile was based on the general Taiwanese population according to age and sex [16].

Exclusion criteria

Patients with acute illness, oropharyngeal diseases, organic diseases, chromosome anomalies, congenital gastrointestinal anomalies, and prior abdominal surgery were excluded.

Data collection

The data collected included demographic information [age, sex, gestational age (full-term, pre-term), birth weight, birth order, plurality, mode of delivery], and clinical data [, presentation features, weight, feeding methods (breastfeeding, bottle feeding), biochemistry profile (blood gas, electrolytes), US findings (pyloric length and pyloric muscle thickness), surgical methods (laparotomy, laparoscopy), length of hospitalization (LOH), complications, post-operative feeding recovery, and post-operative nutritional recovery].

Analysis of factors related to the severity of pyloric hypertrophy, electrolyte imbalance and outcomes

Variables such as plurality, mode of delivery, birth order, birth weight, and feeding methods were not included in the analysis due to their inapplicability. The severity of pyloric hypertrophy was assessed by pyloric muscle thickness and pyloric length. Factors analyzed for the association with pyloric hypertrophy included sex, gestational age (full-term or pre-term), age, weight, and symptom duration. Correlation analysis between symptom duration and serum electrolyte levels (sodium, potassium, chloride, and bicarbonate) was performed to evaluate the association between disease progression and electrolyte imbalance.

Parameters evaluated for post-operative outcome included LOH, complications, feeding recovery and nutritional recovery. Post-operative feeding recovery was measured as the time to start of feeding after surgery. Post-operative nutritional recovery was assessed by two weight-for-age percentile measurements. One assessment was performed at first follow-up (1–2 weeks after surgery) and the second assessment was performed 6–8 weeks after surgery. A weight-for-age increase >5% at the first assessment was categorized as early nutritional recovery and a weight-for-age increase >20% at the second assessment was categorized as significant nutritional recovery. Clinical characteristics including age at diagnosis, symptom duration, pyloric length, pyloric muscle thickness, post-operative time to start feeding, serum bicarbonate level, and serum chloride level were compared between patients with nutritional recovery and patients without nutritional recovery. Serum bicarbonate and chloride levels were used for analysis due to metabolic alkalosis may cause several physiological consequences to affect the nutritional recovery. To reduce bias, patients with conditions that impede weight gain (post-operative complications or acute illness like respiratory infection, diarrhea, and urinary tract infection) were excluded.

Outcomes including post-operative LOH, post-operative feeding recovery (the time to start of feeding and the time to achieve normal feeding volume after surgery), and post-operative nutritional recovery were compared between patients with laparotomy and patients with laparoscopy.

Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) software (version 20). All numerical variables with normal distribution are presented as mean ± standard deviation; group comparisons were performed using Student's *t*-tests. The chi-square test was used to compare between categorical variables in the two groups. Pearson's correlation coefficients were applied to assess linear relationships in paired sets of data with normal distribution. Spearman's correlation coefficients were applied in variables without normal distribution. Potential risk factors affecting nutritional recovery (p-value < 0.05 or approaching 0.05 by univariate analysis) were analyzed by multivariable logistic regression. Statistical significance was defined as p-values < 0.05.

Ethical approval

The study was approved by the Ethics Committee of Chang Gung Memorial Hospital. (No.201901522B0). Parents or guardians of eligible participants provided informed written consent. The study was carried out in accordance with the approved guidelines and regulations.

Results

Between January 2009 and December 2018, 89 cases of IHPS were diagnosed at Chang Gung Memorial Hospital (Linkou branch). Of the 89 eligible patients, 4 were excluded based on the exclusion criteria of chromosomal anomaly (1), ileal atresia (1), and imperforated anus (2). Thus, 85 cases were included in the analysis. Of these, 75 were male, and 10 were female (male: female ratio = 7.5:1). Forty-eight patients (57.8%) were the first birth. The mean age was 39.9 ± 17.2 days, and the mean age of symptom onset was 28.1 ± 13.2 days. Twenty-nine patients (34.1%) had symptom onset before 28 days of age, and 17.6% first experienced symptoms after 56 days of age. The average birth weight and average weight at diagnosis were 3122.3 ± 486.9 g (range = 1626–4100 g), and 3909.6 ± 755.3 g (range = 2250–6000 g), respectively. The most common type of delivery was natural spontaneous delivery (n = 57, 67.1%), followed by cesarean section (n = 28, 32.9%). Associations with family history, chromosomal anomalies, and gastrointestinal malformation were uncommon. Only one patient had a family history of IHPS (1.2%).

