Pancreatitis in Children: A Single Center Experience
Çocuklarda Pankreatit: Tek Merkez Deneyimi

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ABSTRACT

Objective: The aim of this study was to evaluate the clinical, laboratory and etiological differences between children having acute pancreatitis, acute recurrent pancreatitis and chronic pancreatitis.

Material and Methods: Medical records of children who were diagnosed with pancreatitis between January 2014 and December 2017 were evaluated retrospectively. The study was approved by the Ethics Committee of Afyonkarahisar University of Health Sciences.

Our cases were classified as acute pancreatitis, acute recurrent pancreatitis and chronic pancreatitis according to INSPPIRE group definitions.

Results: Etiology, demographic characteristics, laboratory and radiological findings were compared between acute pancreatitis (group 1) and acute recurrent and chronic pancreatitis (group 2) groups. 43 patients (78.2%) were enrolled in acute pancreatitis group (group 1). In group 2; 8 cases had acute recurrent pancreatitis and 4 cases had chronic pancreatitis [a total of 12 cases (21.8%)].

When the etiologies of our cases were examined; Group 1 had idiopathic (88.5%), stone (2.3%), trauma (2.3%), infections (4.6%) and choledochal cyst (2.3%), respectively. In group 2, they were found to be idiopathic (50%), congenital anomalies of the pancreatic duct (8.3%), allergy (8.3%), autoimmunity (8.3%) and genetic causes (25%).

There was no statistical difference between the groups in terms of laboratory values. In our study, the cause of pancreatitis could not be generally identified in all groups.

Conclusion: In cases having acute pancreatitis, infections were the second most common etiology; and common causes of acute recurrent and chronic pancreatitis have been found as genetic causes.

Key Words: Acute pancreatitis, Chronic pancreatitis, Etiology

ÖZ

Amaç: Bu çalışmada akut pankreatit, akut reküren pankreatit ve kronik pankreatit tanısı ile izlenen çocukların klinik, laboratuvar ve etyolojik farklılıklarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Ocak 2014-Aralık 2017 tarihleri arasında pankreatit tanısı ile izlenen çocukların tıbbi kayıtları retrospektif olarak değerlendirilmiştir. Çalışımımız Afyonkarahisar Sağlık Bilimleri Üniversitesi Tip Fakültesi Etik Kurulu’ndan onay almıştır. Olgularımız INSPPIRE grubu tanımlamalarına göre akut pankreatit, akut reküren pankreatit ve kronik pankreatit olarak sınıflandırılmıştır. Akut pankreatit (grup 1) ve akut reküren ve kronik pankreatit (grup 2) grupları arasında etyolojik, demografik özellikleri, laboratuvar ve radyolojik bulgular karşılaştırılmıştır.
INTRODUCTION

Childhood pancreatitis has begun to be detected more frequently in recent years due to the increase in the awarenesses of healthcare professionals and more detailed evaluation of the etiologies of pancreatitis (1).

According to International Study Group of Pediatric Pancreatitis (INSPPIRE), childhood pancreatitis was classified as acute pancreatitis (AP), acute recurrent pancreatitis (ARP) and chronic pancreatitis (CP). AP has been described as a reversible inflammatory process which can be limited only in pancreas or causes multisystemic failure of organ functions. ARP includes recurrent acute pancreatic attacks including normal periods during one month and longer. CP has been characterized by irreversible damage in the pancreatic tissue such as fibrosis and necrosis; and causes endocrine or exocrine failure in the pancreas (1-2).

The diagnosis of childhood AP is made according to the criteria by INSPPIRE. According to these, it has been shown that two out of three following criteria are required for the diagnosis of AP: 1-characteristic abdominal pain (epigastric with or without back invasion or upper right quadrant), 2-increase in serum amilase and/or lipase values three or more times of the upper limit of normal and 3-imaging findings that are consistent with AP (2). MRI was performed if the patient’s clinical findings worsened or magnetic resonance cholangiography (MRCP) were also evaluated. In addition, in cases where optimal evaluation could not be performed due to the gases in the peripancreatic area, CT was performed. In cases where optimal evaluation could not be performed due to the gases in the peripancreatic area, CT was performed. MRI was performed if the patient’s clinical findings worsened progressively. MRCP was performed in patients who were diagnosed with pancreatitis were retrospectively assessed. The study was approved by Ethics Committee of Afyonkarahisar University of Health Sciences. The diagnosis of AP was made; based on the presence of 2 of these 3 variables: (i) clinical symptoms associated with AP such as abdominal pain, nausea and vomiting, (ii) elevated serum amylase levels [>3xUNL (upper normal limit); normal range <100 U/L] and/or elevated serum lipase levels (>3xUNL; normal range <70 U/L), and (iii) radiological changes associated with pancreatitis (1).

