Article published online: 2024-07-22

Corticomedullary Differentiation in Fetal Kidneys: A Necessary Evil?

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J Fetal Med 2024;11:139–144.

Abstract

Renal corticomedullary differentiation (CMD) is a crucial indicator of fetal renal health and is detectable as early as 15 to 16 weeks of gestation. Abnormalities in CMD, such as accentuation or loss, may signal underlying renal diseases. CMD assessment via prenatal ultrasound evolves dynamically throughout gestation, reflecting changes in cortical echogenicity and cystic structures. While CMD alterations can indicate conditions like glomerulonephritis or obstructive uropathies, they also offer prognostic insights into future renal function. This case report highlights the importance of early detection and comprehensive evaluation of CMD for optimising prenatal renal care.

Keywords
- corticomedullary differentiation
- fetal kidneys
- GFR
- loss
- NCCT
- (PET)-SPECT
- indicator
- prenatal diagnosis

Introduction

The hallmark of kidney corticomedullary differentiation (CMD) is characterized by a relatively hyperechoic cortex relative to the medulla. CMD can be identified as early as weeks 15 to 16 and is more noticeable by 20 to 21 weeks. Its absence, accentuation, or reversal is a warning indicator of underlying fetal renal disease.[1]

Cortical echogenicity of the kidneys is compared with that of the liver and spleen, and the cortical and medullary echogenicities are compared.

Early in the second trimester, normal renal cortex is hyperechoic compared with the liver and spleen, which changes to hypoechogenicity by 32 weeks of gestation. Renal cortical hyperechogenicity is the most prevalent pattern from 21 to 25 weeks of pregnancy (92%), while hypoechogenicity becomes the most common pattern by 34 to 37 weeks (70%).

Renal cystic structures can reflect dilated tubules, cystic dilatation of the glomeruli or actual cysts. They might be confined to the cortex, medulla or both. Secondary to multiple interfaces formed by dilated tubules, tiny cysts,

DOI https://doi.org/10.1055/s-0044-1787665.
ISSN 2348-1153.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

interstitial fibrosis and inflammation renal hyperechogenicity are accentuated.[2]

Renal disorders like glomerulonephritis (GN), acute tubular necrosis, end-stage renal disease, obstructive hydronephrosis, Fabry's disease and other conditions can also be secondary causes of the loss of CMD seen in renal insufficiency.[3–7]

Loss of CMD in renal insufficiency has been explained by several potential underlying mechanisms, most likely connected to the variations in water content between the cortex and medulla.

In boys with posterior urethral valve disorder, increased renal cortical echogenicity and loss of CMD may be useful indicators of future poor renal function. While only a small percentage of patients with impaired renal function had normal kidneys, the initial renal ultrasonography (US) study revealed echogenic kidneys in a considerable number of patients with normal renal function.[8–12]

Unlike renal hyperechogenicity, which is seen in neonates with growth restriction, cortical hyperechogenicity can occur without any structural abnormalities at any point during pregnancy. Hyperechogenic renal medullae have been linked to prenatal infections, caesarean sections brought on by fetal distress, intrauterine growth restriction and admission to the neonatal intensive care unit (NICU). It has been discovered that fetuses with hyperechoic medullae are 1.5 times more likely to have an aberrant outcome. To evaluate prenatal intrauterine hypoxia and identify potentially problematic fetal problems in utero, renal parenchymal echogenicity may be a helpful signal.[12]

Case Report

A primigravida at the Fetal Medicine Centre at Artemis Hospital, Gurgaon, Haryana, India had a loss of CMD in both kidneys during routine prenatal US at 28 weeks of pregnancy. Ultrasound was performed on GE Voluson E8 with 2D Convex probes C 2–9 and C 1–6.

At the time of the anomaly scan, the fetus appeared to be free of any obvious congenital defects. Upon observation, both the kidneys exhibited typical dimensions and morphology, matching the size of the fetal kidney relative to gestational age. There were no cystic lesions and renal parenchyma was not hyperechogenic.

The kidneys could not be clearly distinguished from the surrounding structures on a follow-up ultrasound performed at 28 weeks. After some effort, both kidneys were eventually found. Both kidneys had no abnormalities but had lost their CMD, which made it challenging to distinguish them from surrounding structures. The amniotic fluid index remained within the normal range throughout pregnancy, the fetal bladder was clearly defined and both renal arteries were sufficiently defined (►**Fig. 1**).

