Long-Term Renal Consequences of Preterm Birth

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KEYWORDS

• Glomeruli • Preterm • Chorioamnionitis • Diabetes • Preeclampsia
• Growth restriction • Antenatal steroids

KEY POINTS

- Several antenatal factors have the potential to impair kidney development, including fetal growth restriction, maternal hypertension, and diabetes.
- Preterm birth is associated with several postnatal risk factors for kidney development, including increased physiologic requirements related to ex utero life, nephrotoxic medications, acute kidney injury, and postnatal growth failure.
- Children and adults born preterm may have reduced kidney size and increased blood pressure (BP), which likely predispose to renal disease later in life.
- The population of individuals born preterm continues to increase worldwide; it is expected that further evidence of renal dysfunction after preterm birth will continue to emerge in the future.

CLINICAL SCENARIO 1

A woman presented to the delivery suite at 26+1 weeks' gestation with ruptured membranes and was managed with intravenous ampicillin 500 mg 6 hourly, gentamicin 120 mg daily for 48 hours and then converted to oral azithromycin 500 mg every three days. She received antenatal steroids (betamethasone 12 mg daily for 2 doses) and was admitted to the antenatal ward. Four days later, she developed a fever and tachycardia, with an associated increase in white cell count on full blood picture and increased C-reactive protein levels. Labor ensued, and she delivered a

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26+6 week gestation male infant weighing 900 g (50th centile), who required intubation for resuscitation, received a dose of surfactant, and was extubated at 48 hours of age. Placental histology later confirmed the diagnosis of chorioamnionitis and funisitis. Certain components of this history have long-term implications on renal health (Fig. 1).

Chorioamnionitis

Chorioamnionitis (bacterial infection that causes inflammation of the amnion and chorion), is widely recognized as a significant contributor to preterm birth, as a cause of both spontaneous preterm labor and premature rupture of the amniotic membrane.[1,2] Chorioamnionitis also produces the fetal inflammatory response syndrome (FIRS), characterized by an inflamed umbilical cord and increased fetal serum levels of proinflammatory cytokines.[3] Consequently, FIRS can adversely influence neonatal organ development, including the lungs,[4] brain,[2,5] thymus,[6,7] and kidney.[8] In an ovine model, intrauterine exposure to chorioamnionitis (bolus intra-amniotic high dose of endotoxin [10 mg lipopolysaccharide (LPS)] at a time in gestation when nephrogenesis was near completion) was found to cause a 20% reduction in nephron endowment.[8] In response to the reduction in nephron number, there was also a significant increase in glomerular volume, most likely resulting from compensatory hypertrophy; these adverse effects on nephrogenesis occurred in the absence of fetal growth restriction.[8] This finding is clinically important, because a reduction in nephron number can lead to increased susceptibility to renal injury and disease in later life.[9–14] In a more recent ovine study,[15] it was found that exposure to a chronic low-dose intra-amniotic infusion of endotoxin (1 mg LPS), during a time when fetal nephrogenesis was still rapidly ongoing, did not lead to any observable deleterious effects on nephron endowment. Together, these findings are indicative that the extent of infection as well as the timing (acute vs chronic) may influence the impact of chorioamnionitis on renal development.

Antenatal Steroids

Besides the beneficial effects on lung function and postnatal survival, antenatal glucocorticoid treatment is also associated with increased mean arterial BP, and increased

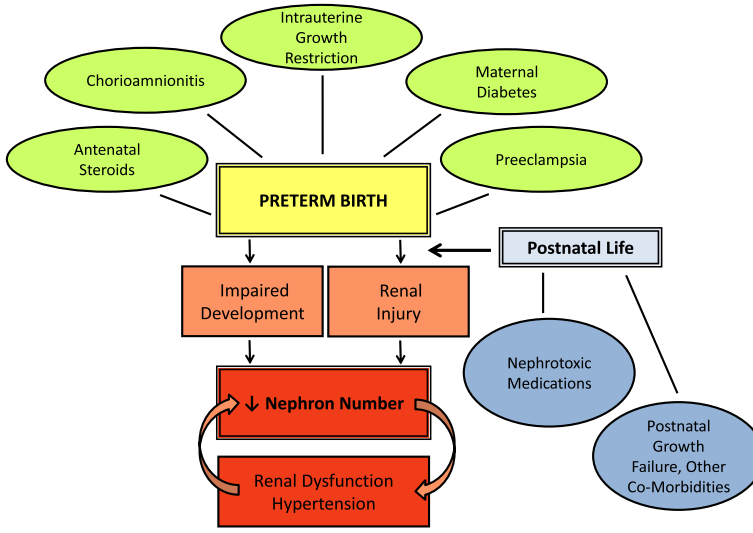

Fig. 1. Prenatal and postnatal risk factors for renal developmental injury.