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ORIGINAL ARTICLE

Fecal elastase-1 and ultrasonography for assessment of exocrine pancreatic function in children with cystic fibrosis

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Abstract

Background: Cystic fibrosis (CF) is an autosomal recessive disorder affecting the exocrine functions of many organs including the pancreas. Clinical and laboratory recognition of pancreatic insufficiency is important for proper treatment. Early radiologic detection of pancreatic pathologic changes can help better evaluation. **Objective**s: To correlate exocrine pancreatic function with pancreatic ultrasound changes in CF children. **Methods:** This was a prospective cross-sectional study to assess the exocrine pancreatic function by measuring fecal elastase-1 (FE-1) level and doing pancreatic ultrasound for CF patients. **Results:** A total of 30 CF patients with age range from 3 months to 10 years were included in the study. They were categorized into three age groups; below one year, from 1 to 4 years and above 4 years old. None of our cases was exocrine pancreatic sufficient regarding FE-1 level and most of them (86.7%) had severe fecal elastase deficiency. Before 1 year of age there was no detected abnormal ultrasound findings in pancreas; only 8 older patients had abnormal US detected as hyper-echogenicity of pancreas. Abnormal US was more detected among patients with severe pancreatic insufficiency. The sensitivity of ability of fecal elastase level to predict abnormal ultrasound was 80%, with 84% specificity at cut of point 15.2 µg/g. **Conclusions:** Fecal-elastase-1 measurement in cystic fibrosis children can diagnose the exocrine pancreatic insufficiency even without clinical manifestations of steatorrhea. FE-1 level can predict pathologic changes of pancreas detected by transabdominal ultrasound.

Key words: Cystic fibrosis, pancreatic insufficiency, ultrasound, fecal elastase

Introduction

Cystic fibrosis (CF) is a multisystem disorder inherited as autosomal recessive and caused by more than 2000 different mutations in a single gene on chromosome 7 encoding the cystic fibrosis transmembrane conductance regulator (CFTR) protein, which function as chloride channel and regulatory protein in all exocrine tissues **(1)**. The prevalence of CF in USA populations is reported to be 1 to 4000 live births and higher frequencies are reported in some European countries **(2)** while still the

prevalence of CF in Egypt is not well known **(3).**

Cystic fibrosis foundation consensus report had established the different diagnostic criteria for cystic fibrosis **(2)**.The clinical manifestations in CF are attributed to the disturbed cellular transport of sodium, chloride and bicarbonate leading to thick, viscous secretions in many organs, and increased salt content in secretions of sweat gland **(4)**.

Patients with cystic fibrosis develop progressive loss of exocrine pancreatic function due to defective acinar secretion and obstruction of the intra-pancreatic ducts by thick mucus secretion, leading to the retention of digestive enzymes and establishing a chronic inflammatory process with consequent adipose tissue, and fibrous tissue replacement **(5, 6)**. So, the main pathological findings in the pancreas of CF patients are atrophy, fibrosis and fatty infiltration **(1, 7)**, these pathogenic processes may be implicated in the development of pancreatic dysfunction **(8)**. Pancreatic insufficiency is the most common gastrointestinal complication of cystic fibrosis **(9)**.

Although the exocrine pancreatic insufficiency (EPI) is expected in CF patients, the clinical diagnosis can be challenging, as symptoms are often nonspecific overlapping with other gastrointestinal conditions, with maldigestion or malabsorption particularly for the fat and fat-soluble vitamins including weight loss, colic, bloating, dyspepsia and steatorrhea **(5)**. EPI can negatively impact health of CF children because of the high energy needs for their growth and development **(10)**. The evaluation of exocrine pancreatic function is mandatory for all CF children to confirm EPI either for the screened neonates or the symptomatic older patients, with the purpose of determining the need for pancreatic enzyme replacement therapy (PERT) and nutritional management **(1)** and to follow the decline of pancreatic function in pancreatic sufficient (PS) patients (11).

There is a large number of exocrine pancreatic function tests, most of which are limited in their use, whether due to high cost, low availability and/or difficulty of collecting stool samples for a long period **(12)**. Measurement of fecal elastase-1 (FE-1) is an accurate, easily obtained, FDA approved screening test to classify pancreatic status in patients with CF with a 90-100% sensitivity and a 96-100% specificity, so it becomes a standard of care for patients with CF**(1)**. In pancreatic sufficient (PS) patients with CF, fecal elastase-1 values lie within the normal range, but in those who are pancreatic insufficient (PI) the values are very low **(13)**. Notably, it is low in neonates but reaches normal adult levels by 2 weeks of age (**14**).

