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# Association of Obesity in Children with Pancreatitis in a Predominantly Hispanic Population at the US-Mexican Border: A Single Center Outpatient Study

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## **Abstract**

**Importance:** The incidence of pancreatitis has been increasing over the last decade. Limited data are available for pancreatitis in the Hispanic population. The clinical profile of pancreatitis and its association with obesity in a Mexican American population has not been well studied. Objective: To describe prevalence, the characteristics of pancreatitis cases, and determine its association with obesity. Design and Setting: Retrospective review of children from February 2012 to February 2015, at the Texas Tech University Health Sciences Center of El Paso (TTUHSC- El Paso) outpatient center. Case/non-case study was used to determine the association of overweight and obesity with pancreatitis. Participants: Children ages 2 - 18 years, only the newly diagnosed pancreatitis cases irrespective of its type excluding patients with traumatic and repeat visit for pancreatitis. Main Outcome and Measures: Pancreatitis and obesity. Results: The prevalence of pancreatitis was estimated as 20 cases in 21,444 patients seen in the outpatient clinic. In multivariable analysis, only obesity and ethnicity were significantly associated with pancreatitis. Obesity was found to be more than 7-fold likely with pancreatitis as compared to non-cases. Overweight was found to be more than 6-fold likely with pancreatitis as compared with non-cases. Our study demonstrates an association between obesity and pancreatitis in the study population. Conclusions and Relevance: Appropriate intervention for managing obesity may reduce the prevalence of pancreatitis and associated co-morbidities. A larger prospective study should be done to determine underlying causes of association between obesity and pancreatitis.

# **Keywords**

Pancreatitis, Obesity, Body Mass Index (BMI)

#### 1. Introduction

Pancreatitis is a growing health burden in children. It is a comparatively uncommon painful inflammatory condition but with a significant health impact. Very limited studies are available in children with pancreatitis. The Hispanic population had a higher prevalence of biliary pancreatitis compared with the non-Hispanic population [1]. During the last decades, the incidence of acute pancreatitis has been increasing [2]. Incidence estimates can be done to best approximate the burden of disease because acute pancreatitis is not a chronic condition. Two studies showed the incidence of acute pancreatitis in children, one from the United States (US) (the Children's Hospital of Pittsburgh) which estimates an incidence of 13.2 cases in 100,000 children per year, or about 1 in 7500/year [3], and the other from Australia (the Royal Children's Hospital, Melbourne), which estimates an incidence of 3.6 cases in 100,000/year or about 1 in 28,000/year. For the United States, the incidence estimates, for example, imply that there are about 11,000 children who are affected with acute pancreatitis per year [4]. The etiology and pathogenesis of pancreatitis still remain unclear and no specific medical treatment except supportive therapy is available [5]. Recently, with the increasing incidence of acute pancreatitis in children globally, different causes have been proposed. Some studies showed that in infants and toddlers, multisystem disease was the most common cause. Other studies showed a 53% increase in pancreatitis cases, of which, biliary disease is the most common cause [6]. In children, the underlying etiologies vary greatly from those in adults, including traumas, drugs, multisystem diseases, and infections [7]. Despite that, the burden of pancreatitis in children, especially in the Mexican-American population, is unknown. Thus, our primary aim is to describe the prevalence and clinical profile of pancreatitis in children from a primary care center in El Paso, a large US-Mexico border city.

Few studies demonstrated that overweight and obesity are risk factors for pancreatitis [8]. Obesity is a major problem in US particularly in the Hispanic population. Among children and adolescents, the prevalence of obesity was higher among Hispanics (22.4%) and non-Hispanic blacks (20.2%) than among non-Hispanic whites (14.1%), as per Centers for Disease Control and Prevention (CDC) 2011-2012 data [9]. Increasing cases of childhood obesity recently have been noted in developing countries undergoing changes in dietary habits, such as Latin America. Prior to this transformation, being underweight and having poor growth were the primary health concerns. This can be explained by inexpensive, readily available, high-caloric food along with sedentary lifestyle. With increasing prevalence of obesity, the health implications are more apparent. Obesity is related with many health problems in children and is a significant early risk factor for considerable causes of adult morbidity [10]. Obesity-asso-

ciated metabolic and cardiovascular complications are identified to be related to insulin resistance or hyperinsulinemia, the most common abnormality found in these patients [10]. A research showed that Hispanic ethnicity is a risk factor for biliary pancreatitis in children who have gallstone- or sludge-induced pancreatitis. One research showed that obesity is noted to be a risk factor for gallstone pancreatitis [1]. Another finding was that Hispanic children were inexplicably overweight in contrast to white and black children [1]. Moreover, several clinical investigations, primarily using adult studies, showed that obesity increases the severity of the disease by favoring local complications within the pancreas and injuries in remote organs as well as by increasing mortality rate [5]. It is therefore imperative to determine whether obesity associates with the occurrence of pancreatitis in our study population.

