

Women with kidney diseases: Whatever we understand and lack of knowledge.

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ABSTRACT

About 10% of adults worldwide suffer from chronic kidney disease, which is among the top 20 causes of death globally and can have a devastating effect on patients and their families. In 2018, World Kidney Day and International Women's Day fell on the same day, providing a chance to consider the significance of women's health, particularly their kidney health, on the community and the next generation. We should also endeavour to increase our curiosity about the particular features of kidney disease in women so that we can apply the knowledge we gain more broadly. Women and girls, who comprise over half of the global population, play significant roles in their families' and society's lives. Gender disparities persist in global access to education, healthcare, and clinical research participation. Pregnancy is a special time for women to get screened for kidney illness, but it's also a time when acute and chronic kidney problems might appear, which can have an effect on the health of future generations' kidneys. Numerous autoimmune diseases and other illnesses have a higher propensity to affect women, having significant effects on both the foetus and the ability to carry children. In addition to being more likely to be kidney donors than recipients, women experience distinct consequences from dialysis than do males. This editorial focuses on the knowledge gaps regarding women, kidney health, and renal disease.

Keywords : *Women; Access to care; Kidney health; Acute and chronic kidney disease; inequities.*

INTRODUCTION

About 10% of adults worldwide suffer from chronic kidney disease (CKD), which is among the top 20 causes of death globally¹. The condition can have a catastrophic effect on patients and their families. 2018 marks both World Kidney Day and International Women's Day, providing a chance to consider the significance of women's health, particularly their kidney health, on the community and the coming generations. We should also endeavour to be more inquisitive about the particular features of kidney disease in women so that we can apply the knowledge we gain more broadly.

Women and girls, who comprise over half of the global population, play significant roles in their families' and society's lives. In addition to carrying children, women play a crucial role in raising them and helping to maintain. In the twenty-first century, women still aim for parity in business, trade, and other professional pursuits, even if they are aware that parity does not always exist. Men and women do not always have equal access to education and healthcare; women are still underrepresented in many clinical research studies, which reduces the amount of data that can be used to provide recommendations for the best possible outcomes (Figure 1). This editorial centres on the current state of knowledge on kidney health and illness in women, as well as potential future research directions to enhance overall results.

What Is and Is Not Known

For women of childbearing age, pregnancy presents a special set of challenges. AKI and pre-eclampsia (PE) can result in future chronic kidney disease (CKD), but the extent of the risk is unknown. Pregnancy is negatively impacted by 2–5 CKD, especially in the earliest phases.⁶⁻⁷ As CKD progresses, the dangers rise, raising potentially difficult ethical questions about getting pregnant and keeping a child.⁶⁻⁸ We are aware that PE raises the risk of hypertension and chronic kidney disease (CKD) in later life, but we haven't looked into surveillance or renoprotective measures to see if renal function may be gradually reduced.⁹⁻¹²

Certain systemic diseases, such as rheumatoid arthritis (RA), systemic scleroderma (SS), and systemic lupus erythematosus (SLE), are more likely to impact women more than men. The proportionate impact of these acute and chronic diseases on the development of end-stage renal disease (ESRD) in females remains unknown. Women are always less common than men in CKD cohorts, and their progression to ESRD is slower.^{13–15} We don't know why and to what extent this is caused by variations in the way kidney impairment is diagnosed, variations in patient access to care, or actual variations in the incidence and severity of the disease.

Though still lower than males with comparable levels of kidney impairment, women with CKD had a greater cardiovascular risk than women without the disease¹⁶. There are variations in the vascular access types between men and women in hemodialysis cohorts, which could be caused by biological. Donating kidneys for transplantation is more common among women than receiving them. We are unsure if this is due to other causes, cultural factors, or the difference incidence of CKD in men and women. In certain places of the world, particularly the poorest, there are still gender disparities in access to care, and the degree of these discrepancies cannot be clearly assessed due to a lack of data.

