Congenital Hepatic Hemangiomas in Children

Most hepatic hemangiomas in infants are benign and are typically divided into two groups: 1) focal hepatic hemangiomas which are congenital and limited in size and 2) infantile hepatic hemangiomas which are diffuse in nature. The authors of this study evaluated the clinical course of infantile hepatic hemangiomas over time. The study used a patient database which included all patients diagnosed with congenital hepatic hemangiomas from 2004 to 2022. Data for the study included initial age at presentation, presence of anemia or thrombocytopenia, and an analysis of all radiographic images involving the hepatic hemangiomas over time.

A total of 96 infants in the patient database with hepatic congenital hemangiomas were studied. An equal number of male and female infants were present, and the patient group had a median gestational age of 37 weeks. Anemia was present in 48% of infants, and thrombocytopenia was present in 57% of infants. There was a significant statistical relationship between increasing infantile hepatic hemangioma size and risk of anemia and thrombocytopenia. Only 11% of infants had cutaneous hemangiomas, and no patient developed hypothyroidism in relation to their hepatic hemangioma.

Congenital hepatic hemangiomas were detected prenatally in approximately one third of infants in which ultrasound imaging detected lesions between 18 to 37 weeks gestation. Such initial prenatal lesions were noted to be single and hypervascular. Often these lesions continued to grow in the prenatal period with 24% of patients developing arterial or venous shunting.

In patients who had serial hepatic hemangioma imaging (47 patients), a residual hemangioma volume of 43% was present at 12 months while a residual volume of 16% was present at 24 months. Medical intervention did not change the rate of hemangioma involution. Biopsy specimens were available for 16 patients, and 13 of these biopsy specimens demonstrated a rapidly involuting congenital hemangioma. The other three patients had either partially involuting congenital hemangiomas or non-involuting congenital hemangiomas.

In patients who had data available, 46% of patients with congenital hepatic hemangiomas underwent medical therapy for which the most common therapies were corticosteroids (34%) and propranolol (31%). A total of nine patients underwent procedural therapy which included embolization, surgical resection, embolization /surgical resection, and embolization/liver transplantation. Extra-hepatic complications associated with this disorder included cardiomegaly (31%), heart failure (23%), and respiratory failure (23%). Although cardiac dysfunction was not significantly associated with hemangioma size, there was a significant correlation between hemangioma size and risk of respiratory failure. The mortality rate in this study was 4% because of hemorrhagic shock, sepsis, or complications of prematurity.

This study provides insight into the natural history of congenital hepatic hemangiomas. Most infants seem to tolerate this disorder with involution of hemangiomas over time. However, some infants with congenital hepatic hemangiomas can have lift-threatening consequences which should be considered early in the care of such children.

Ostertag-Hill C, Fevurly R, Kulungowski A, Christison-Lagay E, McGuire A, Rialon K, Duggan E, Murillo R, Zurakowski D, Staffa S, Alomari A, Kozakewich H, Al-Ibraheemi A, Fishman S, Dickie B. The natural history of congenital hepatic hemangiomas. Journal of Pediatrics 2025; doi: 10.1016/j.jpeds.2025.114523. Online ahead of print.

Infant Colic and Atopy

Infant colic is characterized by excessive crying and irritability and is a common cause of clinic visits to both general pediatricians and pediatric gastroenterologists. Proposed causes of colic have included functional, neurological, allergic, migraine-related, or potential dysbiosis components. The authors of this study previously

determined that risk factors such as prematurity, low birth weight, first born status, and maternal factors (atopy, severe nausea during pregnancy, and postpartum depression) may lead to infant colic. These risk factors led the authors to study if infant colic is associated with an increased long-term risk of atopy or respiratory symptoms as these children become older.

Data for this study was obtained from Project Viva which evaluates the long-term health of mother-infant pairs in eastern Massachusetts. Mothers were recruited between 1999 and 2002 before their 22nd week of pregnancy. Research visits to obtain clinical information were performed at the second and third trimester of pregnancy as well as several time points including: just after delivery or during infancy, toddler years, early childhood, middle childhood, early adolescence, and middle adolescence. A total of 1249 infants had data available for potential colic and excessive crying symptoms. These infants also had long-term data for the following symptoms: allergic rhinitis, reactive airway disease, and respiratory infections. Maternal information included education history, smoking history, marital status, income, number of prior births, use of oral antibiotics during pregnancy, and atopy of the mother and her partner. Infant data consisted of sex, mode of delivery, and infant feeding method.