# 2. Methodology

To estimate the acute pancreatitis prevalence in children, a retrospective review of children from February 2012 to February 2015 was conducted. Thereafter, we designed a case/non-case study to determine the association of overweight and obesity with pancreatitis. This study was planned as 1:3 case/non-case study. The inclusion criteria were the following: children ages 2 - 18 years, only the newly diagnosed pancreatitis cases only, and diagnosis of pancreatitis irrespective of its type. As per the International Study Group of Pediatric Pancreatitis: In Search for a Cure (INSSPIRE) definitions and Atlanta criteria, having 2 of the 3 criteria support the diagnosis of acute pancreatitis: clinical findings, including abdominal pain, nausea, vomiting; levels of serum pancreatic amylase and/or lipase  $\geq 3$  times the upper limit of normal, radiographic evidence of acute pancreatitis including pancreatic edema on ultrasound or computed tomography [8]. These were the criteria followed in this study. Excluded are patients with traumatic pancreatitis and patients with repeat visit for pancreatitis. Cases included all confirmed diagnosis of pancreatitis in children during February 2012 to February 2015 in Pediatric Gastroenterology clinics at Texas Tech University Health Sciences Center in El Paso (TTUHSC-El Paso) while a random selection of 3 times of pancreatitis cases from the non-pancreatitis group of age 2 to 18 years during February 2012 to February 2015 from outpatient Pediatric clinics were made and served as controls (non-cases). We extracted all socio-demographic variables routinely collected from the electronic medical records along with laboratory values for pancreatitis cases. Our primary exposure variable was Body Mass Index (BMI, kg/m2). Children and adolescents 2 - 19 years old of the same age and sex with a BMI at or above the 95th percentile are considered obese. Children and adolescents of the same age and sex with BMI at or above the 85th percentile and below the 95<sup>th</sup> percentile are considered overweight [9].

**Statistical Analysis:** Appropriate summary measures were used to describe the patients' characteristics and outcomes. Proportion of obesity and overweight was summarized along with 95% confidence interval (CI) using binomial distribution. Unadjusted and adjusted association of BMI was obtained with pancreatitis using logistic regression analysis. Further, a stepwise logistic regression was used to determine the risk factors of

pancreatitis in children. Results were reported using odds ratio (OR) along with 95% CI and p-values. P-values less than 5% were considered as significant results. All the analysis was carried out using SAS (Statistical Analysis System) 9.3.

#### 3. Results

In a 3-year period, out of 21,444 pediatric patients seen in the outpatient clinic, 20 were found to have pancreatitis. The demographic characteristics and comorbidities are shown in **Table 1**. The mean age of the patients with pancreatitis seen was 11 years old. Among those who have pancreatitis, 45% was found to have obesity. The prevalence of obesity was the same for males and females. Among the 20 patients, 15 were Hispanics (75%). Among patients with pancreatitis, 65% had Medicaid, the rest was either under a private insurance or self-pay. The comorbidities identified among the cases were 10% gastroenterology related, 5% endocrinology related.

Table 2 describes the abnormal values for pancreatitis. The laboratory tests that are

Table 1. Baseline characteristics according to patient group.

Variable Age, <i>years</i> (mean, SD)	Entire cohort (n = 83)		Pancreatitis (n = 20)		Control (n = 63)		p-value
	10.40	4.52	11.6	4.83	10.02	4.39	0.1739
Body Mass Index, kg/m² (mean, SD)	21.77	6.76	26.53	8.83	20.26	5.19	0.0061
Body Mass Index (BMI) categorized (n, %)							0.0053
Normal	50	60.24	6	30	44	69.84	
Obese	21	25.3	9	45	12	19.05	
Overweight	12	14.46	5	25	7	11.11	
Gender (n, %)							0.4428
Female	41	49.4	8	40	33	52.38	
Male	42	50.6	12	60	30	47.62	
Ethnicity (n, %)							0.0177
Hispanic or Latino	75	90.36	15	75	60	95.24	
Non-Hispanic	8	9.64	5	25	3	4.76	
nsurance (n, %)							0.0101
Medicaid	66	79.52	13	65	53	84.13	
Private	7	8.43	5	25	2	3.17	
Self-Pay	5	6.02	0	0	5	7.94	
Others	5	6.02	2	10	3	4.76	
Comorbidities (n, %)							0.5137
Endocrine-related (Endo)	3	3.61	1	5	2	3.17	
Gastroenterology-related (GI)	4	4.82	2	10	2	3.17	
None	53	63.86	12	60	41	65.08	
Others	23	27.71	5	25	18	28.57	

