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Impact of Obesity on Pediatric Acute Recurrent and Chronic Pancreatitis

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Abstract

Objective—To assess the impact of obesity on pediatric acute recurrent pancreatitis (ARP) or chronic pancreatitis (CP).

Methods—We determined body mass index (BMI) status at enrollment in INSPPIRE (**IN**ternational **S**tudy group of **P**ediatric **P**ancreatitis: **I**n search for a cu**RE**) cohort using CDC criteria for pediatric-specific BMI percentiles. We used Cochran-Armitage to assess trends, Jonckheere-Terpstra to determine associations.

Results—Of 446 subjects (ARP = 241, CP = 205), 22 were underweight, 258 normal weight, 75 overweight, 91 obese. The BMI groups were similar in sex, race, age at presentation. Hypertriglyceridemia was more common in overweight or obese. Obese children were less likely to have CP and more likely to have acute inflammation on imaging. Compared to children with normal weight, obese or overweight were older at first acute pancreatitis (AP) episode and diagnosed with CP at an older age. Obese or overweight were less likely to undergo medical or endoscopic treatment, develop exocrine pancreatic insufficiency, require total pancreatectomy with islet autotransplantation (TPIAT). Diabetes was similar among all groups.

Conclusions—Obesity or overweight seems to delay the initial AP episode and diagnosis of CP compared to normal weight or underweight. The impact of obesity on pediatric CP progression and severity deserves further study.

Keywords

Children; Body Mass Index; Pancreatitis

INTRODUCTION

Within the last decade, pediatricians have observed an increased incidence of children with acute pancreatitis (AP).[1–5] In general, children with AP recover without long-term sequelae, but a subset has recurrent attacks of AP (defined as acute recurrent pancreatitis or ARP); some develop chronic pancreatitis (CP).[6] CP is characterized by irreversible structural damage in the pancreas, fibrotic replacement of the parenchyma and finally failure of both exocrine and endocrine functions. [6] In children, genetic risk factors play a major role in

recurrent pancreatic inflammation and progression to chronic disease.[7–10] This is in contrast to adult CP, where environmental factors (namely alcohol and tobacco) pose the most significant risk.[11,12] As with adults,[13] ARP most likely precedes CP in children.[14] Importantly, children with CP carry significant disease and socioeconomic burden,[7,8,10,15] underscoring the importance of identifying predisposing factors early to avoid progression of ARP to CP.

Obesity is an important risk factor for severe AP in adults. Obese patients with AP are prone to more severe inflammation with high morbidity and mortality, as well as local and systemic complications, compared to patients with normal weight.[16–20] It is not clear whether obesity is also a risk factor for the development of acute recurrent pancreatitis or chronic pancreatitis, in adults or children. A single prospective study in adult patients, reported a greater presence of overweight or obesity compared to normal controls before disease onset of alcoholic CP. Interestingly, the only impact in this alcoholic pancreatitis cohort with obesity was delayed progression to CP if they had prior history of pancreatic surgery.[21]

In this report, we studied the impact of overweight or obesity on pediatric pancreatic disease characteristics in our well-phenotyped INSPPIRE (**IN**ternational **S**tudy group of **P**ediatric **P**ancreatitis: **I**n search for a cu**RE**) cohort of children with ARP and CP.[22]