Pregnancy, preterm birth, hypertensive disorders associated with pregnancy, and foetal health. WOMEN'S HEALTH IS ESSENTIAL FOR BOTH CURRENT AND FUTURE KIDNEY HEALTH

What is Acknowledged

The primary cause of AKI and maternal mortality, especially in underdeveloped nations, is PE.^{2,17} The most frequent cause of AKI in women who are fertile is pregnancy.^{10, 18, 19} Numerous illnesses and various regions have various causes. In nations without access to legal abortion services, septic abortion following an illicit operation is the primary cause of early AKI; in wealthy nations, on the other hand, PE following aided fertilisation is increasingly the predominant cause.^{12, 20–22} Three to ten percent of pregnancies result in PE and hypertensive problems.^{2–3,18}; in these conditions, an imbalanced pro- and anti-angiogenic dysregulation primarily targets the kidney, resulting in endothelial damage throughout the body, hypertension, and proteinuria. The incidence of PE rises at the extremes of reproductive age for the reasons previously indicated. It is higher in low-middle income nations

(perhaps reflecting undetected predisposing conditions). The kidney and placenta have an unambiguous link, and having chronic kidney disease (CKD) increases the risk of PE and hypertensive problems during pregnancy (Figure). In addition to CKD, additional illnesses mentioned as risk factors for PE include diabetes and immunologic CKD risk factors may include obesity, metabolic syndrome, illnesses, and baseline hypertension. Since many of these conditions exhibit even slight changes in renal function, the role of kidney function in the development of PE is recognised indirectly. Based on novel angiogenic-antiangiogenic markers, more recent classifications of PE distinguish between “placental” and “maternal” causes of PE, which may be crucial for care both during and after pregnancy.

PE has long-term repercussions on the health of both the mother and the foetus, but there are still many unanswered questions in this field of active research. PE increases the mother's risk of developing CKD and ESRD in the future. The causes are not entirely known, although podocyte loss—a defining feature of PE—suggests long-term glomerular injury.²⁵ Endotheliosis may signal glomerulosclerosis; tubular and vascular damage may coexist. Endotheliosis is linked to PE but is also seen in healthy pregnancies.^{26, 27}

PE is linked to premature delivery, reduced intrauterine growth, intrauterine and perinatal death, and “small babies” in addition to maternal concerns.^{2, 3, 5} Preterm and small babies are much more likely to experience neurological impairments and postnatal problems, including sepsis.^{28–32} Since postnatal intensive care is necessary for both survival and deficit-free survival, the dangers might be larger in low-income nations.^{20, 21} Over time, infants are vulnerable to adult onset diabetes, metabolic syndrome, cardiovascular diseases (CVDs), and chronic kidney disease (CKD). Since the kidneys finish developing in the latter stages of pregnancy, delayed or insufficient kidney growth leading to a low number of nephrons is most likely the cause of small for gestational age and preterm newborns' elevated risk of chronic kidney disease (CKD) and hypertension.^{33–37}

CHRONIC KIDNEY DISEASE PREGNANCY: DIALYSIS AND TRANSPLANTATION

What is Acknowledged

persistent renal illness From the beginning of the pregnancy,

CKD increases the chance of unfavourable outcomes (Table 1).^{6, 38, 39} The risks may be increased in glomerular nephropathies, autoimmune disorders, and diabetic nephropathy, and they rise from CKD stage 1 to CKD stage 5.^{6, 7, 38–41} Pregnancy outcomes following kidney donation indicate that a lower amount of renal parenchyma may be linked to an increased risk of PE and pregnancy-related hypertension problems.^{42, 43}

Baseline hypertension and proteinuria are significant predictors of pregnancy-related risks. Among these, we know that malformations are not more common than in the general population (except in cases of inherited diseases like reflux nephropathy, polycystic kidney disease, or congenital kidney and urinary tract anomalies), maternal death is rare (except in highly resourced countries), and small for gestational age babies and preterm deliveries are intrinsically linked, more common in patients with stage 1 chronic kidney disease, and their frequency increases as kidney function deteriorates). Similar to this, the impact of pregnancy on the advancement of CKD remains incompletely recognised due to variations in research methodologies, obstetric practices, and follow-up periods. Overall, in early CKD, short- and long-term declines in kidney function are uncommon, but one possible reason for the first CKD diagnosis to occur is pregnancy. Pregnancy may be the only time advanced CKD is detected in nations with inadequate or unequal resources. When CKD is diagnosed in earlier stages, more rigorous therapy and surveillance may be required; in well resourced nations with well-established prenatal care, the implications of starting dialysis may raise significant clinical and ethical difficulties.^{49–51}