Participant demographic information, clinical characteristics, imaging findings, and laboratory results are summarized in Table 1. Two patient records lacked data on gestational age, birth order, and plurality. The most common presentations were non-bilious projectile vomiting (100%) and palpable olive-like mass (25.3%). Of patients with available data, 73 were born at term (88%), 10 were born preterm (12%), and none was post-term. The laboratory findings included five cases of hyponatremia (5.9%), 12 of hypokalemia (14.1%), 36 of hypochloremia (46.8%), and 32 cases of bicarbonate elevation (47.1%) (Table 1). The mean pyloric thickness and pyloric muscle length were 5.5 ± 0.8 (range = 4.1–8.2 mm) and 20.8 ± 3.0 mm (range = 15.0–32.6 mm), respectively. The correlations of demographic data and clinical parameters with pyloric hypertrophy severity are reported in Table 2. Sex and gestational age (full-term or pre-term) showed no association with the pyloric length or pyloric muscle thickness (Table 2). In Pearson's correlation analysis results shown positive correlation between the pyloric muscle thickness and age (r = 0.308, p = 0.004), weight (r = 0.321, p = 0.003), and symptom duration (r = 0.294, p = 0.008). Pyloric muscle length was not significantly correlated with age (r = 0.115, p = 0.293), weight (r = 0.187, p = 0.089), or symptom duration (r = - 0.029, p = 0.794) (Table 2). The Pearson's correlation coefficients for symptom duration with serum sodium, potassium, chloride, and bicarbonate were −0.147 (p = 0.192), −0.155 (p = 0.168), −0.065 (p = 0.583) and 0.326 (p = 0.007), respectively. The serum bicarbonate is the only parameter associated with symptom duration.

All patients received Ramstedt pyloromyotomy and underwent surgery without severe complications. No patients received atropine as treatment. Seventy patients (82.4%) received laparotomy, and 15 (17.6%) received laparoscopic surgery. Several minor complications were identified, including 42 cases of vomiting (49.4%), one case of upper

Table 1 Demographic and clinical characteristics of infants with IHPS.

Characteristics	n (%)/mean ± SD (min, max)
Total patients	85
Birth order (unknown, n = 2)	
First order	48 (57.8%)
Non-first order	35 (42.2%)
Mode of delivery (unknown, n = 2)	
Vaginal delivery	57 (67.1%)
Cesarean section	28 (32.9%)
Plurality (unknown, n = 2)	
Twin birth	2 (2.4%)
Gestational age (unknown, n = 2)	
Full-term	73 (88%)
Preterm	10 (12%)
Gender	
Male	75 (88.2%)
Female	10 (11.8%)
Birth weight (gm)	3122.3 ± 486.9 (1626–4100)
Age (days)	39.9 ± 17.2 (15–92)
Symptom duration (days)	11.6 (1–60)
Weight (gm)	3909.6 ± 755.3 (2250–6000)
Palpable olive-like mass	21 (25.3%)
Serum levels of electrolytes	
Sodium/Hyponatremia	137.6 ± 3.0 mEq/L (127–145)/5 (5.9%)
Serum potassium/Hypokalemia	4.9 ± 0.7 mEq/L (3.1–6.7)/12 (14.1%)
Serum chloride/Hypochloremia (Unchecked, n = 8)	101.2 ± 6.8 mEq/L (82–112)/36 (46.8%)
Serum bicarbonate/Elevated bicarbonate (Unchecked, n = 17)	26.6 ± 6.6 mmol/L (11.9–51.3)/32 (47.1%)
Pyloric size (ultrasound measurement)	
Pyloric length	20.8 ± 3.0 mm (15.0–32.6)
Muscle thickness	5.5 ± 0.8 mm (4.1–8.2)
Operation	
Laparotomic	70 (82.4%)
Laparoscopic	15 (17.6%)
Time to start feeding (hours)	9.3 ± 5.7 (1.8–21.8)
Length of hospitalization (days)	7.3 ± 5.7 (3–53)

gastrointestinal bleeding with coffee-ground vomitus (1.2%), and two cases of poor wound healing after surgery (2.4%). The vomiting gradually resolved within 2–3 days. No significant difference in the occurrence of vomiting between laparotomic and laparoscopic operations was observed (50% vs. 46.6%, $p = 0.815$, chi-square analysis). The upper gastrointestinal bleeding resolved 2–3 days after administration of intravenous H2-blocker. Poor wound healing cases were treated with topical antibiotics and wound care. Subsequent wound hemorrhage, discharge, or cellulitis was not observed.

