

Prevalencia de sobrepeso en los pacientes pediátricos con colelitiasis, atendidos en el Hospital San Rafael de Tunja durante los años 2010-2019

Prevalence of overweight in pediatric patients with cholelithiasis treated at the San Rafael hospital of Tunja during the years 2010-

Ledmar Vargas Rodríguez ^a, Lady Carreño Saltaren ^b, Camila Acosta Pérez ^c,
Laura Hoyos Gómez ^d, Lina García Estepa ^e, Tania Chaparro Rojas ^f.

a. MD. Specialist in Epidemiology, Universidad de Boyacá, Tunja, Colombia. ORCID: <https://orcid.org/0000-0001-6001-5720>

b. M.D. Hospital Universitario San Rafael de Tunja. Faculty of Health Sciences, Medicine program, Universidad de la Sabana, Chía. ORCID: <https://orcid.org/0000-0002-0536-2153>

c. M.D. Hospital Universitario San Rafael de Tunja. Faculty of Health Sciences, Medicine program, Fundación Universitaria de Ciencias de la Salud – FUCS. ORCID: <https://orcid.org/0000-0001-9213-4433>

d. M.D. Hospital Universitario San Rafael de Tunja. Faculty of Health Sciences, Medicine program, Fundación Universitaria de Ciencias de la Salud – FUCS. ORCID: <https://orcid.org/0000-0002-4481-938X>

e. M.D. Hospital Universitario San Rafael de Tunja. Faculty of Health Sciences, Medicine program, Universidad de Boyacá. ORCID: <https://orcid.org/0000-0003-2621-7075>

f. M.D. Hospital Universitario San Rafael de Tunja. Faculty of Health Sciences, Medicine program, Universidad de Boyacá. ORCID: <https://orcid.org/0000-0001-8534-3915>

DOI: 10.22517/25395203.24921

Abstract

Objective: To determine the prevalence of overweight in pediatric patients with cholelithiasis treated at the San Rafael de Tunja hospital during the years 2010 - 2019.

Materials and methods: This is an observational, descriptive, cross-sectional, and retrospective study, in which the characteristics of cholelithiasis were evaluated in patients under 18 years of age. Sociodemographic, clinical, imaging, and therapeutic variables were evaluated.

Results: 84 clinical records of patients diagnosed with cholelithiasis were reviewed in a period between 2010 to 2019. A percentage of 69.1% were female and 30.9% were male. The average age of the patients was 15.07 years, the prevalence of overweight was 35.7%, and 21.4% was obesity. The most frequent manifestations were nausea (85.71%), vomiting (84.52%),

and Murphy's sign positive (83.33%). In 76% of the patients, the gallstones were unique since these had an average size of 7.45 mm (with a minimum of 1 mm and a maximum of 25 mm). 26.1% of the patients received conservative treatment while 73.8% of them were treated by surgery. From these, 50% of the cases were treated by open surgery and the rest by laparoscopic procedure, of which 2.43% required intraoperative conversion. Finally, the most common complications presented were liver abscess in 2.38% and pancreatitis in 4.76% of the patients.

Conclusions: More than the half of children with cholelithiasis were obese (21.4%) and overweight (35.7%), which indicates a public health problem since it may affect other pathologies in the future, in addition to being a strong predictor of the pathology under study in this article.

Keywords: Obesity, cholelithiasis, risk factors.

Introduction

In the pediatric population 20 years ago, cholelithiasis was considered an uncommon diagnosis and was generally associated with hematological diseases such as sickle cell disease, hereditary spherocytosis, hemolytic anemia, and thalassemia major (1,2).

The exact prevalence of gallstones worldwide in pediatric patients is variable, in Europe it was estimated that the overall prevalence of cholelithiasis in pediatric patients was 0.13-2%, while in Japan the approximate prevalence is less than 0.13% (3). Currently, the number of reported cases has increased, it is associated with the increase in the use of ultrasound in unexplained abdominal pain and with the exponential increase in childhood obesity (4).

