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*Case Report*

# Cystic Fibrosis in two Ghanaian Children

Sandra Kwarteng Owusu[1], Gabrielle Obeng-Koranteng[2], Sandra Laryea Odai[2], Marie Charlyne Fatima Kilba[3], Parbie Abbeyquaye[2], Kwabena Onwona-Agyeman[3], Sheila Asamoah-Okyere[2], Prince Matthew Oduah-Odoom[2], Naomi Dianna Adjetey[1], Kevin Bonsu[2], Stella Elikplim Lawerteh[2], Selorm Afidemenyo[2], Marco Zampoli[4]

[1]Department of Paediatrics, Komfo Anokye Teaching Hospital, Kumasi, [2]Department of Paediatrics, Millitary Hospital, Accra, [3]Department of Paediatrics, Greater Accra Regional Hospital, Accra, Ghana, [4]Department of Paediatrics, Division of Paediatric Pulmonology, Red Cross War Memorial Children's Hospital, University of Cape Town, Rondebosch, Cape Town, South Africa.

***Corresponding author:**
Sandra Kwarteng Owusu, Department of Child Health Komfo Anokye Teaching Hospital, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana.

abenaboamah18@gmail.com

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## ABSTRACT

Cystic fibrosis (CF) is a severe life-limiting genetic disorder resulting from mutations in the cystic fibrosis transmembrane regulator gene and is reported to be more prevalent among Caucasians than people of African descent. The past three decades have seen a gradual increase in the reporting of CF in non-European populations with CF in all regions including Africa. We report on the first two known Ghanaian children diagnosed with CF presenting early in infancy. The first patient presented with severe acute malnutrition and persistent diarrhea resulting from severe exocrine pancreatic insufficiency. In the second patient, there were recurrent wheeze and recurrent pneumonia, severe dehydration with metabolic alkalosis. Diagnosis of CF in Ghana is challenging due to the absence of diagnostic tools such as sweat testing equipment. In the first patient, sweat testing and genetic testing were done in South Africa. In the second patient, sweat testing was not done but diagnosis was confirmed by genetic testing. Both patients presented with classical CF symptoms including *Pseudomonas aeruginosa* airway infection before age 6 months. Both children are currently alive and healthy on appropriate treatment. These case reports highlight the growing evidence of CF occurring in people of African descent and the diagnostic challenges faced in Africa.

**Keywords:** Cystic fibrosis, Ghana, Africa, Case reports

## INTRODUCTION

Cystic fibrosis (CF) is a severe life-limiting monogenic disorder more prevalent among Caucasians affecting 1 in 3300 newborns compared to 1 in 15,300 newborns among people of African descent.[1] The past three decades have seen a gradual increase in the reporting of CF among non-European populations such as in Africa and in all regions worldwide.[2] This rise in incidence may reflect the growing awareness among medical practitioners in non-European regions about existence of CF. In regions such as Africa, confirming the diagnosis of CF remains challenging due to the absence of newborn screening, sweat testing equipment, and expensive genetic testing. These challenges contribute to cases of CF going undiagnosed.[2]

CF is caused by mutations in the cystic fibrosis transmembrane regulator (CFTR) gene, located on the long arm of chromosome 7q31.2 and codes CFTR channels found on cell membranes.[3] Worldwide, the most common mutation is the pPhe508del previously called F508del mutation. It is a severe Class II missense mutation resulting from deletion of a single phenylalanine residue at amino acid position 508 (F508del)[4,5] Among Africans, the most common CFTR mutation reported is the c.2988+1G>A previously called 3120+1G>A, a severe Class I non-sense mutation which may occur as homozygous or

compound heterozygous form.[1] This mutation was first reported by Macek *et al*., among African-Americans.[6] CF commonly presents in early life with exocrine pancreatic insufficiency resulting in severe failure to thrive, electrolyte abnormalities, especially metabolic alkalosis. Recurrent pneumonia associated with wheezing and persistent wet cough is another common manifestation of CF.[7]

The diagnosis of CF requires the presence of clinical symptoms, a sibling with CF, or a positive newborn screening test plus two disease causing CFTR gene mutations or two positive sweat tests (sweat chloride > 60 mmol/L).[7,8] In Ghana and many other African countries, diagnosis of CF remains challenging as sweat testing is not available and genetic testing expensive. This can contribute to delayed or missed diagnosis in patients with CF[9] which leads to poor outcomes and early mortality.