Eighty-five patients participated in the initial follow-up. There were no reports of IHPS, gastrointestinal complications, inadequacy of feeding or poor weight gain. After excluding three cases where weight measurements were not possible and three cases with post-operative complications (gastrointestinal bleeding or wound infection), a total of 79 patients were included in our nutritional recovery analysis. Of these 79 cases, the mean pre-operative weight-for-age percentile was 18.2 ± 20.6, and it reached 24.8 ± 23.3 (increase of 6.36 ± 11.8%) 1–2 weeks (mean, 9.6 ± 1.8 days) after operation. Thirty-one cases (39.3%) reached early nutritional recovery (weight-for-age increase >5%). Age and pyloric length tended to be associated with nutritional recovery by post-operative weeks 1–2 ($p = 0.062$ and 0.067, respectively, Table 3). In multivariable analysis, pyloric length related to nutritional recovery at week 1–2 postoperatively (OR = 1.42, $p = 0.030$, 95% CI = 0.03–1.94).

After the first follow-up, 13 patients continued follow-up at their local hospital. Of the remaining 66 patients, 59 completed follow-up and weight measurements 6–8 weeks after surgery. Gastrointestinal complications, poor wound healing or wound infection were not noted. Seven patients suffered acute illness (three acute diarrhea, two respiratory tract infections, and two urinary tract infections), which influenced feeding volume and weight gain at follow-up. These subjects were excluded from the second nutritional recovery assessment. A total of 52 cases were analyzed for nutritional recovery at 6–8 weeks after surgery. Mean weight-for-age percentile reached 41.6 ± 21.6 (mean post-operative follow-up, 44.8 ± 2.9 days). The average increment of weight-for-age percentile was 23.4 ± 11.8 compared to pre-operative status. Twenty-six cases (50%) achieved significant nutritional recovery (increase of weight-for-age percentile >20). As shown in Table 4, pyloric muscle thickness was the only parameter related to significant nutritional recovery after surgery. Those patients achieving significant nutritional recovery had greater pyloric muscle thickness than those without significant nutritional recovery (5.8 ± 0.6 vs. 5.2 ± 0.9, $p = 0.003$, Table 4). In multivariable analysis, pyloric muscle thickness remained independently related to significant nutritional recovery (OR = 4.08, $p = 0.032$, 95% CI = 1.13–14.7) (Table 4).

Table 2 The correlation coefficient between infant's characteristics and pyloric hypertrophy among IHPS patients.

Infant's characteristics	Pyloric length (mm) r (95% CI)	Pyloric muscle thickness (mm) r (95% CI)
Age[a]	0.115 (−0.102, 0.332)	0.308 (0.100, 0.516)*
Sex[b]	0.298 (−0.422, 0.787)	0.433 (−0.302, 0.845)
Gestational age[b]	0.483 (−0.250, 0.864)	−0.050 (−0.659, 0.599)
Weight[a]	0.187 (−0.029, 0.405)	0.321 (0.113, 0.531)*
Symptom duration[a]	−0.029 (−0.253, 0.194)	0.294 (0.080, 0.514)*

*$p < 0.05$.
[a] Data with normal distribution were analyzed by Pearson's correlation coefficients.
[b] Data with non-normal distribution were analyzed by Spearman's correlation coefficients.

Table 3 Correlation between patients with early nutritional recovery and patients without early nutritional recovery (1–2 weeks post operation) of 79 IHPS patients.

Variables	Early nutritional recovery[a]		*p*-value	Multivariable logistic regression	
	Positive (n = 31)	Negative (n = 48)		OR (95% CI)	*p-value*
Age at diagnosis (days)	34.2 ± 13.5 (31)	41.1 ± 17.2 (48)	0.062	0.96 (0.91–1.01)	0.083
Symptom duration (days)	9.3 ± 7.6 (31)	12.1 ± 12.9 (45)	0.283		
Pyloric length (mm)	21.5 ± 3.4 (31)	20.2 ± 2.1 (48)	0.067	1.42 (1.03–1.94)	0.030*
Pyloric muscle thickness (mm)	5.4 ± 0.8 (31)	5.5 ± 0.9 (48)	0.654		
Time to start feeding (hours)	9.6 ± 5.5 (31)	8.5 ± 5.7 (47)	0.418		
Serum bicarbonate (mmol/L)	26.8 ± 4.7 (28)	26.8 ± 7.7 (35)	0.999		
Serum chloride (mmol/L)	99.2 ± 6.7 (31)	101.0 ± 8.8 (43)	0.335		

*Data of continuous variables were expressed as mean ± SD, and analyzed by student *t* test; mean values were significantly different between variables ($p < 0.05$*).
*Odds ratio (OR) and 95% confidence intervals (CI) were estimated using multivariable logistic regression analysis. Statistical analyses were considered significant at $p < 0.05$.
[a] Early nutritional recovery: increment of weight-for-age percentile >5 within 1–2 weeks post operation.