Dialysis and organ replacement

Reduced fertility is associated with end-stage renal disease (ESRD); data from Australia and Europe indicate a 1:10 ratio between the general population and transplantation, as well as a 1:1100 chance between transplantation and dialysis.^{52, 53} The earliest reported instances of successful pregnancies while receiving dialysis were in the 1970s; nevertheless, in the new century, this was recognised as a legitimate therapeutic prospect. There have been over a thousand documented pregnancies among dialysis patients.⁵⁵ The most significant development has been the proof of a strong correlation between the frequency and duration of dialysis sessions and successful pregnancy outcomes; as a result, the current standard of care calls for strengthening dialysis up to daily.^{8, 54}

Given the benefits of dialysis for women and their children, views towards counselling women with severe CKD may need to change. After receiving a kidney transplant, fertility is partially recovered.^{56–60} But even in the best of circumstances (normal renal function, no Women who have kidney transplants are more likely to experience problems than women in the general population if they have hypertension or proteinuria at least two years following transplantation and have not experienced any recent bouts of rejection. On the other hand, if teratogen medications (mycophenolicThere is little experience with pregnancy among patients who have failed kidney transplants or diminished renal function, and therapy is still compelled to be based on anecdotal data or personal experience.^{61, 62} Multiple pregnancies may have an increased risk in CKD patients, with both native and transplanted kidneys. Assisted fertilisation procedures are becoming more and more common in various settings, although there are few focused research in this population.

Women, kidney disease, and autoimmune diseases

What is Acknowledged

Women are more likely to be affected by autoimmune illnesses including SLE, RA, and SS, which are characterised by systemic inflammation that damages target organs, including the kidneys. Hormonal, genetic, and epigenetic variables interact in a complicated way to cause disparities in the prevalence and severity of various diseases across the sexes (Table 2). The impact of autoimmune illnesses on public health, which five million people worldwide suffer from SLE, an autoimmune illness that affects various organs. Women and persons of non-European heritage are disproportionately affected, with a female to male ratio of nine to one. During the prime years of reproduction, there is the greatest female predominance (up to 15:1). The biology underlying these variations has been investigated; genetic variants on X chromosomes^{66–68} and the number of X chromosomes provide one reason; the involvement of oestrogen in SLE is another significant etiological explanation. The transcription activity of intracellular oestrogen receptors, whose profile is changed in T-cells from female SLE patients, mediates the main effects of oestrogen.^{69, 70} The protein known as cathepsin S has been implicated in the development of lupus by inciting the immune system to target healthy cells, especially in women. People of European, Hispanic, and Afro-American descent may be more susceptible to lupus due to a variety of non-HLA genetic markers.⁷² Pregnancy-related

susceptibility to SLE is similarly complex, with increased IFN- α expression being one of the contributing factors. The placenta's expression of elevated IFN- α contributes to the harmful role of SLE by increasing vulnerability to the disease as well as placental reproduction success.⁷³ Due to their aberrant form and function, regulatory T-cells—which may be the key to cell regulating fetomaternal tolerance—may be more difficult to manage during pregnancy in women with SLE and may contribute to prenatal pathology in these cases.⁷⁴ About 50% of people with SLE have kidney problems, including vascular, interstitial, and glomerular abnormalities. Despite effective treatments, lupus nephritis remains a significant risk factor for total morbidity and mortality in SLE. In addition, women are more commonly affected by RA than males (4:1), with a peak incidence occurring between the perimenopausal years of 45 and 55. This implies a potential link between the start of disease and an oestrogen deficit. incidence of females to males ratio is roughly 1:1 after the age of 60, which may indicate that sex hormone changes play a role in the development of RA. It is also widely known that pregnant women often experience an improvement in or complete remission from RA symptoms.^{79–81} In patients with RA, renal involvement is a complex and reasonably common predictor of mortality. Patients with RA have a much higher risk of developing CKD than those in general. The development of chronic kidney disease (CKD) can be caused by multiple continuing processes, such as interstitial nephritis and glomerulonephritis, which are conditions related to RA, chronic inflammation, combined with nephrotoxic anti-rheumatic medications. The primary cause of ESRD with RA and nephropathy is AA amyloidosis, which has a high correlation with RA activity. This correlation worsens morbidity. Crucially, a few of the long-term negative effects of combination RA medication can affect the kidneys.^{82–84}

