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ACTA PÆDIATRICA NURTURING THE CHILD WILEY

ORIGINAL ARTICLE

Impaired renal clearance among Swedish adolescents born preterm

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Abstract

Aim: To determine whether adolescents born before 28 gestational weeks have an increased risk for renal impairment.

Methods: Swedish infants, born before 28 gestational weeks in 2001 and 2002, were identified from a local register. A total of 16 children, 12 females and 4 males, were examined at 16–17 years of age with ^{51}Cr-EDTA clearance. A comparison group ($n = 26$) was used.

Results: Most study participants ($n = 13$) had normal blood pressure; one individual had hypertension stage 1. All study participants had results within the reference interval for ionised calcium, parathyroid hormone, intact fibroblast growth factor-23 and for urinary albumin-to-creatinine ratio. Four out of 16 participants (25%) had a ^{51}Cr-EDTA clearance less than 90 ml/min/1.73 m^2, indicating a reduced kidney function. Measured ^{51}Cr-EDTA clearance values were significantly lower in the study group than in the comparison group ($p = 0.0012$). Five study participants (31%) were referred for further investigations.

Conclusion: Swedish children born before 28 gestational weeks have an increased risk of renal impairment later in life, suggesting that the kidney function in these individuals should be assessed, at least once, during adolescence.

KEYWORDS
adolescent, kidney function tests, extremely preterm infant, neonatology, nephrology

1 | BACKGROUND

Neonatal intensive care has undergone a technological revolution during the past 20 years. Consequently, more infants born preterm survive, and a larger share of children born extremely preterm enjoy better health.[1,2] In the standard Swedish national follow-up programme, all children born before 28 gestational weeks are followed at the neonatal outpatient clinic from birth until the age of 5.5 years by a neonatologist and are then referred, if needed, to continued follow-up in the paediatric outpatient clinic.

It is unusual for children born preterm to have kidney-specific problems at the age of 5.5 years; hence, long-term follow-up of

Abbreviations: ADHD, attention deficit hyperactivity disorder; BMI, body mass index; BPD, bronchopulmonary dysplasia; eGFR, estimated GFR; FGF23, fibroblast growth factor-23; GFR, glomerular filtration rate; ICD, International Classification of Diseases; IVH, intraventricular haemorrhage; mGFR, measured glomerular filtration rate; NEC, necrotising enterocolitis; PDA, persistent ductus arteriosus; PTH, parathyroid hormone; ROP, retinopathy of prematurity; SGA, small for gestational age.

kidney function is seldom done.[3] However, recent data suggests that preterm birth affects an individual's renal health throughout life.[4,5] Most of the nephrons are formed during the last trimester of the pregnancy.[6] Children born before 36 gestational weeks have an increased risk of suffering from reduced nephrogenesis.[7] In addition, several studies have shown that low birth weight, due to intrauterine growth restriction as well as prematurity alone, is correlated to fewer nephrons and reduced kidney volume.[8,9] As early as in 1988, Brenner et al.[10] stated that children with low birth weight have fewer nephrons and that compensatory hyperfiltration by the remaining nephrons may cause glomerulosclerosis and loss of kidney function. They showed that individuals with a congenital reduction of the number of nephrons have a greater likelihood of developing adult hypertension and subsequent kidney failure.[10] Recent studies have also shown that children born preterm have an increased risk of developing elevated blood pressure as they go through adolescence.[11,12] This is in good agreement with today's evidence that there is a strong linkage between low birth weight and the risk of developing metabolic syndrome in adulthood.[13,14]

Reduced kidney function affects calcium and phosphate homeostasis early on in life,[15] leading to altered levels of mineral-regulating hormones such as fibroblast growth factor-23 (FGF23) and parathyroid hormone (PTH). The main function of FGF23 is to regulate the circulating levels of phosphate. FGF23 is secreted by osteocytes, cells residing within the bone matrix, and inhibits phosphate reabsorption directly in order to increase the kidney excretion of phosphate. The circulating levels of FGF23 increase even with a slightly decreased glomerular filtration rate (GFR), and such increase is therefore an early sign of decreased kidney function.[16]

The aim of this study was to investigate whether children born before 28 gestational weeks have an increased risk of developing renal impairment already during adolescence.