MATERIALS AND METHODS

Study Design and Participants

Demographic and clinical information were collected at the time of enrollment of children who fulfilled the criteria for ARP and CP from 18 pediatric academic medical centers. INSPPIRE study design and enrollment criteria have been previously described.[22] All patients were <19 years of age at the time of enrollment. As previously defined, ARP diagnosis required 2 episodes of AP along with resolution of pain (≥ 1 month between episodes) or normalization of pancreatic enzymes and resolution of pain in between episodes irrespective of time interval.[6] Diagnosis of CP required at least one of the following: (a) abdominal pain plus imaging findings suggestive of chronic pancreatic damage; (b) exocrine pancreatic insufficiency and imaging findings; (c) endocrine pancreatic insufficiency and imaging findings.[6] Weight and height measurements were collected from physician questionnaires. Centers for Disease Control and Prevention (CDC) Growth Charts and pediatric age- and gender-specific body mass index (BMI) percentiles to classify children as underweight (<5th percentile), normal weight (5th–<85th percentile), overweight (85th–<95th percentile), or obese (≥95th percentile).[23] Diabetes mellitus was defined by 2006 WHO criteria as fasting glucose ≥ 7.0 mmol/L (126 mg/dL) or plasma glucose ≥ 11.1mmol/L (200 mg/dL) 2 hours after glucose load of 1.75g/kg children (to maximum 75g glucose load) or elevated HbA1c over 6.5% or 48 mmol/mol.[24] Clinical and demographic data were entered into the REDCap™ (Research Electronic Data Capture, Vanderbilt University, Nashville, Tenn) database at 18 centers from September 2012 to March 2017, through standardized patient and physician questionnaires and represented baseline information of the INSPPIRE cohort. All centers obtained Institutional Review Board approval or the equivalent for their

country for this study. Most of the 446 patients included in this study have been previously reported.[7,8,15]

Statistical Analysis

Summary statistics use mean with standard deviation (SD) or median with interquartile range (IQR) according to the normality of distribution. Categorical variables were analyzed using Cochran-Armitage trend test to examine whether prevalence of findings increased/decreased with BMI. The Jonckheere-Terpstra test was used to assess the association between BMI and levels of pain and missed school days. A P value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 446 INSPPIRE subjects were reviewed with 241 having ARP and 205 having CP. Of these patients, 22 (4.9%) were underweight, 258 were normal weight (57.8%), 75 (16.8%) were overweight, and 91 were obese (20.4%) based on BMI. Demographics of the cohorts are shown in Table 1. The groups were not different in age at first diagnosis of AP, sex or race, but obese children were more likely to be of Hispanic ethnicity ($P = 0.002$). The distribution of BMI at centers with a high prevalence of Hispanic children (Children's Hospital of Los Angeles, UCSF, UTSW, Baylor) were not different when compared to other centers ($P = 0.94$).

Risk Factors of ARP and CP Per BMI Groups

Table 2 shows the distribution of risk factors for ARP and CP among the groups. Patients with normal BMI were more likely to have *cationic trypsinogen (PRSS1)* mutations ($P = 0.05$). There were no differences among the groups for mutations in *serine protease inhibitor Kazal-type 1 (SPINK1), cystic fibrosis transmembrane conductance regulator (CFTR),* or *chymotrypsin C (CTRC).* Hypertriglyceridemia (as defined by treating physician) was found almost exclusively in overweight or obese patients ($P = 0.02$). Other risk factors, including obstructive risk factors were not different among the groups.

Diagnosis of CP Per BMI Groups

Obese or overweight children were less likely to have CP ($P = 0.009$) and were diagnosed with first AP attack and with CP at an older age than normal weight or underweight children ($P = 0.01$) (Table 3). Imaging findings were determined by endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP); computed tomography (CT) or endoscopic ultrasound (EUS). Acute inflammatory changes, such as gland enlargement, peripancreatic inflammation/fat stranding consistent with AP/ARP were more commonly found in overweight or obese children ($P<0.01$). Chronic changes indicative of CP (pancreatic atrophy, pancreatic fibrosis, pancreatic duct irregularity, pancreatic duct dilatation, pancreatic duct stone, calcifications, abnormal side branches) were found at similar rates in all groups (Table 4). The exception was pancreatic ductal strictures which were significantly

less common in obese or overweight ($P = 0.008$) (Table 4). Overweight or obese children were also less likely to have ERCP done for diagnostic or therapeutic purposes ($P = 0.03$).

Impact of Weight Category on Disease Burden and Complications of CP

Weight category had no impact on the frequency or pattern of abdominal pain, missed school days, emergency room visits or hospitalizations related to pancreatitis (Table 5). Obese children were significantly less likely to undergo medical treatments (specifically pancreatic enzyme therapy), endoscopic interventions and total pancreatectomy/islet autotransplantation (TPIAT) than other groups ($P < 0.001$, 0.01, and 0.002 respectively) (Table 6). Finally, overweight or obese children were less likely to have exocrine pancreatic insufficiency ($P = 0.013$) and there were no differences in the diagnosis of diabetes among the groups (Table 7).

