SciMedCentral

Journal of Family Medicine & Community Health

Research Article

Prevalence of Pancreatitis in Female and Male Pediatric Patients in Eastern Kentucky in the United States

Sabrina L. McIlwrath and Karin N. Westlund*

Department of Physiology, University of Kentucky, USA

Abstract

Background & aims: Studies in the past decade report worldwide increase of pediatric pancreatitis. The present study focuses on aUnited States region where the first genes associated with hereditary pancreatitis were identified. Aim of the study was to investigate incidences of acute pancreatitis, recurrent acute pancreatitis, and chronic pancreatitis, collecting demographics, etiologies, and comorbid conditions using charted ICD-9-CM codes.

Methods: Retrospective chart review was performed on de-identified patient records of hospitalizations at University of Kentucky hospitals between 2005 and 2013.

Results: Of 234 children diagnosed during the 9 year time period, 69.2% (n=162) had a single episode of acute, 27.8% (65) recurrent acute, and 16.2% (38) chronic pancreatitis. Surprisingly, the annual incidence for first time diagnosis of acute pancreatitis was significantly higher for female patients (16.1, 95% CI: 13.5-18.7 per 100,000, P<0.005) compared to males (9.1, 95% CI: 6.8-11.4). Comorbid conditions varied widely depending on patients' age. Between 33.3-46.2% presented with digestive system symptoms, 12.8-26.3% with diseases of stomach and duodenum, and 10.6-31.6% with systemic diseases. Biliary disease was the most common etiology for single acute (28.4% of cases) and recurrent acute pancreatitis (16.9% of cases). Nineteen of 65 patients with recurrent acute pancreatitis developed chronic pancreatitis (29.2%), while only 3 of 162 with a single bout of acute pancreatitis returned with chronic pancreatitis (P<0.0001).

Conclusions: These findings identify a prevalent disease progression from recurrent acute pancreatitis to chronic pancreatitis in the Kentucky pediatric patient population that could be due to hereditary predisposition and other geographically relevant health factors.

***Corresponding author**

Karin N. Westlund, Department of Physiology, University of Kentucky, MS-508 Medical Science Building, 800 Rose, Lexington, KY, 40536-0298, USA, Tel: 859-323-0672 or -33668; Email: kwhigh2@uky.edu

Submitted: 23 August 2016

Accepted: 10 November 2016

Published: 12 November 2016

ISSN: 2379-0547

Keywords

- Epidemiology
- Gender difference
- Recurrent acute pancreatitis
- Tobacco use
- Obesity

ABBREVIATIONS

AP: Acute Pancreatitis; BMI: Body Mass Index; CCTS: Center for Clinical and Translational Science; CDC: Center For Disease Control; CFTR: Cystic Fibrosis Transmembrane Conductance Regulatory; CI: Confidence Interval; CLDN2: Claudin; CP: Chronic Pancreatitis; CPA1: Carboxypeptidase A1; CTRC: Chymotrypsin; ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification; PRSS1: Protease, Serine 1; SPINK1: Serine Peptidase Inhibitor, Kazal-type 1; UK: University of Kentucky

INTRODUCTION

Pancreatitis is a progressive inflammatory disease of the pancreas with the highest incidence in older male patients with a mean age of 57 [1,2]. It is generally categorized into reversible acute (AP) and irreversible chronic pancreatitis (CP) [3-6]. Several recent studies have investigated the population-based incidence of pancreatitis in pediatric patients. Predominantly conducted in metropolitan areas, an incidence rise of pediatric cases has been reported between 1990 and 2005 [6-10]. It has been speculated that this increase may be due to an epidemiological increase or improved clinical awareness.

The population of Kentucky is of special interest to the study of pancreatitis as the first gene mutations associated with hereditary pancreatitis were identified in a kindred living in eastern Kentucky and western Virginia in the United States of America [11,12]. These autosomal-dominant mutations are associated

with the onset of recurrent AP and CP in children by the age of 5-10 years [10,13-15]. The University of Kentucky, Lexington, USA, hospitals and clinics serve a catchment area located in eastern and central Kentucky. In contrast to previous studies, 2/3 of the population resides in rural Appalachian counties and only 1/3 in urban counties. The aim of our retrospective chart review study of the 9-year period between 2005 and 2013 was to examine the frequency and clinical characteristics of pancreatitis in this pediatric population.

