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ORIGINAL ARTICLE

Chylous Disorders: A Rare Entity in Children

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ABSTRACT

Objective: The aim of this study is to share our experience about this rare disorder including clinical features, management and outcome perspectives.

Study Design: Retrospective, cross sectional study.

Place and Duration of Study: This study was conducted at the department of Gastroenterology, The Children's Hospital & Institute of Child Health, Lahore, between the periods of January 2013 to December 2017.

Patients and Methods: The database included age (months), gender, clinical presentation, laboratory parameters, management and outcome. The data was analyzed by SPSS version 22.

Results: Twenty-four children were identified who met the criteria as chylous disorder. There were 15 (65.2%) females with interquartile range (IQR) of 144(1) months. Fourteen (58.3%) patients had primary etiology while rest 10 (41.6%) had secondary cause. Intestinal lymphangiectasia was the leading cause in 7 (50%) followed by idiopathic chylous ascites, effusion and syndromic chylous disorder. Among the secondary causes were post-surgical and tuberculosis in 4 (40%) each and two (20%) of malignancy (adenocarcinoma of colon, myxoma of heart and intestine). Majority of patients had lymphopenia and hypoalbuminemia. Acute management included stabilization with albumin, fluid aspirations to decompress, octreotides and dietary intervention. Eight children required ascitic tap and five pleurodesis for effusion and ascites. The majority of children did well on follow-up on medium chain triglycerides (MCT) oil and 3 (12.5%) children expired due to non-compliance issues, severe hypoalbuminemia and concurrent infections.

Conclusion: Chylous disorder is a rare entity; symptoms control is good on dietary modification with MCT oil and supplemented deficient vitamins and required surgical intervention when medical measures have failed.

Key Words: *Chylous disorder, Intestinal lymphangiectasia, Children*

INTRODUCTION

First description about the lymphatic system was given by Asellius, centuries ago followed by Waldmann's who published his paper on chylous disorder (Waldmann's disease) in 1961.[1] Chylous disorders are still considered a rare disease in children and literature is quite sparse about the prevalence studies.[2] Chylous disorders are

broadly categorized into primary (hereditary) and secondary (acquired) forms with variable age of presentation.[3] Primary disease presents in younger age group and secondary form is more prevalent in older children and adults.

Excessive productions of lymph or obstruction to lymphatic system leads to leakiness of lymph from lacteals leading to various manifestations. Gastrointestinal presentation includes malabsorptive diarrhea, abdominal distension with or without pain and failure to thrive. Hypoalbuminemia leads to generalized body swelling, worsening ascites, pleural effusion or pericardial effusion. Chylous pleural effusion presents with tachypnea, respiratory distress and labored breathing.[4]

The diagnostic triad include lymphopenia, hypoalbuminemia and hypogammaglobinemia for patients primarily presenting with malabsorption in addition to hypocalcemia.[5] Fluid aspiration from pleural and peritoneal cavities has milky appearance, triglyceride content of >210mg/dl, ratio of pleural fluid to serum cholesterol<1.0. Intestinal lymphangiectasia is diagnosed on endoscopic findings of characteristic starry sky appearance on fat protocol and biopsy suggestive of dilated lacteals. Lymphangiogram and lymphangiosynctigraphy are important diagnostic tools but facilities and risk of anaphylaxis are limitations.[5-7]

Medical management is based on acute stabilization of these children with albumin, fluid aspirations to decompress, octreotides and dietary intervention. Fat free diet and medium chain triglycerides (MCT) oil are the two long term treatment option in these children with good outcome in addition to managing underlying secondary causes. Refractory cases are the candidates for more advanced options like Sirolimus with variable results.[8]Surgical interventions is required in those cases where the child is non-complaint and refractory cases mainly for chylous ascites and pleural effusions. Outcome is mainly dependent on the main underlying cause and secondary/acquired form has excellent prognosis as compared to primary form.[8,9] Mortality is mainly due to non-compliance issues, severe hypoalbuminemia and concurrent infections.

The aim of study is to share our experience about this rare disorder including various clinical forms and features, management and outcome perspectives.

PATIENTS AND METHODS

It was a retrospective, cross-sectional study conducted at the Department of Pediatrics, Division of Gastroenterology, The Children's Hospital & Institute of Child Health, Lahore. The data base of children admitted or seen with the diagnosis of chylous disorders during the period from January 2014 to December 2018 was collected and reviewed. Chylous disorder was defined as any child who has presented with lymphopenia, hypoalbuminemia, hypogammaglobulinemia (low IgG) in addition to chylous fluid (milky) aspiration from serous cavities.