Key Notes

- Preterm birth may affect an individual's renal health throughout life, but long-term follow-up of kidney function is seldom done.
- Our study indicates that adolescents born before 28 gestational weeks have an increased risk of renal impairment, four out of 16 (25%) individuals had a ^{51}Cr-EDTA clearance less than 90 ml/min/1.73 m^2.
- We suggest a kidney-focused follow-up of adolescents born extremely preterm, to prevent future kidney disease and cardiovascular complications of prematurity.

2 | MATERIAL AND METHODS

2.1 | Ethical approval and informed consent

The study was conducted according to and approved by the research ethics committee of Gothenburg (#089-18, #2021-03327), and the study was also approved by the Swedish Radioactivity Protective Authorities, since the participants were given a single injection of 3.7 MBq ^{51}Cr-EDTA. Written informed consent was obtained from the study participants and their caregivers.

2.2 | Subjects

Study participants were identified from a local register at The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg, including all infants admitted to the neonatal intensive care unit. A total of 86 infants, born before 28 gestational weeks during the period January 2001 and December 2002, were identified. Of these, 17 died shortly after birth, and one child a few years later. Of the remaining 68 children, 24 lived more than 100 km from Gothenburg and were excluded for practical reasons. No additional exclusion criteria were set initially. The remaining 44 children were contacted by mail and phone by the same investigator (C.S.). Three individuals could not be reached due to missing phone numbers, and 21 agreed to participate, of whom two individuals later retracted their consent. Three children were excluded for medical reasons; one female with Rett syndrome and two children with a solitary kidney, in both cases discovered during the neonatal period. A total of 16 children, 12 females and 4 males, 16.4–17.5 years of age, fulfilled the study protocol. The mean age was 16.9 years with a median of 16.9 years. The study was conducted between June 2018 and February 2019.

Information on neonatal characteristics was collected from the Swedish national birth records; that is, date of birth, gestational age, birth weight and sex. The medical charts from the neonatal and ophthalmic care were reviewed for diagnostic codes related to neonatal morbidity. The diagnostic codes according to the 10th revision of the International Classification of Diseases (ICD) were used, and the following conditions were noted: small for gestational age (SGA) P05.1, necrotising enterocolitis (NEC) P77.9, retinopathy of prematurity (ROP) H35.1, bronchopulmonary dysplasia (BPD) P27.1, intraventricular haemorrhage (IVH) P52.0–2 and treatment for persistent ductus arteriosus (PDA) P29.3A.

Clinical characteristics for the investigated adolescents are presented in Table 1. The lowest gestational age at birth was 24 weeks +0 days and the highest gestational age at birth was 27 weeks +6 days, with a median age of 25 weeks +6 days. The mean birth weight was 815 g, with minimum and maximum birth weights of 545 g and 1125 g, respectively.

The study participants and their caregivers filled in a questionnaire about the children's medical history, relatives with hereditary kidney diseases, current health and use of medications and nutritional supplements.

One female had been treated for an uncomplicated urinary tract infection during childhood. Another female had a twin sister with solitary kidney and a grandmother who underwent dialysis

TABLE 1 Clinical characteristics of the study participants

ID No.	Gender	Age (years)	Gestational age	Birth weight (g)	Diagnosis[c]					
1	F	17	24 week +5 days	650	BPD	ROP1				
2[a]	M	17	27 week +0 days	625		ROP2		SGA		
3	M	17	27 week +4 days	1125		ROP3				NEC
4	M	17	27 week +6 days	1065		ROP1				
5	F	17	24 week +0 days	545		ROP1	IVH1		PDA	
6	F	17	25 week +0 days	760	BPD					
7	F	17	25 week +3 days	865	BPD		IVH1			
8[a]	M	17	25 week +1 days	950		ROP2			PDA	
9	F	16	26 week +2days	1085		ROP3			PDA	
10[b]	F	16	25 week +5 days	725		ROP1		SGA		
11	F	16	25 week +0 days	650	BPD	ROP1				
12	F	16	24 week +2 days	640	BPD					
13[a]	F	16	25 week +5 days	785					PDA	
14[a]	F	16	26 week +1days	830		ROP2	IVH1			
15	F	16	25 week +6 days	850	BPD	ROP3			PDA	
16[a]	F	16	25 week +6 days	895		ROP2				

Abbreviations: BPD, bronchopulmonary dysplasia; F, Female; IVH1, intraventricular haemorrhage stage 1; M, Male; NEC, necrotising enterocolitis; PDA, patent ductus arteriosus; ROP: retinopathy of prematurity stage 1–3; SGA, small for gestational age.