In CF, injury to the pancreas occurs early in life. The extent of injury is variable, proved by the variable degree of exocrine insufficiency at birth. In general, about 85% of the CF patients are PI before the age of 1 year **(5)**. Diabetes may also develop in 8-18 % of CF patients over longer time due to impaired endocrine functions of the pancreas as the structural changes progress to affect insulin secreting islets cells **(15)** and it is suggested that worse exocrine pancreatic disease in infancy predicts cystic fibrosis–related diabetes (CFRD) at an older age **(16).**

Although multiple imaging techniques are highly accurate for diagnosing the morphologic changes in pancreas of CF patients, their utility for diagnosing or predicting PI is questionable **(5)**. Therefore, it was important to visualize these morphologic changes and correlate them to the degree of pancreatic insufficiency in the young age.

Imaging of the pancreas using transabdominal ultrasound is a well-known and verified procedure **(1, 5)**. Sonography remains the technique of choice for initial evaluation of the pancreas in patients with CF because it is a fast, accurate, less costly, non-invasive and does not require sedation of the pediatric patients, it also allows examination of the adjacent organs **(6)**. Ultrasonography characteristics of the pancreas in cystic fibrosis are described in earlier studies, and correlated well to CT and MRI findings **(6, 17, 18)**. Some previous studies have

correlated pancreatic function and radiological findings in adult CF patients with pancreatic exocrine failure **(1, 19)**. In this study, we aim to correlate exocrine pancreatic function assessed by faecal elastase-1 to pancreatic ultrasound characteristics in CF infants and children. To our knowledge, this is the first study making this correlation in infancy and young children by US visualization of pancreatic pathologic changes and its relation to age and severity of pancreatic insufficiency.

2-Methods

We conducted a prospective cross-sectional study to assess the exocrine pancreatic function by measuring the concentration of fecal elastase-1 (FE-1) and doing pancreatic ultrasound for cystic fibrosis patients who were diagnosed, followed up, and treated in Pediatric Pulmonology, Allergy and Immunology unit and clinic, in collaboration with Radiology and Clinical Pathology Departments, Faculty of Medicine, Zagazig University, Egypt. This single-center study was conducted in the period between January 2023 and July 2023 including patients with documented diagnosis of cystic fibrosis according to the C.F foundation guideline by positive sweat chloride test and/or presence of two heterozygous mutations or one homozygous mutation on the gene encoding CFTR protein **(2)**.

2.1-Sample size:

Assuming all cases fulfilled the inclusion and exclusion criteria would be included in the study. During the study period (6 months), 5 cases/month, 30 cases were included as a comprehensive sample. By using OPEN-EPI at CI 95% and Power 80%.

2.2-Operational design:

We included CF patients from 1 month to 10 years old of both gender presented with or without clinical evidence of steatorrhea, pancreatic enzymes replacement therapy (PERT) were not discontinued during the study. All cases were recorded in their stable general condition during regular follow up.

The involved patients were assessed for their exocrine pancreatic functions. Exocrine pancreatic insufficiency (EPI) is laboratory defined by a fecal elastase (FE-1) level < 200 µg/g stool, and abdominal ultrasound was performed to detect radiological changes in the pancreas and correlate them with severity of pancreatic insufficiency.

We excluded patients taking drugs to regularize bowel habits, patients with liquid stool three or more times a day during the two weeks preceding the examination, presence of enterostomy/colostomy, short bowel syndrome, dehydrated patients or during pulmonary exacerbations. Also patients who didn't sign the informed consent form were excluded.

We collected data on patient demographics (gender, age, order in family, consanguinity), family history of CF diagnosed cases, history of symptoms (respiratory, gastrointestinal, failure to thrive), anthropometrics (weight, height and related Z score), and pancreatic testing/imaging (FE-1 and US findings) and enrolled the patients in 3 age groups for better interpretation of results.

