

## Congenital Chloride Diarrhoea

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**Abstract:** Congenital chloride losing diarrhea (CLD) is a medical emergency case in pediatrics. It is a rare genetic disorder caused due to mutation of chromosome 7. It is commonly seen in Saudi Arabic countries, It is seen in early neonates with features of absence of meconium, "urine like diarrhea", antenatal finding shows hydramnious child in fetus, fecal chloride concentration is more than 90mmol/l. The main treatment for CLD is continuous lifelong replacement of faecal loss water, NaCl and KCl by salt substitution therapy, use of proton pump inhibitor etc, with early diagnosis long term outcome is favourable.

### I. Article

Congenital chloride diarrhea (CLD) is rare autosomal recessive disorder caused by mutation in the CLD gene called the solute carrier family 26 member 3 gene in the chromosome 7. It is also known as Synonyms Darrow Gamble Syndrome. It first came to knowledge by Gamble et al and Darrow simultaneously in 1945, both describing it by a child who had persistent watery diarrhea, a high faecal concentration of chloride, hypochloramia and metabolic alkalosis. It is particularly common in Kuwait and Finland with an incidence of 1/3200 due to high consanguinity marriage. Till date only 1 case has been diagnosed in India at Jaslok Hospital. While it is mostly seen in Finland Poland, Saudi Arabia and Kuwait.

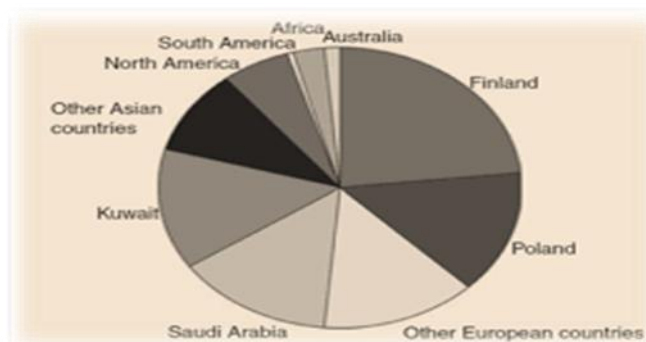


fig1: countrywise distribution of CLD

Congenital chloride diarrhea is caused by an abnormality in the active transport of chloride from the distal ileum and colon. The basic defect of CLD is the loss of SLC26A3 mediated transport in surface epithelium of distal ileum and colon. It is probably resulting from an absence or impairment of  $\text{Cl}^-/\text{HCO}_3^-$  exchange mechanism in these segments of intestine. The absence of  $\text{HCO}_3^-$  causes the intestinal content to become acidic resulting in restriction of  $\text{Na}^+$  absorption and increase in secretion of  $\text{K}^+$ . This defect leads to intestinal loss of both NaCl and fluid, and watery  $\text{Cl}^-$  rich diarrhea. If untreated there will be hypochloremia, hyponatremia and dehydration which results in activation of rennin angiotensin system. The above finding together with hydramnious invariably presents and meconium lacking in strong evidences of intrauterine diarrhea.

The resulting hyperaldosteronism induces  $\text{Na}^+$  reabsorption in the distal colon and especially in the distal tubules of the kidney, resulting in the secondary  $\text{K}^+$  depletion which leads to an increase in both hypokalemia and metabolic alkalosis in untreated CLD, giving main laboratory finding as hypochloremia, hypokalemia and metabolic alkalosis.

### II. Clinical Presentation

- **Antenatal** - Fetus develops "urine like diarrhea" in utero resulting in polyhydraminous, giving evidence of lack of meconium at birth. The babies are born prematurely presumably as a consequence of the hydramnious. During the fetal growth, the mean length is normal for the duration of gestation, while the mean weight is slightly higher probably due to intestinal accumulation of water.



Fig 2:Urine like diarrhea

Amniocentesis reveals that there is an elevated bilirubin and alpha fetoprotein level. The ultrasonographic report shows that there is distended and large bowel loops for which it is often misdiagnosed as bowel atresia or intestinal occlusion and often go for unnecessary surgical intervention after birth

- **Neonatal** - There is absence of meconium was noticed on the first day of life. Diarrhea is often unnoticed because of the fluid in the diaper is thought to be urine. In fact several patients in whom diarrhea was not observed were reported to pass large volume of urine. On the very first day of life about 150 ml fluid was lost in the stool. In the first 3 months of life, the sum of concentration of  $\text{Na}^+$  and  $\text{K}^+$  usually exceeds the concentration of  $\text{Cl}^-$ . Stool ph remains between 4 to 6 against normal range is 7- 7.5.