Females, Chronic Kidney Disease, and Renal Replacement Treatment Access

What is Acknowledged

Not all patients obtain renal replacement therapy (RRT), despite the fact that it is a life-sustaining treatment that includes dialysis and transplantation. The rate of ESRD treated with RRT varies widely throughout nations and areas and is highly dependent on a nation's health care system and economy.^{90, 91} Only 50% of patients in the world who need RRT receive it⁹²; this number is significantly lower in low- and middle-income nations and regions; in certain Sub-Saharan African countries, fewer than Disparities by sex in access to dialysis With treatment gaps

being greater in low-income countries, at least 2.284 million persons may have died before their time from not having access to RRT; conservative estimates in Asia and Africa put the number of those without RRT at 1.907 million and 432,000, respectively. With the greatest rise in Asia (0.968 million to a projected 2.162 million [1.71–3.14 million]), the expected number of RRT could more than quadruple to 5.439 million (3.899–7.640 million) by 2030.⁹² These figures come from a thorough, comprehensive review.

There is insufficient data to compare treatment gaps by gender. Men were more likely than women to receive RRT, according to studies conducted in Africa. In Japan, the number of female patients treated for end-stage renal disease (3,287 in males vs. 1,764 women per million treated) was less than half that of male patients.⁹¹ no justifications are provided in support of this discovery. According to a US study, women had a 1.70 odds ratio, which is much greater than men's, for starting dialysis later in life.⁹⁸ Women reported being far less aware of their past kidney disease than males did (2.9%±1.6% vs. 17.9%±5.9%), which could explain why RRT was started later in life in women.⁹⁹

Men and women receiving dialysis have comparable mortality rates, although women experience greater incidence rates of some complications and morbidity related to the treatment. Women experience greater hospitalisation rates than males, according to a US survey on hospitalisations among 111,653 patients on maintenance hemodialysis. Additionally, compared to male hemodialysis patients, female patients are less likely to use arteriovenous fistulas, which are linked to decreased rates of death, complications, and expenses.¹⁰¹ This could be caused by various variables such as differences in attitude, timing of referral, and anatomical/surgical problems with regard to vessel size. This hasn't been thoroughly investigated.

Given that the dialysis dose is determined by Kt/V, women with lower average urea distribution volumes or total body water than men may have underdialysis.¹⁰² It has also been shown that clinical indices such as anaemia, nutrition, and quality of life (QoL) are worse in women undergoing dialysis.¹⁰³ There are ambiguous reasons.

Disparities by sex in the availability of kidney transplants

The most effective RRT for those without contraindications is transplantation. Global data indicates that while women are more likely than men to become living donors for kidney

transplantation, they are less likely to have kidney transplants themselves, whether from cadaveric or living donors.¹⁰⁴ Data from several nations, such as the US, France, China, and India, confirm that women have lower kidney transplant rates than men do, that women are less likely to be listed on national transplant waiting lists, and that it takes longer for women to start dialysis than for men to do so. Mothers and female spouses are the groups most likely to donate.^{91,105–108} There is a gender gap in the paediatric population as well. A survey from 35 nations taking part in the European Dialysis and Transplant Association-European Renal Association-European Society for Paediatric Nephrology Registry was released.

CONCLUSION

Women are particularly vulnerable to renal illnesses because these conditions have a significant effect on both the present and future generations, not to mention problems with access to care. Promoting better access to care for women is essential to preserving the health of populations, families, and communities. To enhance our comprehension of the development of kidney disorders, targeted research on the distinct role of sex hormones or the interplay between sex hormones and other physiology is crucial. Better research on immunological disorders like SLE and other autoimmune and systemic illnesses that are frequent in women, as well as pregnancy (which is thought of as a state of tolerance to non-self), could result in advances in knowledge and paradigms for treatment. Since the kidneys finish developing in the latter stages of pregnancy, delayed or insufficient kidney growth leading to a low number of nephrons is most likely the cause of small for gestational age and preterm newborns' elevated risk of chronic kidney disease (CKD) and hypertension.

