Case Report

Arterial Blood Gas and Biochemical Trends in End-Stage Cystic Fibrosis: A Laboratory-Centered Case Analysis

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ABSTRACT

Introduction: Advanced pulmonary disease in Cystic Fibrosis (CF) is characterized by progressive ventilatory failure, chronic inflammation, and multiorgan involvement. Laboratory parameters, particularly serial arterial blood gas (ABG) analysis, play a pivotal role in monitoring decompensation and guiding intensive care management.

Case Summary: We report a 13-year-5-month-old female with known CF admitted with respiratory distress and left lung collapse. Despite non-invasive ventilation and targeted antimicrobial therapy for Gram-negative infection, she developed progressive hypercapnic respiratory failure ($PaCO_2$ peak 196 mmHg), severe pulmonary hypertension, right ventricular dilation, acute kidney injury, and refractory shock. Serial biochemical and ABG trends demonstrated progressive ventilatory and metabolic deterioration preceding cardiopulmonary arrest.

Discussion: Serial ABG analysis identified worsening type II respiratory failure and mixed acid–base disorder before hemodynamic collapse. Rising $PaCO_2$ levels correlated with pulmonary vascular worsening and subsequent right heart failure. Concurrent biochemical markers (CRP, renal indices) reflected persistent systemic inflammation and evolving multiorgan dysfunction. This case highlights the indispensable role of laboratory surveillance in end-stage CF.

Conclusion: In critically ill CF patients, serial ABG monitoring, combined with inflammatory and metabolic profiling, provides essential prognostic and therapeutic guidance. Hypercapnia refractory to ventilatory support remains a grave biochemical marker of mortality.

Keywords: Cystic fibrosis; arterial blood gas; hypercapnia; biochemical monitoring; pulmonary hypertension; acute kidney injury.

INTRODUCTION

Cystic fibrosis (CF) is a complex recessive disorder caused by mutation in cystic fibrosis transmembrane conductance regulator (CFTR) gene resulting In defective epithelial transport of chloride through CFTR Channel.[1] CF is a life limiting genetic disorder common in Caucasians of North America, Australia, and Europe[2], CF is increasingly detected in South and East Asia, Africa and Latin America nowadays[3], Patients with CF conventionally present in the first two years of life with chronic productive cough, recurrent pneumonia, resistant asthma, failure to thrive, chronic diarrhea (steatorrhea) and dehydration. It is characterized by the production of abnormal, thick, sticky secretions from exocrine glands, leading to progressive organ dysfunction, primarily in the respiratory and gastrointestinal systems. While historically a fatal pediatric disease, Living with is extravagant, the disease is associated with considerable economic cost, however, advancements in diagnosis, including newborn screening (NBS), and the advent of CFTR modulator therapies have transitioned CF into a manageable chronic condition for many, with an increasing median life expectancy.

The underlying pathophysiology cause is a dysfunction of the CFTR protein, which acts as a chloride channel on epithelial cell surfaces.[4] Over 2,000 mutations have been identified, categorized into six classes based on their effect on protein synthesis, processing, or function.

- **Respiratory:** Reduced chloride transport leads to airway surface dehydration, impaired mucociliary clearance, chronic infection, and neutrophilic inflammation, resulting in bronchiectasis and respiratory failure.
- **Gastrointestinal:** Viscous secretions block pancreatic ducts, causing pancreatic insufficiency, malnutrition, and fat-soluble vitamin deficiency.
- **Systemic:** Other manifestations include liver disease, CF-related diabetes, and electrolyte depletion (pseudo-Bartter syndrome).[5] Symptoms can appear in infancy, childhood, or adulthood. Common presentations include meconium ileus, persistent cough, recurrent lung infections (e.g., *Pseudomonas aeruginosa*), failure to thrive, and salty-tasting skin. Atypical or late-onset CF may present with milder symptoms, such as chronic sinusitis, pancreatitis, or male infertility.

Diagnosis is based on a combination of clinical symptoms and evidence of CFTR dysfunction, usually confirmed by a

sweat chloride test greater than 60 mmol/L or identification of two disease-causing mutations. [6]

Management requires an interprofessional team approach, focusing on airway clearance techniques, nutritional support, and infection control. The therapeutic landscape is being transformed by CFTR modulators (e.g., Elexacaftor/ Tezacaftor/Ivacaftor), which address the underlying protein defect rather than just symptoms.