METHODS

The retrospective chart review of de-identified patient data for hospitalizations was approved by the Institutional Review Board of the University of Kentucky (protocol No. 14-0061-X2B). It was conducted using archival database information for admissions at the University of Kentucky (UK) hospitals and clinics in Lexington, the second largest city in Kentucky. The catchment area was defined as counties from which at least 5% of the population sought treatment at the University of Kentucky hospitals and clinics. Counties were classified as urban or rural in accordance with the US census bureau [16]. Within the catchment area there are 10 urban counties (Anderson, Bourbon, Boyle, Fayette, Franklin, Harrison, Jessamine, Mercer, Scott, Woodford) and 45 rural Appalachian counties (Bath, Bell, Breathitt, Carter, Casey, Clark, Clay, Clinton, Elliott, Fleming, Floyd, Garrard, Harlan, Jackson, Johnson, Knott, Knox, Laurel, Lawrence, Lee, Leslie, Letcher, Lewis, Lincoln, Madison, Magoffin, Mason, McCreary, Menifee, Montgomery, Morgan, Nicholas, Owsley, Perry, Pike, Powell, Pulaski, Robertson, Rockcastle, Rowan, Russell, Wayne, Whitley, Wolfe).

Data source

Patient records from University of Kentucky HealthCare Clinical data were extracted and de-identified by the biomedical intelligence reporting officers within the Biomedical Informatics core facility of the University of Kentucky Center for Clinical and Translational Science (CCTS) center. Data from patients treated at the University of Kentucky hospitals in Lexington, Kentucky, were available starting January 2005 onward. Patient data sets contained demographic information (age, sex, race, county of residence, marital and employment status, payment source), data of admission, discharge (date, discharge disposition, inpatient mortality), diagnoses codes.

Inclusion criteria

Patients with pancreatitis were diagnosed by the treating physician. To identify and characterize incidence and prevalence of comorbid diseases, disorders, and symptoms, ICD-9-CM codes were investigated in accordance with the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), as listed in (Table 1). All patients under the age of 20 treated between January 2005 to December 2013, who received a charted diagnosis of either acute pancreatitis (ICD-9-CM 577.0) or chronic pancreatitis (ICD-9-CM 577.1), were included in this study. Recurrent acute pancreatitis does not have a separate ICD-9-CM code. Typically it is described as the incidence of two

Table 1: ICD-9-CM codes of diseases, disorders, and symptoms investigated in the pediatric patients.

Generalized disease/disorder name	ICD-9-CM codes
Acute pancreatitis	577.0
Chronic pancreatitis	577.1
Abdominal pain	789.00-789.09, 789.60-789.69
Anemia	280-285
Anxiety and depression	300, 311
Biliary disease (cholelithiasis & disorders of the gallbladder and biliary tract)	574-576
Cachexia (malaise, fatigue, cachexia)	780.79, 783.21, 783.22, 783.40, 783.41, 783.7, 799.3, 799.4
Cardiovascular symptoms (congenital symptoms & abnormal heartbeat)	745, 746, 747, 780.2, 785.0-785.3, 785.9
Cystic fibrosis (cystic fibrosis & polycystic kidney disease)	V83.81, 277.0, 753.10-753.19
Diabetes mellitus	249- 250
Disease of stomach & duodenum (gastritis &duodenitis, stomach, stomach & duodenum)	535-537
Disease of the lung (chronic bronchitis, emphysema, asthma)	491-493
Disorder of the kidneys (chronic kidney disease, hydronephrosis, calculus of kidney & ureter)	585, 591-593
Gastroesophageal reflux disease	530.18
Hepatitis	070
Human immunodeficiency virus infection	V08, 042
Hyperlipidemia	272.0-272.4
Inflammatory bowel disease	555-556, 564.1
Liver disease (non-alcoholic liver disease& necrosis)	570, 571.40-571.9, 572-573
Lupus	710.0
Obesity	V85.30-V85.54, 278.00-278.01
Other pancreatic disease (cysts & other diseases of the pancreas)	577.2, 577.8, 577.9
Sepsis (septicimia& systemic inflammatory response syndrome)	038, 995.90-995.94
Digestive system symptoms (diarrhea, vomiting, nausea)	787.01-787.03, 787.60, 787.7, 787.91, 787.99
Tobacco use disorder	V15.82, 305.1

or more episodes of AP with a documented resolution of pain and normalization of enzymes. As this cannot be assessed in the present study, we defined recurrent AP as at least 2 bouts of acute pancreatitis separated by a minimum of 2 months. All other patients under the age of 20 were combined in the control group. Race of the patients in this study was not a factor considered since rural counties are over 90% white and urban counties are ~80% white.

Statistical analysis

All normally distributed data are presented as mean ± standard error or mean (SEM) and 95% confidence interval (CI). Data were compared using Student's *t*-test or Chi square test when appropriate. Analysis of the annual incidence of pancreatitis in males and females during the study period was analyzed using linear regression. In all cases statistical significance was achieved when $P<0.05$.