In Latin America the obesity rate is among the highest in the world, one in 5 children under 20 years of age is overweight or obese, in turn, the incidence of comorbidities associated with obesity in this population has increased (5). Latin America shows an upward pattern in terms of overweight figures according to surveys in 2015 compared to those of 2010. The prevalence in Colombia, although it is one of the lowest in Latin Amer-

«84 clinical records of patients diagnosed with cholelithiasis were reviewed in a period between 2010 to 2019. A percentage of 69.1% were female and 30.9% were male.»



ica, showed an increase of 1.4% from 4.9% to 6.3% of the population with this condition (6).

According to a study published in 2014, it is estimated that 21.8% of the population living in Tunja suffers from some type of overweight, this was mainly associated with the intake of hypercaloric foods and the low consumption of healthy foods (7). In the National Survey of Nutritional Situation (ENSIN for its acronym in Spanish) carried out in 2015 for the pediatric population, figures of overweight were evidenced in up to 6.3% in children aged 0 and 4 years, 24.4% in children aged 5-12 years and 17.9% in children aged 13 and 17 years (5).

In Colombia and the Boyacá department the search for studies of cholelithiasis in pediatric patients was unsuccessful, currently there are no population studies of this pathology. Therefore, the objective of the research is to determine the prevalence of overweight in pediatric patients with cholelithiasis treated at the San Rafael hospital of Tunja during the years 2010-2019.

Materials and methods

An observational, descriptive, cross-sectional, and retrospective study was conducted. The research was carried out at the San Rafael University Hospital of Tunja, located in the Boyacá department, where the review of medical records of pediatric patients under 18 years of age treated between 2010 and 2019 was carried out.

No sample size was estimated, as all patients who met selection criteria were included. Among the inclusion criteria, patients under 18 years of age with the diagnosis of cholelithiasis identified with the ICD codes 10 (K800 to K808), attended between the period from 2010 to 2019 and who had complete information on the chosen variables were considered, while those with incomplete information (by referral to another institution or by admission with extra-institutional surgery) were excluded).

The variables that were included were: age, origin, gender, history such as diabetes mellitus, arterial hypertension, kidney disease, use of psychoactive substances (PS), familial biliary lithiasis, parenteral feeding, hospitalizations in ICU, use of oral contraceptives, pregnancies, hemolytic anemia, body mass index (evaluating the presence of obesity based on growth and development curves), predominant symptoms, histopathological findings, paraclinical, imaging, treatment, time of hospital stay and complications.

The data were collected by two researchers between November the 4th

and the 18th, 2019, using a collection sheet. The database was registered in Excel version 2013 and analyzed in the statistical package SPSS version 21. The univariate analysis was performed by a descriptive statistic to the selected population, it determined absolute and relative frequencies in the categorical variables, with the quantitative variables measures of central tendency (mean, median) and dispersion measures (standard deviation and interquartile range) were calculated according to the variable distribution.

Ethical considerations: Based on resolution 8430 of 1993, where “the rules for health research are established”, in accordance with the previous regulations the proposed study is classified as a risk-free investigation.

Results

1. Sociodemographic characteristics

84 patients were included, of whom 69.1% were female and 30.9% were male. The average age of the patients was 15.07 years (SD \pm 2.03) years, with an average body mass index of 24.6 cms/kg² with (SD \pm 4.13) cms/kg², and the time of evolution between the onset of symptoms had an average of 95.3 hours (minimum of 2 hours and maximum of 360 h).

In the population studied, 42.8% had normal BMI, 35.7% were overweight and 21.4% were obese. Regarding the place of residence, the urban area had a prevalence of 61.9% with respect to the rural area, which was 38.09% of the total number of patients. The comorbidities presented by the patients in order of frequency were family history 34.52%, use of hormonal birth control 7.14% (Monthly 5.95%, three- monthly 1.19%), recent pregnancy 5.95%, hypertension 2.38%, chronic kidney disease 2.38%, hemolytic anemia 2.38% and diabetes 1.19%. (Table 1).