Ultrasound results were recorded, and the couple was informed of the uncertain course and prognosis of the aforementioned concerns. They were also encouraged to follow-up every 3 weeks. There were no kidney abnormalities found during the parental abdomen ultrasound.

The same prenatal findings, loss of CMD and difficulty in differentiating from surrounding tissues with normal amniotic fluid index at the 50th centile for gestational age were seen and recorded on the subsequent follow-up ultrasound performed at 34 weeks of gestation (►**Fig. 2**).

The fetus underwent follow-up US and renal nuclear scans to evaluate renal functioning, as well as counselling regarding the need for a renal workup post-delivery.

The pregnant woman and the fetus were under constant observation, and there was no untoward incident that required the mother to take non-steroidal anti-inflammatory drugs (NSAIDs) or antibiotics. The postpartum period was also uneventful, with no event of septicaemia, NICU admission, hypovolaemia in the baby or antepartum bleeding.

A postnatal abdominal ultrasound was performed to corroborate the prenatal findings. The scan revealed a renal outline based on the presence of renal arteries (►**Fig. 3**).

The couple visited the medical facility when the baby was 7 months old, complaining of oliguria, even though the infant was getting enough water and had a normal hydration status. The infant underwent a renal diethylenetriamine pentaacetate (DTPA) scan as part of a follow-up for renal function. After injecting 2 mCi of 99mTc DTPA intravenously, posterior projection dynamic pictures were obtained. A single-photon emission computerized tomography (SPECT) or low-dose non-contrast CT (NCCT) was acquired 60 minutes after the injection of frusemide was administered. After the kidneys' positions were examined, they both seemed to be in their typical sizes and locations (►**Fig. 4**).

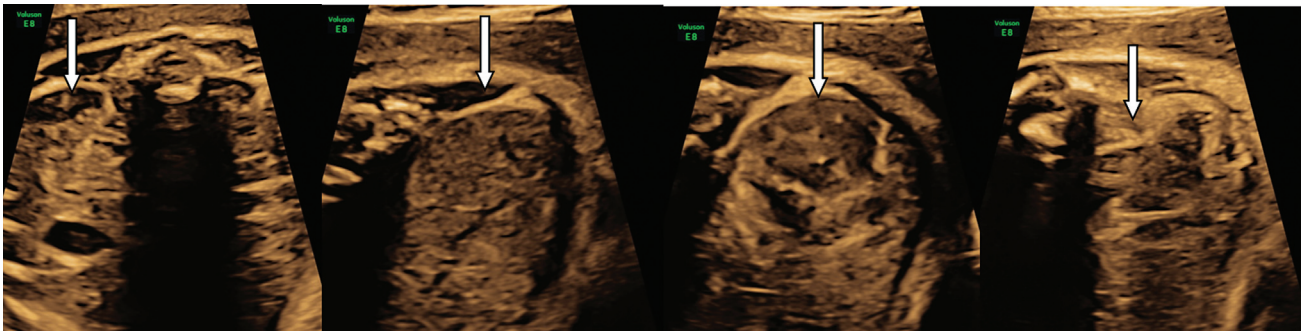

Fig. 1 Antenatal ultrasound at 28 weeks of gestation showing both the kidneys with lack of corticomedullary differentiation, with normal amniotic fluid at 28 weeks.

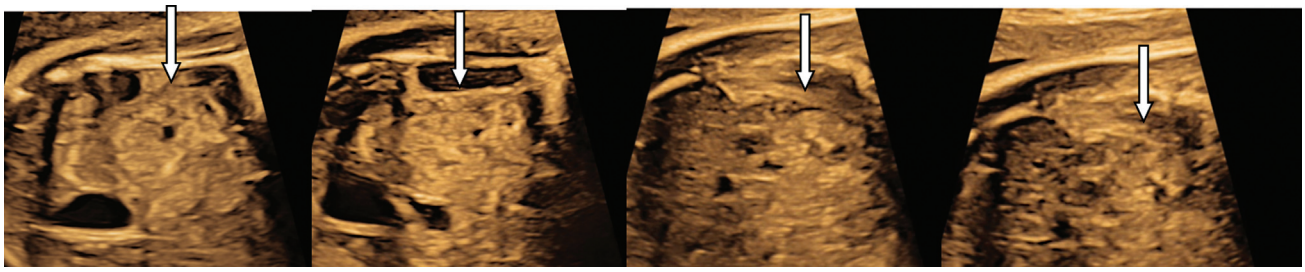

Fig. 2 Follow-up antenatal ultrasound at 34 weeks of gestation showing the same finding; both kidneys showing lack of corticomedullary differentiation, with normal amniotic fluid at 34 weeks.