The inclusion criteria were; included children from neonatal age to 18 years of age of both sexes and who had any two of the following

1. Milky (chylous fluid) aspirate
2. Hypoalbuminemia <2.5 g/dl
3. Lymphocytopenia<30%
4. Hypogammaglobulinemia

We excluded all other causes of low albumin, hypogammaglobulinemia and lymphopenia like celiac disease, primary immunodeficiency states and inflammatory bowel disease.

The database was searched from manual and electronic record with the search key using intestinal lymphangiectasias, starry sky appearance, chylous ascites or chylothorax in addition to lymphangiography and lymphoscintigraphy. The demographic database, clinical forms and presentation, physical examination, absolute lymphocyte count, albumin level, immunoglobulins G, chylous fluid analysis and triglyceride level and imaging studies if done were recorded.

Statistical analysis was carried out by using the Statistical Package for Social Sciences version 22 (SPSS Inc., Chicago, IL, USA). Categorical data were summarized as number and percentages whereas continuous data were summarized as mean, standard deviation (SD), and range. Comparison between groups for categorical

variables was carried out using Chi-square test or Fisher's exact test whereas for continuous data student t-test or Mann Whiteny U test were used. A p-value less than 0.05 was considered significant where applicable. This study was approved by the Institutional Review Board and conducted according to the principles of the Helsinki Declaration.

RESULTS

Twenty-four children were identified who met the criteria as chylous disorder. There were 15 (65.2%) females with median age of 144(1%) months. Fourteen (58.3%) patients had primary etiology and intestinal lymphangiectasia was the leading cause in 7 (50%) followed by idiopathic chylous ascites and effusion in 4 (28.5%), syndromic with chylous disorder and total agenesis of lymphatic vessels. Ten (39.1%) children had secondary cause and among them were post-surgical and tuberculosis in 4 (40%) patients each and 2 (20%) patients had primary malignancy with chylous fluids in the peritoneal cavity.

Majority 18 (75%) of patients had lymphopenia and hypoalbuminemia as well as low immunoglobulins G levels. In addition, 19 (79.1%) had hypocalcemia and eight children had manifested with tetany in both the group. Acute management included stabilization with albumin, fluid aspirations to decompress, octreotides and dietary intervention. Eight children required multiple ascitic tap and catheter placement for continuous decompression. Five children underwent pleurodesis for recurrent pleural effusions and ascites. The majority of children did well on follow up on MCT oil and three (12.5%) children expired due to non-compliance issues, severe hypoalbuminemia and concurrent infections.

TABLE 1: Different forms of chylous disorders in Pakistani children (n = 24)

Etiology	Number (%)
Age	
<12month	6 (25.0)
12-60 month	7 (29.1)
>60 month	11 (45.8)
Gender	
Female	15 (62.5)
Male	9 (37.5)
Primary chylous disorder	**14 (58.3)**
Intestinal lymphangiectasia	7 (50.0)
Idiopathic Chylous ascites and chylothorax	4 (28.5)
Agenesis of lymphatics	1 (7.1)
Syndromic with chylous disorder	2 (14.2)
Secondary chylous disorder	**10 (41.6)**
Post-surgical	4 (40.0)
Tuberculosis	4 (40.0)
Malignancy	2 (20.0)
Well on medical management	**16 (66.6)**
Surgical intervention	
(Pleurodesis, thoracic duct ligation)	5 (20.8)
Resection of intestinal myxoma	1 (4.1)

TABLE 2: Clinical characteristics of patients with primary and secondary chylous disorders (n = 24)

Characteristics	Primary chylous disorders (n=14)	Secondary chylous disorders (n=10)	p-value
Loose stools	**13**	**02**	**< 0.001**
Body swellings	14	10	0.50
Failure to thrive	14	06	0.20
Tetany	06	02	0.38
Clubbing	**11**	**02**	**< 0.001**
Chylothorax	06	06	0.68
Chylous ascites	05	06	0.40
Expired	02	01	1.00

TABLE 3: Biochemical parameters in patients with different chylous disorders (n=24)

Characteristics	Mean
Age (Months)	71.1±66.20
Haemoglobin g/dl	10.47±1.46
Lymphocyte count 10^9/l	24.30±5.48
Albumin g/dl	1.99±0.24
Serum calcium mg/dl	7.31±0.66
Serum immunoglobulin G mg/dl	371±135.5
Ascitic fluid triglyceride mg/dl	243±35.67

DISCUSSION

Chylous disorders are rarely reported from Asian countries and broadly classified as primary and secondary chylous disorders.[3] The exact prevalence of this condition is not known even in the developed world because of lack of epidemiological studies. Previously reported incidence of chylous ascites was 1 in 20000 in adult population and none of the studies have mentioned about children.[2,10] The mean age at

presentation was 71.1 ± 66.2months in chylous disorders which is consistent with the world literature.[10] There is no gender predilection in the previous studies but in our study, females clearly outnumbered males.