MATERIALS and METHODS

The study was conducted in a tertiary hospital between January 2014 and December 2017. Medical records of children who were diagnosed with pancreatitis were retrospectively assessed. The study was approved by Ethics Committee of Afyonkarahisar University of Health Sciences. The diagnosis of AP was made; based on the presence of 2 of these 3 variables: (i) clinical symptoms associated with AP such as abdominal pain, nausea and vomiting, (ii) elevated serum amylase levels [>3xUNL (upper normal limit); normal range <100 U/L] and/or elevated serum lipase levels (>3xUNL; normal range <70 U/L), and (iii) radiological changes associated with pancreatitis (1).

Patients were classified as acute pancreatitis, acute recurrent pancreatitis and chronic pancreatitis according to INSPPIRE group definitions (2). Etiologic factors, demographic characteristics, laboratory and radiological findings were compared between acute pancreatitis (group 1) and acute recurrent and chronic pancreatitis (group 2) groups. The choice of diagnostic imaging methods was based on the criteria published by Grover et al. (8) Imaging techniques performed to the patients, including ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI) and/or magnetic resonance cholangiography (MRCP) were also evaluated. Ultrasonography was applied to all patients because it is a useful and non-invasive method. However, in cases where optimal evaluation could not be performed due to the gases in the intestine due to paralytic ileus and patient movement CT was performed. In addition, in cases of increased pancreatic size, edema and peripancreatic area could not be evaluated adequately by US and in the presence of suspicion of fluid collection or necrosis in the peripancreatic area, CT was performed.

MRI was performed if the patient’s clinical findings worsened progressively. MRCP was used in biliary tract and pancreatic duct examination. MRCP was performed in patients...
with suspected choledochus, pancreatic duct and pancreatic pathology.

The severity of AP was classified as mild, moderately severe and severe AP according to the criteria defined by NASPGHAN Pancreas Committee (9).

**Statistical Analysis**

Descriptive statistics for the whole sample were generated as follows: Frequency for categorical variables; mean and standard deviation for continuous variables with normal distributions; median with minimum and maximum values for continuous variables without normal distributions. Chi-square test was used to compare the percentage distributions of categorical data between groups. In order to compare the averages of the groups, the normal distribution of the data was evaluated by Shapiro Wilk test. In the independent groups; T test was used to compare when means’ distributions were normal. Otherwise, Mann Whitney U test was used to compare. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 22.0 package program. Values of P <0.05 were considered as statistically significant.

**RESULTS**

The total number of patients included in the study was 55 and 43 (78.2%) were diagnosed with AP, 8 with ARP and 4 with CP. There was not a statistically significant difference between groups in terms of age, gender and BMI z scores (Table I). BMI Z scores of the patients also did not change according to gender (p=0.303) and age (p=0.133).

When the initial complaints of the patients were examined, it was found that the most common cause was abdominal pain in both groups. The ratio of patients with abdominal pain, vomiting and nausea was 95.3%, 56.3%, 37.5% in group 1, and 91.7%, 66.7%, 33.3% in Group 2, respectively.

In the evaluation of the initial laboratory tests; complete blood count, transaminases, renal function tests and serum levels

**Table I:** Demographic and body mass index Z score characteristics of the patients.

|                      | Group 1 | Group 3 | p      |
|----------------------|---------|---------|--------|
| Age (years), Mean ± SD | 9.9 ± 4.46 | 10.03 ± 4.98 | 0.900  |
| Male, n (%)          | 23 (53.5) | 8 (66.7)  | 0.400  |
| Body mass index Z score, kg/m² | -0.12 ± 1.23 | -0.61 ± 1.54 | 0.300  |

