Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 7 (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

Pathogenic Deletion in the CLCNKB Gene in Parents of a Double First-Cousin Consanguineous Marriage: Bartter Syndrome with Delayed Diagnosis and Fatal Renal Outcomes in Two Siblings- a Case Report

Ali A. Al-Makramani

Department of Pediatrics, Faculty of Medicine, Jazan University, Jazan, Saudi Arabia.

Email ID makra3@yahoo.com. , aalmakramani@jazanu.edu.sa,

***Corresponding Author:**

Ali A. Al-Makramani

Department of Pediatrics, Faculty of Medicine, Jazan University, Jazan, Saudi Arabia.

Email ID makra3@yahoo.com. , aalmakramani@jazanu.edu.sa

Cite this paper as: Ali A. Al-Makramani, (2025) Pathogenic Deletion in the CLCNKB Gene in Parents of a Double First-Cousin Consanguineous Marriage: Bartter Syndrome with Delayed Diagnosis and Fatal Renal Outcomes in Two Siblings- a Case Report. *Journal of Neonatal Surgery*, 14 (7), 1001-1006.

ABSTRACT

The uncommon Bartter syndrome (BS) type III (classic) results from chloride voltage-gated channel Kb (CLCNKB) gene mutations affecting the chloride channel ClC-Kb in the kidneys' distal tubules. Nephrocalcinosis, premature birth, failure to thrive, and early-onset maternal polyhydramnios can or cannot manifest as their symptoms. We present the unique, rare, and novel case of type III BS associated with consanguineous parents (double first cousins) of two children [male 7.5 years, female 4 months] with a fatal outcome [mortality due to end-stage renal failure]. The male patient is also the first case with Type III BS that has been followed up for such a long time. Antenatal polyhydramnios was associated in both cases. The two siblings had different courses of their clinical presentations, signs, symptoms, and complications. Observations at different times revealed metabolic alkalosis, growth retardation, hypokalemia, hyponatremia, hypochloremia, anemia, hepatomegaly, superinfections, and high levels of serum bicarbonates. After their death, the CP was advised to undergo genetic counseling, which recommended preimplantation genetic diagnosis, which they willingly agreed to and are currently in the process of preparing for.

Keywords: *CLCNKB; Bartter syndrome; hypokalemia; metabolic alkalosis; consanguineous marriage..*

1. INTRODUCTION

Consanguinity, the practice of marriage between genetically related individuals, raises concerns about the increased risk of genetic disorders in offspring. This is because both parents are more likely to have the same genetic mutation [1], which can cause autosomal recessive disorders (ARD) like cystic fibrosis and thalassemia [2]. Consanguineous parents (CP) carrying the same recessive gene have been found to have a higher incidence of ARDs. Around 20% of the global population prefers consanguineous marriages, with prevalence varying across societies depending largely upon geolocation, culture, social benefits, migration, and religion [3]. Rural areas tend to have a higher number of consanguineous marriages due to younger marriages, lower socio-economic status, and education. Western/European nations have lower than 0.5%, while India has 9.9%. Arab nations have 20-50% prevalence, with first-cousin marriages being common [3,4]. A study found that children born after first-cousin marriages had a 4.4% higher risk of dying before they were born [5] and a range of 0.7% to 3.8% more birth defects [6]. Consanguinity is a significant predictor of cardiovascular conditions, but not other diseases like psychiatric disorders, epilepsy, asthma, cancer, or diabetes [7]. Studies in Croatia, Qatar, and Morocco have however linked consanguinity to various non-communicable diseases such as uni/bipolar depression, cancer, stroke, cardiovascular disease, diabetes, leukemia, asthma, and epilepsy [8,9], in another study consanguineous marriage significantly affected autosomal recessive diseases (78.8%), including neurodegenerative, disease cases, mucopolysaccharidosis, epidermolysis bullosa dystrophica, Phenylketonuria, and sensorineural deafness [5,6]. Saudi Arabia has a higher rate of hereditary kidney diseases in children compared to global counterparts, including familial nephrotic syndrome, renal tubular acidosis, marble brain disease, polycystic kidney disease, nephrocalcinosis syndrome, and familial juvenile nephronophthisis [10].

