Gastrointestinal Complications of Childhood Obesity

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Disclosures

• None
Objectives

• Increase knowledge around the assessment of gastrointestinal conditions associated with childhood obesity.
• Increase knowledge around the treatment of the gastrointestinal conditions associated with childhood obesity.
Obesity Prevalence

Weight Status among US Children 2003-2006

- Non-Overweight: 31.9%
- Overweight: 15.6%
- Obese: 16.3%

Ogden et al. JAMA, 2008.
Comorbidities:

- Migraine Headaches
- Depression
- Obstructive Sleep Apnea
- Asthma
- Cardiovascular Disease
- Hypertension
- Nephropathy
- Metabolic Syndrome
- Non-Alcoholic Fatty Liver Disease
- GERD
- Type II Diabetes Mellitus
- Degenerative Joint Disease
Common Gastrointestinal Issues of Obesity

• NAFLD
• Constipation
• Gastroesophageal Reflux Disease
• Disorders of the Biliary Tree
Case

- You are seeing Jose, a 10 yo Hispanic male who has moved from San Diego to Portland
- He is registering for school and is here for a school entry exam
- Obesity and diabetes are “genetic” and run in the family
- Jose is otherwise healthy with no complaints
- Jose has not been active in physical activity outside of PE class; he loves his video games
- Snacks regularly; no breakfast; regular with 2nds at dinner table
Exam

- Height 123 cm
- Weight 36 kg
- BMI 23.8 kg/m² (97%)
- At his neck you notice acanthosis nigricans
- The exam of the abdomen is limited but you feel he does not have any HSM
Action

- You attempt to discuss weight management with the family but they are having none of it – “My son is fine without any problems.”
- The family is however agreeable for lab screening.
- You send him for the typical obesity lab screening and get the following results
  - ALT 52 U/L
  - AST 55 U/L
- Your lab’s ULN is 60 U/L for both ALT and AST
- Now what?
Case – Elevated LFTs

- 95% ALT healthy boys 25.8 U/L
- 95% ALT healthy girls 22.1 U/L
- TRUE ELEVATION

Schwimmer et al. SAFETY Study 2010.
Common Gastrointestinal Issues of Obesity

- NAFLD
- Constipation
- Gastroesophageal Reflux Disease
- Disorders of the Biliary Tree
What is NAFLD?

• Nonalcoholic fatty liver disease
• American Liver Foundation
  – The build up of extra fat in liver cells that is not caused by alcohol.
  – If more than 5% of the liver’s weight is fat - called a fatty liver (steatosis).
Not all Fatty Liver is NAFLD

Definitions

• Fatty Liver
  • ≥ 5% steatosis of any etiology
• NAFLD
  • ≥ 5% macrovesicular steatosis
  • Appropriate exclusions
• NASH
  • NAFLD + inflammation and liver cell injury

Courtesy of Jeff Schwimmer, MD fattyliver@ucsd.edu
Prevalence of NAFLD in Children

**Prevalence of Fatty Liver in Children and Adolescents**

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**ABSTRACT**

OBJECTIVE: Fatty liver disease is diagnosed increasingly in children, but the prevalence remains unknown. We sought to determine the prevalence of pediatric fatty liver disease by histology in a population-based sample.

METHODS: We exploited a retrospective review of 75,123 children between the ages of 0 and 18 years who had an outpatient performed by a county medical examiner from 2001 to 2003. Fatty liver was defined as >5% of hepatocellular fat.

RESULTS: Fatty liver was present in 33% of subjects. For children and adolescents age 2 to 19 years, the prevalence of fatty liver adjusted for age, gender, race, and ethnicity was estimated to be 9.8%. Fatty liver prevalence increases with age, ranging from 5.7% for ages 2 to 4 up to 17.8% for ages 15 to 19 years. Fatty liver prevalence differs significantly by race and ethnicity (Asian: 10.2%, Black: 1.1%, Hispanic: 13.4%, white: 8.0%). The highest rate of fatty liver was seen in obese children (10%).

CONCLUSIONS: Fatty liver is the most common liver abnormality in children age 2 to 19 years. The presence of macrovesicular hepatic steatosis in 9% of every 10 children has important ramifications for the long-term health of children and young adults. The influence of the risk factors identified should be taken into consideration in the development of pediatric dietary advice for children and adolescents.