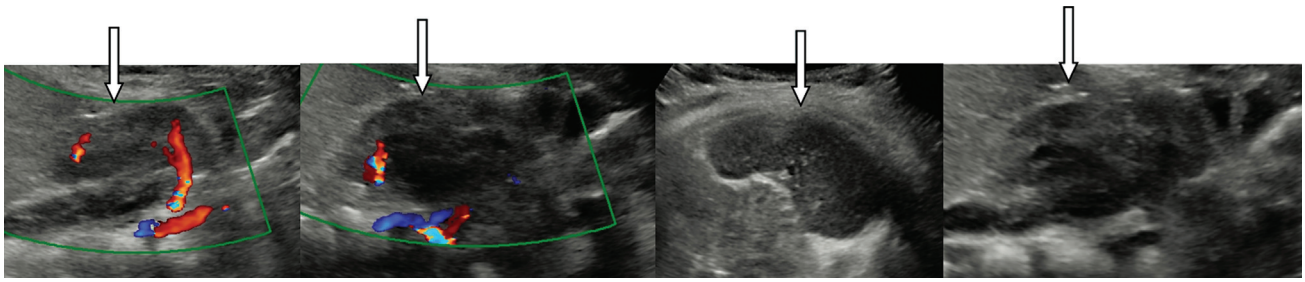

Fig. 3 Postnatal ultrasound of the baby confirming lack of corticomedullary differentiation in both kidneys.

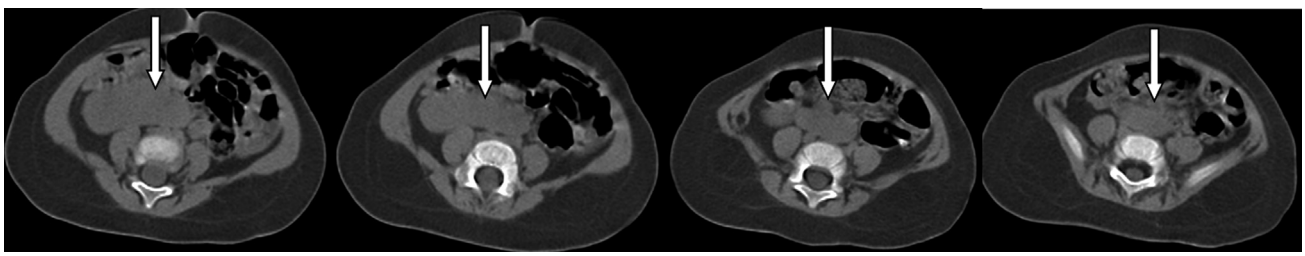

Fig. 4 Computed tomography (CT) of the baby at around 7 months postnatal showing no corticomedullary differentiation in both kidneys.

The arrival of the tracer in the abdominal aorta corresponded with the perfusion of both kidneys. Normal cortical uptake of both kidneys and normal pelvicalyceal system drainage were observed. Within 2 to 3 minutes of the tracer injection, bladder activity was also observed (►**Fig. 5**). Left renal function was at 43%, whereas that of the right kidney was at 57% (►**Table 1**).

Postnatal renal imaging by US (►**Fig. 3**) and NCCT (►**Fig. 4**) confirmed the antenatal documentation of the lack of CMD in both kidneys (►**Figs. 1** and **2**). When the patient was 7 months old, a positron emission tomography (PET)-SPECT (►**Fig. 5**) revealed that renal functioning had deteriorated, which can be assessed by plasma 51Cr-EDTA clearance (►**Fig. 6**)[13] and insulin clearance (►**Fig. 7**).[14]

Discussion

Nonetheless, there is a chance that a fetus with bilateral hyperechoic kidneys and a normal volume of amniotic fluid will fare well in the short term, and there are reports that the parenchymal hyperechogenicity will decrease over time. To ascertain the long-term natural history of this phenomenon, more observation is necessary.[9]

Non-invasive ultrasound modality can properly measure estimates of renal parenchymal quantity (total renal parenchymal area) and quality (CMD and renal echogenicity); if necessary, NCCT or PET scan can also be performed.