Findings Controlling for Hispanic Ethnicity

Because Hispanic ethnicity is associated with obesity, we performed additional analysis of the parameters associated with obesity to control for Hispanic ethnicity. These showed that the same trends persisted in the study sub-population of non-Hispanics as in the entire cohort (see Supplemental Table 1).

DISCUSSION

In this large, multicenter and multinational cohort of children with acute recurrent pancreatitis, we found that overweight or obese children were less likely to suffer from chronic pancreatitis, exocrine pancreatic insufficiency and less likely to undergo medical therapies, endoscopic procedures or TPIAT.

Obesity is a well-recognized risk factor of severe AP in adults, associated with high morbidity and mortality.[16–20] During AP episodes, obese patients may be prone to both local complications (i.e. pancreatic pseudocyst, necrosis or abscess), systemic complications (sepsis, lung and kidney failure) and increased risk of death. Increased risk of local complications may be related to greater volume of retroperitoneal, peripancreatic or intrapancreatic fat found in obese people with AP,[20,25,26] as fat will have a higher propensity for necrosis. Indeed, there is a direct correlation between BMI, amount of intrapancreatic fat and severity of AP.[20] The mechanisms leading to higher levels of complications of AP in obesity are not well-understood. A recent study has suggested that unsaturated fatty acids released from intrapancreatic fat could be responsible of local necrosis and systemic complications.[20] Similar to adults, obese children with AP have worse outcomes compared to non-obese: severe AP, length of stay, medical costs, mortality are significantly higher in obese individuals.[27]

The role of obesity as a risk factor for ARP or CP is largely unknown. In a study by Ammann et al, progression to CP in a group of adult patients was slower over time if BMI was >25 and they underwent a drainage surgery previously.[21] However, it should be noted that this was a cohort of alcoholic CP patients, about half of patients were obese and the effect was not seen in obese patients without prior surgical history. The outcome may be

quite different in the pediatric cohort where alcohol is a negligible risk factor of ARP and CP.[7,8]

In our cohort, obese or overweight children were diagnosed with CP at an older age and their imaging findings were overwhelmingly supportive of acute inflammatory changes in the pancreas. These data suggest that obesity may induce a delayed-onset disease, a prolonged proinflammatory state, with delayed progression to a chronic inflammatory state. According to the popular sentinel acute pancreatitis event (SAPE) hypothesis or repeated inflammation-recovery-fibrosis theory, massive inflammatory response develops with AP consistent of both early and late phases.[28] Initially inflammation in the pancreas attracts inflammatory cells (neutrophils, lymphocytes) along with cytokines and causes oxidative stress.[28] During later phases of the inflammation, profibrotic cells and stellate cells predominate. Once the inciting factor is removed, the pancreas heals to baseline, but recurrent inflammation sets the stage for progressive fibrosis. It is possible that the peri- or intrapancreatic fat creates a proinflammatory or prooxidant state that prevents or delays the transition to chronicity. We have not analyzed the pancreatic imaging studies to verify the presence of pancreatic fat in our patients. This will be an important addition to the study questionnaires as the INSPPIRE consortium moves forward.

Although diagnosis of CP was less common in obese or overweight children, the only significant difference between the groups was the presence of ductal strictures in children with normal weight. It is possible that differences could be detected in a larger cohort.

The high percentage of obese children in our population reflects the increased prevalence of obesity in the US and other countries observed within the last few decades.[29,30] Twenty-three percent of our study population was obese, which is a slightly higher than expected US prevalence for this age group.[29] We observed a much higher percentage of Hispanic children with obesity in our cohort (40%) compared to the general US population (<24% for all Hispanic pediatric age groups).[29] This raises an interesting question about the potential role of genetic variations among ethnic groups in disease presentation or evolution. The distribution of BMI was similar at all centers including centers that enrolled a higher number of Hispanic children, therefore it is unlikely that the results were skewed by an enrollment bias.