**SCALE**

Study of Child and Adolescent Liver Epidemiology

**STANDARDIZED NAFLD Prevalence**

9.6%


Courtesy of Jeff Schwimmer, MD  fattyliver@ucsd.edu
Rates of NAFLD are highest in Hispanic and Asian children

SCALE: Fatty Liver by Race/Ethnicity

Prevalence

Asian | Black | Hispanic | White


Courtesy of Jeff Schwimmer, MD  fattyliver@ucsd.edu
Obesity is a major risk factor for NAFLD

SCALE: Fatty Liver by Weight Category


Courtesy of Jeff Schwimmer, MD fattyliver@ucsd.edu
60% of children with NAFLD are obese

SCALE: Fatty Liver Distribution by Weight Status

Overweight
Normal

OBESE


Courtesy of Jeff Schwimmer, MD fattyliver@ucsd.edu
NAFLD is a Spectrum Disorder

Spectrum of NAFLD

Normal Liver

Fatty Liver

Steatohepatitis

Cirrhosis

Courtesy of Jeff Schwimmer, MD  fattyliver@ucsd.edu
Multiple-Hit Hypothesis of NAFLD Pathogenesis

Traditional view of NAFLD pathogenesis

**Simple steatosis**
- First hit
  - Insulin resistance
  - Deposition of lipids in the hepatic parenchyma

**NASH**
- Second hit
  - Oxidative stress
  - Adipokines

**Cirrhosis**
- Increased susceptibility to multiple injuries
  - Progressive fibrosis
  - Liver failure, hepatocellular carcinoma
“Distinct-hit” hypothesis of NAFLD

Simple steatosis and NASH are two distinct entities with different pathogenetic pathways

Insulin resistance

Steatosis

NASH

Progression?
There are (at least) 2 types of NASH

In children Type 2 NASH is common

Histopathology of Pediatric Nonalcoholic Fatty Liver Disease

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Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are common in children and adolescents. However, standard histological criteria for pediatric NASH are not well defined. We reviewed consecutive patients aged 4 to 18 years with biopsy-proven NASH diagnosed between 1987 and 2000. Histopathologic tests were evaluated for individual cases of pediatric NASH. Appearance of liver tissue varied from different levels of fibrosis. Type 1 was characterized by steatosis, ballooning, and portal inflammation, and portal cholestasis. The study included 50 children with NASH. Simple steatosis was present in 30% of patients, and advanced fibrosis was present in 4%. Type 2 NASH was present in 30%, and type 3 and type 4 were present in 50%. Biopsy was performed in 50%. The pathologic findings were identical to type 2 NASH in 10 of 10 cases. Type 3 NASH was more common in patients with type 2 fibrosis. In most patients with type 2 NASH, the pattern was generally that of type 2 NASH, and type 3 and type 4 NASH were distinctly separate in pediatric NASH. As type 2 is the most common pattern in children, NASH categories should be considered when interpreting liver biopsies and when using studies of the metabolic syndrome, genetics, and cytokines or response to treatment in pediatric patients. Schwimmer et al Hepatology 42: 641-8, 2005

Schwimmer et al. Hepatology 42: 641-8, 2005

Courtesy of Jeff Schwimmer, MD fattyliver@ucsd.edu
Type 2 NASH is more common in boys

Schwimmer et al. Hepatology 42: 641-8, 2005

Courtesy of Jeff Schwimmer, MD fattyliver@ucsd.edu
Type 2 NASH is more common in Asian, Hispanic, and Native American children

Schwimmer et al. *Hepatology* 42: 641-8, 2005

Courtesy of Jeff Schwimmer, MD fattyliver@ucsd.edu
Treatments for NAFLD/NASH

• No medications approved for NAFLD/NASH
Vitamin E, Metformin, and NAFLD

- Randomized, double-blind, placebo-controlled clinical trial conducted at 10 university clinical research centers in 173 patients (aged 8-17 years) with biopsy-confirmed NAFLD conducted between September 2005 and March 2010.

- Youth randomized to
  - Vitamin E with metformin placebo
  - Vitamin E placebo with metformin
  - Double Vitamin E and metformin placebo
Vitamin E, Metformin, and NAFLD

• Neither vitamin E nor metformin was superior to placebo in attaining the primary outcome of sustained reduction in ALT level in patients with pediatric NAFLD.