Infant colic was present in 320 infants (26%) and excessive crying was present in 118 infants (9%). Infants with colic were statistically more likely to be of white ethnicity, have a history of prematurity, be born to a nulliparous mother, and be born to a mother with a history of atopy. The presence of eczema at all childhood time points was increased in patients who had a history of colic or excessive crying compared to children with no history of such symptoms, but this increase was not statistically significant except at follow up during middle childhood (median 7.7 years). Children with allergic rhinitis had an increased risk of colic during infancy, but the increase was only significant during the follow-up periods of early childhood (median 3.1 years) and middle childhood. Children with excessive crying as infants also were noted to have an increased risk of allergic rhinitis as they became older, but the risk was not statistically significant. Children in the age range of middle childhood and middle adolescence (median 17.5 years) had a higher risk of reactive airway disease if they had colic as infants although no such relationship was seen between colic and reactive airway disease in the other age ranges as well as with excessive crying and all age ranges. Respiratory infections in the age range of the toddler years (median 2.1 years), early childhood, and middle adolescence had a higher relative risk of respiratory infections if they had colic as infants although no such effect was seen between colic and the other age ranges as well as with excessive crying during infancy and all age ranges. Children with a history of colic were more likely to have more than one atopic disorder long term compared to children with no history of colic although no such effect was present in children with a history of excessive crying during infancy.

This study suggests that infant colic symptoms may be a marker of future atopic disease. Perhaps colic is associated with infant atopic symptoms which become more obvious as children become older.

Switkowski K, Oken E, Simonin E, Nadeau K, Rifas-Shiman S, Lightdale J. Associations of infant colic and excessive crying with atopic outcomes in childhood and adolescence. Journal of Pediatrics 2025; 283: 114623

Ondansetron Use in the Setting of Pediatric Gastroenteritis

Acute gastroenteritis (AGE) is a frequent reason that children present to the emergency department (ED). Besides utilization of intravenous fluid, ondansetron can reduce both nausea and emesis symptoms while such children are being seen in the ED. The authors of this study evaluated the utility of ondansetron continuing into the outpatient setting for children initially presenting to the ED with AGE.

This study was a double-blind, placebo-controlled randomized study that occurred at six pediatric EDs in Canada. Children from 6 months to less than 18 years of age were enrolled in the

study if that had AGE defined as at least 3 emesis episodes in the 24 hours prior to study enrollment, emesis or diarrhea at least 72 hours before enrollment, and emesis 6 hours before enrollment. All enrolled patients received ondansetron in the ED. These study patients were randomized with patients receiving ondansetron or placebo for a total of 6 doses at time of ED discharge. Besides collecting basic patient data, patient AGE severity was defined by using a modified Vesikari scale (range 0 – 20) in which a higher score on the scale was associated with more severe AGE.

The study occurred over an approximately 5-year period, and 517 patients received ondansetron while 512 patients received placebo. Baseline characteristics were the same between the two groups. Post enrollment scores of children with AGE demonstrated that Vesikari scores of 9 or higher were lower in the ondansetron group compared to the placebo group (unadjusted risk difference, −7.4 percentage points, 95% confidence interval, −11.2 to −3.7). A linear regression model demonstrated less AGE symptoms for patients using ondansetron after leaving the ED (adjusted odds ratio, 0.50, 95% confidence interval 0.40 to 0.60 and risk difference, −6.6 percentage points, 95% confidence interval, −10.9 to −2.3). A multivariable analysis demonstrated that patients taking ondansetron had a decreased risk of having a Vesikari score of 9 or higher (adjusted odds ratio, 0.46, 95% confidence interval, 0.27 to 0.78). Although both study groups had equal numbers of patients who had emesis during the study, the patients who received ondansetron had significantly a smaller number of emesis episodes. Interestingly, the percentage of children who had unscheduled medical visits within 7 days after study enrollment as well as the percentage of children who required intravenous fluid within 7 days after study enrollment was not statistically significant between groups.

This study demonstrates that sending pediatric patients home with a limited number of ondansetron doses after being seen in the ED for AGE may be beneficial in reducing gastrointestinal symptoms. The authors of the study noted that no patient developed symptoms of QT prolongation after being sent home on ondansetron, and it is always prudent to send children home with only limited amounts of this medication to prevent this side effect.

Freedman S, Williamson-Urquhart S, Plint A, Dixon A, Beer D, Joubert G, Pechlivanoglou P, Finkelstein Y, Heath A, Zhang J, Wallace A, Offringa M, Klassen T, and the Pediatric Emergency Research Canada Innovative Clinical Trials Study Group. The New England Journal of Medicine 2025; 393: 255-266.

Autoimmune Hepatitis Treatment Outcomes in Children

Autoimmune hepatitis (AIH) in children is a progressive and destructive autoimmune disease of the liver which can be fatal. Treatment of pediatric AIH often consists of two regimens: 1) prednisolone with possible addition of azathioprine or 2) tacrolimus (a calcineurin inhibitor). The authors of this study compared the efficacy of these two treatments.

This retrospective study occurred using data from 5 European medical centers in which children with AIH were studied over a 13-year period (2005-2018). Children included in the study were younger than 18 years of age, had liver biopsies obtained within 6 months of therapy, and had at least 2 years of follow-up care. Initial patient data and follow-up data at 3, 6, and 12 months on therapy were analyzed. Four medical centers utilized prednisolone starting at 1-2 mg/kg/day with azathioprine at 1-2 mg/kg/day either added or not added after 14 days of AIH diagnosis. Prednisolone weaning was guided by the treating physician. The fifth medical center used tacrolimus at a dose starting at 0.025-0.050 mg/kg/day in order to obtain a tacrolimus trough of 3-6 ng/mL with the addition of prednisolone (10-20mg daily) at the discretion of the treating physician. Chart review occurred to evaluate for the presence of other medical disorders, AIH parameters (autoantibodies, liver biopsy results), and the presence of any imaging (ultrasound or magnetic resonance cholangiopancreatography (MRCP)).

