**Abstract.** Data on kidney failure in patients with congenital adrenal hyperplasia are rare. To the best of our knowledge, there is no data on how to manage patients with congenital adrenal hyperplasia during hemodialysis sessions. We report a case of a fifteen-year-old boy with a known case of congenital adrenal hyperplasia since 8 months of age who presented with advanced uremia and severe hyperkalemia for which he was initially started on hemodialysis without pre-HD hydrocortisone, during which he developed recurrent intradialytic hypotension. Subsequently, when intradialytic serum cortisol levels were monitored with different hydrocortisone regimens, a serum cortisol level greater than 25 mcg/dl during HD was not associated with significant intradialytic complications. The target was 28 mg of injected hydrocortisone followed by a maintenance dose of 6 mg/hr starting at the end of the first hour of dialysis. He developed intradialytic hypertriglyceridemia-associated priapism, which improved after the correction of the iron deficiency. Intradialytic hypertriglyceridemia was of higher magnitude during heparin-free HD than during HD with heparin. In conclusion, when intradialytic serum cortisol levels were monitored with different hydrocortisone regimens, a serum cortisol level greater than 25 mcg/dl during HD was not associated with significant intradialytic complications. The target was 28 mg of injected hydrocortisone followed by a maintenance dose of 6 mg/hr starting at the end of the first hour of dialysis. He developed intradialytic hypertriglyceridemia-associated priapism, which improved after the correction of the iron deficiency. Intradialytic hypertriglyceridemia was of higher magnitude during heparin-free HD than during HD with heparin. In conclusion, a target serum cortisol concentration > 25 mcg/dl during HD helps reduce intradialytic complications in patients with congenital adrenal hyperplasia and renal failure. Exogenous glucocorticoid administration can be associated with intradialytic hypertriglyceridemia-associated priapism in iron-deficient patients.

**Keywords:** adrenal insufficiency, congenital adrenal insufficiency, hemodialysis, hypertriglyceridemia, priapism.

**Conflict of interest.** The authors declare no conflict of interest.


Correspondence should be addressed to Nabadwip Pathak: kirtigd@gmail.com
Introduction. The prevalence of congenital adrenal hyperplasia (CAH) is 1 case per 16,000 people [1]. Kidney failure in patients with CAH is rare (1). To the best of our knowledge, no data have mentioned how to manage adrenal insufficiency during hemodialysis sessions in CAH patients. A study by Alhabari et al. showed that predialysis hydrocortisone administration reduces the risk of intradialytic hypotension, and the same protocol was initially attempted in our patient [2]. We report a case of CAH with end-stage kidney disease on maintenance hemodialysis. In this study, we also mentioned how we managed adrenal insufficiency without adverse effects in the patient and mentioned one episode of dialysis-related hypertriglyceridemia-associated priapism. To the best of our knowledge, there is no data on glucocorticoid-associated hemodialysis-related hypertriglyceridemia causing priapism.

Case presentation. A fifteen-year-old boy with a known case of congenital adrenal hyperplasia since the age of eight months presented with nausea and vomiting with a serum creatinine of 14.0 mg/dl, blood urea 300 mg/dl, serum sodium 137 mmol/l and serum potassium of 7 mmol/l. He was started on hemodialysis via a temporary hemodialysis catheter while continuing his usual daily hydrocortisone dosing. Although his ultrafiltration volume in the HD session was nil, he developed recurrent intradialytic hypotension, and the hemodialysis session was stopped after 1.5 hrs. Ultrasound of the abdomen revealed bilateral shrunken kidneys. He was diagnosed with congenital adrenal insufficiency due to 21 hydroxylase deficiency at the age of eight months based on elevated 17-OH progesterone levels and very low early morning serum cortisol.

Later, two-3 hemodialysis sessions were performed with an injection of 100 mg of hydrocortisone 1 hr before starting the hemodialysis session (the protocol used by Alhawari et al.), with a UF goal of 1-1.5 l depending on intradialytic weight gain. Although there were no episodes of intradialytic hypertension, he developed severe intradialytic hypertension (SBP increased from 140 mmHg to more than 200 mmHg), which was followed by a pulmonary edema. The subsequent two HD sessions were performed while keeping DNa 2 mmol/l less than SNa, but he developed severe intradialytic hypertension with pulmonary edema.

Subsequent three sessions were performed with the same dialysate prescription with a similar ultrafiltration goal but with a reduction in pre-HD hy-
drocortisone from 100 mg to 50 mg, following which an intradialytic hypertension episode did not occur. He developed tiredness and intradialytic hypotension in the last 2 hrs of dialysis and 4th hour of HD, respectively, in all three sessions. During the evaluation, the serum cortisol levels were 15.8 mcg/dl and seven mcg/dl at the end of the 3rd and 4th hours of hemodialysis, respectively (Fig. 1).