Frederic C. Bartter wrote about a syndrome in 1962 [11] that included metabolic alkalosis caused by low potassium levels

and hyperaldosteronism caused by high renin levels in a person who did not have any signs of high blood pressure. Since then, the condition has been named “Bartter syndrome (BS)” and is known to have five recognized and distinct genotypic/phenotypic indicators. The most common type of BS is Type I BS, which is caused by changes in the SLC12A1 gene (sodium-potassium-chloride cotransporter). People with this type of BS lose a lot of salt, have low levels of streptokinase in their urine, and don't grow [12]. Antenatal Bartter syndrome (Type II BS) is characterized by extreme dehydration, early delivery, polyhydramnios, and other symptoms that manifest either before or soon after birth. The

chloride channel ClC-Kb in the kidneys' distal tubules is affected by mutations in the (Chloride Voltage-Gated Channel Kb) CLCNKB gene, which causes type III BS [12,13]. “Mutations in the (Barttin CLCNK Type Accessory Subunit Beta)” BSND and the CLCNKA/CLCNKB genes are linked to polyhydramnios, premature birth, and poor urine concentration [14,15]. These genes are part of Type IVa and Type IVb, which are subgrouped. Treatment for BS depends on the severity and type of symptoms, but it usually includes drugs like aldosterone antagonists, non-steroidal anti-inflammatory drugs, and salt supplements given by mouth or through an IV. The literature primarily reports BS and its associated types through case reports and short case series [15]. According to a recent systematic review, a total of 18 cases of type III BS were reported between the years 2012 and 2022 [15], with five of them being associated with consanguinity [16-20]. The period of follow-up in these cases has been 4 weeks [20] to a maximum of 2.9 years [17], with three cases reported in females [16, 17, 20] and two in males [18,19]. The age range of consanguinity-associated BS in these cases has been between 28 days [16] and 48 years [17]. We present a case report of a brother and sister, aged 7.5 years and 4 months, respectively, associated with the consanguinity of double first cousins, with both cases failing to thrive till the mentioned age, respectively.

Case presentation

This narrative case report is being reported by the author, who is related to the family concerned. The parents of both deceased children are the nephew and niece of the author, who had a consanguineous marriage in the year 2004. The ages of the male and female parents at the time of marriage were 22 and 19 years, respectively. Fig 1 presents the family pedigree of the two affected deceased patients, identifying them as probands 1 and 2. Both parents were cousins, while their grandparents were also cousins. The report illustrates the medical history and complex consequences of the family suffering due to shared genetic mutations. Both patients presented with severe health complications and succumbed to their condition at ages 7.5 years and 4 months, respectively. After the death of their children, the genetic analysis of both parents revealed a diagnosis of type III BS. The couple has experienced three pregnancies to date, with the first one ending in a spontaneous miscarriage at 5 months of gestation (2 years after marriage), with the cause of the miscarriage being not determined.