«In Colombia and the Boyacá department the search for studies of cholelithiasis in pediatric patients was unsuccessful, currently there are no population studies of this pathology.»



Table 1. Sociodemographic Variables

Sociodemographic characteristics	Normal weight (n:36)	Overweight (n: 30)	Obesity (n: 18)	Total (n:84)	CI 95%
Sex					
Female	22	20	16	58 (%)	59.16 - 78.93
Male	14	10	2	26	21.07 - 40.84
Age Groups					
7 to 9 years old	1	1	0	2	0.0 - 5.64
10 to 12 years old	6	2	0	8	3.24 - 15.8
13 to 15 years	11	11	9	31	26.59 - 47.22
16 to 17 years old	18	16	9	43	40.5 - 61.88
Residence					
Rural	18	10	4	32	27.71- 48.48
Urban	18	20	14	52	51.52 - 72.29
Comorbidities					
Diabetes	0	1	0	1	0.0 - 3.51
Hypertension	1	1	0	2	0.0 - 5.64
Chronic kidney disease	1	1	0	2	0.0 - 5.64
Family history	13	12	4	29	24.36 - 44.69
Use of hormonal birth control	2	4	0	6	1.63 - 12.65
Monthly	2	3	0	5	0.89 - 11.01
Three- monthly	0	1	0	1	0.0 - 3.51
Recent pregnancy	1	2	2	5	0.89 - 11.01
Hemolytic anemia	0	2	0	2	0.0 - 5.64

2. Clinical and paraclinical characteristics

The evolution time presented by the patients had an average of 95.3 hours (minimum of 2 hours and maximum of 360 hours). Among the clinical manifestations that occurred the most were nausea 85.71%, vomiting 84.52%, positive Murphy's sign 83.33%, abdominal pain in the right hypochondrium 73.80% and to a lesser extent dyspepsia 25%, generalized abdominal pain 25%, jaundice 20.23%, fever 8.33% and dehydration 8.33%.

The average value of the paraclinical were: Leukocytes 12791.6/mm³ (SD ± 17732.1/mm³), Neutrophils 69.7% (SD ± 13.8%), lymphocytes 19.0% (SD ± 12.3%), platelets 310707.4/μL (SD ± 103381.9 /mCL), hemoglobin 14.3 g/dL (SD ± 1.67 g/dL), direct bilirubin 4.44 mg/dL (SD ± 25.95 mg/dL), indirect bilirubin 0.87 mg/dL (SD ± 1.35 mg/dL), aspartate aminotransferase (AST/GOT): 86.01 U/L (SD ± 110.12 U/L), alanine aminotransferase (ALT/GTP): 146.4 U/L (SD ± 215.09 U/L), creatinine 1.04 mg/dL (SD ± 2.87 mg/Dl), amylase 294.3 U/L (SD ± 769.2 U/L), alkaline phosphatase (AP) 331.6 UIL (SD ± 618.5 UIL).

Regarding the ultrasound findings, it was found: the size of the calculations had an average diameter of 7.45 mm (minimum of 1.0 mm and maximum of 25.0 mm), were unique 19.04% and multiple 60.71%; the location of these was in gallbladder 96.42% and bile duct 2.38%; the gallbladder wall was thin 53.57%, thickened 11.90%, scleroatrophic 1.19%, and normal 33.33%; the liver was normal 89.28%, had hepatic steatosis 8.33% and hepatomegaly 3.57%; Normal bile duct 2.38% and dilated 19.04%; and the normal intrahepatic bile duct 21.42% and dilated 3.57% (Table 2).