Table 4 Correlation between patients with significant nutritional recovery and patients without significant nutritional recovery (6–8 weeks post operation) of 52 IHPS patients.

Variables	Significant nutritional recovery[a]		*p*-value	Multivariable logistic regression	
	Positive (n = 26)	Negative (n = 26)		OR (95%CI)	*p-value*
Age at diagnosis (days)	41.2 ± 18.5 (26)	37.1 ± 12.5 (26)	0.342		
Symptom duration (days)	13.7 ± 15.8 (26)	10.5 ± 11.4 (26)	0.401		
Pyloric length (mm)	20.6 ± 2.6 (26)	20.4 ± 2.8 (26)	0.838		
Pyloric muscle thickness (mm)	5.8 ± 0.6 (26)	5.2 ± 0.9 (26)	0.003*	4.08 (1.13–14.7)	0.032*
Time to start feeding (hours)	8.2 ± 5.0 (26)	9.3 ± 6.3 (26)	0.499		
Serum bicarbonate (mmol/L)	25.5 ± 6.5 (24)	28.4 ± 5.4 (24)	0.096		
Serum chloride (mmol/L)	100.9 ± 8.4 (24)	103.3 ± 5.4 (24)	0.251		

*Data of continuous variables were expressed as mean ± SD, and analyzed by student *t* test; mean values were significantly different between variables ($p < 0.05$*).
*Odds ratio (OR) and 95% confidence intervals (CI) were estimated using multivariable logistic regression analysis. Statistical analyses were considered significant at $p < 0.05$.
[a] Significant nutritional recovery: increment of weight-for-age percentile >20 within 6–8 weeks post operation.

Table 5 Relationship of outcome parameters between laparotomic and laparoscopic groups of IHPS patients.

Variables	Laparotomy (n = 70)	Laparoscopy (n = 15)	*p*-value
Mean LOH (days)	7.4 ± 6.3 (70)	7.0 ± 2.4 (15)	0.818
Time to start feeding post-operation (hrs)	9.4 ± 5.6 (70)	9.0 ± 6.3 (15)	0.800
Post-operative LOH (days)	4.3 ± 2.3 (70)	4.3 ± 1.8 (15)	0.947
Increment of weight-for-age percentile (1–2 weeks)	6.4 ± 14.9 (65)	6.3 ± 14.9 (14)	0.980
Increment of weight-for-age percentile (6–8 weeks)	24.1 ± 25.2 (41)	24.9 ± 23.7 (11)	0.945

*Abbreviations: LOH: length of hospitalization; SD: standard deviation.
#Data of continuous variables were expressed as mean ± SD and analyzed by t-test; mean values were significantly different between variables ($p < 0.05$*).

Table 5 shows the outcome parameters in the laparotomic and laparoscopic groups. The mean LOH was 7.3 ± 5.7 (pre-operative LOH = 3.0 ± 4.7 days, post-operative LOH = 4.3 ± 2.2 days). Of 70 patients who received laparotomic pyloromyotomy, the mean LOH, post-operative LOH, and time to start of feeding after surgery were 7.4 ± 6.3 days, 4.3 ± 2.3 days, and 9.4 ± 5.6 h, respectively. Of 15 patients receiving laparoscopic pyloromyotomy, the mean LOH, post-operative LOH, and time to start of feeding after surgery were 7.0 ± 2.4 days, 4.3 ± 1.8 days, and 9.0 ± 6.3 h, respectively. No significant differences between the laparotomic and laparoscopic groups were observed in the mean LOH ($p = 0.818$), post-operative LOH ($p = 0.947$), and time to start of feeding after surgery ($p = 0.800$). There was no significant difference in mean LOH and increment of weight-for-age status (1–2 weeks and 6–8 weeks after surgery) between patients with and without bicarbonate elevation ($p = 0.156$, 0.980, and 0.945, respectively).

Discussion

This 10-year retrospective study involved collection of clinical and laboratory medical record data from IHPS patients at a single tertiary center. Our aims were to investigate the factors that relate to pyloric hypertrophy severity and feeding and nutritional recovery. This is the first report to correlate clinical and laboratory parameters with feeding and nutritional recovery in IHPS.