**Table 2.** Summary of lab variables of pancreatitis patients (n = 20).

Lab Variable	N	Proportion (%)
Amylase (Units/L)		
Abnormal	7	35
Normal	7	35
Not applicable	6	30
Lipase (Units/L)		
Abnormal	17	85
Not applicable	3	15
Aspartate Aminotransferase (AST) (Units/L)		
Abnormal	3	15
Normal	15	75
Not applicable	2	10
Alanine Aminotransferase (ALT) (Units/L)		
Abnormal	4	20
Normal	14	70
Not applicable	2	10
otal Bilirubin (mg/dL)		
Abnormal	4	20
Normal	14	70
Not applicable	2	10
Direct Bilirubin (mg/dL)		
Normal	10	50
Not applicable	10	50
-Glutamyltransferase (GGT) (Units/L)		
Abnormal	4	20
Normal	4	20
Not applicable	12	60
$Ca^{2+}$ (mg/dL)		
Abnormal	7	35
Normal	10	50
Not applicable	3	15
Ca <sup>2+</sup> (Ionized) (mmol/L)		
Abnormal	1	5
Normal	4	20
Not applicable	15	75

#### Continued

Glucose (mg/dL)		
Abnormal	5	25
Normal	12	60
Not applicable	3	15
Prothrombin time (sec)		
Abnormal	4	20
Normal	7	35
Not applicable	9	45
International normalized ratio		
Abnormal	4	20
Normal	7	35
Not applicable	9	45
Partial thromboplastin time (sec)		
Abnormal	1	5
Normal	8	40
Not applicable	11	55

most commonly ordered are comprehensive metabolic panel, amylase, lipase, total and direct bilirubin, Gamma-glutamyltranferase (GGT), ionized calcium, and coagulation factors. The lipase level was the most common abnormality found as seen in 85% (17 out of 20) of the cases. Amylase was abnormal in 35% of the cases, and not done in 30%. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin were found to be normal in >70% of the cases. Glucose was found to be normal in 60% of the cases. Direct bilirubin was found to be normal in 50% of the cases. Gamma-glutamyltransferase (GGT) was not done in 60%. Ionized calcium was not done in 75%.

Table 3 and Table 4 provide unadjusted/adjusted association of patient socio- demographic characteristics with pancreatitis. BMI, ethnicity, and insurance status were found to be significantly associated with pancreatitis in the univariate analysis. However, in multivariable analysis, only BMI and ethnicity remain to be significantly associated with pancreatitis. Obesity was found to be approximately 7-fold more likely with pancreatitis as compared to non-cases. Overweight was found to be approximately 6-fold more likely with pancreatitis as compared with non-cases. Hispanics/Latinos were 89% less likely to have pancreatitis compared to Non-Hispanics.

#### 4. Discussion

Acute pancreatitis in children is uncommon and studies done are limited in this population [6]. The incidence of acute pancreatitis according to recent studies is estimated to be at nearly one in 10,000 children per year, which approaches the incidence reported in adults. This incidence may represent a true rise in the pediatric pancreatitis or im-

proved awareness of the condition [11]. Based on the National Health and Nutrition Examination Survey (NHANES) data in 2003-2006, it has been estimated that 31.9% of children 2 - 19 years old had a BMI at or above 85 the percentile and 16.3% were at or above the 95<sup>th</sup> percentile of BMI for age [12]. Studies have been done to correlate obesity and pancreatitis in adults but not for the pediatric population.

In our cohort of patients, the prevalence of pancreatitis was estimated as 20/21,444. This reflects the prevalence of acute pancreatitis as reported in recent studies [11]. The prevalence of pancreatitis in the Hispanic population is not well studied to date. In our study, the most important cofactor was BMI. The way which obesity increases the severity of pancreatitis is unclear, but several hypothesis have been suggested, including increased inflammation and accumulation of fat within the pancreas where necrosis is often located; increased peri- and intra-pancreatic fat and inflammatory cells; systemic

Table 3. Unadjusted association of variables with pancreatitis.