With advances in clinical research and CF care, life expectancy of people living with CF has improved remarkably to the fourth decade in high-income countries. We describe the first two Ghanaian children diagnosed with CF in early infancy and discuss possible approaches to the diagnostic challenges throughout Africa.

## CASE REPORTS

### Case 1

A 3-month-old male born prematurely at 34 weeks to non-consanguineous parents presented to the emergency unit with a 10-day history of persistent cough, fever, and poor weight gain. He was referred from a private facility as a case of recurrent pneumonia. The mother of the patient had a history of three previous first trimester fetal losses. Other routine pregnancy tests were negative including HIV, hepatitis B, and sickle cell disease. The patient was delivered through emergency cesarean section on account of premature rupture of membranes. His birth weight was 2.7 kg and he did not require resuscitation. He was exclusively breastfed and missed week 10 immunizations due to ill health. He had no history of contact with a person with tuberculosis. The patient is the second child of the couple. The first child of the same union died at age 6 months after a protracted hospital admission while been managed for severe pneumonia.

On examination, the patient appeared ill. His temperature was 38.5°C and was severely dehydrated despite no history of vomiting or diarrhea. He was in severe respiratory distress with a respiratory rate of 77 breaths/min. He weighed 3.2 kg, he had no dysmorphic features and normal appearance of the chest wall. Air entry was reduced bilaterally with wheezes bilaterally. All other systems were unremarkable.

The patient received intranasal oxygen, 3% hypertonic saline nebulization, and intravenous broad-spectrum antibiotics. He was also rehydrated with lactated Ringers. Complete blood count, serum creatinine, urea, and tests of liver function were normal. The arterial blood gas measurement showed severe metabolic alkalosis with hyponatremia, hypochloremia, hypokalemia, and hypocalcemia [Table 1]. Hyponatremia and hypokalemia were also corrected. Urinalysis was normal.

Chest X-ray [Figure 1] showed hyperinflation and abdominal ultrasound scans were non-contributory. Based on all the findings above, CF was considered. Sweat testing facility is currently not available in Ghana. Stool samples were taken for fecal elastase tests and blood samples for genetic testing to India and the United States of America. Fecal elastase level was 64.7 ug/g (normal range is 200–500 ug/g) which was consistent with exocrine pancreatic insufficiency. Based on the evidence of pancreatic insufficiency, our suspicion of CF was heightened and treatment with prolonged antibiotics to cover *Pseudomonas aeruginosa* was continued. Daily pancreatic enzyme replacement therapy (PERT) was initiated and oral 3% hypertonic saline and multivitamin supplementation were started. The physiotherapist supported twice daily chest physiotherapy to enhance airway clearance. Dietary intervention ensured adequate daily caloric intake of at least 120 Kcal/Kg/day. The patient's condition improved,

**Table 1:** Arterial blood gas profile for case 1 at first presentation showing metabolic alkalosis, hyponatremia, hypokalemia, and hypocalcemia.

| **Blood gas results for case 1** | |
|---|---|
| pH | 7.54 |
| $PO_2$ | 76.2 mmHg |
| $PCO_2$ | 82 mmHg |
| $HCO_3$- | 47 mmol/L |
| $Na^+$ | 123 mmol/L |
| $K^+$ | 1.23 mmol/L |
| $Ca^{2+}$ | 0.77 mmo/L |

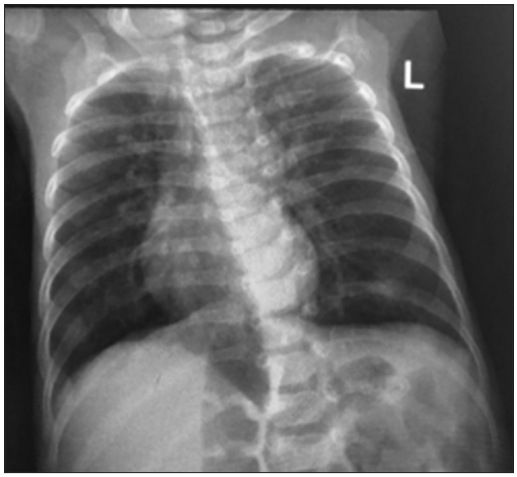


**Figure 1:** Chest Xray of case 1 showing hyperinflation.

and he was discharged home while awaiting the genetic testing results. Over the period, the patient was readmitted twice with recurrent chest infections treated with intravenous antibiotics. Genetic testing results received later confirmed a CF diagnosis with two pathogenic CFTR mutations: c1364C→Ala455Glu and a large deletion on exon 12.