![Figure 1](image.png)

**Fig. 1.** During hemodialysis sessions, serum cortisol(microgram/dl) hourly trends with three intravenous hydrocortisone regimens.

By measuring the serum cortisol concentration every 30 minutes during HD, we found that the serum cortisol concentration decreased to 50% within approximately 1 hour. Based on a study by Charmandari et al., the serum cortisol concentration was checked at 10 min post i.v. administration of 50 mg of hydrocortisone to obtain a peak concentration of 120 mcg/dl, resulting in a volume distribution of approximately 40 L. The cortisol concentration reached approximately 60 mcg/dl and 30 mcg at the end of the 1st and 2nd hr, respectively. Based on a study by Letizia et al., we kept the target serum cortisol concentration above 35 mcg/dl throughout the HD session. We targeted a peak double the planned target concentration, 70 mcg/dl, to address the possibility of uremia-associated glucocorticoid resistance. To achieve the same results, a 28 mg loading dose was given with a probable Vd of 40 to obtain a peak of 70 mcg/dl, and at the end of the first hour, the dose reached 35 mcg. To maintain the level above 35 mcg, 7 mg/hr was added as a continu-nous infusion to add 17.5 mcg/l/hr at a probable Vd of 40 liters and prevent a decrease in the hydrocortisone level below the target serum cortisol value. The above regimen reduced intradialytic hypotension episodes with occasional intradialytic hypertension episodes. Later, whenever he was tired or hypotensive, his serum cortisol concentration was less than 25 mcg/dl. The target serum cortisol concentration was maintained above 25 mcg/dl, for which the regimen consisted of a 28 mg bolus f/b 6 mg/hr (starting at the end of the 1st hr). The last hydrocortisone protocol was not associated with intradialytic hypertension or intradialytic hypotension. We followed the same hydrocortisone prescription during the next three years during hemodialysis sessions without any intradialytic complications (see Fig. 1).

Two years later, he developed post-hemodialysis prolonged penile erection, which lasted for 24 hours and gradually resolved but recurred again after the subsequent 2 HD sessions, and it lasted for one day both times. During the biochemical evaluation, he was found to have milky plasma due to hypertriglyceridaemia (serum triglyceride > 1000 mg/dl), but his fasting serum triglyceride level was 124 mg/dl the next day in the early morning. The subsequent hemodialysis was heparin-free, given the possible need for need for surgical intervention, and hourly serum triglyceride levels were checked during HD, which showed increasing serum triglyceride levels (Fig. 2).
Fig. 2. Serum triglyceride levels before dialysis and during hemodialysis: hemodialysis without heparin, hemodialysis with heparin, and hemodialysis after iron deficiency is corrected.

During subsequent hemodialysis with heparin, there was also an increasing trend in the serum triglyceride level, but to a lesser degree (see Fig. 2). On evaluation, Doppler did not show any evidence of reduced flow in a penile vessel or any collection abutting the penile vessel. Hence managed conservatively. His Hb was 6.0 gm/dl, and his serum ferritin level reached 45 ng/ml; hence, he received parental iron supplementation. In subsequent hemodialysis sessions, the hourly serum cortisol values did not indicate intradialytic hypertriglyceridemia (see Fig. 2). He did not develop any such events in the future.

**Discussion.** In the general population, early morning fasting cortisol levels less than five mcg/dl suggest adrenal insufficiency, which is confirmed by an ACTH stimulation test, in which serum cortisol levels less than 18 mcg/dl indicate adrenal insufficiency [3]. Whether these cut-off values apply to end-stage kidney disease patients is unclear. An early morning serum cortisol concentration less than 8.45 mcg/dl has the highest sensitivity and specificity for detecting adrenal insufficiency in hemodialysis patients [4, 5]. A higher early morning cortisol level for the diagnosis of adrenal insufficiency in hemodialysis patients could be due to end-organ glucocorticoid resistance as observed in kidney failure patients [6].

In our case, the cortisol cut-off during hemodialysis was initially more than 35 mcg/dl based on a study by Letizia et al., in which the mean (+ standard deviation) serum cortisol post-HD was 34.56 ±14.3 mcg/dl [7]. However, later, whenever his serum cortisol concentration was less than 25 mcg/dl, he developed intradialytic hypotension and tiredness despite a minimal ultrafiltration target. Hence, we later changed the target to more than 25 mcg/dl, after which no additional intradialytic complications were observed. Considering the above observation, we kept serum cortisol above 25 mcg/dl due to the dialysis session, which is higher than the cutoff for the definition of adrenal insufficiency post-ACTH stimulation test. Similarly, higher baseline and post-ACTH stimulation serum cortisol cut-offs are observed in severe sepsis patients for the diagnosis of adrenal insufficiency, which could be due to end-organ glucocorticoid resistance, as observed in kidney failure patients [8, 9].