RESULTS

Incidence of pancreatitis diagnosis in pediatric patients

A total of 234 pediatric patients were diagnosed with pancreatitis at the University of Kentucky hospitals and clinics during the 9-year study period from 2005 to 2013 in this retrospective chart review. Acute pancreatitis (AP) was diagnosed in 227 children (97%), and during the study period this group f patients was diagnosed a total of 407 times. A single diagnosis of AP was made in 71.4% of these cases (162 children). Recurrent AP was identified in 28.6% of pediatric patients (65 children). A diagnosis of CP was made in 38 children, including16.2% of pediatric patients with pancreatitis who sought treatment a total of 85 times. The mean age at first time diagnosis of pancreatitis was 12.7 (95% CI: 12.0-13.4) irrespective of the type of pancreatitis, patient's gender, or county of residence.

Differentiation by sex

In contrast to other studies, all forms of pancreatitis were diagnosed in significantly more female than male pediatric patients. The mean annual incidence of a principal diagnosis of AP was 7.8 per 100,000 female and 5.3 (95% CI: 4.3-6.4) per 100,000 male children (95% CI: 6.5-9.0; $P<0.01$, Student's *t*-test). For all diagnoses of AP the mean annual incidence of hospitalization was 11.4 per 100,000 female and 7.8 (95% CI: 6.5-9.2) per 100,000 male children (95% CI: 10.2-12.7; $P<0.01$, Student's *t*-test) in the catchment area. First time diagnosis of AP was made in 145 female and 82 male children ($P<0.001$, df = 4, Chi square test). Annually, AP was diagnosed for the first time in a mean of 16.1 (95% CI: 13.5-18.7) female and 9.1 (95% CI: 6.8-11.4) male patients ($P<0.005$, Student's *t*-test). The number of patients with first time diagnosis of AP increased with age and was highest in the 15 to 19 year old children (Figure 1A).

Comparison of AP versus CP

The annual number of CP diagnoses was ten-fold lower than for AP, yet, showed similar significant gender differences. A mean of 2.9 per 1,000,000 female (95% CI: 2.1-3.6) and 1.3 per 1,000,000 male (95% CI: 0.6-2.1) pediatric patients were

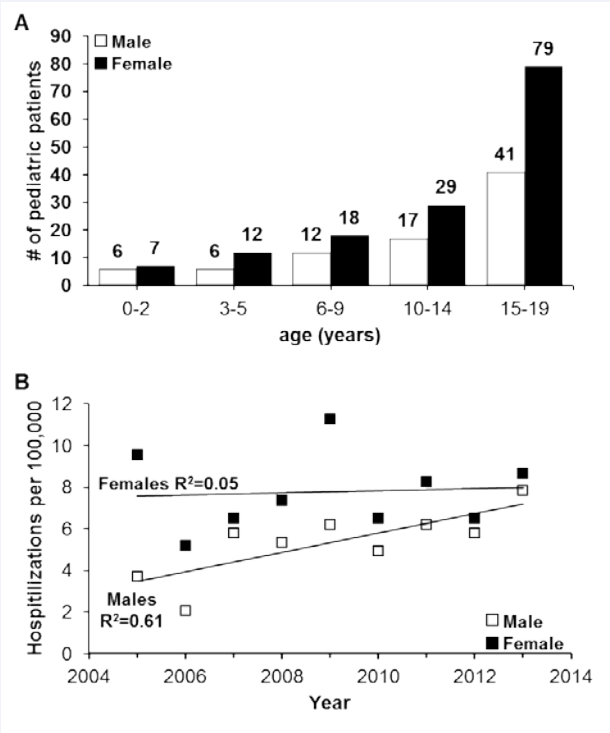

Figure 1 Acute Pancreatitis Diagnoses in Pediatric Patients
A. Age of male and female pediatric patients when first diagnosed with acute pancreatitis.
B. Incidence of annual clinic and hospital admissions of pediatric patients with acute pancreatitis per 100,000 children in catchment area from 2005 through 2013.

diagnosed with CP ($P<0.05$, Student's *t*-test). The actual totals during the study period were twice as many females [17] than males [12] with diagnosis of CP. Mean annual hospitalizations were 5.5 per 1,000,000 children for the female population and 4.0 for the male population which was not a significant difference.

During the study period a consistent increase in the hospitalizations of male pediatric patients by age was detected using linear regression (R^2 = 0.6074) while hospitalization numbers for females remained constant per year (Figure 1B). No gender differences were noted for length of hospital stay (females: 3.5 ± 0.4 days; males: 2.8 ± 0.2 days). The incidence of AP was not different between patients living in urban or rural Appalachian counties. In urban counties 9.6 per 100,000 and in rural Appalachian counties 8.5 per 100,000 children were treated annually for AP.