Obese children were less likely to have exocrine pancreatic insufficiency diagnosis. They were less likely to receive medical treatments (specifically pancreatic enzyme therapy), endoscopic or surgical procedures, such as TPIAT. TPIAT is directed primarily to the treatment of CP by removing the pancreas that has lost its exocrine function while attempting to preserve its islet cell mass and maintain the endocrine function. [31]

Hypertriglyceridemia is known to be associated with acute pancreatitis,[32,33] and a recent study in adults has shown that even mild elevations in serum triglycerides may be a risk factor.[34] Elevated serum triglycerides are well-described in obese children as a risk factor for cardiovascular disease.[35,36] It is possible that elevated triglyceride levels in our cohort of overweight or obese children is due to obesity and unrelated to pancreatitis.

We did not observe different rates of diabetes among the groups, but diabetes is a late complication of CP (18%, 20 years after diagnosis).[37] It may be too early to observe diabetes in our cohort. Overall, the percentage of children with diabetes in our cohort (7.0%; 95% confidence interval, 5%–10%) was higher than that observed in the US population (0.25–0.5% under the age 20 years old).[38–40] Our report of diabetes is based on physician's diagnosis and does not differentiate between the types of diabetes, including Type 1, 2, or Type 3c (pancreatogenic) diabetes, therefore it is possible that it was under-reported. Type 3c diabetes is emerging as a distinct form of diabetes, although there are yet no clear guidelines to differentiate it from other forms of diabetes.[41,42] Our future efforts will include a detailed phenotyping of patients for all types of diabetes, including prediabetes.

Obesity or overweight present with the initial AP attack later and are diagnosed with CP later compared to normal weight or underweight. In the INSPPIRE cohort, overweight or obese children were less likely than normal weight or underweight children to suffer from chronic pancreatitis, exocrine pancreatic insufficiency and undergo medical therapies, endoscopic procedures or TPIAT. The full impact of obesity on pediatric pancreatitis severity, recurrence, progression and chronicity will only become clear with longer follow-up of our cohort.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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TABLE 1

Demographic Characteristics of the INSPPIRE Cohort by BMI Status

	Underweight (n = 22)	Normal (n = 258)	Overweight (n = 75)	Obese (n = 91)	*P*[*]
Sex, Female	12 (55)	161 (62)	39 (52)	45 (49)	0.11
	(n = 19)	(n = 239)	(n = 66)	(n = 84)	
Ethnicity (Hispanic)	5 (26)	46 (19)	16 (24)	34 (40)	**0.002**
Race	(n = 21)	(n = 230)	(n = 63)	(n = 68)	
White	17 (81)	186 (81)	53 (84)	59 (87)	0.69[†]
Multi-racial	2 (10)	16 (7)	2 (3)	6 (9)	
Black	1 (5)	8 (3)	4 (6)	1 (1)	
Asian	1 (5)	12 (5)	4 (6)	2 (3)	
Other	0 (0)	8 (3)	0 (0)	0 (0)	
Age at first diagnosis AP		(n = 245)	(n = 69)	(n = 84)	
Mean (SD)	9.4 (5.0)	8.7 (4.7)	9.5 (4.6)	9.6 (4.5)	0.26
Age at enrollment					
Mean (SD)	12.3 (4.3)	11.9 (4.5)	11.7 (4.4)	12.3 (4.1)	0.64

Data expressed as n (%) unless otherwise specified.

Statistically significant values are in bold.

[*]Categorical variables were compared using Pearson chi-square test, and ANOVA for Age.

[†]Comparison for race was categorized as White and non-White.