To ascertain the serum cortisol level cut-off to prevent adrenal crisis, we relied on symptoms such as intradialytic hypotension and intradialytic tiredness rather than serum 17OHP, as there is a lag period of 60-90 min between the change in the serum cortisol level and 17OHP, which makes it a poor marker [10].

Details of loading dose calculation and maintenance dose calculation were done with the help of previous studies, as mentioned below.

As shown in previous studies, the loading dose was calculated by estimating the volume of distribution after measuring peak serum cortisol levels after 10 min of intravenous 50 mg of hydrocortisone [11].

$$\text{Volume of distribution} = \frac{\text{Total drug amount}}{\text{Peak drug concentration}}$$

Vd=50 mg/120 mcg/dl =41.6 liter

Initially, the dosage was calculated to maintain a serum cortisol concentration greater than 35 mcg/dl during HD

$$\text{Loading dose} = \frac{\text{Desired concentration}}{\text{Volume of distribution}} \times \text{Vd}$$

(to make calculation easy, Vd was kept 40 l, which is close to the calculated value)

= 70 mcg/dl 40 litres=28 mg
The target concentration of cortisol at the onset of HD was kept twice as high as that during the rest of the HD duration due to the possibility of maximum glucocorticoid resistance at the onset of HD compared to that during the HD session due to the higher concentration of uremic toxins. Studies have shown reduced glucocorticoid receptor affinity in chronic kidney failure patients, but to the best of our knowledge, there is no data on the effect of dialysis therapy on glucocorticoid resistance [13].

The subsequent concentration was > 35 mcg/dl, for which maintenance dosing was started after the completion of the 1st hr of HD, as the concentration was expected to reach > 35 mcg/dl by that time. At the end of the 2nd hour without any hydrocortisone supplementation, the serum cortisol concentration was reduced to 17.5 mcg/dl; to prevent further decreases in the serum cortisol concentration after the 1st hour of HD, we calculated the maintenance dose:

\[
\text{Maintenance dose} = \text{Clearance} \times \text{Target concentration} \]

(half-life-1 hr; Vd 40 l hence clearance-20 l/h)

\[
\begin{align*}
\text{20 l/h} & \times \text{35 mcg/l} \\
& = 7 \text{mg/hr}
\end{align*}
\]

Later, we reduced the maintenance dose to 6 mg/hr to maintain the target between 25 and 30 mcg/dl.

Two years after the initiation of HD, he developed recurrent episodes of priapism lasting for more than 24 hrs, starting on the day of HD, and was observed to be associated with intradialytic hypertriglyceridemia. Studies have shown an association between hypertriglyceridemia and priapism due to increased viscosity, distortion of erythrocyte morphology, increased erythrocyte aggregation and adhesiveness, and decreased capillary flow [14]. One possible reason for intradialytic hypertriglyceridemia could be acute exposure to high-dose glucocorticoids, although there is little literature supporting this possibility [15]. Glucocorticoid exposure has been shown to be associated with increased lipolysis and to potentiate lipogenesis via insulin [16].

The intradialytic hypertriglyceridemia did not recur after he received parental iron therapy for iron deficiency. Experimental data have shown the role of iron deficiency in reducing the beta-oxidation of fatty acids and promoting hepatic lipogenesis. In the iron deficiency state, the hepatic carnitine required by long-chain fatty acid transporters is reduced, as iron is a cofactor of the enzyme synthesizing it [17]. The severity of intradialytic hypertriglyceridemia was greater in patients with heparin-free HD than in those with heparin HD, possibly due to the role of heparin in increasing lipoprotein lipase activity [18].

From the findings of our study, we can suggest the following recommendations. Firstly, the Intradialytic serum cortisol target must be kept higher than the general population’s post-ACTH stimulation cutoff of serum cortisol.

Secondly, Intradialytic hypertriglyceridemia could be a possible cause of priapism in hemodialysis patients who are receiving hydrocortisone during hemodialysis sessions.

Thirdly, an Iron deficient state could be a cause of steroid-associated acute hypertriglyceridemia. Hence, in patients with steroid-associated acute hypertriglyceridemia, iron status should be evaluated.

To confirm all the above observations, a study with a larger sample size is required.

**Conclusion:** To the best of our knowledge, this is the first study to discuss the management of adrenal insufficiency in end-stage kidney disease patients. A target serum cortisol concentration > 25 mcg/dl during HD helps reduce intradialytic complications in patients with congenital adrenal hyperplasia and renal failure. This is also the first study to state that exogenous glucocorticoid administration can be associated with intradialytic hypertriglyceridemia-associated priapism in iron-deficient patients.

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**Data availability.** The data used during the current study are available from the corresponding author on request.

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**Author’s contributions.**

**Nabadwip Pathak:** Manuscript writing and making the main contribution to its content;

**Sunil Kumar Nanda:** Data collection and editing;

**Moses Ambriose:** Editing the manuscript.

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