Comorbidities and etiology of pancreatitis in pediatric patients

After diagnoses with AP, the incidence of diseases of the lungs, kidneys, biliary diseases, diabetes, chronic pancreatitis, and other pancreatic diseases was increased in 25% of males and 31.7% of females. Comorbid conditions diagnosed similarly in all age groups include metabolic diseases such as obesity (0-29.8%) and diseases of the stomach and duodenum (12.8-26.3%), systemic diseases of the kidney or lung (10.6-31.6%), and sepsis (4.8-13.3%) (Table 2). Comorbid conditions such as anemia

(8.5-46.2%), cardiovascular symptoms (6.7-38.5%) diseases of the kidney and ureter (15.8-61.5%), symptoms of cachexia (5.3-38.5%), and gastroesophageal reflux disease (5.3-30.8%) were highest in the 0-2 year age group and decreased with age. Other pancreatic diseases (0-20.0%), diabetes (0-25.5%), and biliary disease (7.7-39.7%) increase with the age of pediatric patients as do abdominal pain (15.4-48.4%) and anxiety / depression (0-39.7%).

Of the 227 pediatric patients with AP almost one-third (29.6%) had recurrent episodes. The etiological time course of disease presentation in female and male patients diagnosed with single or recurrent AP is summarized in (Table 3). Digestive system symptoms were noted in 12.2-25.0% of patients later diagnosed with recurrent AP. Abdominal pain was elevated in patients of both AP groups.

DISCUSSION

In the last two decades there has been an increasing rise in the recognition and diagnoses of pancreatitis in children. The overall age-adjusted incidence of pancreatitis at the University of Kentucky Hospitals was 7.8-11.4 per 100,000 in males and females in the catchment area. This was lower than previously reported in Pittsburgh, Pennsylvania, USA (13.2 per 100,000) and higher than in Melbourne, Australia (3.6 per 100,000) [6,9,18]. This retrospective study identified a significantly higher incidence of diagnosis of pancreatitis (62%) in female pediatric patients similar to a recent international study [15]. Similar to previous studies, the incidence of pancreatitis diagnoses was highest in the oldest pediatric patients (ages 15-19 years) [6,21], shifting from digestive system such as diarrhea and vomiting to abdominal pain and mood disorders (anxiety and depression). These variations may be attributable to developmental differences, changes in diet, and may also reflect cumulative environmental impact [6,9,18,19]. Reduced incidence of digestive symptoms and pain may be attributed to the study design. The present study utilized medical codes only for the retrospective chart review. Integral symptoms of a pancreatitis diagnoses are not charted separately by ICD-9-CM code by definition. Thus, the incidence of systemic diseases decreased with increasing age, the number of metabolic and biliary disease cases such as cholelithiasis increased.

Approximately 30% of pediatric cases of AP are classified as idiopathic, lacking any distinct medical etiology [9,20, 21]. An association with underlying autoimmune or hereditary mechanisms has been suggested. A recent study reported that 8 of 10 pediatric patients with CP had hereditary pancreatitis associated with gene mutations in the cationic trypsinogen

Table 2: Incidence of comorbidities by age of patients.