The baby shows large and distended abdomen , with X-ray showing loops of ileum and colon as dilated with air and fluid , misdiagnosed as intestinal occlusion or aganglionic segment due to the fact of bowel distension ,normal peristalsis and polyhydraminous.

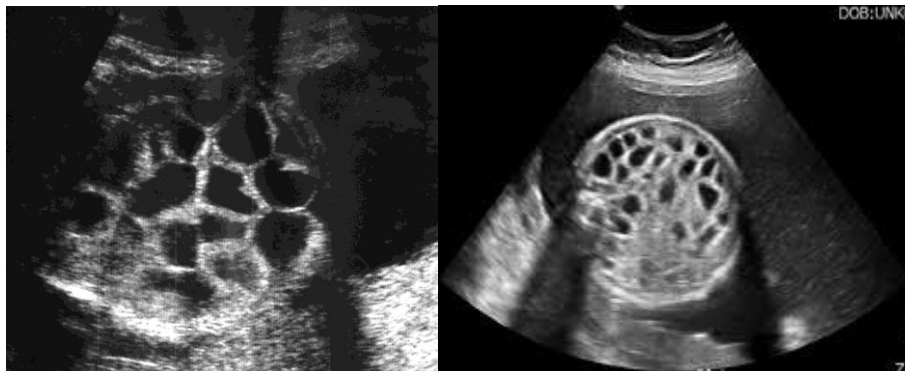


Fig:3-Antenatal sonogram showing multiple dilated bowel loops

Serum electrolyte and ph at first hour of life shows low concentration of  $\text{Na}^+$  and  $\text{Cl}^-$ . This inability to maintain normal concentration of  $\text{Na}^+$  in the first week of life suggesting immaturity of aldosterone system.

#### Complication Of CLD

- Diarrhea and fecal incontinence - the amount of stool per day ranges from 2 to 7 liters /day.
- Renal injury
- Male sub fertility
- Hyper uremic and gout
- Increase concentration of sweat  $\text{Cl}^-$

### III. Management

The most important treatment is to maintain the normal serum electrolyte level by salt replacement therapy immediately after birth

- Salt Substitution Therapy With NaCl And KCl** – In early neonatal period the amount of NaCl and KCl in substitution therapy is added to intravenous maintenance fluid as follows 120-300 ml/day (in patients aged 0-7 days) and 500-700 ml/day(in patients more than 7 days).Administration of salt substitution is gradually changed from intravenous to per oral therapy with 3-4 daily dose.

- ii) **Proton pump Inhibitor-** Treatment with omeprazole was associated with reduction in the volume and frequency of stools and the cessation of inconsistency in case of CLD. This improvement is due to the inhibition of gastric chloride secretion .
- iii) **Oral butyrate** – It is easily administered, useful in preventing severe dehydration episodes. It stimulates the intestinal water and ion absorption through a variety of mechanism, including activation of parallel Cl<sup>-</sup>/butyrate and Na<sup>+</sup>/H<sup>+</sup> exchanger.
- iv) **Cholestyramine** – It binds acid and reduces intestinal secretion resulting in moderate reduction in diarrhea for 2-4 weeks. In children short courses can be used to temporarily reduce diarrhea and prevent soiling..
- v) **Captopril** – It prevents the conversion of angiotensin I and angiotensin II by inhibition of ACE, a peptidyl dipeptide carboxyl hydrolase .Angiotensin II also stimulates aldosterone secretion from the adrenal cortex, thereby contributing to sodium and fluid retention.

#### IV. Outcome

During last 40 years CLD has been changed from most fatal disorder to a treatable disease with an established genetic basis .Prompt recognition and an adequate replacement of faecal loss of chloride ,sodium ,potassium and water are mandatory for satisfactory disease outcome.

#### V. Acknowledgement

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