2.3. Fecal Elastase-1:

For all patients, FE-1 test was determined using a commercial kit (Bioassay Technology Lab., Human Elastase ELISA Kit, Cat.No E0811Hu. China) that employs enzyme-linked immunosorbent assay (ELISA) of monoclonal antibody-based detection system specific for pancreatic elastase-1. Based on lab references, normal FE-1 level is greater than 200 mcg/g. Moderate EPI is defined as 100-200 mcg/g, and severe EPI is defined as less than 100 mcg/g **(20)**. 1g stool sample was added to the 9 mL phosphate-buffered saline and centrifuged for 5 minutes at 5000 rpm then the supernatant was separated and stored at -20°C till used according to the assay procedure of the kits. (www.bt-laboratory.com) The ELISA is human elastase specific, thus exogenous pancreatic enzyme supplements, which are of porcine origin, have no effect on the results.**(21)**

2.4. Abdominal ultrasound findings:

Abdominal ultrasound was performed for each patient in the study group by one of the most expert sonographers to detect radiological changes in the pancreas using convex probe (from 3.5 to 5 MHz) (Phillips IU22) according to body built.

Patients fasted for 4 hours and were examined in the supine position with a transverse or oblique epigastric probe-position using a sufficient amount of probe gel. Axial and para-axial images of the pancreas were derived at the level of pancreatic body and tail; the pancreas was clearly visualized. The US findings were reviewed for parenchymal changes regarding pancreatic echo level. Evaluating the echogenicity of the pancreas was related to signal intensity ratios between liver and pancreas echo levels. Patients with diffuse echogenicity throughout the pancreas were considered to have a fatty pancreas **(22, 23)**.

Pancreatic size was also evaluated by measuring the greatest anteroposterior diameters of the head, body, and tail compared with standardized age-related dimensions of the pancreas **(8)**.

2.5. Statistical Analysis:

Data was statistically described in terms of mean± standard deviation (±SD) or frequencies and percentages when appropriate. The comparison of means of the 3 studied groups was done by one-way ANOVA test. For comparing categorical data, Monte Carlo test was performed. ROC curve was performed to detect the cut-off point and sensitivity and specificity of fecal elastase in differentiation of normal and abnormal ultrasound. Two-sided p values less than or equal 0.05 was considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 25for Microsoft Windows.

2.6. Ethical consideration:

Informed consents were obtained from all the parents or caregivers before inclusion in the study, explaining the value of the study and the procedures that were commenced. The whole study design was approved by the Institutional Research Board of Zagazig Faculty of Medicine, Zagazig, Egypt (IRB#:9387-22-3-2022). Confidentiality and personal privacy were respected in all levels of the study.

3-Results

3.1. Study Characteristics:

A total of 30 CF patients were included in the study. The study population demographic and anthropometric characteristics are shown in [Table 1]. Overall, 19 males and 11 female patients were included. Documented history of CF in the family was reported in 13 out of 30 patients (43.3%), and another 13 patients had a history of positive consanguinity. The mean age of our patients was 41.87± 35.1 months with a ranged from 3 months to 10 years. They were categorized into three age groups; below one year, from 1 to 4 years and above 4 years old. The mean Z score for weight was -2.4± 1.7. patients below 1 year-old and 1-4 years old had lower weight Z score values (-2.8± 1.7 and -2.4± 1.95 respectively) than the >4 years old patients' values (- 1.9± 0.93). The mean Z score for height was -1.9± 2.17 with the age group 1-4 years old had the lowest weight score value (-2.6± 2.7). Regarding clinical presentation, 24 patients (63.3%) presented by steatorrhea as an evidence of pancreatic insufficiency, 70% presented by dehydration and electrolyte disturbance and 63.3% had pulmonary manifestations.

Table 1: Socio-demographic characteristics, anthropometric measures and clinical presentation among the studied CF patients

		Total (30)	<1 year (7)	1-4 years (15)	>4 years (8)
Age in months	(mean± SD)	41.87± 35.1	7.14± 2.97	30.16± 12.4	91.65± 21.25
	Min- Max	(3-120)	(3-12)	(12-48)	(60-120)
Age at diagnosis in months	(mean± SD)	21.6± 32.7	3± 1.53	13.77± 13.7	52.6± 49.8
	Min- Max	(1-120)	(1-5)	(1-48)	(4-120)
Sex Male	Number	19	3	10	6
	%	63.3%	42.9%	66.7%	75 %
Female	Number	11	4	5	2
	%	36.7%	57.1%	33.3%	25%
Family history of diagnosed CF cases	Number	13	4	4	5
	%	43.3%	57.1%	26.7%	62.5%
Consanguinity	Number	13	4	6	3
	%	43.3%	57.1%	40%	37.5%
Z score for weight	(mean± SD)	-2.4± 1.7	-2.8± 1.7	-2.4± 1.95	- 1.9± 0.93
Z score for height	(mean± SD)	-1.9± 2.17	-1.4± 1.67	-2.6± 2.7	-1± 0.64
Weight	(mean± SD)	11.81± 9.1	5.5± 1.63	10.29± 2.87	20.18± 4.17
Height	(mean± SD)	87.1± 23.38	64.14± 6.8	80.8± 13.53	118.88± 9.63
Pulmonary manifestations	Number	19	2	11	6
	%	63.3%	28.6%	73.3%	75 %
Dehydration & hyponatraemia	Number	21	7	9	5
	%	70 %	100 %	60 %	62.5%
Steatorrhea	Number	24	5	14	5
	%	80%	71.4%	93.3%	62.5%

