Potassium abnormalities in CKD and in COVID-19 infection

Reviewed by:

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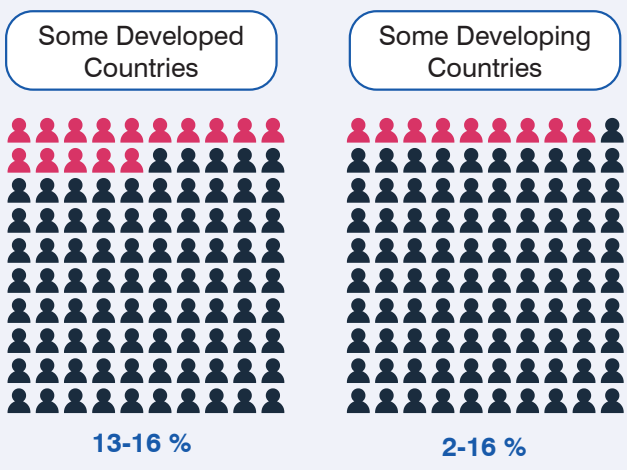
Potassium abnormalities in CKD

Chronic kidney disease (CKD) is progressive loss of renal functions eventually requiring renal replacement therapy. It is a cause of major health concern, particularly because of the high morbidity and mortality rates it is associated with. It is defined as kidney damage or an estimated glomerular filtration rate (eGFR) < 60 ml/min per 1.73 m^2, persisting for ≥ 3 months.[1] The last few years have witnessed progressive increase in the burden of CKD, with its prevalence ranging from 13-16% in some of the developed countries and between 2-16% in the developing countries (Figure 1).

Kidneys are a major regulator of body's potassium balance. Potassium is the most common intracellular cation, with most of the ingested potassium excreted by kidneys. Poor renal functions, therefore, is frequently associated with increase in the serum potassium levels (hyperkalemia). Use of low sodium salts and certain medicines like pain killers and Ace-inhibitor group of hypertension medicines also contribute to hyperkalemia in renal patients. Nonetheless, low serum levels of potassium (hypokalemia) are not uncommon in CKD, particularly in the elderly patients with reduced intake and also repeated loss of potassium during dialysis in patients with advanced CKD; it can also be seen after the use of select drugs (such as insulin) which can either promote intracellular shift of potassium or increase potassium excretion (diuretics), thereby reducing their serum levels.[2]

Both hyperkalemia and hypokalemia can be detrimental to patient outcomes. While hyperkalemia is a well-documented cause of arrhythmias and resultant mortality, hypokalemia also appears to be associated with poor outcome and higher mortality rates in CKD patients. The significance of screening for hypo- and hyperkalemia in CKD patients therefore cannot be overemphasized.[3] Early management and correction of potassium abnormalities in these patients improves patient outcomes.

Figure 1: Prevalence of CKD in some developed and developing countries



Adapted from: Vaidya SR, Aeddula NR. Chronic Renal Failure. [Updated 2022 Aug 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535404/.

Hypokalemia in COVID-19: What do we know?

Since the last 3 years, we have been in the midst of the COVID pandemic that has led to high morbidity and mortality rates across the globe. COVID-19 infection, caused by severe acute respiratory syndrome CoV-2 (SARS-CoV-2), has been associated with widespread abnormalities. Hypokalemia has been reported in patients with COVID-19 infection, and is a cause of concern due to its potential to cause frequent fatal arrhythmias. Hypokalemia, therefore, may deteriorate treatment outcomes in patients with COVID-19. Several causes of hypokalemia in these patients have been proposed,

including anorexia and diarrhea due to COVID-19 illness, increased gastrointestinal losses, hyperactivation of the renin-angiotensin aldosterone system (RAAS) by binding of the virus to and degradation of ACE2 (ACE2 regulates RAAS), and ischemia- or drug-induced renal tubular damage. It is noteworthy that SARS-CoV-2 virus has also been associated with direct renal tubular damage (Figure 2).[4]

A retrospective study[4] performed in a tertiary care center in Italy that evaluated non-critical patients with COVID-19 showed hypokalemia in 41% of the admitted patients. Female gender and use of diuretics were identified as risk factors for hypokalemia. Similar results were reported in another study[5] performed in China that also evaluated hospitalized patients with COVID-19 infection, and confirmed diagnosis of hypokalemia in 48.1% of the patients. That hypokalemia can confer poor prognosis in COVID-19 patients has been suggested by findings of increased risk of ICU transfers in COVID-19 patients with hypokalemia compared to their counterparts with normal serum potassium, though the difference has not been statistically significant. A case report[6] showed that hypokalemia after COVID-19 infection is often times persistent, present more than 5 months after the patient recovers from COVID-19 infection, and is asymptomatic. These reports emphasize the need for evaluating potassium levels in patients with COVID-19, and further following-up them in the post-COVID phase to detect its persistence.

