Original Article

Complications, Associations and Outcome in Children with Congenital Chloride Diarrhoea

Iqtadar Seerat and Muhammad Arshad Alvi

ABSTRACT

Objective: To determine the complications and associations of congenital chloride diarrhoea to improve prognosis.
Study Design: Retrospective study.
Place and Duration of Study: This study was conducted at the Paediatric Gastroenterology, Hepatology & Nutrition, King Faisal Specialist Hospital & Research Centre, Jeddah, Kingdom of Saudi Arabia from September, 2003- September, 2016
Materials and Methods: A total of 19 confirmed cases of children with congenital chloride diarrhoea between birth and 14 years of age were included in this study. The data was collected from the ICIS used in hospital power chart system. The data was presented in form of a pie chart and a table.
Results: Out of these 19 cases we found 12(63%) patients with failure to thrive,12(63%) patients with motor developmental delay, 12 (63%) patients with short stature, 13(68.4%) patients with renal abnormalities, 6(31.5%) with vitamin D deficiency, 3(15.7%)with iron deficiency anaemia, 2(10.4%) with congenital heart disease (Transposition of great arteries& Ventricular septal defect) and 1 case of colitis (5.2%).
Conclusion: Due to various associations and complications of congenital chloride diarrhoea we conclude that early diagnosis and regular follow up with multidisciplinary team comprisingPaediatric Gastroenterologist, Nephrologist, Endocrinologist, General Paediatrician for developmental assessment and Dietician are required to improve prognosis.

Key Words: Congenital Chloride Diarrhoea (CLD), multidisciplinary team, complications, associations

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INTRODUCTION

Congenital chloride diarrhoea (CLD) is an autosomal recessive disease caused by mutations in the SLC26A3 gene. It is characterized by secretory watery diarrhoea of prenatal onset with high faecal chloride concentration and metabolic alkalosis.[1,2,3]
Due to the loss of the SLC26A3 mediated transport in the surface epithelium of the ileum and colon there is an impairment of active chloride/bicarbonate exchange which ultimately results in hyponatraemia, hypokalaemia, hypochloraemia and metabolic alkalosis. The intra-uterine diarrhoea leads to polyhydramnios and premature birth.[4] If not treated adequately most patients will die due to severe dehydration within the 1st few months of life.

Department of Paediatric Gastroenterology, Hepatology & Nutrition, King Faisal Specialist Hospital & Research Centre, Jeddah, Kingdom of Saudi Arabia.

Correspondence: Dr. Iqtadar Seerat, Consultant Paediatric Gastroenterology, Hepatology & Nutrition, King Faisal Specialist Hospital & Research Centre, Jeddah, Kingdom of Saudi Arabia
Contact No: 00966559629265
Email: iseerat@hotmail.com

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The diagnosis is established when faecal chloride concentration exceeds 90 mmol/l after correction of dehydration. Congenital chloride diarrhoea should be treated with full oral replacement of sodium and potassium salts to achieve normal growth and avoid renal damage. In the literature there is mentioning of a variety of complications and associations in relation with congenital chloride diarrhoea. In this study we focused on this important aspect of disease. In our all 19 cases the genetic testing revealed a novel homozygous mutation in exon 5 of the SLC26A3 gene that encodes the protein regulating chloride bicarbonate absorption in distal ileum and colon.[5]

MATERIALS AND METHODS

A total of 19 confirmed cases of children with congenital chloride diarrhoea between birth and 14 years of age were included in this retrospective study. The study was carried out for the time period from September, 2003- September, 2016.The data was collected from the ICIS used in hospital power chart system. The data was presented in form of a pie chart and a table.

RESULTS

The table 1 shows the salient features in history and also embarks on important clinical manifestations in

our group of patients. The figure 1 reveals the number of complications and associations which our patients have come across over a period of time. Out of these 19 cases we found 12 patients (63%) were failure to thrive (weight below the 5th centile), 12 patients (63%) with motor developmental delay, 12 (63%) patients with short stature, 13 patients (68.4%) with renal abnormalities, 6 patients (31.5%) with vitamin D deficiency, 3 patients (15.7%) with iron deficiency anaemia and 2 patients (10.4%) with congenital heart disease (Transposition of great arteries & Ventricular septal defect) and 1 patient (5.2%) with colitis.