The patient had a fourth admission 3 months after initial presentation with severe hyponatremia (121 mmol/l), fever, and persistent cough. Induced sputum sample isolated *P. aeruginosa*. He was again initiated on a 2 weeks course of intravenous 3rd generation cephalosporin, an aminoglycoside and nebulized gentamycin alternating with 3% hypertonic saline, and continued with a prolonged oral course of ciprofloxacin as eradication attempt for *P. aeruginosa*. The clinical psychologist also provided counseling and support for the family. The patient is currently 18 months old and thriving since the last admission. He is currently on 3% saline supplementation, PERT, and cotrimoxazole prophylaxis. He also receives daily chest physiotherapy and is seen in the clinic every 4 weeks for monitoring.

### Case 2

A 4-month-old male born prematurely at 35 weeks to non-consanguineous couple presented to the emergency room with a history of poor weight gain since birth. He was referred from a tertiary health facility in Ghana for investigation of failure to thrive to the Red Cross War Memorial Children's Hospital in South Africa. The patient had a history of persistent diarrhea, generalized edema, and extensive peeling of the skin. He had been extensively investigated including bone marrow aspirate for anemia. He had also received two blood transfusions due to severe anemia. His mother's medical and obstetric history was all unremarkable. He did not require resuscitation at birth and had a birth weight of 2.7 kg. He was breastfed exclusively and weaning foods were started at age 5 months. He had missed immunizations due to ill health and had no history of contact with anyone with TB. The patient is the 3rd child of the couple. Patient's older siblings aged 4 and 2 years at the time of his presentation were growing well with no known medical conditions.

On examination, the patient appeared ill and had bilateral pitting edema and extensive dermatosis with a weight of 3.1 kg at age 5 months. He was also pale, afebrile, and anicteric. He was not in respiratory distress with a respiratory rate of 30 bpm, a normal cardiac examination, and hepatomegaly on abdominal examination.

His random blood sugar was 106 mg/dl at presentation. In addition, he had low hemoglobin level, hypoalbuminemia with raised liver transaminases. His fecal elastase was <15 ug/g. CF was confirmed in South Africa with two positive sweat chloride tests (126 mmol/l and 117 mmol/l). He was initiated on PERT. In addition, oral 18% sodium chloride supplementation, multivitamin supplementation, and a high caloric diet were commenced. During his admission, *P. aeruginosa* was isolated from induced sputum and ear swab samples. He received *P. aeruginosa* eradication treatment for 3 months with oral ciprofloxacin and nebulized gentamicin twice daily (80 mg/2 ml intravenous solution). His chest X-ray showed hyperinflation but was otherwise unremarkable. His genetic tests showed two pathogenic CFTR mutations, c1397C>G→Ser466 and c1373G>T→Gly458Val. The boy is currently 7 years old and healthy.

## DISCUSSION

This is the first report on CF in young Ghanaian children to the best of our knowledge. Both cases presented with typical signs of CF. Neither patient had the 3120+1G<A mutation most commonly reported in people with African ancestry.[4,6,10] In case 1, CFTR mutation c1364C→Ala455Glu and deletion of exon 12 were found while case 2 was heterozygous with c1397C>G→Ser466 and c1373G>T→Gly458Val. These unusual mutations illustrate the need for extensive CFTR genotyping through sequencing to confirm CF diagnosis in people with African ancestry and other untested populations that are not of European descent.[2] Due to the extent of heterogeneity of mutations in CF, it is possible that as more reports continue to emerge from Africa, other mutations will be reported to reflect a more diverse genetic profile in the African population.[11] The c1364C→Ala455Glu mutation has been reported among French, Canadian, and Dutch patients and usually characterizes milder forms of disease.[12] We, however, found features suggestive of severe disease in case 1 who had the above mutation.