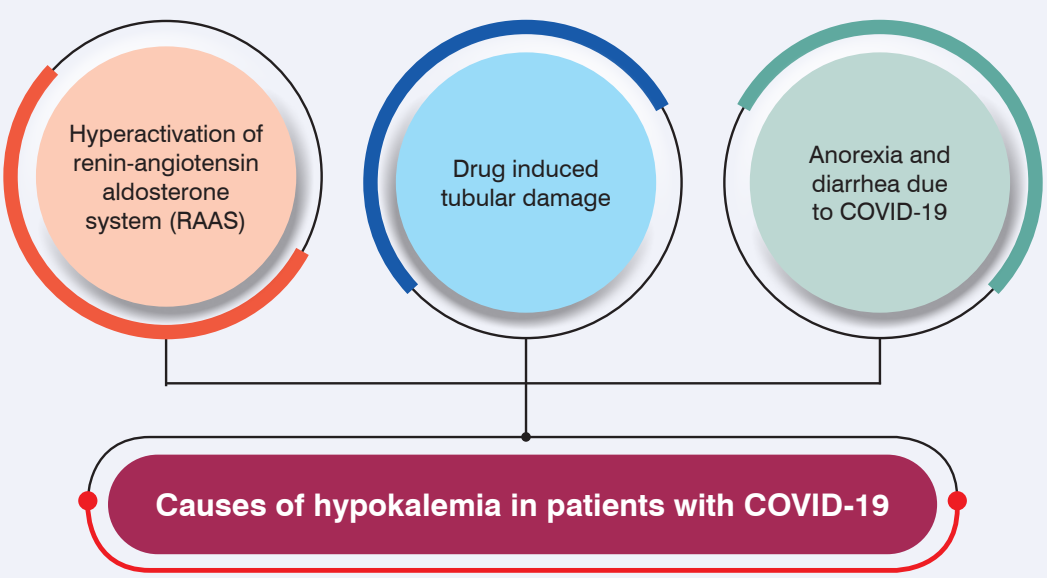
Management of hyperkalemia

- Several treatment options for lowering potassium are available
- Emergency care includes use of injectable calcium gluconate to decrease cardiac toxicity
- Use of Dextrose and insulin infusion intravenously can promote intracellular shift of potassium, thereby lowering its serum levels
- Beta-2 adrenergic agents, such as albuterol (salbutamol), can also be used though for hypokalemia it needs to be administered in doses higher than those used for bronchodilation
- Diuretics, both loop and thiazide diuretics, also reduce potassium levels by increasing renal excretion. They should be used carefully to prevent dehydration
- Oral potassium binding agents can be used to decrease absorption of potassium from the intestines
- Dietary review to decrease potassium rich diet and correction of metabolic acidosis helps in long term management of potassium levels.

Management of hypokalemia

Given the serious and often life-threatening complications that hypokalemia can be associated with, early detection and appropriate management of hypokalemia is desirable. Treatment of hypokalemia aims to correct potassium deficits, treat the underlying cause, and prevent or treat

Figure 2: Some possible patho physiological mechanisms associated with hypokalemia in COVID-19 infection



Adapted from: Alfano G, Ferrari A, Fontana F, et al; Modena COVID-19 Working Group (MoCo19). Hypokalemia in Patients with COVID-19. Clin Exp Nephrol. 2021 Apr;25(4):401-409.

> Mild-to-moderate hypokalemia needs oral potassium supplementation while severe hypokalemia needs more aggressive treatment, usually intravenous (IV) or sometimes oral potassium replacement

life-threatening events which it can predispose to. Many patients can have co-associated hypomagnesemia, which if present, should also be diagnosed and treated to optimize treatment outcomes.[8] Severity of hypokalemia is based on serum potassium levels. Broadly, potassium levels of 2.5–3.5 mEq/L is referred to as mild-to-moderate hypokalemia, while potassium levels < 2.5 mEq/L is severe hypokalemia.[9] Overall mild-to-moderate hypokalemia needs oral potassium supplementation while severe hypokalemia needs more aggressive treatment, usually intravenous (IV) or sometimes oral potassium replacement.[8,9] Intravenous potassium should be carefully administered after admission to hospital, with close monitoring of ECG and serum potassium levels.[9]

- For mild-to-moderate hypokalemia, oral potassium, typically as potassium chloride, is provided at 60-80 mmol/day in divided doses over several days to weeks. Oral potassium should be administered with plenty of fluids, preferably with or after meals[9]
- For managing severe hypokalemia, potassium replacement at a dose of 40 mmol/day every 3-4 hours is preferred[8]
- It is recommended to choose IV over oral potassium replacement in patients with nausea, vomiting, abdominal distress, cardiac dysrhythmias, recent or ongoing cardiac ischemia, and digitalis toxicity[8,9]
- For IV replacement, 0.9% sodium chloride is preferred to 5% dextrose as the infusion fluid, to avoid dextrose-induced transcellular shift.

Conclusion

Potassium is an important intracellular cation, serum levels of which are frequently altered in patients with CKD and in those with COVID-19 infection. Both hypo- and hyperkalemia have been reported in patients with CKD. Given that overwhelming majority of serum potassium is excreted by the kidneys, CKD expectedly increases serum potassium (hyperkalemia). However, low potassium (hypokalemia) is also documented in elderly patients with anorexia and poor diet; potassium is also lost after repeated dialysis and can be reduced after use of select drugs in CKD patients. Additionally, studies have also shown hypokalemia in hospitalized patients with COVID-19 infections, with one case report suggesting its persistence for up to 5 months after COVID infection. Treatment of hypo- and hyperkalemia is crucial for improving treatment outcomes.

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