TABLE 2

Risk Factors of ARP and CP by BMI Groups

	Underweight (n = 22)	Normal (n = 258)	Overweight (n = 75)	Obese (n = 91)	*P*
Genetic mutations					
PRSS1	4/15 (26)	63/188 (34)	9/46 (20)	15/62 (24)	0.05
SPINK1	2/14 (14)	40/175 (23)	5/42 (12)	9/56 (16)	0.12
CFTR	3/15 (20)	62/185 (33)	15/46 (34)	14/62 (23)	0.28
CTRC	0/9 (0)	7/121 (6)	0/27 (0)	4/39 (10)	0.77
Obstructive factors	6/22 (27)	81/257 (32)	19/73 (26)	30/90 (33)	0.87
Pancreas divisum	0/21 (0)	31/251 (12)	7/72 (10)	11/84 (13)	0.88
Sphincter of Oddi disorders	1/20 (5)	5/244 (2)	2/70 (3)	3/88 (3)	0.66
Gallstones	2/21 (10)	11/252 (4)	3/70 (4)	5/89 (6)	0.92
Pancreaticobiliary malunion	1/20 (5)	9/250 (4)	1/72 (1)	3/88 (3)	0.54
Traumatic PD stricture	1/21 (5)	1/254 (0.4)	0/71 (0)	0/86 (0)	0.19
Duodenal diverticulum	0/21 (0)	1/253 (0.4)	0/72 (0)	0/87 (0)	1.0
Duct obstruction	0/20 (0)	5/255 (2)	1/72 (1)	1/88 (1)	0.67
Annular pancreas	0/21 (0)	2/254 (1)	0/72 (0)	1/88 (1)	1.0
Biliary cyst	0/20 (0)	5/255 (2)	2/55 (4)	4/76 (5)	0.11
Toxic/metabolic factors					
Alcohol	0/22 (0)	5/257 (2)	0/74 (0)	2/90 (2)	0.84
Tobacco (active or passive)	2/20 (10)	23/253 (9)	5/66 (8)	9/86 (10)	0.95
Hypertriglyceridemia	0/16 (0)	8/228 (4)	3/63 (5)	8/73 (11)	**0.02**
Autoimmune pancreatitis	0/17 (0)	7/200 (4)	3/57 (5)	1/67 (18)	0.88
Other autoimmune diseases	1/20 (5)	21/244 (9)	8/70 (11)	4/86 (5)	0.72
Inflammatory bowel disease	0/20 (0)	4/243 (2)	0/68 (0)	0/85 (0)	0.28

Denominators represent data available for each group; data expressed as n (%) unless otherwise specified.

Statistically significant values are in bold.

*Cochran-Armitage trend test was used for statistical comparisons.

ARP indicates Acute Recurrent Pancreatitis; CP: Chronic Pancreatitis; PD: pancreatic duct; *CFTR, cystic fibrosis transmembrane conductance regulator; PRSS1, cationic trypsinogen; CTRC, chymotrypsin C; SPINK1, serine protease inhibitor Kazal-type 1.*

TABLE 3

Diagnosis of CP by BMI Status

	Underweight (n = 22)	Normal (n = 258)	Overweight (n = 75)	Obese (n = 91)	*P* *
Diagnosed with CP	9 (41)	133 (52)	30 (40)	33 (36)	**0.009**
Age first diagnosis AP in CP	(n = 9)	(n = 128)	(n = 28)	(n = 31)	
Mean (SD)	8.1 (4.2)	8.2 (4.5)	10.2 (4.4)	10.4 (4.1)	**0.01**
Age at first diagnosis CP	(n = 9)	(n = 122)	(n = 26)	(n = 29)	
Mean (SD)	9.4 (3.4)	9.8 (4.3)	11.6 (4.2)	11.6 (4.0)	**0.01**
Time from AP to CP, yrs	(n = 20)	(n = 229)	(n = 67)	(n = 80)	
Median (IQR)	7.0 (1.7–7.0)	3.0 (0.7–7.7)	3.7 (1.1–>8.0)	5.3 (1.7 to >13.0)	0.11

Data expressed as n (%) unless otherwise specified.

Statistically significant values are in bold.

* From Cochran-Armitage trend test for CP diagnosis; linear regression for age at CP; Cox proportional hazard regression for time from AP to CP.