3.2. fecal elastase level:

Most of our cases had sever fecal elastase deficiency, only 4 cases (26.7%) in the age group (1-4 years) had moderate deficiency with no statistically significant difference in the mean FE-1 level between the 3 age groups [Table 2]. None of our cases was considered exocrine pancreatic sufficient regarding FE-1 level.

Table 2: Degree of exocrine pancreatic insufficiency according to Fecal Elastase-1 level

Degree of exocrine pancreatic insufficiency		Total	<1 year	1-4 years	>4 years	P value
Fecal elastase level (µg/g)	Mild to Moderate (100-200)	4	0	4	0	0.139(1)
		13.3%	0%	26.7%	0%	
	Severe (<100)	26	7	11	8	
		86.7%	100%	73.3 %	100%	
	(mean± SD)	51.33±38	32.6± 22.7	63.9± 46.81	44.1± 20.5	0.164(2)

SD: Standard deviation (1) Monte Carlo test (2) One way ANOVA test *: Statistically significant at P ≤ 0.05

3.3. Ultrasound Findings:

Before 1 year of age there was no detected abnormal ultrasound finding of pancreas. Enlarged hyperecheoic pancreas was evident in 2 cases (13.3%) among patient group (1-4 years), and 3 cases (37.5%) among the age group >4 years. Both pancreatic and renal abnormal US finding in the form of enlarged, hyperechogenic pancreas [Figure 1] and mild increased renal parenchymal echogenicity with ill definition of the cortico-medullary outlines denoting

renal affection were more in the older patients; 2 cases (25%) older than 4 years and only one case in the age group (1-4 years) without statistically significant difference in the ultrasound findings in the 3 different age groups [Table 3].

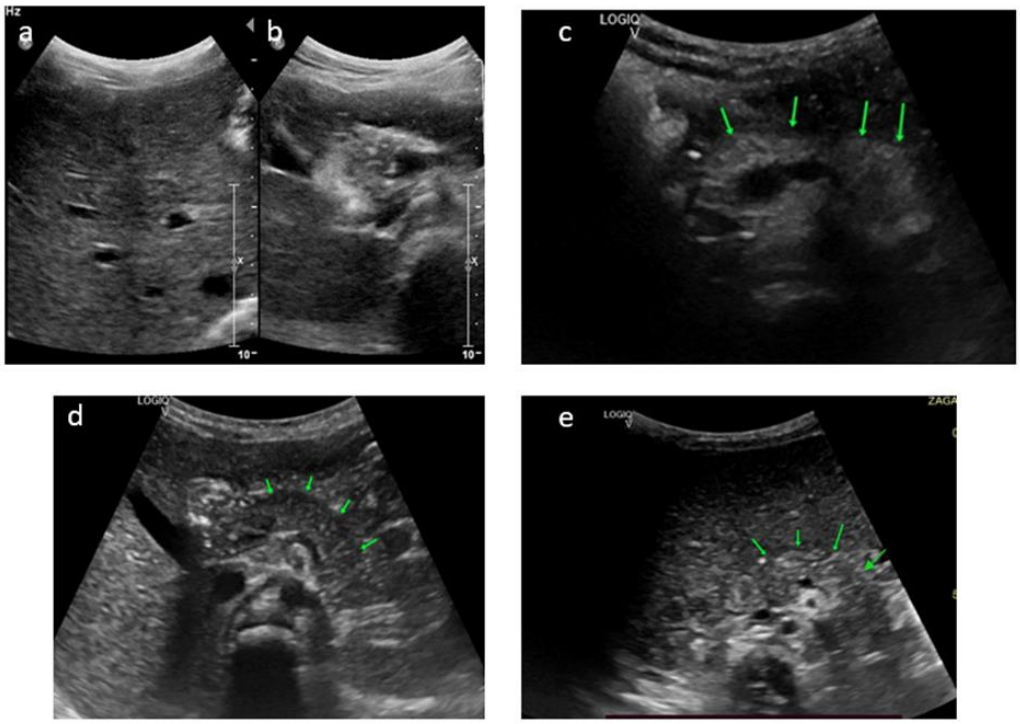

Figure (1): Axial ultrasound images showing:

a. the liver b. pancreas: Images shows mild increased echogenicity of the pancreatic tissue compared to the liver parenchyma.

c. marked enlarged pancreas and increased parenchymal echogenicity.

d. average size pancreas with normal parenchymal echogenicity.

e. slightly enlarged pancreas with increased parenchymal echogenicity.

Table (3): Ultrasound finding among studied group

Ultrasound finding	Total	<1 year No.=7	1-4 years No.=15	>4 years No.=8	P value
Normal	22	7	12	3	#0.062
	73.3%	100%	80%	37.5%	
Pancreatic finding (hyper-echogenic pancreas)	5	0	2	3	
	16.7%	0%	13.3%	37.5%	
Pancreatic and kidney finding	3	0	1	2	
	10%	0%	6.7%	25%	

#Monte Carlo test *: Statistically significant (*P-value≤0.05)*.

3.4. Relations between fecal elastase level and ultrasound findings:

Patient who developed ultrasound changes either in pancreas only (16.7%) or in both pancreas and kidney (10%) were more detected among those who had severe pancreatic insufficiency, only 1 out of the 4 moderate cases had pancreatic and renal ultrasound abnormality. However, these differences were statistically insignificant [Table 4].

The sensitivity of ability of fecal elastase level to predict abnormal ultrasound was 80%, with 84% specificity at cut of point 15.2 µg/g with statistically significant different at (0.02) [Table 5- Figure2].

Table (4): Relation between fecal elastase and US findings among the studied group

Ultrasound	Fecal elastase			P value
	Total (30)	Moderate Insufficiency (4)	Severe Insufficiency (26)	
Normal	22	3	19	0.405
	73.3%	75%	73.1%	
Pancreatic finding	5	0	5	
	16.7%	0%	19.2%	
Pancreatic and kidney finding	3	1	2	
	10 %	25 %	7.7%	

*: Statistically significant at P ≤ 0.05 Monte Carlo test

Table (5): The predictive ability of fecal elastase level to detect pancreatic abnormal US.

Variables	*Fecal elastase*
Cut off	15.2 µg/g
Area under curve (95%CI)	0.68 **(0.01-0.87)**
P-value	**0.02***
Sensitivity	80%
Specificity	84%
PVP	50%
PVN	95.5%
Accuracy	83%

**Statistically significantly different. CI confidence interval*

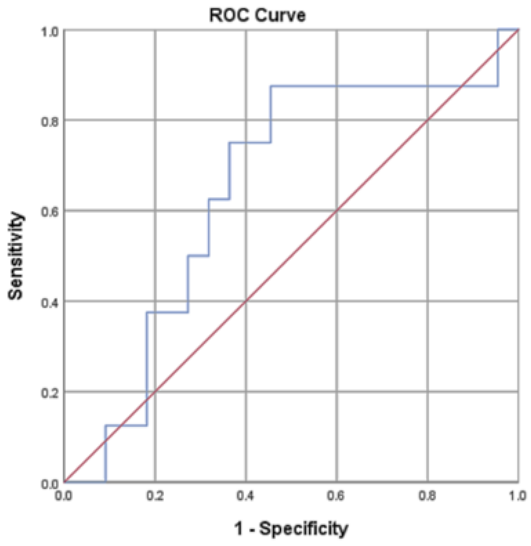

Figure (2): ROC curve for the predictive ability of fecal elastase level to detect abnormal US.

