

## SHORT REPORT

## Cholelithiasis in Down's syndrome

E Toscano, V Trivellini, G Andria

**Abstract**

**Cholelithiasis is considered uncommon in infancy, childhood, and adolescence. We performed a prospective, controlled study showing that children with Down's syndrome have a significantly higher prevalence of cholelithiasis (4.7%) compared with controls (0.2%). Clinicians should be aware of the risk of gallstones in children with Down's syndrome.**

(Arch Dis Child 2001;85:242-243)

Keywords: Down's syndrome; cholelithiasis; gallstones

Cholelithiasis is uncommon in newborns, infants, children, and adolescents, with a prevalence no greater than 0.5%.<sup>1-3</sup> In paediatric patients, the predisposing factors include prematurity, phototherapy, parenteral nutrition, sepsis, abdominal surgery, short bowel syndrome, anatomic abnormalities of the biliary system, haemolytic disease, and the use of diuretics, narcotic, analgesics and ceftriaxone.<sup>4</sup>

In addition to anecdotal clinical reports, an increased prevalence of cholelithiasis in Down's syndrome (DS) was reported by Llerena and colleagues,<sup>5</sup> who investigated 145 patients and detected 10 with asymptomatic biliary calculi (6.9%).

We describe the first prospective, controlled study showing an association between DS and cholelithiasis in children.

**Patients and methods**

A total of 139 children with DS (age range 1 month to 19 years, median 36 months), from the area around Naples, referred between March and December 1999 were recruited to the study. Abdominal ultrasound examination was performed in 126. Thirteen patients referred were not studied for various reasons. None had undergone cholecystectomy. The control group consisted of 577 children (age range 1 month to 19 years, median 40 months), living in the same area, referred to our department for problems unrelated to gallstones. None had a known risk factor for cholelithiasis. Their clinical problems included urinary tract infections and/or urinary tract obstruction (145/577), hepatitis B carriers (117/577), recurrent abdominal pain (114/577), disorders of pubertal development (58/577), inborn errors of metabolism (57/577), multiple congenital anomalies (29/577), and others (57/577). The examinations were performed after

an eight hour fast, using a real time ultrasound scanner with a 3.5 MHz linear transducer.

Patients were recruited with informed parental consent. The study was approved by the local ethical committee.

**Results**

Of the 126 patients with DS who underwent abdominal ultrasound examination, six (4.7%) were found to have cholelithiasis. The four girls were aged 6, 12, 18, and 21 months, respectively; both boys were 6 years old. Among the controls, only one (0.2%) 7 year old girl had gallstones. All seven children with cholelithiasis in our study were born at term, were asymptomatic, and did not have identifiable risk factors for gallstones. The six with DS had normal serum bilirubin, haptoglobin, lipase, and ceruloplasmin concentrations, whole blood carboxyhaemoglobin concentration, reticulocyte count, and liver function tests (alkaline phosphatase, aspartate and alanine aminotransferase,  $\gamma$  glutamyltransferase, prothrombin time, and activated partial thromboplastin time).

In the six children with DS and cholelithiasis, abdominal *x* ray did not show radiopaque gallstones. In five of the six patients there were between two and five gallstones, varying in diameter between 3.5 and 5.2 mm. In two cases gallstones were present in the infundibulum. In one case a single gallstone was present with a diameter of 3.7 mm. There was no evidence of biliary obstruction.

**Discussion**

Ultrasonography in 3500 neonates without known risk factors for gallstones has indicated a prevalence of cholelithiasis of 0.5%.<sup>1</sup> Palasciano and colleagues<sup>2</sup> reported a prevalence of 0.13% in a population study of 1570 subjects aged 6-19 years, living in Southern Italy, as were our patients and controls. Nomura and colleagues<sup>3</sup> reported that none of 742 Japanese infants and children had gallstones. Gallstone prevalence in adults is known to vary greatly among ethnic groups and geographic regions. We performed a case-control study, because the previous report of Palasciano and colleagues<sup>2</sup> only investigated children aged 6-19 years. The prevalence rate of cholelithiasis in our controls was similar to that reported in the general population under 19 years of age.