Age groups	0-2	3-5	6-9	10-14	15-19
Patients n (%)	13 (5.5)	19 (8.1)	30 (12.8)	47 (20.0)	126 (53.6)
Females n	7	12	18	30	83
Metabolic diseases					
Other pancreatic disease	0	2 (10.5)	6 (20.0)	7 (14.9)	17 (13.5)
Diabetes	0	2 (10.5)	4 (13.3)	12 (25.5)	12 (9.5)
Obesity	2 (15.4)	0	4 (13.3)	14 (29.8)	17 (13.5)
Hyperlipidemia	0	1 (5.3)	0	2 (4.3)	2 (1.6)
Disease of stomach & duodenum	3 (23.1)	5 (26.3)	4 (13.3)	6 (12.8)	20 (15.9)
Systemic diseases					
Anemia	6 (46.2)	9 (47.4)	6 (20.0)	4 (8.5)	23 (18.3)
Cardiovascular Symptoms	5 (38.5)	3 (15.8)	2 (6.7)	5 (10.6)	20 (15.9)
Disease of the kidney & ureter	8 (61.5)	3 (15.8)	11 (36.7)	9 (19.1)	29 (23.0)
Disease of the lung	3 (23.1)	6 (31.6)	6 (20.0)	5 (10.6)	24 (19.0)
Sepsis	1 (7.7)	2 (10.5)	4 (13.3)	3 (6.4)	6 (4.8)
Biliary & liver disease					
Biliary disease	1 (7.7)	3 (15.8)	4 (13.3)	15 (31.9)	50 (39.7)
Liver disease	0	2 (10.5)	4 (13.3)	4 (8.5)	11 (8.7)
Non-dependent drugs of abuse					
Tobacco use disorder	0	0	0	0	38 (30.2)
Hereditary/inflammatory diseases					
Cystic fibrosis	3 (23.1)	1 (5.3)	0	2 (4.3)	13 (10.3)
Inflammatory bowel disease	0	0	0	2 (4.3)	15 (11.9)
Lupus	0	0	0	0	4 (3.2)
Viral infection					
Hepatitis	0	0	0	1 (2.1)	4 (3.2)
Common symptoms					
Abdominal pain	2 (15.4)	7 (36.8)	10 (33.3)	13 (27.7)	61 (48.4)
Cachexia	5 (38.5)	1 (5.3)	10 (33.3)	3 (6.4)	12 (9.5)
Digestive system symptoms	6 (46.2)	7 (36.8)	10 (33.3)	16 (34.0)	47 (37.3)
Gastroesophageal reflux	4 (30.8)	1 (5.3)	2 (6.7)	4 (8.5)	19 (15.1)
Anxiety and depression	0	1 (5.3)	1 (3.3)	9 (19.1)	22 (39.7)

Table 3: Etiology of single episode and recurrent Acute Pancreatitis
Time course of comorbid disease determination in male and female patients diagnosed with a single bout of acute or recurrent acute pancreatitis

	Diseases preceding first episode of acute pancreatitis		Diseases diagnosed at time of first acute pancreatitis episode		Diseases diagnosed after first episode of acute pancreatitis	
	Single	Recurrent	Single	Recurrent	Single	Recurrent
Systemic diseases						
Sepsis Male n (%) Female n (%)	 0 1 (1.0)	 0 0	 3 (5.2) 4 (3.8)	 2 (8.3) 1 (2.4)	 1 (1.7) 2 (1.9)	 2 (8.3) 1 (2.4)
Anemia Male n (%) Female n (%)	 1 (1.7) 5 (4.8)	 2 (8.3) 1 (2.4)	 6 (10.3) 14 (13.5)	 1 (4.2) 1 (2.4)	 3 (5.2) 6 (5.8)	 1 (4.2) 4 (9.8)
Disease of the lung Male n (%) Female n (%)	 1 (1.7) 3 (2.9)	 0 0	 3 (5.2) 6 (5.8)	 7 (29.2) 3 (7.3)	 3 (5.2) 4 (3.8)	 2 (8.3) 5 (12.2)
Disease of the kidney Male n (%) Female n (%)	 4 (6.9) 9 (8.7)	 1 (4.2) 3 (7.3)	 5 (8.6) 16 (15.4)	 0 2 (4.9)	 5 (8.6) 4 (3.8)	 1 (4.2) 8 (19.5)
Biliary diseases						
Biliary diseases Male n (%) Female n (%)	 1 (1.7) 4 (3.8)	 0 0	 9 (15.5) 37 (35.6)	 2 (8.3) 9 (22.0)	 0 3 (2.9)	 4 (16.7) 5 (12.2)
Metabolic diseases						
CP Male n (%) Female n (%)	 1 (1.7) 1 (1.0)	 2 (8.3) 0	 0 4 (3.8)	 1 (4.2) 0	 0 3 (2.9)	 6 (25.0) 13 (31.7)
Other pancreatic disease Male n (%) Female n (%)	 1 (1.7) 1 (1.0)	 1 (4.2) 1 (2.4)	 3 (5.2) 4 (3.8)	 2 (8.3) 2 (4.9)	 1 (1.7) 3 (2.9)	 5 (20.8) 7 (17.1)
Diabetes Male n (%) Female n (%)	 4 (6.9) 4 (3.8)	 0 1 (2.4)	 2 (3.4) 4 (3.8)	 1 (4.2) 2 (4.9)	 1 (1.7) 2 (1.9)	 1 (4.2) 4 (9.8)
Obesity Male n (%) Female n (%)	 3 (5.2) 0	 0 2 (4.9)	 4 (6.9) 11 (10.6)	 2 (8.3) 3 (7.3)	 2 (3.4) 3 (2.9)	 2 (8.3) 4 (9.8)
Hyperlipidemia Male n (%) Female n (%)	 0 1 (1.0)	 0 0	 0 3 (2.9)	 1 (4.1) 0	 0 0	 0 0
Non-dependent drugs of abuse						
Tobacco use disorder Male n (%) Female n (%)	 1 (1.7) 3 (2.9)	 0 0	 2 (3.4) 13 (12.5)	 0 2 (4.9)	 5 (8.6) 2 (1.9)	 0 3 (7.3)
Viral infection						
Hepatitis Male n (%) Female n (%)	 0 2 (1.9)	 1 (4.1) 0	 2 (3.4) 6 (5.8)	 1 (4.1) 1 (2.4)	 0 2 (1.9)	 0 3 (7.3)
Prevalent Symptoms						
Digestive system symptoms Male n (%) Female n (%)	 4 (6.9) 8 (7.7)	 6 (25.0) 5 (12.2)	 5 (8.6) 11 (10.6)	 1 (4.2) 2 (4.9)	 7 (12.1) 7 (6.7)	 6 (25.0) 11 (26.8)
Abdominal pain Male n (%) Female n (%)	 2 (3.4) 14 (13.5)	 4 (16.7) 2 (4.9)	 2 (3.4) 9 (8.7)	 1 (4.2) 2 (4.9)	 9 (15.5) 14 (13.5)	 8 (33.3) 14 (34.1)