IHPS affects infants at a reported male: female ratio of between 4:1 and 6:1 [2–4]. Previous studies on the incidence of IHPS in Taiwan found male: female ratios of 4.30:1 and 5.09:1 [6,17]. In this study, the ratio was 7.5:1, which was higher than previous national studies. A study based in Anhui, China, found that a higher ratio may be associated with the family-planning policy in previous years [18]. Strong familial aggregation of IHPS has been reported, which indicates hereditary character and may explain racial differences in incidence [19]. Firstborn infants have been reported to have a 1.8 times higher risk of IHPS than other birth orders [20]. A recent study of IHPS in developing countries reported the highest incidence of IHPS among third-born infants [21]. However, no definite conclusion was drawn from that result. In the present study, first-born infants had the highest incidence of IHPS, accounting for 57.8% of all cases. These findings were consistent with the existing literature. A family history of IHPS has been reported among 14.7% of IHPS patients in European populations, 12% in the Australian population, and 9% in the Canadian population [22–24]. Here, only one case with a positive family history of IHPS was identified. Although it is possible that data were omitted during the medical record review, the rarity of IHPS-positive family history among Asians likely contributed to the observed low incidence. Previous studies have described the association between chromosomal anomalies and IHPS. Two studies have identified separate anomalies, including partial trisomy 9q and unbalanced 8; 17 translocation [25,26]. In this study, one patient with IHPS was identified with an inv (1) (p36.3; q11) chromosomal anomaly; however, the clinical linkage between this chromosomal anomaly and IHPS remains unknown.

In this study, the mean age of IHPS diagnosis was 39.9 days, similar to two other studies in Taiwan, which reported mean ages of 36.5 days and 43.1 days [6,17]. These findings are similar to studies conducted in Israel, Western Australia, Tanzania, Denmark, and Los Angles [27–31]. In a study based in Nigeria, Ezomike et al. reported an older age at diagnosis, 49.16 days, likely due to late presentation and prior peripheral hospital visits [21]. With the availability of US for early identification and diagnosis of IHPS, the use of physical examination to identify the olive mass in IHPS has declined. Glatstein et al. reviewed several studies across decades and observed a decline in "palpable olive" presentations among IHPS patients, despite the absence of a change in the mean age of IHPS [32]. This result may apply to our country, given our well-established health care system. In the present study, the epigastric olive-like mass was palpated in 25.3% of cases. The identification of an olive-like mass during physical examination may be underestimated due errors associated with the retrospective medical record review as well as the progress and availability of US for patients with pyloric stenosis, which allows for diagnosis soon after symptom onset.

Among this study population, elevated bicarbonate was the most common biochemical abnormality, followed by hypochloremia. These results are consistent with previous studies [18,23,33,34]. Previous reports have indicated that symptom duration affected biochemical imbalances [18,35–37]. Touloukian et al. found that the vomiting duration was twice as long for the higher bicarbonate group as for the lower bicarbonate group [37]. Anhui et al. observed that nearly two-thirds of IHPS patients exhibited electrolyte imbalance [18]. Metabolic alkalosis with hypokalemia was more common in patients presenting with symptoms of >3 weeks' duration [35]. Other studies have noted that electrolyte data may be normal in early presenting patients due to resuscitation following early diagnosis [21,35,37]. This study identified a positive correlation between symptom duration and serum bicarbonate level. Similar to Ezomike et al., this study found a negative correlation between serum potassium level and serum bicarbonate level, which was caused by an influx of potassium and alkalosis [21].

Here, the average pyloric muscle thickness was 5.5 mm. Statistical analysis found that pyloric muscle thickness was positively correlated with age, weight, and symptom duration. The literature had identified variable correlation between the size of pyloric mass and patient characteristics. The results of our study are compatible with two retrospective studies evaluating the relationship between US measurements and patient characteristics found that pyloric thickness was positively correlated with age and weight in patients with IHPS [27,38]. However, no significant relationship between pyloric length and age, weight, or symptom duration was observed. A variable measurement of pyloric length would be made by technologists which are contributed to the similarity between spastic antral muscle proximal to pylorus and hypertrophic pylorus [27]. Iqbal et al. observed that age and weight were negatively correlated with pyloric measurements in infants without pyloric stenosis [38], the authors provided some insight into the pathophysiology of IHPS where the normal pylorus undergoes an ontogenetic change that leads to a decrease in the pyloric muscle thickness and length. Pathologic disruption of this preprogrammed morphological change may lead to ongoing pyloric growth and subsequent hypertrophy. Our research disclosed a similar result that only pyloric thickness displayed a positive relationship with age, weight and symptom duration. We expect a future prospective study of serial pyloric measurements to clarify such relationship.