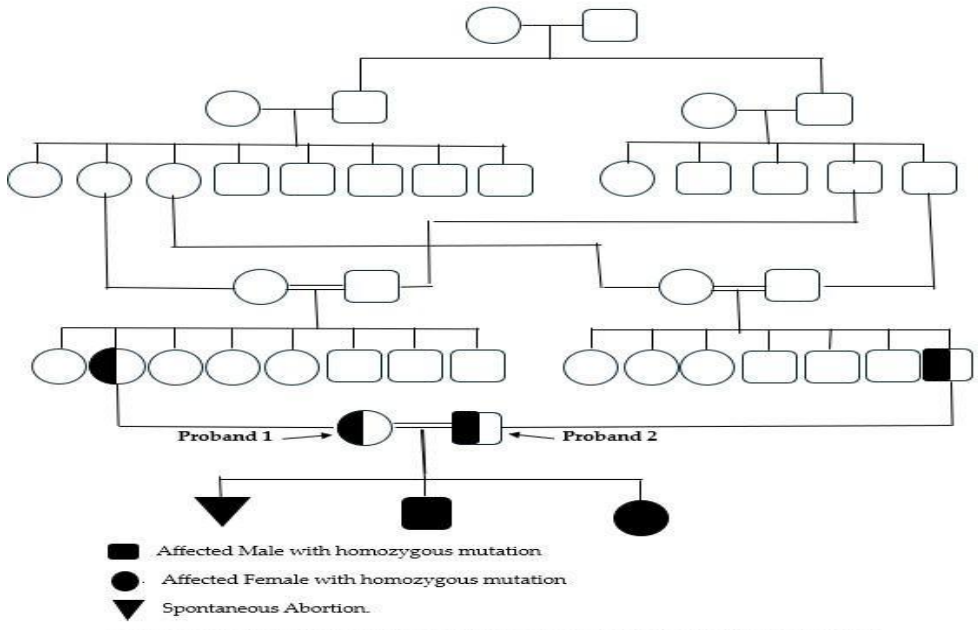

Figure 1: Family pedigree of the two affected children (boy and girl) aged 7.5 years and 4 months respectively, showing the affected proband 1 and 2. Both parents being the disease carriers. Both parents are cousins to each other, and the grandparents were cousins as well.

Case 1: Male child.

The first child born to the consanguineous parents (CP) was 4 years after marriage (2 years after the first pregnancy/miscarriage), born from a full-term normal vaginal delivery, but the pregnancy was complicated by the development of polyhydramnios (at 2nd trimester end). The birth of child weight was 3 kg, 50 cm in height, 35 cm in head circumference, and “Apgar score” was 8, which was well within the normal range. After one week after birth, the child was admitted to Al-Thawra General Modern Hospital, Sana'a, Yemen, with signs and symptoms of hypoglycemia, and

after preliminary treatment was discharged in stable condition. At 4 months, the child started vomiting persistently, which led to him being admitted again to the hospital. The child also had signs of growth retardation at this age. At that time, tests showed low potassium levels, anemia (Hb 6 g/dL), a low number of white blood cells, and a slightly enlarged liver. There were also positive results for cytomegalovirus (CMV) (IgM and IgG) and Toxoplasma (IgM and IgG). Table 1 displays the results obtained for each investigation parameter over various time periods. The child's condition was managed with parenteral administration of potassium followed by ongoing oral supplementation. At 3 years, during a routine follow-up, the child was diagnosed with mild mitral valve regurgitation, which was resolved successfully after medical treatment. At 4 years, the child showed obvious signs of lagging in normal growth, which prompted hormonal investigations. The test for growth hormone stimulation showed low levels of [basal - 1.0 ng/ml, 30 minutes - 4.4 ng/ml, 60 minutes - 5.1 ng/ml, 90 minutes - 2.0 ng/ml] and low levels of both total and free testosterone (Table 1). The child's end-stage of renal failure (RF.) was diagnosed at 6 years old with symptoms of metabolic alkalosis (growth retardation, muscle weakness, nausea and vomiting, and dehydration). Hemodialysis was initiated and continued for 11 months, with the child being recommended for kidney transplantation. A kidney transplant failed within 2 weeks due to graft thrombosis, which led to nephrectomy of the transplanted kidney. Persistent recurring infections and sepsis followed this event. At the age of 7 years and 5 months, the child finally succumbed to end-stage of renal failure (RF) and died, with sepsis after nephrectomy being the main cause.

Table 1: Laboratory findings of the two died (male and female) sibling patients as a result of consanguinity associated type III Bartter Syndrome

