Introduction

We report a child with COVID-19 infection, severe metabolic acidosis, polyuria and proximal renal tubular acidosis.

Case

A 5-year female, with Thalassemia, on regular chelation, presented with fever and altered sensorium. Her GCS was 11/15, with no other neurological deficit. She was in shock and her systemic examination was unremarkable. The PCR for SARS CoV-2 was positive.

Blood gas revealed a severe non anion gap metabolic acidosis, elevated lactate and base deficit. She was treated with fluid boluses and bicarbonate. She improved hemodynamically; lactate normalised but metabolic acidosis persisted. Reports revealed normal renal function, sodium, potassium, calcium and magnesium, very low bicarbonate and phosphorus. A remarkable finding, was an elevated urine output of 6-8 ml/kg/hr.

Urine examination revealed proteinuria, ketonuria and glucosuria. For 48 hours the urine output remained 5-6 ml/kg/hr and she developed hypokalemia. Aggressive intravenous fluids, bicarbonate supplementation up to 12 meq/kg/day, phosphorus and potassium corrections were needed. 24-hour urine, collected on day 2, revealed significant proteinuria and elevated beta2-microglobulin. She had low tubular reabsorption of phosphorus, implying renal phosphate losses. The urinary losses were transient with the urine routine examinations on day 3 and on follow up being normal. The urine output decreased by day 4 to 3-4 ml/kg/hr. The metabolic acidosis and electrolyte abnormalities improved significantly. She was discharged on bicarbonate supplementation of 8meq/kg/day. On follow up she had normal urine output, electrolytes, bicarbonate and no metabolic acidosis.

Table 1:Serial laboratory parameters

	D 1	**D 2**	**D 10**	**D 20**
Sr. Sodium (mEq/L)	146	151		140
Sr Potassium (mEq/L)	4.5	2.9		4.1
Sr Creatinine (mg/dL)	0.3	0.33		0.3
Sr Bicarbonate (mEq/L)	4.7	6.7	14.4	22.0
Sr Phosphorus (mg/dL)	1.9	2.2		5.5
Urine Sodium (mEq/L)	-	246	-	-

Urine glucose (mg/dL)	100		Absent	Absent
24-hour Urine protein	-	547 (39mg/kg/day)	-	-
Tubular resorption of phosphate	-	87%	-	-
TmP/GFR (mg/dL)	-	1.88	-	-
Urine beta2 microglobulin (ng/ml) Normal range <300	-	6108	-	-

Discussion:

Fanconi syndrome is a defect in the proximal tubule of the renal nephron leading to malabsorption of electrolytes, proteins, glucose and phosphorus. It can be due to an inherited genetic defect or secondary to drugs, heavy metals, amyloidosis, multiple myeloma and post renal transplant. Ours is the first reported case of Fanconi syndrome in paediatrics, secondary to COVID-19 infection.

The spectrum of symptoms caused by COVID-19 encompass multiple organs. Renal involvement in the form of acute kidney injury, proteinuria and proximal tubular injury has been documented in several adult case series. A study of 710 patients admitted with COVID-19 in Wuhan has documented renal involvement in the form of proteinuria, haematuria, azotemia in 44%, 27% and 14% respectively [1].

The mechanism of virus induced damage of the kidneys is not elucidated clearly, although the possible theories include injury due to cytokine storm or direct cellular invasion by the virus. Wenhui Li et al proposed that angiotensin converting enzyme 2 (ACE2) is a functional receptor for the virus [2]. ACE2 is expressed in the endothelial lining of lungs, kidneys, heart and gut. Covid-19 causes endotheliitis, which then triggers a host immune response. This, along with apoptosis causes a microcirculatory dysfunction leading to organ injury [3].

In a post mortem study of renal histopathological findings of 26 patients with COVID-19, the features of proximal tubular injury on light microscopy were - loss of brush border, vacuolar degeneration and dilatation of tubule lumen with cellular debris. These were possibly due to direct viral invasion. The electron microscopy revealed corona virus like particles in the cytoplasm of proximal tubular cells, in the podocytes and distal tubular cells. ACE2 is expressed in the apical brush border of the cells in the proximal tubule and to a lesser extent in podocytes and the presence of virus like particles correlates with this distribution of the ACE 2 receptors [4]. These histopathological findings clinically present as transient function loss of the channels in the proximal tubules,

manifesting as Fanconi syndrome. A more profound injury could present as acute tubular necrosis and acute kidney injury. A retrospective study of 42 patients in France, found that incomplete Fanconi syndrome was a frequent occurrence, sometimes preceding acute kidney injury. Proximal tubulopathy was diagnosed in 68%, 85% had proteinuria, 48% had renal phosphate leakage and 44% had glycosuria [5]. More commonly, the proximal renal tubular acidosis is self-limiting, with resolution of polyuria, hypokalemia, hypophosphatemia, metabolic acidosis, non-nephrotic proteinuria and glycosuria on recovery from the infection.

Transient renal tubulopathy has been reported in 2 adults with COVID-19 infection. One presented with nephrogenic diabetes insipidus and the other with hypophophatemia, hyperphosphaturia, metabolic acidosis and proteinuria, all suggestive of Fanconi syndrome [6].

Conclusion

The incidence and long-term effects of renal involvement in children with COVID-19 merits further study and awareness of this is essential while managing Covid-19 in children.

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