In the present study, no morbidity or mortality was reported after surgery. The outcome in terms of post-operative complications, recovery, and recurrence was comparable in the laparotomy and laparoscopy groups, similar to the findings of Agrawal et al. [39]. Vomiting remained the most common symptom after surgery, with 49.4% of IHPS patients experiencing at least one vomiting episode. These findings are comparable to those in a previous study where 48.8% of patients with IHPS experienced post-operative emesis [40]. Forced feeding protocols, viral infection, gastroesophageal reflux, restenosis, incomplete myotomy, mucosal perforation may result in post-operative emesis. Patients with incomplete myotomy might receive re-operation to overcome hypertrophic pylorus. Nevertheless, in our study, there was no patients received second operation because of incomplete myotomy. All post-operative emesis recovered from conservative management. Inadequate myotomy may have contributed to post-operative emesis. However, both laparotomic and laparoscopic procedures can lead to prolonged emesis after surgery. In this study, two patients experienced poor wound healing. One received sutures and antibiotics and had a prolonged hospital stay (12.4 days longer than the mean hospital stay), and the other was readmitted a week post-operation and received wound closure in the operation room. Unlike Hall et al. and St. Peter et al., who reported the benefits of shorter hospital stays, shorter post-operative recovery, lower complication rates, and less post-operative pain with laparoscopic surgery compared to laparotomic surgery [41,42], this study showed no significant differences in the time to start of feeding after surgery and the length of hospital stay between the laparoscopic and laparotomic groups.

Most (92.9%, 79/85) patients participated in the initial follow-up, which enhanced the reliability of our findings and data analysis. The IHPS patients tend to have metabolic alkalosis resulting from excessive HCl, $K+$ and H_2O loss from the stomach via continued vomitus. Continued depletion of H^+, Cl^- lead to influx of potassium and subsequent elevation of serum bicarbonate caused by alkalosis. Metabolic alkalosis could cause several physiological consequences including decreased myocardial contractility, arrhythmias, decreased cerebral blood flow, confusion, increased neuromuscular excitability, and impaired peripheral oxygen unloading secondary to the shift of the oxygen dissociation curve to left [43]. In our series, we observed more episodes of suggestive features for metabolic alkalosis including weak feeding, lack of energy, lethargy, onset of desaturation, and vomitus in the patients with elevated serum bicarbonate before and after operation. There were limited number of patients had weight records at 6–8 weeks after surgery but we found there were some differences in the serum bicarbonate level between patients with significant weight gain and patients without significant weight gain 6–8 weeks after surgery (25.5 ± 6.5 v.s. 28.4 ± 5.4 mmol/L), suggesting serum bicarbonate elevation may be a trend to promote unfavorable nutritional recovery although it is not statistically significant in univariate analysis ($p = 0.096$, Table 4). Although current information cannot be verified, we emphasize that bicarbonate imbalance and dehydration should be corrected promptly in initial management of pyloric stenosis.

We identified a positive correlation between pyloric muscle thickness and both age and symptom duration (Table 2). However, pyloric length and pyloric muscle thickness were positively correlated with significant nutritional recovery 1–2 weeks and 6–8 weeks after surgery, respectively (multivariable logistic regression, Tables 3 and 4). In our series, most patients with IHPS did have a recovery of weight-for-age percentile in 6–8 weeks post operation (either with reach of 20 weight-for-age percentile or not). Even in patients with thicker pylorus, the recovery of nutritional status was well from our results. We observed that hospital duration and recovery of feeding to normal range were similar between the patients with thicker and thinner pylorus. These results indicate that the severity of pyloric hypertrophy and symptom duration may not influence nutritional recovery in IHPS patients.

The strengths of this study include the relatively larger sample size and the standardization of perioperative and post-operative management and surgical approaches, which were based on guidelines for pediatric gastroenterologists and pediatric surgeons. In addition, this study statistically evaluated factors related to nutritional recovery, which was not considered in previous studies. Our study has some limitations, as it was a retrospective, nonrandomized, single-center analysis based on demographic and medical data collected by medical chart review. Given the nature of this study, not all data were obtainable, and some post-operative morbidities may have been underdiagnosed, which limits the ability to draw inferences on possible causality. Despite these limitations, the results were comparable to those reported by other Western countries.

Conclusions

This study found that age, weight, and symptom duration were positively correlated with pyloric hypertrophy in patients with IHPS. The results indicate that bicarbonate elevation and hypochloremia are the two most common electrolyte imbalances among patients with IHPS. Overall, nutritional outcomes for IHPS patients were good with significant weight gain at 6–8 weeks after surgery. The clinical and nutritional outcomes were similar among patients who underwent laparotomy and laparoscopy for treatment of IHPS.

Ethics approval and consent to participate

Institutional Review Board of the Human Research Committee of Chang Gung Memorial Hospital approved the study protocol (No. 201901522B0). The informed consent was obtained from the participants.