Test	Results		Normal values
	Boy (7years 5 months)	**Girl (4 months)**	
Serum Potassium	2.5 mmol/L	1.9 mmol/L	3.5-5.1 mmol/L
Serum Sodium	132 mmol/L	120 mmol/L	136-145 mmol/L
Serum Chloride	87 mmol/L	85 mmol/L	97-110 mmol/L
Serum Bicarbonate	-	30 mmol/L	18-24 mmol/L
Serum Bicarbonate	32 mmol/L	-	22-28 mmol/L
Serum Urea	18.6 mmol/L	-	1.7-8.3 mmol/L
Serum Urea	-	281 mg/dl	10-50 mg/dl
Growth Hormone Stimulation Test. Basal:	1.0 ng/ml	N. A	Up to 7.0 ng/ml
Growth Hormone Stimulation: 30 minutes 60 minutes. 90 minutes	4.4 ng/ml 5.1 ng/ml 2.0 ng/ml	N. A	Peak> 10 ng/ml
Somatomedin C (IGF1) (CC)	< 25.0 µg/l	N. A	124-484
Testosterone (Total), Serum Testosterone (Free), Serum	0.00 ng/dL 0.1 ng/dL	N. A	2.00 – 25 5.0 – 21
Thyroid Profile: T3 Free T4 Free TSH	3.8 pg./mL 1.8 ng/dL 3.10 ml U/mL	N. A	(2.3 – 4.4) (0.8 – 2.0) (0.70 – 6.40)
CBC WBC Platelets		24.1 x10^9 /L 21 x10^9/L	4-10x10^9 /L 150-400 x10^9/L

Abbreviations: L = liter; N.A = not applicable; µg = microgram; dL = deciliter; CBC = complete blood count; WBC = white blood cells; TSH = thyroid stimulating hormone;

Case 2: Female Child

The third pregnancy of the concerned parents (CP) was complicated by polyhydramnios, the child was delivered via cesarean section because of weak labor progression. At birth, the child was healthy with no evidence of any abnormality. At approximately one month, the child developed persistent vomiting complicated by recurrent aspiration pneumonia. The symptoms would disappear with routine antibiotics but would soon reappear after completing the drug course.

Hospitalization was required at the age of two and a half months with severe symptoms associated with renal impairment. Metabolic alkalosis linked to low potassium levels, low sodium levels, low chlorine levels, and high levels of bicarbonates in the blood were found in the lab (Table 1). Other significant investigative findings included hypercalciuria, which was suggestive of BS. Despite standard medical management of the condition, the infant progressed to end-stage renal disease (ESRD) with signs and symptoms of renal failure at the age of 4 months, with the final outcome being death.

Genetic analysis of the concerned parents (CP): After the deaths of the two children within a span of five years, the CP was investigated for genetic tests, which included whole exome sequencing, mitochondrial genome analysis, and copy number variations (CNV). The diagnosis of BS involved children of consanguineous parents (CP) who were linked to the CLCNKB gene in both parents. It was found that both father and mother had a gross heterogeneous pathogenic deletion of 29 kb at locus (Chr1:16,360,054-16,389,061), which affected the whole CLCNKB gene. The ACMG concluded it was pathogenic. Once the Multiplex Ligation-dependent Probe Amplification (MLPA) test confirmed Copy Number Variation (CNV). "According to the American College of Medical Genetics and Genomics (ACMG)" genetic counseling for the parents is recommended.