Variable	Odds Ratio	95%	p-value		
Age	1.09	0.97	1.22	2 0.1745	
BMI categorized					
Obese vs. Normal	5.50	1.63	18.52	0.0059	
Overweight vs. Normal	5.24	1.25	21.89	0.0232	
Gender					
Male vs. Female	1.65	0.59	4.59	0.3370	
Ethnicity					
Hispanic or Latino vs. Non-Hispanic	0.15	0.03	0.70	0.0157	
Insurance					
Medicaid vs. Other	0.35	0.11	1.10	0.0715	
Comorbidities					
GI vs. Endo	2.00	0.09	44.35	0.6611	
None vs. Endo	0.59	0.05	7.03	0.6728	
Other vs. Endo	0.56	0.04	7.46	0.6573	

Table 4. Association between BMI and pancreatitis after adjusting ethnicity and insurance.

Variable	Odds Ratio	95% CI		p-value	
BMI categorized					
Obese vs. Normal	7.75	2.00	30.13	0.0031	
Overweight vs. Normal	5.69	1.18	27.44	0.0302	
Ethnicity					
Hispanic or Latino vs. Non-Hispanic	0.11	0.02	0.79	0.0280	
Insurance					
Medicaid vs. Other	0.70	0.17	2.93	0.6251	

inflammatory response associated with hepatic dysfunction by altering detoxification of inflammatory mediators; increased pancreatic enzyme output associated with chronic high-fat diet, which may stress the pancreas in genetically predisposed individuals; and ventilation/perfusion mismatch associated with hypoxia and a low pancreatic flow leading to pancreatic deoxygenation and injury. However, in previous pediatric studies, the association between obesity and pancreatitis was not well documented [6]. Increasing childhood obesity has been well documented, and an associated has been recognized between obesity and severity of pancreatitis in adults [6]. The basic pathogenesis of acute pancreatitis does not differ greatly between adults and children, and the treatments between adults and children are similar. In large part, our understanding of the pathology, optimal treatment, assessment of severity, and outcome of acute pancreatitis in children is taken from adult literature.

Surprisingly, pancreatitis cases are less in Hispanics than in non-Hispanics in our cohort. In contrast, one study reported Hispanic ethnicity is a risk factor for biliary pancreatitis; however, obesity was not [1]. The reason of the low prevalence of pancreatitis in Hispanics might be because of the low prevalence of pancreatitis in the US-Mexico border population. Other factors may be considered are nutrition, environmental factors, and also the Hispanic paradox taking into consideration the genetics involved in the Hispanic population.

Serum amylase and lipase measurements are commonly used in the diagnosis of acute pancreatitis [1]. The prompt measurement of serum amylase is useful for a diagnosis of acute pancreatitis, but it can also be elevated in other gastrointestinal diseases. Serum lipase has a sensitivity of 86.5% - 100%, and specificity of 84.7% - 99% for diagnosing acute pancreatitis. Thus, its sensitivity is higher compared to serum amylase. In severe pancreatitis, serum lipase levels 7 times higher than normal have been reported within 24 h after onset of pancreatitis. The degree of elevation and serial changes, however, generally do not correlate with disease severity [13]. In our study, lipase levels were abnormal in 85% of the cases. Amylase was abnormal in 35%. The comprehensive metabolic panel (CMP) done on the cases demonstrated normal liver function tests.

From our study, the identified co-morbidities among the cases of acute pancreatitis showed no association with acute pancreatitis. To date, there are no published data citing nutritional status or ethnicity as potential risk factors during childhood years. This is opposed to the adult population where obesity and the known co-morbidities, such as cholelithiasis and renal disease, have been identified as major risk factors [14]. Other than BMI and ethnicity, the other factors considered in our study did not show any association with acute pancreatitis. Age, gender, insurance status, and co-morbidities are not associated with acute pancreatitis in our cohort. The retrospective nature of the study limited the information obtained on biochemical markers used for data analysis. The pediatric patient population size used in the study is another limitation. The inpatient population was not included which made the sample population smaller. The pancreatitis cases diagnosed in the hospital were not included in the data. This study is a regional study, which may not represent the general pediatric population. This study

is one of the first studies to take into account the prevalence of pancreatitis and its association with obesity in the US-Mexico border population.

### 5. Conclusion and Recommendations

Pancreatitis is related to significant burden of disease in children. Present and ongoing studies are showing the early phases of understanding the etiology and societal implications of pancreatitis. Our study shows that pancreatitis is significantly associated with BMI and ethnicity. Insurance status demonstrates no association with the incidence of pancreatitis. Appropriate intervention for managing obesity may reduce the prevalence of pancreatitis and associated co-morbidities. A larger longitudinal study should be done to evaluate pancreatitis cases to investigate the fundamental knowledge gaps about underlying causes and association between obesity and pancreatitis.

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