• Histologic improvement in hepatocyte ballooning seen in patients who received vitamin E.

• Vitamin E did not have significant effects on steatosis, inflammation, or fibrosis as individual components.
Current Recommendations

• Screen for NAFLD
• Problematic without effective treatment outside of weight management
Weight loss and NAFLD

• Feldstein et al. performed a retrospective chart review of 66 youth with NAFLD
• Followup for up to 20 years (mean 6 years) with a total of 409.6 person-years of follow-up
• Diagnosis based on imaging, alcohol intake and lab/biopsy results ruling out other etiologies of liver disease
Weight loss and NAFLD

• One year after initiation of the prescribed lifestyle modification, 49% of children were able to lose at least 10% of their baseline weight, and 86% of them showed significant improvement or normalization of aminotransferases.

• At the time of last follow-up, however, most patients (76%) had re-gained weight, and in 46% of them aminotransferases returned to baseline values.
Back to Jose

• Wait time for gastroenterologist is 2-3 months
• You discuss the results with the family and suggest modification of weight related behaviors
  – Healthy diet
  – Physical activity
  – Family involvement

Schwimmer et al. SAFETY Study 2010.
Case – Elevated LFTs

• You see Jose back in 1 month hoping to find improvement in weight parameters but alas
• His weight and BMI have increased from 97 to >99%
• His repeat LFT’s are now in the 80’s range
• Next available GI visit is in 2 months
• Now what?
Case – Elevated LFTs

• Important to assess for severity of liver disease
  – Queries re: liver dysfunction
    • Easy bleeding/bruisability
    • Jaundice
    • Encephalopathy (change in personality, school performance, sleeping habits)
  – Physical examination (jaundice, HSM, ascites, palmar erythema, asterixis, spider angioma)
  – Consider additional laboratory testing
    • PT/INR
    • Bilirubin (Total and direct)
    • Alkaline phosphatase
    • GGT (Gamma glutamyl transpeptidase)
    • CBC (Splenic sequestration – leukopenia, thrombocytopenia)
Case – Elevated LFTs

• Given persistence and rise in LFTs –
  – Appropriate for GI/Hepatology referral
• Other considerations
  – Acute viral hepatitis
  – Autoimmune hepatitis
  – A1AT
  – Celiac disease
  – Wilson’s
  – Thyroid disease
  – Medications
• Consideration for Liver biopsy
Follow Up

• Jose has now seen the gastroenterologist who has performed a liver biopsy and found NAFLD but no evidence of NASH

• Weight management behaviors have again been discussed but the family has not complied

• Jose is back again in your office now with a complaint of abdominal pain and irregular passage of hard stools for the past 2 months
Common Gastrointestinal Issues of Obesity

- NAFLD
- **Constipation**
- Gastroesophageal Reflux Disease
- Disorders of the Biliary Tree
Constipation

- Common in obese and overweight youth
- May reflect unhealthy diet and lack of fiber in diet
- Most likely etiology is functional
- Most common cause of abdominal pain in youth
Rome III Criteria – Functional Constipation

• At least 2 of the following in youth 4-18 y
• Must be present for >= 2 months
  – 2 or fewer defecations per week
  – At least 1 episode incontinence per week
  – History of retentive posturing or excessive volitional stool retention
  – History of painful or hard BM’s
  – Presence of large fecal mass in rectum
  – History of large diameter stools that may obstruct the toilet
Warning Signs

• Constipation extremely early in life (<1 m)
• Passage of meconium >48 hours
• Family history of Hirschsprung’s disease
• Ribbon like stools
• Blood in the stools in the absence of anal fissures
• Failure to thrive (Weight loss/deceleration of linear growth)
• Fever
• Bilious vomiting
Clinical Exam Red Flags

Hypothyroidism:
- *Coarse skin, hypotonia, tachycardia, severe abdominal distension*

Perineum examination:
- *Perianal fistula/ Abnormal position of anus/ Extreme fear during anal inspection/ Anal scars*
- *Absent anal or cremasteric reflex*

Lumbosacral/LE examination:
- *Tuft of hair on spine/ sacral dimple/gluteal cleft deviation/ flat buttocks*
- *Decreased lower extremity strength/ tone/ reflex*
Routine laboratory testing to screen for hypercalcemia, hypothyroidism, celiac disease, and is not recommended in constipated children in the absence of alarm symptoms.
Imaging also not generally recommended