Discussion

Bartter syndrome is an autosomal-recessively inherited condition characterized clinically by growth retardation while laboratory investigations showed metabolic alkalosis, hypokalemia, hypochloremia, and renin-aldosterone axis activation. It is classified into five types based on mutations of various genetic constituents [CASR, CLCNKB, SLC12A1, KCNJ1, BSND]. This article presents a unique case of two siblings who were both diagnosed with BS because of CP, who were both found to show gross heterogenous pathogenic deletion of 29 kb at locus (Chr1:16,360,054-16,389,061). As far as scientific literature is concerned, this is one of the first cases that presents type III BS in a brother and sister, due to consanguineous parents. The report is especially significant since this is the first case to report a fatal outcome in consanguinity-associated Type III BS when compared to previous reports [16-20]. This case report is also unique in that it is only the third case that presented with antenatal polyhydramnios during the third trimester of pregnancy. Abdelgadir IS, et al. [16], and Azzi A, et al. [20], reported antenatal polyhydramnios, while the other three Type III BS [17, 18, 19], associated with consanguinity, did not have antenatal polyhydramnios in their reported cases. Since there are only five Type III BS associated with consanguinity reported in the literature [16-20], specific discussion will be directed with these studies. The first case of the boy aged 7.5 years may also be considered the longest follow-up of consanguinity-associated Type III BS, as other cases were followed up for 20 days [16], 2.9 years [17], 1 year [18], 2 years [19], and 4 weeks [20]. BS management often involves challenges, including prenatal polyhydramnios, necessitating amniotic fluid drainage and maternal indomethacin treatment. Between the years 2012 and 2022, the number of all types of BS patients reported has been approximately 118 patients, out of which 33.05% have been reported to have antenatal polyhydramnios [15]. Premature birth was seen in one tenth of these cases. Symptoms of Type I BS, which include hyposthenuria, acute salt wasting, high PGE2 production, and failure to thrive, usually manifest at birth. Polyhydramnios and preterm delivery are possible outcomes of some symptoms that develop during pregnancy. Mutations in either the BSND gene or the CLCNKA/CLCNKB gene are linked to polyhydramnios, premature birth, and decreased urine concentration [21]. Preemies, polyuria, and polyhydramnios, together with an early postnatal temporary hyperkalemia, may arouse concern for prenatal BS, according to Mani et al. [22], who state that this condition is caused by a "mutation in the KCNJ1 gene". Thakur S. et al. [23] reported a novel finding of a full bladder (fetal polyuria) with severe polyhydramnios in three fetuses, onset around 24-25 weeks, and concluded that it is an antenatal sign of BS provided no structural abnormalities of the fetus exists. The ClC-Kb channel, located in the thick ascending limb (TAL), distal convoluted tubule, and collecting duct, facilitates the transport of chloride ions to the basolateral membrane [22]. Impaired ClC-Kb function in the thick ascending limb leads to the Bartter phenotype (characterized by hypercalciuria and isosthenuria), while dysfunction in the distal convoluted tubule results in the Gitelman syndrome phenotype (marked by hypocalciuria) [24]. Impaired ClC-Kb function in the TAL leads to lower Cl-exit levels, "NaCl reabsorption through Na-K-2Cl" co transport (NKCC2), and subsequent "calcium reabsorption" [22.24]. "Impaired NCC function" in DCT cells leads to hypocalciuria in BS patients. This is due to reduced Na reabsorption, hyperpolarization, and calcium entry through voltage-activated channels, and lowered Na^+ concentration [25]. "Defective basolateral Cl-exit in the DCT" declines chloride reabsorption, leading to the "GLS phenotype, hypocalciuria in type III BS patients" with diminished "ClC-Kb function". Type 2 BS has "isosthenuria and elevated uCa/Cr ratio", suggesting the CLCNKB mutation is in the TAL, while some types and cases of BS have hypocalciuria [17]. BS type III has significant phenotypic heterogeneity, from severe salt-losing nephropathy to a clinically asymptomatic state, with the mutation type possibly affecting the clinical manifestation [17,26]. The prevalence of severe mutations, including substantial deletions, frameshift, crucial splicing, and nonsense, is higher in individuals with severe symptoms and earlier onset [17].

Symptoms of the mild classical illness known as Bartter syndrome type 3 include growth retardation, recurrent vomiting, polyuria, polydipsia, and electrolyte imbalance; the disorder usually starts in infancy. These features are consistent with our case and earlier case reports [16-20]. The traditional Bartter phenotype is frequently caused by CLCNKB mutations, although the disorder can alternatively manifest as nephrocalcinosis or nephrolithiasis, with contributory variables such as hypercalciuria, borderline hyperuricosuria, or hypoeroxaluria [27]. Studies suggest salt replacement and prostaglandin synthase inhibitors may enhance growth retardation in BS patients. Even after receiving the right therapy, long-term follow-ups reveal normal electrolyte readings and development metrics; yet problems with imbalanced electrolytes, acidosis, and stunted growth often continue.

Both parents were counselled after the loss of their two children. The first phase of counselling was focused on the genetic implications of CP [3], and the fatal outcome associated with it [1]. Consanguinity has been implicated in various genetic [1,5,6], physical [7,9] and behavioral disorders [29,30]. Pre pregnancy counselling was essential before the CP plan for the child. The CP were provided with several other options for future pregnancies which included the option of adv wherein

in vitro fertilization could be performed, followed by genetic testing of embryos before implantation to select unaffected embryos. Another option was prenatal testing for Amniocentesis or chorionic villus sampling, between 10-15 weeks of pregnancy to diagnose the condition. Affected fetus could be terminated while non affected would progress. Both parents chose the first option and are currently in the process of achieving it, without having restored to other options like second marriage.