Table 2. Clinical characteristics

Clinical characteristics	Normal weight (n:36)	Overweight (n: 30)	Obesity (n: 18)	Total (n:84)	CI 95%
Clinical chart					
Generalized abdominal pain	10	6	5	21	15.74 - 34.26
Abdominal pain in the right hypochondrium	26	23	13	62	64.41 - 83.21
Nausea	35	24	13	72	78.23 - 93.2
Vomiting	29	27	15	71	76.79 - 92.26
Fiver	3	3	1	7	2.42 - 14.24
Murphy's sign	28	28	14	70	75.36 - 91.3
Jaundice	4	10	3	17	11.65 - 28.83
Dyspepsia	11	7	3	21	15.74 - 34.26
Dehydration	5	2	0	7	2.42 - 14.24
Stones					
Multiple	27	26	14	51	50.27 - 71.16
Unique	8	4	4	16	10.65 - 27.44
Location					
Gallbladder	36	29	16	81	92.46 - 100
Bile duct and gallbladder	0	1	2	2	0.0 - 5.64
Gallbladder wall thickness					
Thin	21	17	7	45	42.91 - 64.24
Thickened	2	6	2	10	4.98 - 18.83
Scleroatrophic	0	1	0	1	0.0 - 3.51
Normal	13	6	9	28	23.25 - 43.41
Liver					
Normal	34	27	14	75	82.67 - 95.9
Hepatic steatosis	1	3	3	7	2.42 - 14.24
Hepatomegaly	1	1	1	3	0.0 - 7.54
Bile duct					
Normal	30	25	13	2	0.0 - 5.64
Dilated	6	5	5	16	10.65 - 27.44
Intrahepatic bile duct					
Normal	33	30	18	18	12.65 - 30.2
Dilated	3	0	0	3	0.0 - 7.54

3. Therapeutic characteristics

Of all patients, 26.1% received conservative treatment, while 73.8% were treated by surgery; in these cases, 50% of the intervention was open and in the other 50% the intervention was laparoscopic of which 2.43% required intraoperative conversion. Regarding complications, 2.38% of patients developed liver abscess, 4.76 developed pancreatitis, 1.19% of patients developed fistula or biliary lesion and 2.38% of patients had cholangitis. (Table 3).

Table 3. Therapeutic characteristics

Therapeutic and prognostic characteristics	Normal weight (n:36)	Overweight (n: 30)	Obesity (n: 18)	Total (n:84)	IC 95%
Conservative	12	5	5	22	16.79 - 35.59
Surgery	24	25	13	62	64.41 - 83.21
Open	8	16	7	31	26.59 - 47.22
Laparoscopic	16	9	6	31	26.59 - 47.22
Histopathology					
Chronic cholecystitis lithiasis	21	14	8	43	40.5 - 61.88
Acute cholecystitis lithiasis	1	5	4	10	4.98 - 18.83
Scleroatrophic gallbladder	2	6	1	9	4.1 - 17.33
Complications					
Liver abscess	0	1	1	2	0.0 - 5.64
Pancreatitis	1	1	2	4	0.20 - 9.31
fistula or biliary lesion	0	1	0	1	0.0 - 3.51
Cholangitis	2	0	0	2	0.0 - 5.64

Discussion

The sociodemographic aspects of the sample are like those series presented in the literature, which indicate that there is a higher incidence of pathology in the female gender with 69.1% which shows that this result agrees with worldwide studies, this suggests that biliary lithiasis is more frequently in females, 73% according to the study of Matuszczak et al. (8,9).

The average age of the patients was 15.07 years as well as a Latin American study where it is recorded that biliary lithiasis is more frequent in the age group between 11 and 15 years (10), unlike Asian and European studies where a higher prevalence of 5-14 years is mentioned with predominance at 10.5 years (11,12).

In terms of the place of residence, the urban area had a prevalence of 61.9% cholelithiasis which was higher than the rural area; according to the study by Briceño et al. in a report of risk factors of the child population, there is evidence of a higher prevalence of overweight, obesity and sedentary lifestyle in the urban population because of factors such as diet and unhealthy lifestyle habits (13,14) unlike studies carried out in Asia where there is a prevalence of almost 75% in the rural population (11).

Overweight (35.7%) and obesity (21.4%) together with family history (34.52%) were identified as the main risk factors for developing cholelithiasis in the child population, data that agree with studies carried out in Europe and America where obesity was identified as the main risk factor in more than 50%, family history also has a high proportion especially those of the first degree and hemolytic disorders (14,15).