[a]Individuals with attention deficit hyperactivity disorder, treated with stimulants.

[b]Individual with chronic NSAID use.

[c]The diagnostic codes from the neonatal care according to the 10th revision of the International Classification of Diseases.

due to diabetic nephropathy. Otherwise, none of the participants had any known renal impairment or relatives with hereditary kidney diseases.

Five of the study participants were diagnosed with attention deficit hyperactivity disorder (ADHD) and treated with stimulants. Two males used melatonin. One female had an isolated minor intellectual impairment and another female had high-functioning autism. Two participants had scoliosis, and one was suffering from migraine, medicating with NSAIDs. Three of the adolescents had asthma and allergies; all of them used a bronchodilator and one used nasal steroids. Two participants were supplemented with vitamin D. Two females used contraceptives.

2.3 | Study protocol

Study participants were examined at the Department of Pediatric Clinical Physiology at The Queen Silvia Children's Hospital, Sahlgrenska University Hospital, Gothenburg. All measurements (i.e., anthropometric data collection, blood pressure and ^{51}Cr-EDTA clearance) were performed during the same study visit by the same research nurse throughout the study. Blood pressure was measured with Medidyne (WelchAllyn, Mississauga, Canada) and the measurements were performed in the right upper arm in a sitting position after 5 min of rest. Three consecutive measurements were performed, and the mean systolic versus the mean diastolic blood pressures were recorded. Elevated office ambulatory blood pressure was confirmed with 24-h ambulatory blood pressure monitoring. High blood pressure was defined as an increased mean blood pressure according to the Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents.[17]

2.4 | Biochemical determinations

The ^{51}Cr-EDTA plasma clearance (mGFR) determination was based on multiple blood samples drawn at 5, 15, 60, 90, 120, 210 and 240 min after an intravenously injection of 3.7 MBq ^{51}Cr-EDTA and analysed according to a two-compartment model.[18] In our clinical practice, a measured GFR (mGFR) <90 ml/min/1.73 m^2, indicates a reduced kidney function and is used as a threshold for further investigations.

Blood samples for analysis of serum phosphate, ionised calcium, creatinine, PTH and FGF23 were taken before the injection of ^{51}Cr-EDTA. The study participants brought a sample of morning urine for analysis of urinary albumin-to-creatinine ratio. All samples were analysed at accredited hospital laboratories in Gothenburg and Uppsala (FGF23), Sweden. EDTA plasma intact FGF23 was measured on the DiaSorin LIASON XL analyzer (DiaSorin, Stillwater, MN) with an assay performance of analytical range 5 to 5000 ng/L, and intra- and inter-assay coefficients of variation of 3.8% and 7.9%, respectively.[19]

2.5 | Comparison group

The comparison group comprised 26 healthy Swedish males ($n = 5$) and females ($n = 21$), aged 15–17.5 years. The mean age was 15.8 years with a median age of 16 years. The individuals in the comparison group had all suffered from a urinary tract infection in childhood, leading to unilateral renal scarring, and were followed-up with ^{51}Cr-EDTA clearance, reported elsewhere.[20] The ^{51}Cr-EDTA measurements, for both groups, were conducted in the same laboratory with the same method.

2.6 | Statistical analysis

The distribution of continuous variables is given as median, mean, minimum and maximum. Wilcoxon rank sum test was used to test for differences between the study group and comparison group. Analyses were performed using the SAS® version 9.4 software (SAS Institute Inc, Cary, NC).

3 | RESULTS

3.1 | Measurements

Anthropometric data, blood pressure and biochemical results are presented in Table 2. The mean body mass index (BMI) for the study participants was 19.9 kg/m^2. The mean blood pressure for the whole study group was 112/69 mmHg. One participant had raised blood pressure (mean 134/85 mmHg) and underwent 24-h ambulatory blood pressure monitoring, with blood pressures above the 95th percentile both day and night, confirming the diagnosis of hypertension stage 1.[17] Further investigations showed no other pathologies such as renal artery stenosis. The participant did not have ADHD and used no other medications. Three other participants had elevated blood pressure with mean blood pressures of 123/78 mmHg, 120/77 mmHg and 122/66 mmHg, respectively. These individuals did not undergo any further investigations. The remaining participants ($n = 12$) had normal blood pressure.