Conclusion

Type 3 BS associated with consanguinity resulted in premature death of two children aged 7.5 years and 4 months respectively. Consanguineous spouses should seek genetic counseling, and hereditary illnesses like BS should be managed with early identification and care, as this instance establishes.

Informed consent statement:

Informed consent was obtained from the father of the patients that were involved in the study.

Data availability statement:

All relevant clinical details are included within the case report. No additional datasets are available.

Author contributions: Single author

Funding: This research received no external funding.

Acknowledgment: None

Conflicts of interest: None

REFERENCES

[1] Shawky RM, Elsayed SM, Zaki ME, El-Din SM, Kamal FM. Consanguinity and its relevance to clinical genetics. Egyptian Journal of Medical Human Genetics. 2013 Apr 17;14(2).

[2] Ben-Omran T, Al Ghanim K, Yavarna T, El Akoum M, Samara M, Chandra P, Al-Dewik N. Effects of consanguinity in a cohort of subjects with certain genetic disorders in Qatar. Molecular genetics & genomic medicine. 2020 Jan;8(1):e1051.

[3] Modell B, Darr A. Genetic counselling and customary consanguineous marriage. Nature Reviews Genetics. 2002 Mar 1;3(3):225-9.

[4] Hamamy H. Consanguineous marriages: preconception consultation in primary health care settings. J Community Genet. 2012;3:185–192.

[5] Bittles AH, Neel JV: The costs of human inbreeding and their implications for variations at the DNA level . Nat Genet. 1994, 8:117-21.

[6] Bittles A: Consanguinity and its relevance to clinical genetics . Clin Genet. 2001, 60:89-98.

[7] El Goundali K, Bouab C, Rifqi L, Chebabe M, Hilali A. Les mariages consanguins et leurs effets sur les maladies non transmissibles dans la population marocaine: étude transversale. Pan African Medical Journal. 2022 Mar 16;41(1).

[8] Bener A, Hussain R. Consanguineous unions and child health in the State of Qatar. Paediatric and perinatal epidemiology. 2006 Sep;20(5):372-8.

[9] Rudan I, Rudan D, Campbell H, Carothers A, Wright A, Smolej-Narancic N, Janicijevic B, Jin L, Chakraborty R, Deka R, Rudan P. Inbreeding and risk of late onset complex disease. Journal of medical genetics. 2003 Dec 1;40(12):925-32.

[10] Khayat AM, Alshareef BG, Alharbi SF, AlZahrani MM, Alshangity BA, Tashkandi NF. Consanguineous marriage and its association with genetic disorders in Saudi Arabia: a review. Cureus. 2024 Feb;16(2).

[11] Frederic C. Bartter, MD, Pacita Pronove, MD, John R. Gill, Jr., MD and Ross C. MacCardle, Ph. D WT. Hyperplasia of the juxtaglomerular complex with hyperaldosteronism and hypokalemic alkalosis. The American Journal of Medicine. 1962;33(6):811-28.

[12] Cunha TD, Heilberg IP. Bartter syndrome: causes, diagnosis, and treatment. International journal of nephrology and renovascular disease. 2018 Nov 9:291-301.

[13] Finer, G.; Shalev, H.; Birk, O.S.; Galron, D.; Jeck, N.; Sinai-Treiman, L.; Landau, D. Transient neonatal hyperkalemia in the antenatal (ROMK defective) Bartter syndrome. J. Pediatr. 2003, 142, 318–323.

[14] Brochard, K.; Boyer, O.; Blanchard, A.; Loirat, C.; Niaudet, P.; Macher, M.-A.; Deschenes, G.; Bensman, A.; Decramer, S.; Cochat, P.; et al. Phenotype–genotype correlation in antenatal and neonatal variants of Bartter syndrome. Nephrol. Dial. Transplant. 2008, 24, 1455–1464.

[15] Qasba RK, Bucharles AC, Piccoli MV, Sharma P, Banga A, Kamaraj B, Nawaz FA, Kumar HJ, Happy MA, Qasba RK, Kogilathota Jagirdhar GS. Bartter syndrome: a systematic review of case reports and case series. Medicina. 2023 Sep 11;59(9):1638.