(PRSS1) gene [22]. An international study on pediatric pancreatitis reported 67% of children diagnosed with chronic pancreatitis had predisposing genetic mutations [15]. Mutations in the autosomal PRSS1 gene were first identified in a kindred living at least in part in the catchment area of the University of Kentucky hospitals [11,12,14]. Other known autosomal genes associated with increased susceptibility of pancreatitis in children include cystic fibrosis transmembrane conductance regulatory (CFTR), chymotrypsin (CTRC), pancreatic secretory trypsin inhibitor (SPINK1), and most recently the carboxypeptidase A1 (CPA1) gene that when mutated increases the susceptibility for pancreatic cancer [13,15,19-30].

Of the 227 cases of AP in the present study, 29% of pediatric patients with recurrent AP were later diagnosed with CP and 18% of them developed other pancreatic diseases in the absence of any predictive etiology. Examination of the etiology and time course of the presentation of comorbid conditions identified higher incidences of metabolic and biliary diseases after the first episode of AP in patients with recurrent AP. No gender differences were noted for the incidence of metabolic diseases, while biliary diseases were more commonly diagnosed in female pediatric patients. This is lower than in previous reports which found that 6/11 pediatric patients with recurrent AP had biliary diseases [9,20]. Recurrent AP poses the risk of further progression to CP, pancreatic cancer, and type 3c diabetes mellitus [31,32]. Underlying causes for this progression have been identified as a combination of environmental and hereditary factors. While no genetic information was available for the present study, we identified almost twice as many female pediatric patients with the diagnosis with pancreatitis. This suggests causal hereditary and geographic restriction differences in the catchment area.

Acausal factor for these children may be related to Kentucky's rank among the highest states for childhood obesity (18%) according to the CDC. Obesity was identified in 7-10% of patients with AP while only 5 of the 227 pediatric patients were diagnosed with hyperlipidemia. The incidence of obesity was higher in patients with recurrent AP. Obesity and hyperlipidemias are known risk factors that can induce lipotoxicity, exacerbate AP, and contribute to recurrent episodes [33].

Another regional environmental influence is smoking. Strikingly, over 30% of 15-19 year old pediatric patients in this study reported tobacco use. Smoking has been associated with pancreatitis and pancreatic cancer since the early 1980s and poses a separate risk factor [34-36]. Due to the known increased risk smoking poses for pancreatitis, we determined that 8.6% of males reported smoking after the diagnosis among pediatric patients with a single bout of AP during the study period. No data was available on the incidence of second hand smoke exposure in this patient population. Thus, as a multifactorial disease, pancreatitis may be caused by one or more combined environmental and hereditary factors in this group of children as has been reported in adults.

LIMITATIONS

The present study is a retrospective patient chart review utilizing ICD-9-CM codes from patients who were treated at the UK clinics and hospitals (2005-2013). Information about medical care received by patients from other medical professionals is not included in this analysis. This unavailability of information about previous care impacts in particular the data from patients residing in rural counties within the UK hospital catchment area. As only ICD-9-CM codes were analyzed, no detailed information on the severity of pancreatitis bouts and only partial information about the pain experienced by patients is available. It is also highly likely that pain is underreported in our study. Pain is the most common symptom used to diagnose pancreatitis and according to the ICD-9-CM code should not be charted separately. Also, although the CDC recommends the use of body mass index (BMI) to assess obesity in children, this is not widely recorded in the medical charts, reflecting the inaccuracy of applying this weight-height ratio on developing children [37]. Information on the use of oral contraceptives and lab tests such as enzyme contents of blood and other body fluids, results of the Sweat test, or DNA tests for hereditary pancreatitis, were not available for this study.