Our results strongly suggest that paediatric subjects with DS are at increased risk of cholelithiasis. It is of interest that in our series four

Department of  
Paediatrics, "Federico  
II" University, Via S.  
Pansini 5, I-80131  
Naples, Italy  
E Toscano  
G Andria

Department of  
Radiology, "Federico  
II" University  
V Trivellini

Correspondence to:  
Dr Andria  
andria@unina.it

Accepted 8 May 2001

patients with DS and cholelithiasis were in the first two years of life.

Bocconi *et al* studied lipid metabolism in DS and showed that trisomy 21 is associated with hypercholesterolaemia during the intrauterine life.<sup>6</sup> Its relation with the increased prevalence of cholelithiasis in the first two years of life requires further study.

Cholelithiasis is often asymptomatic or associated with non-specific symptoms (abdominal pain, vomiting, and fever). Complications including acute cholecystitis, cholangitis, biliary or gall bladder perforation, obstructive jaundice, biliary cirrhosis, and gall bladder carcinoma may occur.<sup>4</sup> Clinicians should be aware of the increased risk of gallstones and their possible complications in children with DS.

We thank Dr PVajro for help in revising the manuscript.

- 1 Wendtland-Born A, Wiewrodt B, Bender SW, Weitzel D. Prevalence of gallstones in the neonatal period. *Ultraschall Med* 1997;18:80-3.
- 2 Palasciano G, Portincasa P, Vinciguerra V, *et al*. Gallstone prevalence and gallbladder volume in children and adolescence: an epidemiological ultrasonographic survey and relationship to body mass index. *Am J Gastroenterol* 1989;84:1378-82.
- 3 Nomura H, Kashiwagi S, Hayashi J, *et al*. Prevalence of gallstone disease in a general population of Okinawa, Japan. *Am J Epidemiol* 1988;128:598-605.
- 4 Rescorda FJ. Cholelithiasis, cholecystitis, and common bile duct stones. *Curr Opin Pediatr* 1997;9:276-82.
- 5 Llerena JC, de Oliveira MCB, Boechat PR, Mustacchi Z. Abdominal ultrasound scan in Down syndrome patients: high frequency of nonsymptomatic biliary tract disease. *Am J Med Genet* 1993;46:612.
- 6 Bocconi L, Nava S, Fogliani R, Nicolini U. Trisomy 21 is associated with hypercholesterolemia during intrauterine life. *Am J Obstet Gynecol* 1997;176:540-3.

### Fat, fat, fat

As more and more children become obese more and more articles describe the ill effects and precursors of obesity. The take home messages from a spate of articles in a single issue of the *Journal of Pediatrics* are: 1) severe obesity may cause renal disease; 2) overweight children are often still obese, and more likely than others to have cardiovascular risk factors, as young adults; 3) C reactive protein concentrations are raised in obese children; 4) American children are eating more snacks than they used to; and 5) gastric bypass surgery may be indicated in very severe obesity.

Over a period of 12 years a diagnosis of obesity related renal disease was made for seven 10-16 year old African American children at two large hospitals (*Journal of Pediatrics* 2001;138:481-5). They had proteinuria, mild hypertension, moderate hypercholesterolaemia, and focal segmental glomerulosclerosis. Weight loss was followed by much reduced proteinuria in one patient.

In Minnesota (*ibid*: 469-73) 31 subjects were studied at age 13 years and again at age 22 years. Body mass index (BMI) at age 13 correlated positively with BMI, serum cholesterol, and insulin resistance at age 22.

The US Third National Health and Nutrition Examination Survey of 1988-94 included data about over 5000 children (*ibid*: 486-92). Those with a high BMI (95th centile or greater) had a fivefold increase in odds for a raised C reactive protein concentration. Adipocytes produce cytokines which induce the production of acute phase reactants.

Data from three national surveys between 1977 and 1996 show an increase in the number of snacks taken by American children outside usual meal times (*ibid*: 493-8).

In New Jersey (*ibid*: 499-504) ten 15-17 year olds had gastric bypass surgery for severe obesity (BMI 41-70 kg/m<sup>2</sup>). Their mean postoperative weight loss was 54 kg and their associated morbidity (hypertension, breathing problems) resolved. Late postoperative complications necessitated more surgery in four patients.

ARCHIVIST