Apart from South Africa and a few North African countries, sweat testing is not available in most sub-Saharan countries which is a major obstacle to diagnosing CF in this setting.[2] Until this can addressed, CF can only be reliably diagnosed through genetic testing where funding is available, as illustrated in our two cases. Strategies to increase CF awareness and improve access to CF diagnostic tests in Africa are needed. Although unknown, it is possible the sibling to case 1 may have succumbed to undiagnosed CF.

Owusu *et al*.[13] reported on 34 children of African ancestry with CF. The mode of presentation was predominantly severe failure to thrive, with few cases presenting with meconium ileus. The median age at diagnosis was 5 months and the 3120+1G>A mutation was the most commonly occurring genotype. This also agrees with an earlier report on CF in African children from Durban,[10] South Africa which also showed similar findings of severe acute malnutrition as the most common mode of presentation among Black African children. Further both reports showed 3120+1G>A mutation as the most commonly occurring genotype.[10,13]

Bowel obstruction including meconium ileus occurs more commonly as a mode of presentation among Caucasians and is an uncommon mode of presentation among people of African descent (19). Neither of our two cases had evidence of bowel obstruction.

These case reports highlight the need for a high index of suspicion for CF among young African children with unexplained severe malnutrition and in those presenting with chronic or recurrent respiratory illness. Electrolyte imbalances, especially hyponatremic hypochloremic metabolic alkalosis, are also a common mode of CF presentation as were seen in our first patient. This needs to be addressed promptly as it can lead to mortality.

## CONCLUSION

Failure to thrive with severe acute malnutrition is the key presenting features of CF in children of Black African descent. Clinicians should consider CF when investigating children with unexplained malnutrition. Access to sweat testing facility and CFTR genetic analysis is not available in Ghana and other African countries and remains a major barrier to CF diagnosis.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Elborn JS. Cystic fibrosis. Lancet 2016;388:2519-31.
2. Bell SC, Mall MA, Gutierrez H, Macek M, Madge S, Davies JC, *et al*. The future of cystic fibrosis care: A global perspective. Lancet Respir Med 2020;8:65-124.
3. Ramsey BW. Management of pulmonary disease in patients with cystic fibrosis. N Engl J Med 1996;335:179-88.
4. Farrell PM. The prevalence of cystic fibrosis in the European Union. J Cyst Fibros 2008;7:450-3.
5. Davis PB. Another beginning for cystic fibrosis therapy. N Engl J Med 2015;373:274-6.
6. Macek Jr M, Davis CL, Hamosh A, Anvet M, Cutting GR.The identification of a novel mutation:3120 +1G>A. The Cystic Fibrosis Genetic Analysis Consortium, 1993;56:1-2.
7. de Boeck K, Wilschanski M, Castellani C, Taylor C, Cuppens H, Dodge J, *et al*. Cystic fibrosis: Terminology and diagnostic algorithms. Thorax 2006;61:627-35.
8. de Boeck K, Vermeulen F, Dupont L. The diagnosis of cystic fibrosis. Presse Med 2017;46:e97-108.
9. Zampoli On Behalf Of The Msac M. Cystic fibrosis: What's new in South Africa in 2019. S Afr Med J 2018;109:16-9.
10. Masekela R, Zampoli M, Westwood AT, White DA, Green RJ, Olorunju S, *et al*. Phenotypic expression of the 3120+1G>A mutation in non-Caucasian children with cystic fibrosis in South Africa. J Cyst Fibros 2012;12:363-6.
11. Stewart C, Pepper MS. Cystic fibrosis in the African diaspora. Ann Am Thorac Soc 2017;14:1-7.
12. de Braekeleer M, Allard C, Leblanc JP, Simard F, Aubin G. Genotype-phenotype correlation in cystic fibrosis patients compound heterozygous for the A455E mutation. Hum Genet 1997;101:208-11.
13. Owusu SK, Morrow BM, White D, Klugman S, Vanker A, Gray D, Zampoli M. Cystic fibrosis in black African children in South Africa: A case control study. J Cyst Fibros 2020;19:540-5.

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