Tabbers et al. JPGN Feb 2014
Constipation Treatment

Disimpaction

• PEG orally 1 to 1.5 g/kg/day for 3 to 6 days
• An enema once per day for 3 to 6 days is recommended if PEG is not available
• PEG as effective as enemas but can cause more fecal incontinence

Tabbers et al. JPGN Feb 2014
Constipation Treatment

Maintenance

• PEG recommended as the first-line maintenance treatment (0.4 g/kg/day)
• Dose adjusted according to the clinical response
• Lactulose is recommended as the first-line maintenance treatment, if PEG is not available
• Use of milk of magnesia, mineral oil, and stimulant laxatives may be considered as an additional or second-line treatment
Titrating the Dose

### Bristol Stool Chart

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Separate hard lumps, like nuts (hard to pass)</td>
</tr>
<tr>
<td>2</td>
<td>Sausage-shaped but lumpy</td>
</tr>
<tr>
<td>3</td>
<td>Like a sausage but with cracks on its surface</td>
</tr>
<tr>
<td>4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>5</td>
<td>Soft blobs with clear-cut edges (passed easily)</td>
</tr>
<tr>
<td>6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>7</td>
<td>Watery, no solid pieces. <strong>Entirely Liquid</strong></td>
</tr>
</tbody>
</table>
Other

• Encourage normal fiber (age + 5 gms) and fluid intake
• Routine use of prebiotics and probiotics not recommended
• Association of cow milk protein allergy and constipation is debatable.
• A 2- to 4-week trial of milk avoidance may be trialed in the child with intractable constipation
Constipation Treatment

- **Education** is important
- Explain encopresis to the parent and child
- Toilet sit 1-2 times daily, 5 to 10 minutes after a meal
- Use positive reinforcement, not punishment
- [www.gikids.org](http://www.gikids.org)
- “The Poo in You” – good for both parent and child
Constipation Treatment

When to stop therapy

• Maintenance treatment should continue for at least 2 months
• All symptoms of constipation should be resolved for at least 1 month before discontinuation of treatment
• Treatment should be decreased gradually
• Good to ensure adequate fiber and liquid intake
Constipation Treatment

Prognosis

• 1 year recovery rate for children ~ 40%.
• 5 year and 10 year recovery rates - 50% and 80% respectively
• 50% of children had at least 1 relapse within the first 5 years after initial recovery.
• 30% of children continue to have constipation into adolescence
Case – Obesity and Hard Stools

• You assess for functional constipation and Jose meets 2 of the Rome criteria –
  – 2 or fewer defecations per week
  – History of painful or hard BM’s
  – History of large diameter stools that may obstruct the toilet
• On exam you find no red flags and palpate a large likely fecal mass at the LLQ
• What now?
Case – Obesity and Hard Stools

• You diagnose functional constipation
• Based on exam and history, likely fecal retention and need for medical disimpaction therapy followed by maintenance therapy
• You also take the opportunity to emphasize dietary changes towards normal fiber and liquid intake (healthier diet) as well as physical exercise
• You set up followup
Case – Persistent Abdominal Pain

• Jose is back
• He reports a successful response to your suggested medical disimpaction and that his stools are now being passed easily and daily
• He has not lost any weight but has not gained any either and his BMI has remained the same
• He is still complaining of abdominal pain
• What now?
Case – Persistent Abdominal Pain

- On further questioning, you determine that Jose actually had a change in his abdominal pain over time
- Before it was vague but now it is occurring much more into his chest and is accompanied by a burning sensation and acid taste in his mouth
- Exam is notable for some discomfort in the epigastric area to pressure
Common Gastrointestinal Issues of Obesity

• NAFLD
• Constipation

• Gastroesophageal Reflux Disease
• Disorders of the Biliary Tree
GERD

• Commonly associated with overweight/obesity
• Common symptoms: Heartburn, acid taste in mouth, regurgitation, nonbilious emesis, chronic cough
• Pathophysiology not completely understood
• Thought related to
  – increasing intragastric pressure and GE pressure gradient
  – Increased TLESR
  – Formation of hiatal hernia
GERD - Treatment