[16] Abdelgadir IS, Elgharbawy F, Salameh KM, Juma BE Antenatal Bartter syndrome presenting with vomiting

and constipation mimicking subacute intestinal obstruction in a 20-day-old neonate. BMJ Case Rep. 2017, 2017, bcr-2017.

[17] Mou, L.; Wu, F. Simultaneous Homozygous Mutations in SLC12A3 and CLCNKB in an Inbred Chinese Pedigree. Genes 2021, 12, 369.

[18] Gargano, G.; Manfredi, M.; Pedori, S.; Di Dio, F.; Spagnoli, C.; Frattini, D. A highly unusual case of osmotic demyelination syndrome and extrapontine myelinolysis in a 3-month-old infant with Bartter syndrome. J. Int. Med. Res. 2020, 48, 0300060520966494

[19] Yang, X.; Zhang, G.; Wang, M.; Yang, H.; Li, Q. Bartter Syndrome Type 3: Phenotype-Genotype Correlation and Favorable Response to Ibuprofen. Frontiers in Pediatrics. 2018

[20] Azzi A, Chehade H, Deschênes G. Neonates with Bartter syndrome have enormous fluid and sodium requirements. Acta Paediatrica. 2015 Jul;104(7):e294-9.

[21] Cunha, T.D.S.; Heilberg, I.P. Bartter syndrome: Causes, diagnosis, and treatment. IJNRD 2018, 11, 291–301

[22] Mani, S.; Nair, J.; Handa, D. Antenatal Bartter syndrome: A new compound heterozygous mutation in exon 2 of KCNJ1 gene.,BMJ Case Rep. 2021, 14, e244685.

[23] Thakur S, Kumar M, Malhotra S, Paliwal P, Thareja V, Sahi G. Severe polyhydramnios with consistent fetal full bladder: a novel sign of antenatal bartter's disease. Journal of Pediatric Genetics. 2020 Dec;9(04):296-300.

[24] Seys, E.; Andrini, O.; Keck, M.; Mansour-Hendili, L.; Courand, P.-Y.; Simian, C.; Deschenes, G.; Kwon, T.; Bertholet-Thomas, A.; Bobrie, G.; et al. Clinical and Genetic Spectrum of Bartter Syndrome Type 3. J. Am. Soc. Nephrol. 2017, 28, 2540–2552.

[25] Zelikovic, I.; Szargel, R.; Hawash, A.; Labay, V.; Hatib, I.; Cohen, N.; Nakhoul, F. A novel mutation in the chloride channel gene, CLCNKB, as a cause of Gitelman and Bartter syndromes. Kidney Int. 2003, 63, 24–32.

[26] Konrad, M.; Vollmer, M.; Lemmink, H.H.; Heuvel, L.P.V.D.; Jeck, N.; Vargas-Poussou, R.; Lakings, A.; Ruf, R.; Deschênes, G.; Antignac, C.; et al. Mutations in the chloride channel gene CLCNKB as a cause of classic Bartter syndrome. J. Am. Soc. Nephrol. 2000, 11, 1449–1459.

[27] Colussi G, De Ferrari ME, Tedeschi S, Prandoni S, Syrén ML, Civati G. Bartter syndrome type 3: an unusual cause of nephrolithiasis. Nephrol Dial Transplant. (2002) 17:521–2.

[28] Nakagawa Y, Toya K, Natsume H, Nasuda K, Takeuchi H, Kubota A, et al. Long-term follow-up of a girl with the neonatal form of Bartter‘s syndrome. Endocr J. (1997) 44:275–81.

[29] Mattoo K, Shubayr M, Al Moaleem M, Halboub E. Influence of parental physical activity and screen time on the BMI of adult offspring in a Saudi population. InHealthcare 2020 Apr 24 (Vol. 8, No. 2, p. 110). MDPI.

[30] Shubayr MA, Mattoo KA. Parental neglect of feeding in obese individuals: a review of scientific evidence and its application among Saudi population. Saudi Medical Journal. 2020 May;41(5):451.