In total of 19 patients 13 developed renal abnormalities like end stage renal disease, nephrocalcinosis, increased echogenicity of both kidneys and renal stones. The renal abnormalities were picked up with help of renal ultrasound scans.

Table No.1: History and Presentation

Salient Features	Number of patients
Premature Birth	6
Polyhydramnios	8
Family History	6
Abdominal distension	14
Diarrhoea	19
Electrolyte Imbalance	19
Dehydration	19

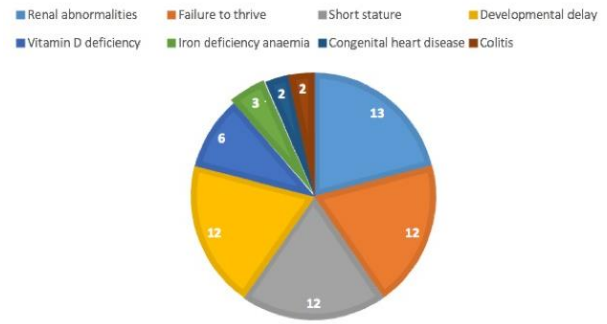

Figure No.1: Number of complications and associations observed in 19 patients with congenital chloride diarrhoea

DISCUSSION

After the two American cases partly of Italian descent more than 250 cases with CLD have been reported worldwide. The incidence of CLD was established to be 1/14,000 in Kuwait compared to that of Finland 1/43,000.This high incidence in Kuwait and Middle East may be due to the multigenerational practice of consanguineous marriages and the autosomal recessive manner of inheritance of the disease.[5,6]

In our group of patients we were able to pick up complications and associations like failure to thrive, motor developmental delay, short stature, vitamin D deficiency, iron deficiency anaemia, renal abnormalities, colitis and congenital heart disease. Congenital chloride diarrhoea seems to be associated with an increased risk for intestinal inflammation. In the Finnish series, at least 3 patients have a diagnosis of unspecified colitis or crohn's disease.[7,8]

As down regulation of SLC26A3 emerges in the inflamed colonic mucosa a link between intestinal inflammation and the primary defect of CLD is possible. In our 19 patients only one child developed rectal bleeding for which he has had both upper GI endoscopy and colonoscopy.

The colonoscopy showed small discreet ulcers and inflammation in left colon. The biopsies from the affected area confirmed colitis. The upper GI endoscopy was unremarkable. After appropriate treatment his symptoms of colitis have settled. Although a slightly increased risk for gastrointestinal malignancies among the carriers of SLC26A3 has been proposed but in our small study no malignancies were found.[9]

In this study we found 2 cases of congenital heart disease with transposition of great arteries and ventricular septal defect, therefore it is worth targeting and screening this group of patients for congenital heart disease with help of echocardiography.

The nutritional status of patients should be improved with the help of a dietician as they are prone to have recurrent episodes of dehydration during which the oral intake decreases. Due to lack of nutrition and calories children lose weight and also exhibit manifestations of nutritional deficiencies like iron, vitamin D. In our twin centre (King Faisal Specialist Hospital & Research Centre) Riyadh, children with congenital chloride diarrhoea requiring renal transplant are given nutrition through gastrostomy to overcome malnutrition.

Although the overall long-term outcome in the Finnish series of CLD is favourable, the relatively high incidence(28%)of chronic renal disease underlines the importance of early diagnosis, adequate salt substitution and regular follow-up of CLD.[10] In our study 68.4% children with congenital chloride diarrhoea were found to have renal manifestations. This is mainly due to inclusion of echogenic kidneys (53.85%) which were picked up on serial renal ultrasound scans.

In the literature many other associations in relation with congenital chloride diarrhoea like hernia, subfertility, cystic fibrosis etc. are reported.[11,12,13,14,15] In our group of patients no other significant complications or associations were observed. We treat our patients with oral sodium chloride, potassium chloride salts and omeprazole. We also emphasise on the importance of keeping good compliance with medications to improve the long term prognosis.[16]

CONCLUSION

We conclude that early diagnosis and regular follow up with multidisciplinary team are required for prevention of complications to improve prognosis.

Conflict of Interest: The study has no conflict of interest to declare by any author.

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