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A total of 157 children with AIH were included in the study, and all children still had their native liver one year after diagnosis. Therapeutic options consisted of prednisolone with possible azathioprine in 111 patients and tacrolimus therapy with possible prednisolone occurring in 46 children. The children treated with prednisolone and possible azathioprine were statistically more likely to have other autoimmune diseases and higher platelet counts. The children treated with tacrolimus and possible prednisolone were statistically more likely to higher Metavir fibrosis scores, have higher bilirubin levels, and have more esophageal varices at diagnosis. A total of 12 children (six patients in each group) had a diagnosis of acute liver failure with an INR greater or equal to 2, and such patients all had eventual response to therapy.

Liver histology confirmed AIH in 112 children, and 41 of these children had biliary involvement. Seven of the 41 children with biliary involvement did not have associated autoimmune sclerosing cholangitis. MRCP testing occurred in 105 children (67%) within the first year of therapy. Statistically more children undergoing therapy with prednisolone and possible azathioprine underwent MRCP. MRCP diagnosed autoimmune sclerosing cholangitis in 42 children with 23 patients having combined large and small duct disease.

Autoantibody testing was positive in 148 patients (94%) and elevated IgG serum levels were present in 125 patients (85%). The most common autoantibody detected was anti-smooth muscle actin antibody occurring in 117 patients. Most patients had high rates of advanced fibrosis/cirrhosis as noted by a Metavir score of 3 or 4 in 46% of patients, and advanced fibrosis/cirrhosis was significantly higher in the patient group treated with tacrolimus and possible prednisolone.

Only one child in the entire patient group did not experience lowering serum alanine aminotransferase (ALT) levels by 6 months of therapy. ALT normalization took a statistically longer time in the patient group receiving tacrolimus with possible prednisolone compared to the prednisolone group with possible azathioprine use at both 3 months (26.8% versus 58% normalization) and 6 months (46.2% versus 68.8% normalization). However, there was no significant difference in normalization at 12 months between the two treatment groups. Serum IgG levels took longer to normalize in patients receiving tacrolimus with possible prednisolone compared to the prednisolone group with possible azathioprine use at 3 months, 6 months, and 12 months although the normalization time was not consistently statistically significant at 3 months and 12 months. No significant difference in Z-scores for height and weight was present between the two treatment groups during the study. The number of children eventually not requiring prednisolone was higher in the group receiving tacrolimus compared to the prednisolone group with possible azathioprine use. However, this finding makes sense as the latter group received prednisolone initially.

This study suggests that starting tacrolimus for pediatric patients with AIH may be preferable as less steroid use may be needed. This study

is retrospective only, and large multi-national prospective studies in the treatment of pediatric AIH are very much needed.

Jorgensen M, Almaas R, Kharrazi G, Urbonas V, Kvistgaard H, Wollen E, Andreassen B, Casswall T, Fischler B. Various regimens for autoimmune hepatitis in northern European children show equivalent outcomes at 1 year: a retrospective study. Journal of Pediatrics 2025; 284: 114635

GI Outcomes After Pediatric Malrotation Repair

Intestinal malrotation in children is a surgical emergency if a resultant intestinal volvulus occurs. The Ladd procedure is a surgical technique to prevent complications from a potential volvulus. However, it is unclear what gastrointestinal (GI) symptoms occur long term in pediatric patients with malrotation after the Ladd procedure. The authors of this study attempted to answer this question using the TriNetX Research Network which contains de-identified patient data from electronic medical records as well as other sources. Using a database of 130 million patients, this retrospective matched cohort study compared pediatric patients with a history of malrotation repair to a control group of general pediatric patients. Patients were matched by sex, race, age, and ethnicity. GI symptoms were determined using International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes. Patients were evaluated at 1 to 5 years post-surgery and 3 to 5 years post-surgery.

A total of 354 patients with a history of intestinal malrotation status post repair were matched to 354 control patients. There was no significant difference in patient demographics across the two groups. At both 1 to 5 post surgery or years 3 to 5 post surgery, patients with a history of intestinal malrotation repair were statistically more likely to have GI symptoms of constipation, diarrhea, abdominal pain, gastroesophageal reflux disease, nausea, and emesis.

This study suggests that GI symptoms may be persistent in patients even after malrotation surgical repair, and these results seem to differ with prior research showing that GI symptoms generally resolve after a Ladd procedure. Perhaps this patient group has an increase in functional GI symptoms in the setting malrotation repair. More research is now needed to determine if this patient group is at a higher risk of mucosal GI disease long term which could include celiac disease, erosive esophagitis, gastritis, and other related disorders.

Corcoran K, Martinez S, Tsikis S, Al-Mamun M, Intestinal Malrotation Clinical Group. Long-term gastrointestinal outcomes in pediatric intestinal malrotation patients following operative treatment. Journal of Pediatric Gastroenterology and Nutrition 2025; online ahead of print (DOI: 10.1002/jpn3.70204)