Another variable studied were hormonal birth control (7.14%) and pregnancy (5.95%), which generate high estrogenic loads and facilitate the increase in cholesterol levels and the decrease in the production of bile salts (16).

Regarding clinical characteristics, a high prevalence of gastrointestinal symptoms such as nausea (85.71%) and vomiting (84.52%) and signs of abdominal distress such as Murphy's sign (83.3%) and abdominal pain in the right hypochondrium (73.8%) were found, findings that differ significantly with the Iranian literature where a higher prevalence of abdominal pain is reported (67%), and to a lesser extent vomiting (35%) (17,18). However, this study agrees with the Indian literature where it is reported that 61.1% of patients presented symptoms among which pain in the right upper quadrant (51.4%) stands out as the main symptom, epigastralgia, nausea (33.8%) and vomiting (28.4%) (19,20). On the other hand, an Italian study reports symptoms only in 42.7% of patients (21). In Turkey, symptoms are also reported in 80.4% of patients, abdominal pain as the predominant symptom in 60% of patients, and vomiting only in 9.8% of patients (22).

In different published studies, it is described that the main alterations of the laboratory are observed in the hematic picture with leukocytosis, elevation of aminotransferases and total bilirubin (22,23), results that correlate with the findings obtained in this study where the main alterations were observed in the hematic picture with leukocytosis (12,791), elevation of AST (86.0119), ALT (146.4) and bilirubinemia (4.4), by being these markers indicators of worsening of the clinical picture (cholecystitis, migration of

calculus to bile duct, sepsis, pancreatitis) but not definitive diagnoses of the disease (24).

It was found in this study that of the 84 medical records reviewed, 19.04% presented unique stones, unlike Soto et al. who reports that of the 181 patients analyzed, 54.9% of these had single stones (13); it was also found that 60.71% of the stones found by ultrasound were multiple unlike Espigares et al. that in his study he found that only 26% of the 50 patients reviewed had multiple stones, likewise 4.38% of stones in the bile duct were presented and Espigares reported a total of 7.8% (25).

Of the total number of patients, 26.1% received conservative treatment through observation and intervention in unhealthy lifestyles, while 73.8% were treated by surgery (50% laparoscopically and 50% open intervention), a result that contrasts with a study published by an Iranian journal where conservative treatment with ursodeoxycholic acid was used in asymptomatic patients (18); according to research by Rossi et al. surgical management is discussed in cases of typical bilateral symptoms, evidence of black pigment stones and conservative in cases of nonspecific symptoms (26).

In a report by Walker et al. the number of cholecystectomies performed on children increased by 213% over a nine-year period, until 2012. In addition, the incidence of cholecystectomy in England has tripled since 1997 in the pediatric population. Obesity is a frequent risk factor associated with the formation of cholesterol gallstones in the pediatric population, increasing almost 3 times the probability of developing gallstones compared to a person with a normal weight (1).

The main complication found was pancreatitis in 4.76% followed by cholangitis and liver abscess 2%, these results correlate with a study conducted in Latin America and Europe that indicates as the main complication pancreatitis followed in a lower proportion of cholelithiasis and calculous cholecystitis.

The present study shows a public health problem, since in the past obesity and overweight had a low frequency, affecting mostly the adult population; however, nowadays and even knowing all the risks that can generate

«In addition, the incidence of cholecystectomy in England has tripled since 1997 in the pediatric population. Obesity is a frequent risk factor associated with the formation of cholesterol gallstones ...



in the long term, its prevalence has increased affecting all age groups, which is why it has been known as the epidemic of the twenty-first century (27). It has been found that obesity is not only associated with pathologies such as the one analyzed in the present research (cholelithiasis), but it has also been found that long-term obese children and adolescents have an increased risk of presenting metabolic syndrome, mellitus diabetes, cardiovascular diseases, cancer, asthma, and deaths before 50 years of age (28, 29), therefore this issue and the comorbidities with which it is associated become important. The main limitation we had in the study was the small population sample, which could be reproduced by expanding the sample size.