Consent for publication

All participants gave consent for publication.

Language editing

The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/8SciBR.

Conflicts of interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

The authors thank all the children and their parents or caregivers for participating in this study, and also thank medical staff (medical residents, medical interns, and nurses) for their clinical care.

REFERENCES

[1] Hirschsprung H. Falle von angeborener pylorus stenose. J Kinderheilk 1888;27:61.
[2] Rogers IM. The enigma of pyloric stenosis. Some thoughts on the aetiology. Acta Paediatr 1997;86:6–9.
[3] To T, Wajja A, Wales PW, Langer JC. Population demographic indicators associated with incidence of pyloric stenosis. Arch Pediatr Adolesc Med 2005;159:520–5.
[4] Krogh C, Fischer TK, Skotte L, Biggar RJ, Oyen N, Skytthe A, et al. Familial aggregation and heritability of pyloric stenosis. JAMA 2010;303:2393–9.
[5] MacMahon B. The continuing enigma of pyloric stenosis of infancy: a review. Epidemiology 2006;17:195–201.
[6] Tiao MM, Tsai SS, Kuo HW, Yang CY. Epidemiological features of infantile hypertrophic pyloric stenosis in Taiwan: a national study 1996-2004. J Gastroenterol Hepatol 2011;26:78–81.
[7] Weinstein MM, Seibert JJ, Erenberg A. Six atypical presentations of congenital hypertrophic pyloric stenosis. Clin Pediatr (Phila) 1979;18:120–2.
[8] Janik JS, Wayne ER, Janik JP. Pyloric stenosis in premature infants. Arch Pediatr Adolesc Med 1996;150:223–4.
[9] Ohri SK, Sackier JM, Singh P. Modified Ramstedt's pyloromyotomy for the treatment of infantile hypertrophic pyloric stenosis. J R Coll Surg Edinb 1991;36:94–6.
[10] Nakayama DK, Taylor LA. Hypertrophic pyloric stenosis in infancy. An analysis of treatment outcome. N C Med J 1998;59:310–3.
[11] Kofoed PE, Host A, Elle B, Larsen C. Hypertrophic pyloric stenosis: determination of muscle dimensions by ultrasound. Br J Radiol 1988;61:19–20.
[12] Hallam D, Hansen B, Bodker B, Klintorp S, Pedersen JF. Pyloric size in normal infants and in infants suspected of having hypertrophic pyloric stenosis. Acta Radiol 1995;36:261–4.
[13] Rohrschneider WK, Mittnacht H, Darge K, Troger J. Pyloric muscle in asymptomatic infants: sonographic evaluation and discrimination from idiopathic hypertrophic pyloric stenosis. Pediatr Radiol 1998;28:429–34.
[14] Steven IM, Allen TH, Sweeney DB. Congenital hypertrophic pyloric stenosis: the anaesthetist's view. Anaesth Intensive Care 1973;1:544–6.
[15] Tigges CR, Bigham MT. Hypertrophic pyloric stenosis: it can take your breath away. Air Med J 2012;31:45–8.
[16] Chen W, Chang MH. New growth charts for Taiwanese children and adolescents based on World Health Organization standards and health-related physical fitness. Pediatr Neonatol 2010;51:69–79.
[17] Leong MM, Chen SC, Hsieh CS, Chin YY, Tok TS, Wu SF, et al. Epidemiological features of infantile hypertrophic pyloric stenosis in Taiwanese children: a nation-wide analysis of cases during 1997-2007. PLoS One 2011;6:e19404.
[18] Li J, Gao W, Zhu JM, Zuo W, Liu X. Epidemiological and clinical characteristics of 304 patients with infantile hypertrophic pyloric stenosis in Anhui Province of East China, 2012-2015. J Matern Fetal Neonatal Med 2018;31:2742–7.
[19] Galea R, Said E. Infantile hypertrophic pyloric stenosis: an epidemiological review. Neonatal Netw 2018;37:197–204.
[20] McAteer JP, Ledbetter DJ, Goldin AB. Role of bottle feeding in the etiology of hypertrophic pyloric stenosis. JAMA Pediatr 2013;167:1143–9.
[21] Ezomike UO, Ekenze SO, Amah CC, Nwankwo EP, Obianyo NE. Infantile hypertrophic pyloric stenosis - our experience and challenges in a developing country. Afr J Paediatr Surg 2018;15:26–30.