4-Discussion

Exocrine pancreatic insufficiency (EPI) is a major clinical manifestation of cystic fibrosis (CF), and its recognition is important for proper diagnosis and management **(24)**. Clinical findings and laboratory tests are used for diagnosis in the pediatric age. Our study was concerning with evaluation of exocrine pancreatic function in 30 CF children either presented with clinical evidence of steatorrhea or not. Exocrine pancreatic function is laboratory defined by a fecal elastase (FE-1) < 200 mcg/g stool, the lower values indicates the severe insufficiency. It is possible that low FE-1 values are associated with secondary pancreatic insufficiency due to mucosal injury for other causes, but in case of a positive sweat test, a low FE-1 is mostly indicative of primary EPI.**(20)**

The role of imaging for assessment of pancreatic function sufficiency in young CF patients is unclear and to our knowledge this study is the first to characterize the US findings in these patients. Abdominal ultrasound was performed to detect any radiological changes in the pancreas and correlate them with severity of pancreatic insufficiency regarding their FE-1 level.

The age of our patients ranged from 3 months to 10 years with mean of 41.87± 35.1 months. They were 19 males and 11 female patients. For more accurate analysis of data, we categorize the included patients into three age groups; <1 year (7 patients), 1-4 years (15 patients) and >4 years old (8 patients).

The mean age at diagnosis of our patients was 21.6± 32.7 months with reported early diagnosis in the first month of age specially in the younger groups below one year and (1-4 years) age groups, on the other hand, one patient was diagnosed late at the age of 10 years. This is not different from previous studies reported the CF diagnosis within the first months of life prior to the age of 1 year in

most patients, while in fewer percent the diagnosis is not established until after age of 10 years.**(25, 26)** The median age at diagnosis was 4 months according to cystic fibrosis foundation (CFF) Patient Registry Annual Data Report in 2017 **(11)**.

As CF is autosomal recessive inherited disease we documented history of CF in the family in 13 out of 30 patients (43.3%), and another 13 patients had a history of positive consanguinity. Higher percent of reported family history and consanguinity were founded in a previous Turkish study (21,6% and 37,5%) respectively.**(27)**

Z scores for weight and length of less than -2 indicate moderate to severe malnutrition and/or stunting **(28)**. Our patients were falling into these high risk categories as the mean Z score for weight was -2.4± 1.7. Patients below 1 year-old and 1-4 years old had lower weight Z score values (-2.8± 1.7 and -2.4± 1.95 respectively). The mean Z score for height was -1.9± 2.17 with the age group 1-4 years old had the lowest height Z score value (-2.6± 2.7).

Clinically, 63.3% of our patients presented by pulmonary manifestations in the form of persistent or recurrent wheezes or pneumonia or chronic cough, most of them were older than 1 year; 73.3% and 75% among patients 1-4 years and >4 years old respectively had chronic pulmonary manifestations. 70 % of our patients presented by dehydration and electrolyte disturbances mainly in the form of hyponatraemia including all patients younger than 1 year and about 60% of each older groups. Clinical evidence of macroscopic steatorrhea (as large volume of offensive, loose stools associated with abdominal distention or colics) was present in 24 patients (80%) more frequently in the 1-4 years old group (93.3%) followed by those <1 year (71.4%) then the older than 4 years' group (62.5%).

As fecal elastase is the most commonly utilized test in clinical practice **(29),** we measured fecal elastase-1 (FE-1) level for laboratory assessment of exocrine pancreatic functions of our patients. In spite we reported 6 patients without clinically evident steatorrhea, none of our cases was considered exocrine PS regarding FE-1 level. Notably, decreased FE-1 concentration in the stool precedes development of steatorrhea in all patients **(5)**. Most of our patients had sever fecal elastase deficiency (FE-1 <100 µg/g), only 4 cases (26.7%) in the age group (1-4 years) had moderate deficiency (FE-1 100-200 µg/g) with no statistically significant difference in the mean FE-1 level between the 3 age groups indicating that severity of PI is not age related. Pancreatic function is preserved in patients who have certain CFTR variants with residual function **(29)**.

Noteworthy that patients who are pancreatic sufficient (PS) at diagnosis may develop PI with time; while 59% to 71% of infants with CF were diagnosed as pancreatic insufficient at birth, an additional 16% to 20% were turned insufficient by 1 year of age or older **(25)**; so infants with a normal FE-1 at their first diagnosis should be tested yearly thereafter, or when develop symptoms of PI.**(4)** Diabetes may also develop over longer time due to impaired endocrine functions of the pancreas (8–18%) as the structural changes of pancreas progress to affect secreting islets cells **(15)**. Therefore, it was important to evaluate these pathologic structural changes.