TABLE 4

Imaging Study Findings in Children With ARP and CP by BMI Status

	Underweight (n = 22)	Normal (n = 258)	Overweight (n = 75)	Obese (n = 91)	*P**
Imaging modality					
ERCP--any	10 (45)	121 (47)	26 (35)	34 (37)	**0.03**
No. ERCP					
1	6	70	14	18	
2	1	23	8	10	
3	1	8	4	3	
≥4	2	20	0	3	
MRCP/MRI	18 (82)	218 (84)	63 (84)	80 (88)	0.55
CT scan	10 (45)	113 (44)	42 (56)	46 (51)	0.07
EUS	2 (9)	29 (11)	9 (12)	12 (13)	0.59
Findings on any imaging					
Focal acute pancreatitis	2/16 (12)	28/184 (15)	9/55 (16)	14/68 (21)	0.35
Inflammatory changes	4/17 (24)	56/186 (30)	25/56 (45)	38/69 (55)	**0.0001**
Enlarged pancreas	1/16 (6)	36/185 (19%)	14/56 (25)	33/70 (47)	**<0.0001**
Cysts/pseudocysts	3/18 (17)	35/236 (15%)	11/68 (16)	13/85 (15)	0.85
Peripancreatic inflammation/fat stranding	2/16 (12)	54/192 (28)	28/56 (50)	28/69 (41)	**0.001**
Gallstones/sludge	1/17 (6)	12/184 (7)	4/56 (7)	7/73 (10)	0.44
Pancreatic atrophy	6/17 (35)	49/185 (26)	16/57 (28)	13/71 (18)	0.29
PD stricture	7/18 (39)	56/226 (25)	9/64 (14)	12/81 (15)	**0.008**
PD irregularity	6/16 (38)	73/185 (39)	20/56 (36)	20/72 (28)	0.12
PD dilatation	7/16 (44)	74/184 (40)	19/57 (33)	23/73 (32)	0.12
PD stone	3/14 (21)	40/205 (20)	9/57 (16)	11/67 (16)	0.42
Calcifications	4/16 (25)	16/185 (9)	2/56 (4)	6/71 (8)	0.26
Abnormal side branches	6/14 (43)	57/299 (28)	12/58 (21)	17/65 (26)	0.25

Denominators represent data available for each group; data expressed as n (%) unless otherwise specified.

Statistically significant values are in bold.

*Cochran-Armitage trend test was used for statistical comparisons.

ERCP indicates, endoscopic retrograde cholangiopancreatography; MRI, Magnetic resonance imaging; MRCP, Magnetic resonance cholangiopancreatography; CT, Computed tomography; EUS, Endoscopic ultrasound; PD, pancreatic duct.

TABLE 5

Disease Burden in Children with ARP and CP by BMI Status

	Underweight (n = 22)	Normal (n = 258)	Overweight (n = 75)	Obese (n = 91)	*P* *
Pattern of abdominal pain	(n = 18)	(n = 236)	(n = 65)	(n = 82)	
No abdominal pain	2 (11)	31 (13)	8 (12)	4 (5)	0.10
Usually pain free; episodes of mild-moderate pain	3 (17)	37 (16)	9 (14)	9 (11)	
Constant mild-moderate pain	2 (11)	10 (4)	3 (5)	7 (9)	
Usually pain free; episodes of severe pain	6 (33)	79 (33)	20 (31)	33 (40)	
Constant mild-moderate pain; episodes of severe pain	5 (28)	65 (28)	18 (28)	23 (28)	
Constant severe pain	0 (0)	14 (6)	7 (11)	6 (7)	
Constant Pain score	(n = 18)	(n = 225)	(n = 59)	(n = 78)	
Median (IQR)	0 (0–34)	0 (0–15)	0 (0–0)	0 (0–17)	0.58
Episodic Pain score	(n = 17)	(n = 212)	(n = 57)	(n = 77)	
Median (IQR)	73 (56–86)	60 (6–80)	65 (30–86)	58 (4–86)	0.81
Number of ER visits-lifelong (average/year)	(n = 12)	(n = 130)	(n = 38)	(n = 43)	
Median (IQR)	1.6 (1.2–2.5)	1.1 (0–2.4)	1.5 (0.9–2.6)	1.7 (0.7–2.5)	0.10
Number of ER visits-past year	(n = 17)	(n = 221)	(n = 61)	(n = 75)	
Median (IQR)	2 (0–2)	2 (0–3)	2 (1–3)	2 (1–3)	0.14
Number of hospitalizations-lifelong (average/year)	(n = 12)	(n = 133)	(n = 39)	(n = 47)	
Median (IQR)	1.8 (0.6–2.2)	1.0 (0.2–2.0)	1.1 (0.7–2.6)	1.5 (0.6–2.3)	0.18
Days missed school past month (school aged children)	(n = 14)	(n = 201)	(n = 54)	(n = 62)	
Median (IQR)	1 (0–5)	2 (0–6)	0.5 (0–6)	2.5 (0–6)	0.93