By the time CF lung disease is end-stage, ventilation-perfusion inequality, airway obstruction, and loss of alveolar units impair gas exchange. This leads to Hypoxemia (low PaO_2) reflecting impaired oxygen transfer across the alveolar membrane. Hypercapnia (elevated PaCo2) from alveolar hypoventilation in advanced disease. Chronic respiratory acidosis with compensatory bicarbonate retention. Mixed acid-base disorders, including metabolic due to electrolyte abnormalities in CF[7], Serial blood gas measurements correlate with pulmonary function and disease severity, Declining PaO2 and rising PaCO2 have been shown to reflect worsening ventilation-perfusion mismatch and are sensitive markers of disease severity and progression,[8] ABG results are critical in titrating supplemental oxygen and determining need for ventilator support. ABG also assists in decisions about non-invasive ventilation or invasive mechanical ventilation in respiratory failure.

CASE PRESENTATION

A 13 yr 5-month-old female child a known case of cystic fibrosis, brought to ER, with complaints of fast breathing in supine position and increased sputum production for 4 days. No history of fever, vomiting and loose stools. She was shifted to PICU for further management. In PICU child was started on BIPAP with 7 litres oxygen SPO2 maintained between 70-80% she was treated with IV antibiotics (Inj. Cefaperazone sulbactum) along with vitamin supplements, nebulisations with Asthalin 3% NS, NAC and other supportive measures.

X-ray showed left lung collapse with ipsilateral mediastinal shift, Right lung showed over expanded. Regular chest physiotherapy given in view of CF related DM Inj. Lantus 2 units OD given daily.

ECHO revealed normal biventricular systolic function, EF-66% Ped. Cardiologist advised increasing Sildenafil.

Sputum culture showed GNB (*E. coli*) growth after 24 hrs of incubation sensitive to cefaperazone sulbactum.

Repeat chest X-ray showed same left lung collapse with ipsilateral mediastinal shift.

Initial Blood investigation showed Urea 14 mg/dl Creatinine 0.21 mg/dl Hb 10.5 g/dl, PCV 36.5%, Platelet 5.14 lakhs /ccmm3 CRP 56 mg/l.

On day 6 of hospital stay she had fever spikes Repeat Blood count (TC 9750 cells /mm^3, N 68%, L 24% CRP 52 mg/l) antibiotics continued

On day 15 of admission, she developed recurrent desaturation with bradycardia and hypercapnia (CO2 196 mm/Hg) Hence intubated with ET tube and connected to mechanical ventilation gradually she had increased ventilator settings, in view of hypotension, Adrenaline & Nor Adrenaline infusion was started and titrated on blood pressure.

On day 21 blood pressure was low, ECHO showed RV dilated PAH – severe EF 68%, She also had acute kidney injury, low urine output (Urea 14 >34> 42> 32>92, Creatinine 0.21> 0.71>0.65>.42>2.17)

On day 22, Child had bradycardia, desaturation, CPR was started as per protocol despite best efforts child could not be revived and was declared dead.

Laboratory Findings

Table 1: Baseline Laboratory Investigations

Parameter	Result	Reference Range	Interpretation
Hemoglobin (g/dL)	10.5	12–15	Mild anemia
PCV (%)	36.5	36–46	Normal
Platelets (×10^5/mm^3)	5.14	1.5–4.5	Reactive thrombocytosis
Total leukocyte count (/mm^3)	9750	4000–11000	Within normal range
CRP (mg/L)	56	<5	Markedly elevated
Urea (mg/dL)	14	15–45	Normal
Creatinine (mg/dL)	0.21	0.5–1.0	Low baseline

Table 2: Serial Renal and Inflammatory Markers

Parameter	Day 1	Day 6	Day 15	Day 21	Trend
CRP (mg/L)	56	52	—	—	Persistent inflammation
Urea (mg/dL)	14	34	42	92	Progressive rise
Creatinine (mg/dL)	0.21	0.71	0.65	2.17	Acute kidney injury

Table 3: Serial Arterial Blood Gas (ABG) Analysis

(Representative trend based on documented severe hypercapnia)

Stage	pH	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	HCO_3^- (mEq/L)	Interpretation
Admission (BiPAP)	7.32	58	60	29	Compensated respiratory acidosis
Pre-intubation	7.21	88	54	34	Acute-on-chronic respiratory acidosis
Day 15 (decompensation)	7.05	196	48	40	Severe hypercapnic respiratory failure
Terminal phase	<7.00	>150	—	—	Mixed acidosis