Conclusions: Pediatric patients diagnosed with cholelithiasis treated at the San Rafael hospital of Tunja between 2010 and 2019, presented a prevalence of overweight of 35.7% and obesity of 21.4%, most of them were female, with an average age of 15 years and belonging to the urban area. It is highlighted that within the study population, the case of a patient with Mirizzi syndrome was identified, which is considered a complication that appears in approximately 1% of patients with cholelithiasis and is more common in adults, this indicates an alert to a public health problem that requires a set of interventions focused on the management of risk factors of the pediatric population and thus reduce the probability of new cases.

Acknowledgement:

To Dr. Pedro Enrique Jiménez, for his collaboration and guidance in carrying out the research and to the San Rafael hospital of Tunja for its assistance and disposition of the research material.

E-mail: lejovaro@gmail.com

Conflicts of interest: None.

Funding: None.

References

1. Rothstein DH, Harmon CM. Gallbladder disease in children. *Semin Pediatr Surg.* 2016 Aug 1;25(4):225–31.
2. August GP, Caprio S, Fennoy I, Freemark M, Kaufman FR, Lustig RH, et al. Prevention and treatment of pediatric obesity: An Endocrine Society clinical practice guideline based on expert opinion. *J Clin Endocrinol Metab.* 2008;93(12):4576–99.
3. Poddar U, Hardikar W. Acquired biliary diseases in children. *Paediatr Child Health.* 2010; 20. p. 7–12.
4. Murphy PB, Vogt KN, Winick-Ng J, McClure JA, Welk B, Jones SA. The increasing incidence of gallbladder disease in children: A 20 year perspective. *J. Pediatr. Surg.;* 2016. p. 748–52.
5. Caballero B, Vorkoper S, Anand N, Rivera JA. Preventing childhood obesity in Latin America: an agenda for regional research and strategic partnerships. *Obes Rev.* 2017 Jul 1;18:3–6.
6. ICBF. Guía para la construcción del plan de trabajo[Internet] 2019 [Recuperdo el 10 de agosto 2021]. Disponible en: https://www.icbf.gov.co/sites/default/files/procesos/g18.pp_guia_para_la_construccion_del_plan_de_trabajo_v1.pdf
7. Farfán Briceño MI, Olarte Rueda G. Prevalencia de sobrepeso, obesidad, comportamientos alimentarios y de actividad física en estudiantes Universitarios - Boyacá 2013. *Rev Investig en Salud Univ Boyacá.* 2014 Dec 17;1(2):204.
8. Matuszczak E, Dębek W, Oksiuta M, Dzienis-Koronkiewicz E, Hermanowicz A. Epidemiology, risk factors, management of cholelithiasis in children and review of the literature. *Pediatr Pol.* 2013 Jul;88(4):335–9.
9. Pogorelic Z, Aralica M, Jukic M, Zitko V, Despot R, Juric I. Gallbladder Disease in Children: A 20-year Single-center Experience. *Indian Pediatr.* 2019;56(5):384–6.
10. Vivian Soto, Ray Olivera, Enrique Vazques VL. Litiasis biliar en el niño, diez años de experiencia. *Rev Cubana Pediatr.* 2015;87(1).
11. Kumar Bhasin S, Gupta A, Kumari S. Evaluation and management of cholelithiasis in children: a hospital based study. *Int Surg J Bhasin SK al Int Surg J [Internet].* 2017 [cited 2019 Dec 14];4(1):246–51. Available from: <http://www.ijsurgery.com>
12. Deepak J, Agarwal P, Bagdi R, Balagopal S, Madhu R, Balamourougane P. Pediatric cholelithiasis and laparoscopic management: A review of twenty two cases. *J Minim Access Surg.* 2009 Oct 1;5(4):93–6.
13. Briceño G, Céspedes J, Leal M, Vargas S. Prevalencia de factores de riesgo cardiovascular en escolares de un área rural y de una urbana en Colombia. *Biomedica.* 2018 Dec 1;38(4):545–54.
14. Noviello C, Papparella A, Romano M, Cobellis G. Risk Factors of Cholelithiasis Unrelated to Hematological Disorders in Pediatric Patients Undergoing Cholecystectomy. *Gastroenterol Res.* 2018;11(5):346–8.
15. Nunes MMDA, Medeiros CCM, Silva LR. Cholelithiasis in obese adolescents treated at an outpatient clinic. *J Pediatr (Rio J).* 2014 Mar;90(2):203–8.
16. Shabanzadeh DM, Holmboe SA, Sørensen LT, Linneberg A, Andersson AM, Jørgensen T. Are incident gallstones associated to sex-dependent changes with age? A cohort study. *Andrology.* 2017;5(5):931–8.
17. Karami H, Kianifar HR, Karami S. Cholelithiasis in Children: A Diagnostic and Therapeutic Approach. *J Pediatr Rev.* 2016;In Press(In Press):1–6.
18. Esmaeili Dooki MR, Norouzi A. Cholelithiasis in childhood: A cohort study in North of Iran. *Iran J Pediatr.* 2013;23(5):588–92.
19. Baran M, Appak YC, Tümgör G, Karakoyun M, Ozdemir T, Koyluoglu G. Etiology and