- Considerations should be given for concurrent constipation and potential contributions to GERD
- Empiric treatment trial with PPI (1 mg/kg/d) suggested x 1 month but not diagnostic
- If severe or persistent symptoms, hematemesis, dysphagia, weight loss, or relapses following PPI discontinuation – consider referral to GI
When weaning therapy

• Be aware of acid rebound
• Consider change to H2 blocker for a week or warn patients to use calcium carbonate for symptoms
Back to Jose

- You diagnose GERD
- Jose has no warning signs indicating need for additional imaging or referral
- You empirically treat with a PPI 1 mg/kg/day
- You set up followup
Back to Jose

- Jose returns for followup
- His GERD symptoms have improved on PPI therapy and not returned on an interim wean 1 month later
- He has lost weight since his last visit with you >20 lbs! The family finally started to take your weight management advice because of all of his abdominal pain issues
However...

- Jose’s abdominal pain has not completely subsided
- The acid taste in his mouth is gone but he continues now to have abdominal pain at the epigastric area
- The pain episodes occur after meals and seem to wax and wane
- He has been belching a lot
Common Gastrointestinal Issues of Obesity

- NAFLD
- Constipation
- Gastroesophageal Reflux Disease
- **Disorders of the Biliary Tree**
Cholelithiasis

Gallstones in gallbladder

Common bile duct
Cholelithiasis

- Cholesterol gallstones occurs 3-6 times as often in morbidly obese persons as compared to controls
- Occurs owing to increased hepatic secretion of cholesterol
- Weight loss increases the risk of gallstones in the obese
  - >24% initial body weight
  - Weight loss >1.5 kg (3.3 lb) per week
Cholelithiasis

• Symptoms vary
• Asymptomatic (lithogenic stage)
• Biliary colic
  – Sporadic and unpredictable episodes
  – Pain localized to the epigastrium or right upper quadrant, sometimes radiating to the right scapular tip
  – Often postprandial pain, described as intense and dull, typically lasts 1-5 hours, increases steadily over 10-20 minutes, and then gradually wanes
  – Nonspecific symptoms (eg, indigestion, dyspepsia, belching, or bloating)
  – OBSTRUCTION - Pain that is constant; not relieved by emesis, antacids, defecation, flatus, or positional changes; and sometimes accompanied by diaphoresis, nausea, and vomiting
Medical v. Surgical

- Uncomplicated biliary colic –
  - Pain poorly localized and visceral;
  - Benign abdominal exam
  - No fever

- Acute cholecystitis –
  - Well-localized RUQ pain, +rebound and guarding;
  - positive Murphy sign (nonspecific); no peritoneal signs
  - frequent presence of fever;
  - frequent presence of tachycardia and diaphoresis;
  - in severe cases, absent or hypoactive bowel sounds
Other concerns

• Choledocholithiasis
• Pancreatitis
• Cholangitis
Evaluation

• Depending on clinical situation
• Targeted labs
  – LFT’s and bilirubin (total and direct) as well as alkaline phosphatase, GGT
  – CBC
  – Amylase, lipase
• Imaging
  – Ultrasound
  – MRCP - choledocholithiasis
Treatment

• ERCP for therapeutic removal of stone in case of choledocholithiasis
• Surgery
  – Cholecystectomy
    • Large >2cm gallstone
• Dietary not effective
Back to Jose

- Jose’s abdomen is benign
- He points at his entire abdomen and epigastrium when asked to describe pain location although he doesn’t have it now
- He has no fever or jaundice
- You calculate his weight loss by week = 5 lbs/week
Laboratory

- Labs reveal elevated LFT’s to the 80 range still which is a bit surprising in light of his NAFLD given his recent weight loss
- His lipase, total and direct bilirubin are normal as are his GGT and alkaline phosphatase
- You decide to get imaging...
Cholelithiasis

Gallstones
Conclusion

• Jose has gallstones which are quite large >2cm
• You send him to surgery
• Laparoscopic surgery occurs without incident
• Jose follows up with you and has been able to curb his weight loss but maintain his weight in a healthy range
• His LFT’s have returned to normal and he reports no abdominal pain, GERD or constipation symptoms
Summary

• Gastrointestinal issues are common in youth with overweight and obesity
• Weight management remains an important treatment mainstay of majority of these conditions
• Gastrointestinal complications can often alert families to health issues related to weight and improve compliance with weight interventions
Acknowledgments

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• www.gikids.org