SUMMARY

In the present study, we identified an increased incidence of CP and other pancreatic disease diagnoses in pediatric patients with recurrent AP. Thirty percent of children with recurrent AP were subsequently diagnosed with CP in the pediatric patient population from the Eastern Kentucky catchment area seen at the University of Kentucky Hospitals between 2005-2013. Child health education and future studies investigating the genetics of this patient population are needed to improve patients' treatment options and decrease the health and economic burden.

ACKNOWLEDGEMENTS

We would like to thank the CCTS Enterprise Data Trust at the University of Kentucky for providing us access to the de-identified patient data. This research was further supported by the National Institute of Health award R01 NS039041 (KNW). The CCTS is funded by the National Institute of Health National Center for Research Resources and the National Center for Advancing Translational Sciences award UL1TR000117.

List of authors and their contribution

SLM designed the experiment, acquired, analyzed and interpreted the data, and wrote the manuscript. KLM designed the experiment, interpreted the data, revised the manuscript, and gave final approval of the version to be published. Both authors agree to being accountable for all aspects of the work.

REFERENCES

1. Roberts SE, Akbari A, Thorne K, Atkinson M, Evans PA. The incidence of acute pancreatitis: impact of social deprivation, alcohol consumption, seasonal and demographic factors. Aliment PharmacolTher. 2013; 38: 539-548.
2. Vidarsdottir H, Möller PH, Vidarsdottir H, Thorarinsdottir H, Björnsson ES. Acute pancreatitis: a prospective study on incidence, etiology, and outcome. Eur J GastroenterolHepatol. 2013; 25: 1068-1075.
3. Sarner M, Cotton PB. Classification of pancreatitis. Gut. 1984; 25: 756-759.
4. Singer MV, Gyr KE, Sarler H. Revised Marseille Classification of Pancreatitis. In: Malferteiner P, Ditschuneit H, eds. Diagnostic procedures in pancreatic disease. New York, NY: Springer. 1986.
5. Steer ML. Classification and pathogenesis of pancreatitis. SurgClin North Am. 1989; 69: 467-480.
6. Morinville VD, Barmada MM, Lowe ME. Increasing incidence of acute pancreatitis at an American pediatric tertiary care center: is greater awareness among physicians responsible? Pancreas. 2010; 39: 5-8.
7. Lopez MJ. The changing incidence of acute pancreatitis in children: a single-institution perspective. J Pediatr. 2002; 140: 622-624.
8. Werlin SL, Kugathasan S, Frautschy BC. Pancreatitis in children. J PediatrGastroenterolNutr. 2003; 37: 591-595.
9. Nydegger A, Heine RG, Ranuh R, Gegati-Levy R, Crameri J, Oliver MR. Changing incidence of acute pancreatitis: 10-year experience at the

Royal Children's Hospital, Melbourne. J GastroenterolHepatol. 2007; 2: 1313-1316.

10. Park A, Latif SU, Shah AU, Tian J, Werlin S, Hsiao A, et al. Changing referral trends of acute pancreatitis in children: A 12-year single-center analysis. J PediatrGastroenterolNutr. 2009; 49: 316-322.

11. Whitcomb DC, Gorry MC, Preston RA, Furey W, Sossenheimer MJ, Ulrich CD, et al. Hereditary pancreatitis is caused by a mutation in the cationic trypsinogen gene. Nat Genet. 1996; 14: 141-145.

12. Whitcomb DC, Preston RA, Aston CE, Sossenheimer MJ, Barua PS, Zhang Y, et al. A gene for hereditary pancreatitis maps to chromosome 7q35. Gastroenterology. 1996; 110: 1975-1980.

13. Srinath AI, Lowe ME. Pediatric pancreatitis. Pediatr Rev. 2013; 34: 79-90.

14. Sossenheimer MJ, Aston CE, Preston RA, Gates LK, Ulrich Charles D, Martin Steven P, et al. Clinical characteristics of hereditary pancreatitis in a large family, based on high-risk haplotype. The Midwest Multicenter Pancreatic Study Group (MMPSG). Am J Gastroenterol. 1997; 92: 1113-1116.

15. Schwarzenberg SJ, Bellin M, Husain SZ, Ahuja M, Barth B, Davis H, et al. Pediatric chronic pancreatitis is associated with genetic risk factors and substantial disease burden. J Pediatr. 2015; 166: 890-896.