Previous studies investigated imaging methods (MRI, computed tomography or ultrasonography) to diagnose EPI in CF patients **(15)**. We performed transabdominal U/S with good visualization for all parts of the pancreas, this is due to the optimal sonic window provided by the relatively low subcutaneous and intra-abdominal adipose tissues and the relative the large left hepatic lobe in children. **(30, 31)**

In this study, we assessed the exocrine pancreatic functions, documented the sonographic changes in the pancreas and correlate them with severity of PI. To our knowledge this is the first time for this correlation in infants and young CF children.

Before the age of 1 year we didn't detect any abnormal ultrasound finding in the pancreas. Enlarged hyperecheoic pancreas was evident in 2 cases (13.3%) among patient group (1-4 years), and 3 cases (37.5%) among

the age group >4 years. Both pancreatic and renal abnormal US finding were detected in the older patients; 2 cases (25%) older than 4 years and only one case in the age group (1-4 years). In spite of our observation that sonographic changes in pancreas occurred in the older patients it didn't have statistical significance, may be attributed to the small number of studied patients.

Previous literatures described the spectrum of pancreatic appearances in CF **(6)**. The only detected parenchymal abnormal finding in our patients was homogenous, hyperechogenic pancreas with enlargement in its size. High pancreatic echogenicity is a measure of fat accumulation in the pancreas to be softer (pancreatic lipomatosis) **(8, 30)** and enlargement of the pancreas corresponds to lipomatous pseudohypertrophy **(6),** while in a previous study conducted on group of older patients more than 15 years old, the US displayed smaller pancreas in CF patients than their matched controls **(8)** which can be attributed to other pathologic sequences in CF including complete atrophy of the pancreas with or without fatty replacement or diffuse pancreatic fibrosis **(6)**. The abnormal changes in the pancreas are a function of the duration and intensity of the CF disease **(31)**. This supports our results as we demonstrated that US evident parenchymal increased echogenicity was recorded after the age of 1 year in the patients with the lowest values of FE-1 levels. And also explain that other pathologic US findings which may need longer time to develop were recorded in previous studies on adult CF patients **(6, 30, 32)**.

In a study by Saglam et al., the pancreas and bilateral kidneys of 60 pediatric patients with type 1 diabetes showed lower shear wave ultrasonographic elastography values than healthy children **(33)**. As 3 of our older patients experienced associated renal parenchymal ultra-sonographic changes; this was an indication of more frequent monitoring for possible endocrine pancreatic affection and development of cystic fibrosis related diabetes.

In this study, we also related transabdominal ultrasound findings of the pancreas in our patients to their exocrine pancreatic function by the measured FE-1 level. We demonstrated that patient who developed ultrasound changes either in pancreas only (19.2%) or in both pancreas and kidney (7.7%) were mainly detected among those who had severe pancreatic insufficiency, only 1 out of the 4 moderate cases had pancreatic and renal ultrasound abnormality. However, these differences were statistically insignificant.

This goes hand by hand with a study which compared endoscopic US findings in patients with FE-1 < 100 mcg/g versus those with 100-200 mcg/g, and found the proportion of patients with abnormal findings was higher among severe than moderate FE-1 defined exocrine pancreatic insufficiency. **(34)**

Our findings support previous studies reporting fatty infiltration of the pancreas as a feature in CF patients with exocrine pancreatic failure **(1, 35)**, they had a hyperechoic pancreas **(8)**. The sensitivity of ability of fecal elastase level to predict abnormal ultrasound was 80%, with 84% specificity at cut of point 15.2 µg/g (P-value 0.02). And vice versa; a recent study reported a link of pancreatic hyper-echogenicity to the exocrine insufficiency. ***Engjom T et. al***, demonstrated that the presence of hyper-echogenic pancreas seems to predicts exocrine pancreatic insufficiency in CF patients in the age group from fifteen to forty-five with an acceptable diagnostic accuracy, also they didn't report other prevalent ultrasonographic parenchymal changes. The prevalence of US changes in CF patients younger than fifteen was not explored in their study **(8)**.

Our study **was limited** by its relatively small sample size especially when evaluating the difference between age groups. Large multicenter studies with longer follow up periods are needed to evaluate detect the prevalence of pancreatic involvement in CF children and determine its severity and the possible affection of endocrine functions of the pancreas.

5-Conclusion

We conclude that fecal-elastase-1 measurement in cystic fibrosis children can

diagnose the exocrine pancreatic insufficiency even without clinical manifestations of steatorrhea. FE-1 level can predict pathologic changes of pancreas detected by transabdominal ultrasound.

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