REFERENCES

1. GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990- 2015: A systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016; 388(10053): 1545-1602. doi: 10.1016/S0140-6736(16)31678-6
2. von Dadelszen P, Payne B, Li J, et al. Prediction of adverse

maternal outcomes in pre-eclampsia: Development and validation of the full PIERS model. *Lancet*. 2011; 377(9761): 219-227. doi: 10.1016/S0140-6736(10)61351-7

3. Mol BWJ, Roberts CT, Thangaratinam S, Magee LA, de Groot CJM, Hofmeyr GJ. Pre-eclampsia. *Lancet*. 2016; 387(10022): 999- 1011. doi: 10.1016/S0140-6736(15)00070-7
4. Vikse BE, Irgens LM, Leivestad T, Skjaerven R, Iversen BM. Preeclampsia and the risk of end-stage renal disease. *N Engl J Med*. 2008; 359(8): 800-809. doi: 10.1056/NEJMoa0706790
5. Theilen LH, Fraser A, Hollingshaus MS, et al. All-cause and cause-specific mortality after hypertensive disease of pregnancy. *Obstet Gynecol*. 2016; 128(2): 238-244. doi: 10.1097/AOG.0000000000001534
6. Piccoli GB, Cabiddu G, Attini R, et al. Risk of adverse pregnancy outcomes in women with CKD. *J Am Soc Nephrol*. 2015; 26(8): 2011-2022. doi: 10.1681/ASN.2014050459
7. Zhang JJ, Ma XX, Hao L, Liu LJ, Lv JC, Zhang H. A systematic review and meta-analysis of outcomes of pregnancy in CKD and CKD outcomes in pregnancy. *Clin J Am Soc Nephrol*. 2015; 10(11): 1964-1978. doi: 10.2215/CJN.09250914
8. Alkhunaizi A, Melamed N, Hladunewich MA. Pregnancy in advanced chronic kidney disease and end-stage renal disease. *Curr Opin Nephrol Hypertens*. 2015; 24(3): 252-259. doi: 10.1097/MNH.0000000000000119
9. Piccoli GB, Cabiddu G, Castellino S, et al. A best practice position statement on the role of the nephrologist in the prevention and follow-up of preeclampsia: The Italian study group on kidney and pregnancy. *J Nephrol*. 2017; 30(3): 307-317. doi: 10.1007/s40620- 017-0390-1
10. Liu Y, Ma X, Zheng J, Liu X, Yan T. Pregnancy outcomes in patients with acute kidney injury during pregnancy: A systematic review and meta-analysis. *BMC Pregnancy Childbirth*. 2017; 17(1): 235. doi: 10.1186/s12884-017-1402-9
11. Jim B, Garovic VD. Acute kidney injury in pregnancy. *Semin*