[22] Pedersen RN, Garne E, Loane M, Korsholm L, Husby S. Infantile hypertrophic pyloric stenosis: a comparative study of incidence and other epidemiological characteristics in seven European regions. J Matern Fetal Neonatal Med 2008;21:599–604.
[23] Gotley LM, Blanch A, Kimble R, Frawley K, Acworth JP. Pyloric stenosis: a retrospective study of an Australian population. Emerg Med Australasia 2009;21:407–13.
[24] Wayne C, Hung JH, Chan E, Sedgwick I, Bass J, Nasr A. Formula-feeding and hypertrophic pyloric stenosis: is there an association? A case-control study. J Pediatr Surg 2016;51:779–82.
[25] Heller A, Seidel J, Hubler A, Starke H, Beensen V, Senger G, et al. Molecular cytogenetic characterisation of partial trisomy 9q in a case with pyloric stenosis and a review. J Med Genet 2000;37:529–32.
[26] Hodgson SV, Berry AC, Dunbar HM. Two brothers with an unbalanced 8;17 translocation and infantile pyloric stenosis. Clin Genet 1995;48:328–30.
[27] Said M, Shaul DB, Fujimoto M, Radner G, Sydorak RM, Applebaum H. Ultrasound measurements in hypertrophic pyloric stenosis: don't let the numbers fool you. Perm J 2012;16:25–7.
[28] Shaoul R, Enav B, Steiner Z, Mogilner J, Jaffe M. Clinical presentation of pyloric stenosis: the change is in our hands. Isr Med Assoc J 2004;6:134–7.
[29] Hitchcock NE, Gilmour AI, Gracey M, Burke V. Pyloric stenosis in western Australia, 1971-84. Arch Dis Child 1987;62:512–3.
[30] Chalya PL, Manyama M, Kayange NM, Mabula JB, Massenga A. Infantile hypertrophic pyloric stenosis at a tertiary care hospital in Tanzania: a surgical experience with 102 patients over a 5-year period. BMC Res Notes 2015;8:690.
[31] Krogh C, Biggar RJ, Fischer TK, Lindholm M, Wohlfahrt J, Melbye M. Bottle-feeding and the risk of pyloric stenosis. Pediatrics 2012;130:e943–9.
[32] Glatstein M, Carbell G, Boddu SK, Bernardini A, Scolnik D. The changing clinical presentation of hypertrophic pyloric stenosis: the experience of a large, tertiary care pediatric hospital. Clin Pediatr (Phila) 2011;50:192–5.
[33] Piroutek MJ, Brown L, Thorp AW. Bilious vomiting does not rule out infantile hypertrophic pyloric stenosis. Clin Pediatr 2012;51:214–8.
[34] Taylor ND, Cass DT, Holland AJ. Infantile hypertrophic pyloric stenosis: has anything changed? J Paediatr Child Health 2013;49:33–7.
[35] Nmadu PT. Alterations in serum electrolytes in congenital hypertrophic pyloric stenosis: a study in Nigerian children. Ann Trop Paediatr 1992;12:169–72.
[36] Beasley SW, Hudson I, Yuen HP, Jones PG. Influence of age, sex, duration of symptoms and dehydration of serum electrolytes in hypertrophic pyloric stenosis. Aust Paediatr J 1986;22:193–7.
[37] Touloukian RJ, Higgins E. The spectrum of serum electrolytes in hypertrophic pyloric stenosis. J Pediatr Surg 1983;18:394–7.
[38] Iqbal CW, Rivard DC, Mortellaro VE, Sharp SW, St Peter SD. Evaluation of ultrasonographic parameters in the diagnosis of pyloric stenosis relative to patient age and size. J Pediatr Surg 2012;47:1542–7.

[39] Agrawal V, Sharma D, Acharya H, Tiwari A. Laparoscopic hybrid pyloromyotomy for infantile hypertrophic pyloric stenosis: a simplified technique. J Minimal Access Surg 2020;16:386–9.
[40] Castellani C, Peschaut T, Schippinger M, Saxena AK. Postoperative emesis after laparoscopic pyloromyotomy in infantile hypertrophic pyloric stenosis. Acta Paediatr 2014;103:e84–7.
[41] Hall NJ, Pacilli M, Eaton S, Reblock K, Gaines BA, Pastor A, et al. Recovery after open versus laparoscopic pyloromyotomy for pyloric stenosis: a double-blind multicentre randomised controlled trial. Lancet 2009;373:390–8.
[42] St Peter SD, Holcomb 3rd GW, Calkins CM, Murphy JP, Andrews WS, Sharp RJ, et al. Open versus laparoscopic pyloromyotomy for pyloric stenosis: a prospective, randomized trial. Ann Surg 2006;244:363–70.
[43] Brinkman JE, Sharma S. Physiology, metabolic alkalosis. 2021. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.