The study participants had negative urine dipsticks, except for one who had 1 + albumin. All participants had results within the age- and sex-specific reference interval limits for ionised calcium, phosphate, PTH, FGF23 and urinary albumin-to-creatinine ratio.

3.2 | Kidney function

Four out of 16 study participants (25%) had a ^{51}Cr-EDTA clearance less than 90 ml/min/1.73 m^2, indicating a reduced kidney function, median 93 ml/min/1.73 m^2 (mean 91; range 68–108 ml/min/1.73 m^2). The study participants ($n = 4$) with ^{51}Cr-EDTA clearance less than 90 ml/min/1.73 m^{2}mGFR were mainly healthy (asthma, $n = 2$, minor intellectual impairment, $n = 1$) and had neonatal clinical characteristics that did not differ markedly from the rest of the group (Table 1). None of the study participants had an mGFR lower than 60 ml/min/1.73 m^2. Two out of 26 (8%) participants in the comparison group had a ^{51}Cr-EDTA clearance less than 90 ml/min/1.73 m^2, median 104 ml/min/1.73 m^2 (mean 105; range 87–126 ml/min/1.73 m^2). We found a significant difference for the measured ^{51}Cr-EDTA clearance values between the study and comparison groups, $p = 0.0012$.

The estimated glomerular filtration rate (eGFR) was calculated with serum creatinine and the Schwartz-Lyon equation, adjusted for body surface area (ml/min/1.73 m^2).[21] Thirteen study participants had an eGFR below 90 ml/min/1.73 m^2. This eGFR method showed a high sensitivity as all individuals with a ^{51}Cr-EDTA clearance less than 90 ml/min/1.73 m^2 were identified.

3.3 | Clinical follow-up

After consulting the medical team at the Department of Nephrology at The Queen Silvia Children's Hospital, Gothenburg, four of the study participants were referred for further kidney investigations (ultrasound and scintigraphy), resulting in continued follow-up. Two additional participants were assessed to need long-term follow-up and were admitted to the primary health care.

4 | DISCUSSION

4.1 | Principal finding

This study showed that children born before 28 gestational weeks have an increased incidence of renal impairment during adolescence. Four out of 16, that is, 25% of the study participants had a ^{51}Cr-EDTA clearance below 90 ml/min/1.73 m^2, indicating a reduced kidney function. In addition, 13 individuals had an eGFR below 90 ml/min/1.73 m^2. The measured ^{51}Cr-EDTA clearance values differed significantly between the study group and the comparison group, $p = 0.0012$. However, in our study population, we found no or very few indirect signs of altered renal health such as hypertension, microalbuminuria or pathological renal markers in blood and urine. This study adds to the existing knowledge by demonstrating a high incidence of renal impairment in Swedish adolescents born preterm, who were unaware of their reduced kidney function.

4.2 | Kidney function and blood pressure

Rakow et al.[22] recently studied 60 Swedish children, at a mean age of 7.7 years, of whom 20 were born before 28 gestational weeks. Kidney function was assessed by analysing biomarkers in blood and urine. GFR was estimated both with Schwartz's simplified formula and with the cystatin C–based CAPA formula. Kidney volume, as a proxy for nephron number, was determined with ultrasound during the neonatal period and at school age. They also

TABLE 2 Anthropometric data, blood pressure and biochemical results

ID No.	BMI[c] (kg/m^2)	BP[c] (mmHg)	Creatinine (μmol/L)	eGFR[d] (ml/min/1.73 m^2)	ACR[e] (g/mol)	FGF23 (ng/L)	^{51}Cr-EDTA clearance[f]
1	24	113/70	93	62	0.3	66.7	82
2[a]	21	123/78	88	75	1.7	69.0	94
3	17	115/71	92	70	1	50.8	78
4	16	108/62	76	91	0.4	50.7	93
5	19	106/67	67	79	0.2	30.3	97
6	17	134/85	65	78	0.5	29.2	95
7	18	111/71	75	71	0.4	49.7	92
8[a]	20	122/66	76	81	0.9	53.0	107
9	21	94/55	59	91	0	63.4	96
10[b]	26	99/65	66	77	0	25.3	101
11	21	116/71	60	82	0.2	43.3	69
12	18	116/68	66	82	2.3	44.2	92
13[a]	20	120/77	68	77	0.3	34.7	92
14[a]	21	110/69	70	82	0.3	34.6	91
15	22	101/63	73	71	1	41.6	68
16[a]	20	112/72	49	106	0.6	45.6	108

Abbreviation: BMI, body mass index.