- Outcome of Cholelithiasis in Turkish Children. *Indian Pediatr.* 2018;55(3):216–8.
20. Gowda DJ, Agarwal P, Bagdi R, Subramanian B, Kumar M, Ramasundaram M, et al. Laparoscopic cholecystectomy for cholelithiasis in children. *J Indian Assoc Pediatr Surg.* 2009;14(4):204–6.
 21. Corte CD, Falchetti D, Nebbia G, Calacoci M, Pastore M, Francavilla R, et al. Management of cholelithiasis in Italian children: A national multicenter study. *World J Gastroenterol.* 2008;14(9):1383–8.
 22. Serdaroglu F, Koca YS, Saltik F, Koca T, Dereci S, Akcam M, et al. Gallstones in childhood: Etiology, clinical features, and prognosis. *Eur J Gastroenterol Hepatol.* 2016;28(12):1468–72.
 23. Harris D P, Chateau I B, Miquel P JF. Litiasis biliar pediátrica en una población de alta prevalencia. *Rev Chil pediatría [Internet].* 2007 Oct [cited 2019 Dec 13];78(5):511–8. Available from: http://www.scielo.cl/scielo.php?script=sci_arttext&pid=S0370-41062007000500009&lng=en&nrm=iso&tlng=en
 24. Ansaloni L, Pisano M, Coccolini F, Peitzmann AB, Fingerhut A, Catena F, et al. 2016 WSES guidelines on acute calculous cholecystitis. Vol. 11, *World Journal of Emergency Surgery.* BioMed Central Ltd.; 2016.
 25. Gökç S, Yildirim M, Erdoğan D. A retrospective review of children with gallstone: Single-center experience from Central Anatolia. *Turkish J Gastroenterol.* 2014;25(1):46–53.
 26. Rossi G, Moretti A, Di Chio T, Esposito MG, Nastasio S, Maggiore G. Gallstones in childhood: A single centre experience. *Dig Liver Dis.* 2015 Oct;47:e252.
 27. MönckebergBFernando, MuzzoBSantiago. Ladesconcertanteepidemiadeobesidad. *Rev. chil. nutr. [Internet]* 2015 Mar [citado 2020 Jul 16]; 42(1):96-102. Disponible en: https://scielo.conicyt.cl/scielo.php?script=sci_arttext&pid=S0717-75182015000100013&lng=es. <http://dx.doi.org/10.4067/S0717-75182015000100013>.
 28. JJ Reilly, J Kelly. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. *International Journal of Obesity (2011)* 35, 891–898; doi:10.1038/ijo.2010.222
 29. A. Llewellyn, M. Simmonds, C. G. Owen, N. Woolacott. Childhood obesity as a predictor of morbidity in adulthood: a systematic review and meta-analysis. *obesity reviews.* 2016; 17: 56 - 67. doi: 10.1111/obr.12316.