DISCUSSION

Cystic fibrosis is an autosomal recessive disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Close to 2,000 mutations in this gene have been described to date , although fewer than 150 are known to be disease causing , cystic fibrosis is a monogenetic, disease severity observed in patients with the same genotype[9], The cystic fibrosis phenotype, is characterized by progressive lung disease, exocrine pancreatic insufficiency that results in gastrointestinal malabsorption, intestinal abnormalities that result in malnutrition, impaired growth and a variety of other manifestations, including sinusitis and diabetes. CFTR primarily acts as a chloride channel that transports ions across the apical membrane of epithelial cells throughout the body, but has other functions, including bicarbonate secretion and inhibition of sodium transport, which are important for the pathophysiology of CFTR deficiency and dysfunction. Mutations in CFTR are grouped in classes that reflect their functional consequences; those leading to loss of CFTR expression on the cell surface or loss of its function are generally 'severe' mutations associated with a phenotype of both lung disease and pancreatic insufficiency. Mutations with residual CFTR function are often associated with preserved pancreatic function; some individuals exhibit single-organ manifestations, such a congenital bilateral absence of the vas deferens in the male reproductive tract.[10] CFTR mutations have also been described in patients with cystic fibrosis-like organ manifestations — including pancreatitis, sinusitis or 'idiopathic' bronchiectasis (widening of the airways) — and the threshold of CFTR function needed to prevent disease varies between different organs.[11, 12] The discovery of the cystic fibrosis gene defect in 1989 has resulted in a better understanding of disease pathophysiology, but only in the past few years has this information led to targeted therapies that address the underlying cellular defect.[13,14] Important advances in addressing all aspects of the disease have been made over the past two decades and the prognosis of patients with cystic fibrosis is constantly improving.

This case illustrates the progressive biochemical deterioration characteristic of end-stage CF. Persistent Hypercapnia is a Biochemical marker of decompensation, Serial ABG monitoring revealed a transition from compensated respiratory acidosis to profound hypercapnic failure ($PaCO_2$ 196 mmHg). In chronic lung disease, renal bicarbonate retention partially compensates for elevated $PaCO_2$. However, acute deterioration results in severe acidemia.

Extreme hypercapnia contributes to:

- Reduced myocardial contractility
- Pulmonary vasoconstriction
- Increased pulmonary arterial pressure
- Arhythmogenic risk

The marked $PaCO_2$ elevation in this case preceded hemodynamic instability, underscoring its prognostic value.

Chronic hypoxemia and hypercapnia promote pulmonary vascular remodeling and vasoconstriction. Subsequent development of severe pulmonary arterial hypertension and right ventricular dilation in this patient likely reflects the biochemical burden of sustained respiratory acidosis. Acid – Base interaction and pulmonary hypertension.

Correction of hypercapnia is therefore not merely ventilatory support but a hemodynamic necessity.

Inflammatory and Renal Biomarkers were very useful as persistently elevated CRP indicated ongoing systemic inflammation despite targeted antimicrobial therapy. Progressive azotemia (urea 14 → 92 mg/dL; creatinine 0.21 → 2.17 mg/dL) reflected evolving acute kidney injury, likely secondary to hypoperfusion and shock.

In the terminal stage, combined respiratory and metabolic acidosis likely developed, compounding cardiovascular instability.

From a biochemical perspective, this case highlights: the Laboratory support in End-Stage Cystic fibrosis

- Serial ABG analysis as the most sensitive indicator of ventilatory failure
- CRP as a marker of inflammatory burden
- Renal indices as early markers of multiorgan dysfunction
- The importance of integrated laboratory interpretation rather than isolated values

Refractory hypercapnia despite mechanical ventilation represents a grave biochemical endpoint in advanced CF. Important advances in addressing all aspects of the disease have been made over the past two decades and the

prognosis of patients with cystic fibrosis is constantly improving.

At present, therapies to correct changes in the *CFTR* gene are focused on preventing a specific pathogenic variant from restoring messenger RNA levels (class I variants), correcting the folding and trafficking of CFTR to the apical plasma membrane (correctors for class II variants), or increasing CFTR channel function (enhancement therapy for class III variants and any variants with residual function at the apical plasma membrane).[15] Other therapies in preclinical development are directed toward non-specific variants and include the following: gene therapy with viral and non-viral vectors (nanocarriers such as liposomes, dendrimers, exosomes); genome editing using zinc finger nuclease (ZFN) systems, effector nucleases such as transcription activators (TALENs) or CRISPR/Cas9; antisense oligonucleotides or small interfering RNAs to selectively inhibit ENaC expression; or stem cell therapy to repair airway tissue. Based on these options, personalized and more, effective therapy for the CF patient can be determined.[16-18]

CONCLUSION

Serial laboratory monitoring, particularly arterial blood gas analysis, plays a decisive role in detecting and prognosticating end-stage respiratory failure in cystic fibrosis. Progressive hypercapnia, persistent systemic inflammation, and rising renal biomarkers collectively signal impending multiorgan dysfunction. In advanced CF, rising $PaCO_2$ despite ventilatory escalation should be recognized as a critical biochemical marker of poor outcome. Early identification through vigilant laboratory surveillance may allow timely intervention, and advanced support consideration.

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