**Table II:** Initial laboratory findings of the patients.

|                      | Group 1       | Group 2      | p     |
|----------------------|---------------|--------------|-------|
| Hb (g/dl)            | 13.3          | 13.66        | 0.250 |
| WBC (/mm³)           | 10170         | 6840         | 0.290 |
| Plt (/mm³)           | 274039        | 287416       | 0.570 |
| Amylase (U/L)        | 943           | 1248         | 0.170 |
| Lipase (U/L)         | 1474          | 1251         | 0.420 |
| BUN (mg/dl)          | 12            | 14           | 0.280 |
| Calcium (mg/dl)      | 9.8           | 9.8          | 0.890 |
| Albumin (mg/dl)      | 4.4           | 4.5          | 0.690 |
| AST (U/L)            | 67            | 41           | 0.810 |
| ALT (U/L)            | 38            | 23           | 0.450 |
| GGT (U/L)            | 32            | 22           | 0.140 |
| ALP (U/L)            | 203           | 384          | 0.560 |
| LDH (U/L)            | 316           | 312          | 0.780 |
| T-bil (mg/dl)        | 0.72          | 0.58         | 0.790 |
| D-bil (mg/dl)        | 0.25          | 0.13         | 0.240 |
| T-chol (mg/dl)       | 140           | 151          | 0.170 |
| TG (mg/dl)           | 67            | 65           | 0.690 |
| D-Dimer (ug/ml)      | 1.6           | 2.2          | 0.160 |

Hb: Hemoglobin (N= 12-17), WBC: White blood cells (N=4000-10000), Plt: Platelets (N=160000-370000), Amylase: N=28-100, Lipase: N=13-60, BUN: Blood urea nitrogen (N=6-23), Calcium: N=8.6-10.2, Albumin: N=3.5-5.2, AST: N=0-40, ALT: N=0-41, GGT: N= 0-60, ALP: Alkaline phosphatase (N=35-130), LDH: N=135-225, T-bil: Total bilirubin (N=0.3-1.2), D-bil: Direct bilirubin (N=0-0.3), T-chol: Total cholesterol (N=0-200), TG: Triglycerides (N=0-150), D-Dimer: N=0-0.05
When durations of hospitalization were compared between groups, it was found to be 7.3 ± 3.6 days in group 1 and 7.4 ± 3.8 days in group 2. There were no statistically significant differences between groups in terms of these parameters (p>0.05).

All patients were performed US and/or CT and/or MRI and/or MRCP were performed according to their clinical characteristics and criteria published by Grover et al. (8). The imaging method applied to the patients and the positive findings are summarized in Table III. The distribution of patients according to the severity of radiological findings are seen in Table IV.

**DISCUSSION**

In this study, we evaluated clinical, laboratory and etiological differences between the children who were diagnosed with AP, ARP and CP. In this retrospective study, 78.2% of our patients had acute pancreatitis, and 21.8% had acute recurrent and chronic pancreatitis. In the study by Poddar et al. (5), 50% of the children were diagnosed with acute and the other 50% were diagnosed with acute recurrent and chronic pancreatitis.

We have also found that AP can have several etiologies during childhood period. The etiologies of our cases were found to be idiopathic (88.5%), stone (2.3%), trauma (2.3%), infections (4.6%) and choledochal cyst (2.3%) in group 1; and idiopathic (50%), congenital anomalies of pancreatic duct (8.3%), allergy (8.3%), autoimmunity (8.3%) and genetic causes (25%) in group 2. In a single center study, the causes of pancreatitis were found as idiopathic (61.9%) and medications (19%) in group 1 and as idiopathic (47%), hereditary pancreatitis (17.6%), abnormality of pancreaticobiliary junction (14.7%) and congenital anomalies of pancreatic duct (8.8%) in group 2 (10).

In the study by Poddar et al. (5), it was reported that no causes could be found in 52.5% of the patients in AP, 70% of the patients in ARP and 88% of the patients in CP. The etiological causes which are mostly described in the literature based on the types of pancreatitis are trauma and biliary causes in acute pancreatitis, biliary causes in acute recurrent pancreatitis and hereditary and pancreas divisum in chronic pancreatitis (5). In a study evaluating 50 cases of acute pancreatitis, etiological reasons were found to be idiopathic (42%) and associated with cholelithiasis (22%), medications (4%), choledochal cyst (4%)

| Table III: Radiological characteristics of patients. |
|-----------------------------------------------------|
| **Number of patients who underwent radiological examination, n** | **Presence of radiological findings n (%)** |
| USG | 55 | 28 (50.9) |
| BT | 23 | 17 (73.9) |
| MRI | 28 | 16 (57.1) |
| MRCP | 30 | 17 (56.6) |

| Table IV: Classification of patients according to the severity of radiological findings (n=55). |
|---------------------------------------------------------------|
| **Findings** | **n (%)** |
| Normal | 27 (49.0) |
| Mild (increase in pancreatic diameter/pancreatic edema) | 23 (42.0) |
| Moderate (peripancreatic inflammation/collection) | 2 (3.6) |
| Severe | 1 (1.8) |
| Necrosis | 2 (3.6) |
| Pseudocyst | 1 (1.8) |