16. U.S. Census Bureau. State and County Quick Facts. Data derived from Population Estimates, American Community Survey, Census of Population and Housing, State and County Housing Unit Estimates, County Business Patterns, Nonemployer Statistics, Economic Census, Survey of Business Owners, Building Permits. 2015.

17. Bourliere M, Barthet M, Berthezene P, Durbec JP, Sarles H. Is tobacco a risk factor for chronic pancreatitis and alcoholic cirrhosis? Gut. 1991; 32: 1392-1395.

18. Meyer A, Coffey MJ, Oliver MR, Ooi CY. Contrasts and comparisons between childhood and adult onset acute pancreatitis. Pancreatology. 2013; 13: 429-435.

19. Bai HX, Lowe ME, Husain SZ. What have we learned about acute pancreatitis in children? J PediatrGastroenterolNutr. 2011; 52: 262-270.

20. Minen F, De Cunto A, Martelossi S, Ventura A. Acute and recurrent pancreatitis in children: exploring etiological factors. Scand J Gastroenterol. 2012; 47: 1501-1504.

21. Sultan M, Werlin S. Venkatasubramani N. Genetic prevalence and characteristics in children with recurrent pancreatitis. J PediatrGastroenterolNutr. 2012; 54: 645-650.

22. Schmitt F, Le Henaff G, Piloquet H, Leclair MD, David A, Heloury Y, et al. Hereditary pancreatitis in children: surgical implications with special regard to genetic background. J PediatrSurg. 2009; 44: 2078-2082.

23. Whitcomb DC. Hereditary pancreatitis: a model for understanding the genetic basis of acute and chronic pancreatitis. Pancreatology. 2001; 1: 565-570.

24. Whitcomb DC. Genetic risk factors for pancreatic disorders. Gastroenterology. 2013; 144: 1292-1302.

25. Masamune A. Genetics of pancreatitis: the 2014 update. Tohoku J Exp Med. 2014; 232: 69-77.

26. Witt H. Gene mutations in children with chronic pancreatitis. Pancreatology. 2001; 1: 432-438.

27. Tukiainen E, Kylänpää ML, Kemppainen E, Nevanlinna H, Paju A, Repo H, et al. Pancreatic secretory trypsin inhibitor (SPINK1) gene mutations in patients with acute pancreatitis. Pancreas. 2005; 30: 239-242.

28. Bishop MD, Freedman SD, Zielenski J, Ahmed N, Dupuis A, Martin S, et al. The cystic fibrosis transmembrane conductance regulator gene and ion channel function in patients with idiopathic pancreatitis. Hum Genet. 2005; 118: 372-381.

29. De Boeck K, Weren M, Proesmans M, Kerem E. Pancreatitis among patients with cystic fibrosis: correlation with pancreatic status and genotype. Pediatrics. 2005; 115: 463-469.

30. Witt H, Beer S, Rosendahl J, Chen JM, Chandak GR, Masamune A, et al. Variants in CPA1 are strongly associated with early onset chronic pancreatitis. Nat Genet. 2013; 45: 1216-1220.

31. Lowenfels AB, Maisonneuve P, Lankisch PG. Chronic pancreatitis and other risk factors for pancreatic cancer. GastroenterolClin North Am. 1999; 28: 673-685.

32. Hardt PD, Brendel MD, Kloer HU, Bretzel RG. Is pancreatic diabetes (type 3c diabetes) underdiagnosed and misdiagnosed? Diabetes Care. 2008; 31: 165-169.

33. Navina S, Acharya C, DeLany JP, Orlichenko LS, Baty CJ, Shiva SS, et al. Lipotoxicity causes multisystem organ failure and exacerbates acute pancreatitis in obesity. SciTransl Med. 2011; 3: 107.

34. Voirol M, Infante F, Brahime-Reteno O, Raymond L, Hollenweger V, Loizeau E. Alcohol, tobacco and food consumption in pancreatic diseases. Preliminary results of a study of 1000 cases. Schweiz Med Wochenschr. 1980; 110: 854-855.

35. Yen S, Hsieh CC, MacMahon B. Consumption of alcohol and tobacco and other risk factors for pancreatitis. Am J Epidemiol. 1982; 116: 407-414.

36. Yadav D, Slivka A, Sherman S, Hawes RH, Anderson MA, Burton FR, et al. Smoking is underrecognized as a risk factor for chronic pancreatitis. Pancreatology. 2010; 10: 713-719.

37. Daniels SR. The use of BMI in the clinical setting. Pediatrics. 2009; 124: 35-41.

Cite this article

McIlwrath SL, Westlund KN (2016) Prevalence of Pancreatitis in Female and Male Pediatric Patients in Eastern Kentucky in the United States. J Family Med Community Health 3(5): 1092.