[a]Individuals with attention deficit hyperactivity disorder, treated with stimulants.

[b]Individual with chronic NSAID use.

[c]Mean blood pressure. The measurements were performed in the right upper arm in a sitting position after 5 min of rest. Three consecutive measurements were done, and mean systolic versus mean diastolic blood pressure were recorded.

[d]The estimated glomerular filtration rate (eGFR) was calculated with serum creatinine and the Schwartz-Lyon equation, adjusted for body surface area (ml/min/1.73 m^2).[21]

[e]ACR: Urinary albumin-to-creatinine ratio.

[f]The ^{51}Cr-EDTA clearance (standardised for body surface), ml/min/1.73 m^2.

measured office and 24-h ambulatory blood pressure. Children born before 28 gestational weeks had significantly smaller kidneys and lower (but normal) cystatin C-based eGFR than term-born controls. Blood pressure was normal in both groups.[22] This is in accordance with the results obtained by Chan et al.,[13] who studied 25 children born preterm (<33 gestation weeks) in Sydney in the early 1990s. They found no abnormalities in blood pressure or kidney function in individuals born with a size appropriate for gestational age. However, they estimated GFR by analysing creatinine in urine and serum following oral protein loading.[13] In this study, we found only one individual with stage 1 hypertension, three additional participants had slightly elevated blood pressures. Both Keijzer-Veen et al.[11] and South et al.[12] showed an elevated risk for hypertension in adolescents born preterm. Our deficiency to prove an elevated risk for hypertension could be due to the small sample size.

4.3 | Biochemical renal markers and estimated glomerular filtration rate

We did not find any significant alteration of biochemical renal markers in blood and urine, or any presence of microalbuminuria. Yet, when we estimated GFR with creatinine and the Schwartz-Lyon equation,[21] 13 participants had an eGFR below 90 ml/min/1.73 m^2. The eGFR values were partly inconsistent with those obtained with ^{51}Cr-EDTA clearance. In general, among our study participants, the Schwartz-Lyon formula underestimated the kidney function but identified all individuals with ^{51}Cr-EDTA <90 ml/min/1.73 m^2.

Accordingly, creatinine-based eGFR measurements might be a good option to find children at risk of renal impairment. The creatinine analysis is highly accessible and cheap. However, when the method is used for children, the eGFR values must be related to gender and age.[23]

4.4 | Fibroblast growth factor-23

Our findings could not confirm those of Isakova et al.[24] regarding FGF23 as an early marker for kidney failure. Wolf[25] wrote in his review that FGF23 levels increase progressively as GFR declines in chronic kidney disease (CKD); a few studies reviewed have detected increased levels of FGF23 already in early CKD stages.[25] Our results of ^{51}Cr-EDTA clearance and FGF23 were inconsistent, and all study participants had FGF23 values within the age- and sex-specific

reference interval.[19] One reason for these opposing results could be that our studied adolescents had a relatively mild reduction of kidney function. With this in mind, we still believe that by using the gold standard of ^{51}Cr-EDTA clearance,[26] we have succeeded in detecting a true, but subtle renal impairment among adolescents born preterm.

4.5 | Preterm birth, kidney function and follow-up

According to Abitbol et al.,[5] over 60% of the nephrons are formed during the pregnancy's last trimester, and children born before 36 gestational weeks are in active nephrogenesis at birth. These children risk having a reduced number of functional nephrons, and consequently, a lowered kidney function.[5] The linkage between preterm birth and renal impairment could also be explained by a stressful postnatal period with exposure to antibiotics, inadequate nutrition and medical complications.

None of our research participants had been monitored for kidney function after leaving the neonatal inpatient care. The renal impairment we found was relatively mild, but the peak of the kidney function is expected to be around the age of 20 years.[27,28] As a result of this study, there seems to be a need for follow-up of kidney function in children born extremely preterm. Levin et al.[14] concluded that premature birth should be regarded as a risk factor for developing impaired kidney function and that information regarding gestational age, birth weight and acute kidney injury during the neonatal period should be apparent in the medical record and follow the patient throughout life.[14]

For children born extremely preterm, we recommend a medical follow-up visit regarding their kidney function, before entering adulthood. Although a small study, we suggest that such a follow-up visit include measurement of anthropometrics, blood pressure, the urinary albumin-to-creatinine ratio and as well, creatinine and eGFR. The use of eGFR will overestimate the frequency of renal impairment. Nevertheless, our best recommendation is yet to use eGFR as a screening, followed by a mGFR method for individuals with low eGFR. Adolescents born extremely preterm form a small patient group. Measuring GFR once during adolescence for many of these individuals should not be too much of a burden on healthcare. Further studies are still needed in larger populations.