The duration of abdominal pain was found to be 2.5 ± 1.6 days in group 1 and 2.8 ± 2.5 days in group 2. The duration of oral intake cessation was 2.5 ± 1.5 days in group 1 whereas it was 1.8 ± 1.1 days in group 2; and the difference between groups was not statistically significant (p>0.05). The number of patients who used antibiotics was 27 (62.8%) and 5 (41.7%) in group 1 and group 2, respectively. No statistically significant difference was found between groups in terms of antibiotics use (p>0.05).
and pancreas divisum (6%) (11). In our study, infections were found to be the most common cause of acute pancreatitis following idiopathic reasons whereas hereditary causes were found to be more common in acute recurrent and chronic pancreatitis groups following idiopathic causes. In acute recurrent and chronic pancreatitis, mutations are observed in PRSS1 leading to gain-of-function and in SPINK1, CTRC and CFTR leading to loss-of-function. In our study, mutations were detected in CTR, PRSS1 and CTRC among the patients who underwent genetic mutation analyses in our study; and all these patients were included in group 2. As suggested in the literature, genetic analyses are indicated especially for consangenerous marriages, and for recurrent and chronic pancreatitis having a previous history of pancreatitis. Therefore, mutation associated with hereditary pancreatitis could not be shown in group 1.

When clinical scores of the patients in group 1 in this study were examined, it was observed that only 2 cases had pancreatitis at a moderate level and other 41 patients were mild pancreatitis cases. In Group 2, 2 of 12 cases had moderate pancreatitis and 10 were mild pancreatitis cases. Pancreatitis-associated mortality has been reported to be 0-11% in children. In our series, there were no cases who died due to pancreatitis (12). It has been known that complications such as endocrine and exocrine disorders, steatore and diabetes mellitus can be observed in the follow ups of chronic pancreatitis cases (13). Also in our study, there was no endocrine failures; and exocrine pancreas failure was observed in only 1 patient in group 2.

Imaging methods have a very crucial place in the diagnosis, treatment and follow up of pancreatitis. Ultrasound is the first preferred method in acute pancreatitis. Imaging sensitivity of ultrasonography for pancreas is 70% whereas sensitivity of BT is 90%. Computerized tomography is less preferred due to its radiation risk and its less reliability in imaging pancreatic duct compared to MR. However, it is used in severe and complicated pancreatitis cases in order to show necrosis, mass and bleeding. MRCP is a highly sensitive method in showing abnormalities of pancreaticobiliary junction and pancreatic duct. Lack of radiation risk is the advantage of the method (14). Also in this study, USG detected edema, fluid, echogenicity increase and pseudocyst in the pancreas and stones in the biliary tract or pancreatic duct. BT showed increase in the thickness and size of the pancreas, dilatation in the pancreatic duct, and fluid and necrosis in the pancreas. Among the patients who were evaluated by MR, increase in the thickness and size of the pancreas and heterogenicity, necrosis, edema, fluid and pseudocyst were observed in the pancreas. MRCP examination showed prominence in the pancreatic duct, choledochal cyst and heterogenicity, necrosis and edema in the pancreas.

The limitation of this retrospective study was having a single center design. In recent years, there has been an increase in childhood pancreatitis cases as parallel to the world. Our results indicate that the incidence of AP is rising among hospitalized children as in adults. Contrary to adults, AP is a mild disease in children. Most of the cases were idiopathic in accordance with the literature. The most common cause is idiopathic in acute pancreatitis. The most common cause is also idiopathic in acute recurrent and chronic pancreatitis; and it is followed by genetic causes. CTR, SPINK1, CTRC and PRSS1 mutations should be investigated among the patients who had a familial history of pancreatitis. The selection and use of imaging methods are highly important in the diagnosis and follow up of pancreatitis. Patients are required to be followed up closely since AP cases may progress to ARP and CP.

**CONCLUSION**

The incidence of acute pediatric pancreatitis has increased in recent years. Since the epidemiology and clinical findings and manifestations of acute pancreatitis in children differ from adults and may progress to ARP and CP, early diagnosis and management of the disease is very important. The selection and use of imaging methods are highly important in the diagnosis and follow up of pancreatitis.

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