Although pediatric renal failures are uncommon, they are dangerous conditions that need to be diagnosed and treated immediately since they can be fatal.[15–20] Prerenal failures (RF) can result from hypotension, hypovolemia (placental haemorrhage or uterine rupture), septicemia, multi-organ system failure, heart disease (patent ductus arteriosus, aortic coarctation), dehydration and hyperviscosity.

Renal CMD may be altered in intrinsic renal diseases, like syndromic nephropathies, congenital hypodysplasia, bilateral renal agenesis, autosomal recessive polycystic kidney disease, congenital nephrotic syndrome (NS), severe urinary tract infection, renal vein thrombosis, hypoxic and toxin-induced renal parenchymal damage and neonatal GN.[17–20]

Reduced CMD, fluctuating cortical hyperechogenicity and numerous cysts are characteristics of congenital hypodysplasia,

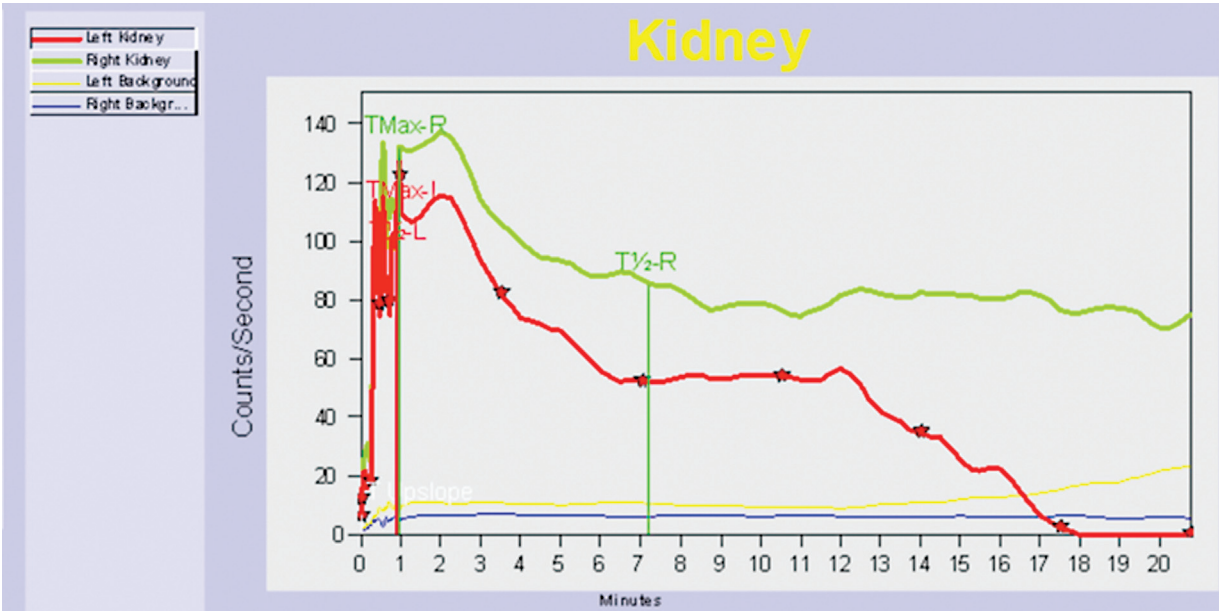

Table of Result Summary

Parameters	Left	Right	Total
Curve Fit	Off	Off	
Split Function (%)	43.4	56.6	
Kidney Counts (cpm)	9692.2	12628	22320
Kidney Depth (cm)	2.340	2.805	
Uptake (%)	1.387	1.808	3.195
GFR (mL/min)	10.6	13.9	24.5
Normalized GFR (mL/min)			123.0
GFR Low Normal (mL/min)			90.0
Mean GFR (mL/min)			118.0
Renal Retention		0.374	
Time of Max (min)	0.868	0.969	
Time of ½ Max (min)	0.885	7.171	
Time from Max to ½ Max (min)	0.016	6.202	

Fig. 5 99mTc diethylenetriamine pentaacetate (DTPA) single-photon emission computerized tomography (SPECT) scan showing perfusion of both kidneys.