4.6 | Strengths and limitations

The main strength of our study is that we have measured the kidney function by ^{51}Cr-EDTA clearance instead of only applying estimated calculations or indirect methods. Another important strength is the longitudinal perspective with a follow- up period of 16–17 years. We succeeded, in a retrospective way, in following 16 children, from the very moment of the preterm birth to early adulthood, with detailed information about their current and past health.

The relatively small study group is a limitation of this study that warrant consideration when interpreting the results in a wider perspective. The individuals in the comparison group have all suffered from a urinary tract infection in childhood, leading to unilateral renal scarring; a newly recruited control group with healthy adolescents would have been preferable. However, the mGFR in our study group was significantly lower than the mGFR in the comparison group, even though the comparison group comprised individuals with renal scarring. Furthermore, the ^{51}Cr-EDTA clearance reference interval,[29] is well defined for the studied ages and these mGFR references corresponds well with the results of our comparison group. Finally, the study group (12 females and 4 males, 16.4–17.5 years) and the comparison group (21 females and 5 males, 15–17.5 years) are similar regarding age and gender distribution.

We suspect that our study participants constitute a selected group of adolescents with relatively good health, because only three participants had mild intraventricular haemorrhage (grade 1) and none had severe haemorrhage (grade 3–4). That differs from the findings of the EXPRESS group,[3] who studied 638 infants born before 27 gestational weeks in Sweden during 2004–2007. Out of the 497 surviving infants, 10% developed severe intraventricular haemorrhage (grade 3–4).[3]

5 | CONCLUSION

In summary, this study demonstrates that children born before 28 gestational weeks have an increased incidence of renal impairment during adolescence. Four out of 16 individuals (25%) had a ^{51}Cr-EDTA clearance less than 90 ml/min/1.73 m^2, indicating a reduced kidney function. However, we found no evidence that adolescents born extremely preterm have an increased incidence of high blood pressure, microalbuminuria, or pathological renal biomarkers.

Individuals surviving extreme preterm birth form a growing patient group. The long-term consequences of being born preterm are partly unknown. In the future we hope that follow-up of kidney function in children born extremely preterm could contribute to preventing future kidney disease and cardiovascular complications of prematurity.