The presentation of primary chylous disorders depend upon the etiology. Generally, the children in the primary disorders are younger as compared to secondary disorders except the post-surgical cases.[4,11] Intestinal lymphangiectasia is the commonest disorder of primary etiology in younger children and presents with malabsorption which is similar to current study as 50% of the primary chylous disorder were intestinal lymphangiectesia.[12]Chylous ascites and pleural effusions are the two other main presentation with abdominal distension and respiratory distress with or without diarrhea. Total agenesis of lymphatic vessels has been described in the literature and presented with chylous ascites or effusion[13], one of our case was of total agenesis of lymphatic vessels and presented with bilateral chylothorax and managed conservatively but finally required surgical intervention. Rarely children have syndromic features and presents with generalized edema, chylous ascites or effusion. In our study, we had two children with syndromic features and genetically proven as Chapel and Hennekam syndromes.[14,15]

The secondary chylous disorders are usually post-surgical, infections, trauma and malignancies. Children with post-cardiac surgery have chylothorax as a complication because of the thoracic duct trauma/obstruction and high right heart ventricular pressure. This is consistent with our study as 40% of secondary etiology cases were post-cardiac surgical patients for different reasons.[16,17] Infection is another common etiology especially abdominal tuberculosis can lead secondary chylous fluid collection in the peritoneal cavity. In this study around 40% cases were due to tuberculosis diagnosed on clinical and laboratory parameters.[18] Malignancies especially abdominal lymphomas are also known to cause secondary chylous disorder in adults and few pediatric cases are also reported in the literature.[19] In our study, two children had primary malignancy (adenocarcinoma of colon, myxoma of heart and intestine) and secondarily developed chylous ascites.

The diagnosis of these cases include the high index of clinical suspicion with support from laboratory parameters including lymphopenia, low levels of albumin and hypogammaglobinemia.[21] Paracentesis from the cavities like ascites or pleural effusion show milky appearance because of chyle in the fluid. High triglyceride content of the aspirated fluid is suggestive of chylous disorder. Intestinal lymphangiectasia is diagnosed on endoscopic findings of characteristic starry sky appearance on fat protocol and tissue biopsy suggested of dilated lacteals.[12] Lymphangiogram and lymphangiosynctigraphy are important diagnostic tools but facilities and risk of anaphylaxis are limitations.[5-7] In this study, the main diagnostic parameters were hypoalbuminemia, lymphopenia and decreased IgG levels in addition to aspiration of milky fluids. Lymphangiogram facility was not available in our center.

Primary management is based on conservative treatment to stabilize these children with paracentesis, albumin infusion, octreotides, dietary intervention and TPN. Acute stabilization of these children require to keep on nothing per oral, daily TPN with correction of electrolytes and albumin in addition to paracentesis and octreotides. Medium chain triglycerides (MCT) oil, fat soluble vitamins and dietary restriction is the mainstay of treatment in these children with good outcome but underlying secondary causes should also be addressed.[21,23] Majority of our children are well on dietary management with MCT oil, fat soluble vitamins and dietary restriction. Few are the candidates for more advanced options like sirolimus with variable results.[24]Two of our children were started on sirolimus and one had good response but other one finally required surgical intervention. Surgery is required in non-complaint and medically failed cases mainly for chylous ascites and pleural effusions. Five of our children underwent pleurodesis and thoracic duct ligation, one child required resection of intestinal myxoma and few had paracentesis for acute distress.[25] Outcome is mainly dependent on the cause and generally primary form has more guarded prognosis as compared to secondary form. Mortality is mainly due to non-compliance issues, severe hypoalbuminemia and concurrent infections. In this study, three children expired and main reason was non-compliance to nutritional

advice complicating with severe hypoalbuminemia and infections.

Limitations of this study include the retrospective, single center study with small sample size but all were referred cases being a tertiary care center, showing the rarity of these cases. More prospective studies are required to understand the natural course of this rare disease and management outcomes.

CONCLUSION

Chylous disorder is a rare entity and primary etiology is more common than secondary pathology in children. Clinical index of suspicion with hypoalbuminemia, lymphocytopenia and hypogammaglobinemia in addition to chylous aspirate have the high diagnostic yield short of lymphangiography and lymphoscintigraphy. Symptoms control is good on dietary modification with MCT oil and supplemented deficient vitamins. Generally, outcome is better if acute crises are handled properly and supervised dietary interventions are applied and followed more closely.

Conflict of interest: None

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