Table 1 DTPA SPECT scan for the baby showing eGFR of the kidneys

	Renal function	GFR (mL/min)
Left kidney	43%	10.6
Right kidney	57%	13.9
	Total GFR 24.5 mL/min	

Abbreviations: DTPA, diethylenetriamine pentaacetate; eGFR, estimated glomerular filtration rate; SPECT, single-photon emission computerized tomography.

a disease characterized by hypoplastic kidneys with abnormal echotexture. Renal dysplasia and altered CMD vary greatly in degree and can be first overlooked as the kidneys may appear normal on US and have normal diameters.[17–19]

Bilateral severe obstructive uropathy (posterior urethral valve, megaureter with ureterovesical junction obstruction and ureteropelvic junction obstruction) is another possible cause of post-renal issues leading to RF.

Age (months)	Mean GFR ± SD (mL/min/1.73 m^2)
<1.2	52.0 ± 9.0
1.2–3.6	61.7 ± 14.3
3.6–7.9	71.7 ± 13.9
7.9–12	82.6 ± 17.3
12–18	91.5 ± 17.8
18–24	94.5 ± 18.1
>24	104.4 ± 19.9

Fig. 6 Plasma 51Cr-EDTA clearance in normal infants and children.[13]

Age (gender)	Mean GFR ± SD (mL/min per 1.73 m^2)
Pre-term babies	
1–3 days	14.0±5
1–7 days	18.7±5.5
4–8 days	44.3±9.3
3–13 days	47.8±10.7
8–14 days	35.4±13.4
1.5–4 months	67.4±16.6
Term babies	
1–3 days	20.8±5.0
3–4 days	39.0±15.1
4–14 days	36.8±7.2
6–14 days	54.6±7.6
15–19 days	46.9±12.5
1–3 months	85.3±35.1
0–3 months	60.4±17.4
4–6 months	87.4±22.3
7–12 months	96.2±12.2
1–2 years	105.2±17.3
Children	
3–4 years	111.2±18.5
5–6 years	114.1±18.6
7–8 years	111.3±18.3
9–10 years	110.0±21.6
11–12 years	116.4±18.9
13–15 years	117.2±16.1
2.7–11.6 years	127.1±13.5
9–12 years	116.6±18.1
Young adults	
16.2–34 years	112±13

Fig. 7 Glomerular filtration rate in healthy infants, children and young adults as assessed by inulin clearance.[14]

An enlarged kidney with a change in the parenchymal echo pattern can also be a symptom of neonatal GN or NS. To date, there is no pathognomonic sign that can be used to make the diagnosis. Changes in the degree and pattern of echogenicity have been observed to be more common in some disorders, such as lupus nephritis, familial NS, Henoch-Schonlein nephritis, immunoglobulin A-nephropathy and para- and post-infectious GN.[19–23]

Prenatal exposure to NSAIDs can occasionally result in severe and irreversible renal insufficiency in neonates exposed through maternal pharmacological exposure.[24–26]

Exposure to antibiotics during pregnancy, especially β-lactams and aminoglycosides, has been linked to detrimental effects on the kidneys in neonates. These drugs have been documented to cross the placenta.[27,28]

Depending on the US appearance of the relative echogenicity of the cortex and parenchyma, CMD can result in higher or decreased CMD and may occasionally even be normal in moderate disease, depending on whether both of these structures are afflicted and to what extent.

The general US appearance makes it impossible to reliably diagnose a specific illness or rule out plausible causes of RF. However, even in utero, abnormal CMD is an extremely sensitive measure to identify renal function, necessitating additional testing to determine the cause.

Our case is likely to be the first to document both the loss of renal function and CMD prenatally, following the Kidney Disease Improving Global Outcomes' guidelines that a glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m^2 be considered a disease regardless of age. This advice is based on estimated GFR (eGFR) and eGFR values below 60 mL/min/1.73 m^2 are associated with a greater risk of death.[29]

Conflict of Interest
None declared.

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