AUTHOR CONTRIBUTIONS

C.S.: Conception and design of the study. Acquisition, analysis and interpretation of data. Drafting the article and revising it critically. Final approval of the version to be published. A.E. and S.H.: Conception and design of the study. Acquisition, analysis and interpretation of data. Revising the article critically for important intellectual content. Final approval of the version to be published. P.M. and D.S.-E.: Conception and design of the study. Analysis and interpretation of data. Revising the article critically for important intellectual content. Final approval of the version to be published.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. EXPRESS Group. One-year survival of extremely preterm infants after active perinatal care in Sweden. JAMA. 2009;301:2225-2233.
2. Norman M, Hallberg B, Abrahamsson T, et al. Association between year of birth and 1-year survival among extremely preterm infants in Sweden during 2004–2007 and 2014–2016. JAMA. 2019;321:1188-1199.
3. EXPRESS Group. Incidence of and risk factors for neonatal morbidity after active perinatal care: extremely preterm infants study in Sweden (EXPRESS). Acta Paediatr. 2010;99:978-992.
4. Gubhaju L, Sutherland MR, Black MJ. Preterm birth and the kidney: implications for long-term renal health. Reprod Sci. 2011;18:322-333.
5. Abitbol CL, DeFreitas MJ, Strauss J. Assessment of kidney function in preterm infants: lifelong implications. Pediatr Nephrol. 2016;31:2213-2222.
6. Carmody JB, Charlton JR. Short-term gestation, long-term risk: prematurity and chronic kidney disease. Pediatrics. 2013;131:1168-1179.
7. Paquette K, Oliveira Fernandes R, Xie LF, et al. Kidney size, kidney function, ang (angiotensin) peptides, and blood pressure in young adults born preterm. Hypertension. 2018;72:918-928.
8. Reid IR, Gamble GD, Bolland MJ. Circulating calcium concentrations, vascular disease and mortality: a systematic review. J Intern Med. 2016;279:524-540.
9. Silver LE, Decamps PJ, Korst LM, Platt LD, Castro LC. Intrauterine growth restriction is accompanied by decreased kidney volume in the human fetus. Am J Obstet Gynecol. 2003;188:1320-1325.
10. Brenner BM, Garcia DL, Anderson S. Glomeruli and blood pressure. Less of one, more the other? Am J Hypertens. 1988;1:335-347.
11. Keijzer-Veen MG, Dülger A, Dekker FW, Nauta J, van der Heijden BJ. Very preterm birth is a risk factor for increased systolic blood pressure at a young adult age. Pediatr Nephrol. 2010;25:509-516.
12. South AM, Nixon PA, Chappell MC, et al. Renal function and blood pressure are altered in adolescents born preterm. Pediatr Nephrol. 2019;34:137-144.
13. Chan PYL, Morris JM, Leslie GI, Kelly PJ, Gallery EDM. The long-term effects of prematurity and intrauterine growth restriction on cardiovascular, renal, and metabolic function. Int J Pediatr. 2010;2010:1-10.
14. Levin A, Tonelli M, Bonventre J, t al. Global kidney health 2017 and beyond: a roadmap for closing gaps in care, research, and policy. Lancet. 2017;390:1888-1917.
15. Haarhaus M, Brandenburg V, Kalantar-Zadeh K, Stenvinkel P, Magnusson P. Alkaline phosphatase: a novel treatment target for cardiovascular disease in CKD. Nat Rev Nephrol. 2017;13:429-442.
16. Isakova T, Cai X, Lee J, et al. Longitudinal evolution of markers of mineral metabolism in patients with CKD: the Chronic Renal Insufficiency Cohort (CRIC) study. Am J Kidney Dis. 2020;75:235-244.
17. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Subcommittee on Screening and Management of High Blood Pressure in Children. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics. 2017;140:e20171904.
18. Bröchner-Mortensen J, Haahr J, Christoffersen J. A simple method for accurate assessment of glomerular filtration rate in children. Scand J Clin Lab Invest. 1974;33:139-143.
19. Souberbielle JC, Prié D, Piketty M-L, et al. Evaluation of a new fully automated assay for plasma intact FGF23. Calcif Tissue Int. 2017;101:510-518.
20. Wennerström M, Hansson S, Jodal U, et al. Renal function 16 to 26 years after the first urinary tract infection in childhood. Arch Pediatr Adolesc Med. 2000;154:339-345.
21. Souza VC, Rabilloud M, Cochat P, et al. Schwartz formula: is one k-coefficient adequate for all children? PLoS One. 2012;7:e53439.
22. Rakow A, Laestadius Å, Liliemark U, et al. Kidney volume, kidney function, and ambulatory blood pressure in children born extremely preterm with and without nephrocalcinosis. Pediatr Nephrol. 2019;34:1765-1776.
23. Björk J, Nyman U, Berg U, et al. Validation of standardized creatinine and cystatin C GFR estimating equations in a large multicenter European cohort of children. Pediatr Nephrol. 2019;34:1087-1098.
24. Isakova T, Wahl P, Vargas GS, et al. Fibroblast growth factor 23 is elevated before parathyroid hormone and phosphate in chronic kidney disease. Kidney Int. 2011;79:1370-1378.
25. Wolf M. Forging forward with 10 burning questions on FGF23 in kidney disease. J Am Soc Nephrol. 2010;21:1427-1435.
26. Soveri I, Berg UB, Björk J, et al. Measuring GFR: a systemic review. Am J Kidney Dis. 2014;64:411-424.
27. Rule AD, Amer H, Cornell LD, et al. The association between age and nephrosclerosis on renal biopsy among healthy adults. Ann Intern Med. 2010;152:561-567.
28. Davies DF, Shock NW. Age changes in glomerular filtration rate, effective renal plasma flow, and tubular excretory capacity in adult males. J Clin Invest. 1950;29:496-507.
29. Piepsz A, Tondeur M, Ham H. Revisiting normal 51Cr-ethylenediaminetetraacetic acid clearance values in children. Eur J Nucl Med Mol Imaging. 2006;33:1477-1482.

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