Data expressed as n (%) unless otherwise specified.

* Jonckheere-Terpstra Test was used for statistical comparisons.

ARP indicates Acute Recurrent Pancreatitis; CP, Chronic Pancreatitis; ER, Emergency Room.

TABLE 6

Treatment Modalities in Children with ARP and CP by BMI Status

	Underweight (n = 22)	Normal (n = 258)	Overweight (n = 75)	Obese (n = 91)	*P* *
Medical Therapies	11/21 (52)	133/248 (54)	29/74 (39)	32/90 (36)	**<0.001**
Pain medications	3/15 (20)	91/194 (47)	16/54 (30)	27/71 (38)	0.07
Pancreatic enzymes	9/21 (43)	109/248 (44)	20/73 (27)	26/90 (29)	**0.001**
Vitamins/antioxidants	0/20 (0)	28/242 (12)	9/71 (13)	8/88 (9)	0.99
Steroids	0/21 (0)	6/239 (3)	1/72 (1)	2/84 (2)	0.96
Octreotide	0/21 (0)	7/245 (3)	2/71 (3)	0/87 (0)	0.34
Endoscopic Therapies	10/21 (48)	116/251 (46)	24/73 (33)	31/88 (35)	**0.01**
Biliary sphincterotomy	4/21 (19)	43/246 (17)	7/71 (10)	17/88 (19)	0.57
Pancreatic duct stent	5/21 (24)	58/245 (24)	15/72 (21)	15/88 (17)	0.21
Biliary stent	3/21 (14)	10/247 (4)	2/71 (3)	3/88 (3)	0.35
Pancreatic duct stone removal	3/20 (15)	32/248 (13)	5/71 (7)	9/88 (10)	0.19
Surgical Therapies	6/21 (29)	66/255 (26)	14/72 (19)	17/89 (19)	0.10
Cholecystectomy	4/21 (19)	36/255 (14)	8/72 (11)	11/88 (12)	0.44
Celiac nerve block	0/21 (0)	4/255 (2)	0/71 (4)	1/89 (1)	0.65
Cyst/pseudo-cyst operation	0/21 (0)	10/255 (4)	3/71 (4)	2/89 (2)	0.76
Lateral pancreaticojejonstomy	0/21 (0)	11/255 (4)	0/71 (0)	3/89 (3)	0.31
Partial pancreatectomy	0/21 (0)	2/255 (1)	2/71 (3)	0/89 (0)	0.82
TPIAT	2/21 (10)	34/255 (13)	2/71 (3)	4/88 (5)	**0.002**

Denominators represent data available for each group; data expressed as n (%) unless otherwise specified.

Statistically significant values are in bold.

*Cochran-Armitage trend test was used for statistical comparisons.

ARP indicates Acute Recurrent Pancreatitis; CP, Chronic Pancreatitis; TPIAT, Total pancreatectomy/islet autotransplantation.

TABLE 7

Complications of CP per BMI Status

	Underweight (n = 22)	Normal (n = 258)	Overweight (n = 75)	Obese (n = 91)	*P*[*]
Exocrine Pancreatic insufficiency	4/19 (21)	36/218 (17)	7/68 (10)	5/79 (6)	**0.013**
Diabetes	0/20 (0)	12/240 (5)	5/72 (7)	3/84 (4)	0.91

Patients who had TPIAT were excluded from analysis.

Denominators represent data available for each group; data expressed as n (%) unless otherwise specified.

Statistically significant values are in bold.

[*]Cochran-Armitage trend test was used for statistical comparisons.