- Nephrol. 2017; 37(4): 378-385.
12. Acharya A. Management of acute kidney injury in pregnancy for the obstetrician. *Obstet Gynecol Clin North Am*. 2016; 43(4): 747-765. doi: 10.1016/j.ogc.2016.07.007
 13. Iseki K. Gender differences in chronic kidney disease. *Kidney International*. 2008; 74(4): 415-417. doi: 10.1038/ki.2008.261
 14. Nitsch D, Grams M, Sang Y, et al. Associations of estimated glomerular filtration rate and albuminuria with mortality and renal failure by sex: A meta-analysis. *BMJ*. 2013; 346: f324. doi: 10.1136/bmj.f324
 15. Levin A, Djurdjev O, Beaulieu M, Er L. Variability and risk factors for kidney disease progression and death following attainment of stage 4 CKD in a referred cohort. *Am J Kidney Dis*. 2008; 52(4): 661-671. doi: 10.1053/j.ajkd.2008.06.023
 16. Weiner DE, Tighiouart H, Elsayed EF, et al. The Framingham predictive instrument in chronic kidney disease. *J Am Coll Cardiol*. 2007; 50(3): 217-224. doi: 10.1016/j.jacc.2007.03.037
 17. Oladapo OT, Adetoro OO, Ekele BA, et al. When getting there is not enough: A nationwide cross-sectional study of 998 maternal deaths and 1451 near-misses in public tertiary hospitals in a low-income country. *BJOG*. 2016; 123(6): 928-938. doi: 10.1111/1471-0528.13450
 18. Tranquilli AL, Dekker G, Magee L, Roberts J, Sibai BM, Steyn W, et al. The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. *Pregnancy Hypertens*. 2014; 4(2): 97-104. doi: 10.1016/j.preghy.2014.02.001
 19. Liu Y, Bao H, Jiang Z, Huang Y, Wang N. Pregnancy-related Acute Kidney Injury and a Review of the Literature in China. *Intern Med*. 2015; 54(14): 1695-1703. doi: 10.2169/internalmedicine.54.3870
 20. Prakash J, Pant P, Prakash S, et al. Changing picture of acute kidney injury in pregnancy: Study of 259 cases over a period of 33 years. *Indian J Nephrol*. 2016; 26(4): 262-267. doi: 10.4103/0971-4065.161018
 21. Ibarra-Hernández M, Orozco-Guillén OA, de la Alcantar-Vallín ML, et al. Acute kidney injury in pregnancy and the role of underlying CKD: A point of view from México. *J Nephrol*. 2017 Oct 11; doi: 10.1007/s40620-017-0444-4
 22. Blázquez A, García D, Rodríguez A, Vassena R, Figueras F, Vernaev V. Is oocyte donation a risk factor for preeclampsia? A systematic review and meta-analysis. *J Assist Reprod Genet*. 2016; 33(7): 855-863. doi: 10.1007/s10815-016-0701-9
 23. O'Gorman N, Wright D, Poon LC, et al. Multicenter screening for pre-eclampsia by maternal factors and biomarkers at 11-13 weeks' gestation: Comparison with NICE guidelines and ACOG recommendations. *Ultrasound Obstet Gynecol*. 2017; 49(6): 756-760. doi: 10.1002/uog.17455
 24. Zeisler H, Llurba E, Chantraine F, et al. Predictive value of the sFlt-1: PlGF ratio in women with suspected preeclampsia. *N Engl J Med*. 2016; 374(1): 13-22. doi: 10.1056/NEJMoa1414838
 25. Garovic VD. The role of the podocyte in preeclampsia. *Clin J Am Soc Nephrol*. 2014; 9(8): 1337-1340. doi: 10.2215/CJN.05940614
 26. Wide-Svensson D, Strevens H, Willner J. Antepartum percutaneous renal biopsy. *Int J Gynaecol Obstet*. 2007; 98(2): 88-92. doi: 10.1016/j.ijgo.2007.03.049
 27. Shiiki H, Dohi K, Hanatani M, et al. Focal and segmental glomerulosclerosis in preeclamptic patients with nephrotic syndrome. *Am J Nephrol*. 1990; 10(3): 205-212. doi: 10.1159/000168082
 28. Linsell L, Malouf R, Morris J, Kurinczuk JJ, Marlow N. Risk factor models for neurodevelopmental outcomes in children born very preterm or with very low birth weight: A systematic review of methodology and reporting. *Am J Epidemiol*. 2017; 185(7): 601-612. doi: 10.1093/aje/kww135

29. Guellec I, Lapillonne A, Marret S, et al. Effect of intra- and extrauterine growth on long-term neurologic outcomes of very preterm infants. *J Pediatr*. 2016; 175: 93-99.e1. doi: 10.1016/j.jpeds.2016.05.027
30. Moore T, Hennessy EM, Myles J, et al. Neurological and developmental outcome in extremely preterm children born in England in 1995 and 2006: the EPICure studies. *BMJ*. 2012; 345: e7961. doi: 10.1136/bmj.e7961
31. Guillén Ú, DeMauro S, Ma L, Zupancic J, Roberts R, Schmidt B, et al. Relationship between attrition and neurodevelopmental impairment rates in extremely preterm infants at 18 to 24 months: A systematic review. *Arch Pediatr Adolesc Med*. 2012; 166(2): 178-184. doi: 10.1001/archpediatrics.2011.616
32. Ranke MB, Schweizer R, Rodemann SM, et al. Schoolchildren born VLBW or VLGA show height-related changes in body composition and muscle function but no evidence of metabolic syndrome risk factors. Results from the NEOLONG study. *J Pediatr Endocrinol Metab*. 2015; 29(2): 163-172. doi: 10.1515/jpem-2015-0266
33. Castanys-Muñoz E, Kennedy K, Castañeda-Gutiérrez E, et al. Systematic review indicates postnatal growth in term infants born small-for-gestational-age being associated with later neurocognitive and metabolic outcomes. *Acta Paediatr*. 2017; 106(8): 1230-1238. doi: 10.1111/apa.13868
34. Ong KK, Kennedy K, Castañeda-Gutiérrez E, et al. Postnatal growth in preterm infants and later health outcomes: A systematic review. *Acta Paediatr*. 2015; 104(10): 974-986. doi: 10.1111/apa.13128
35. Low Birth Weight and Nephron Number Working Group. The impact of kidney development on the life course: A consensus document for action. *Nephron*. 2017; 136(1): 3-49. doi: 10.1159/000457967
36. Luyckx VA, Bertram JF, Brenner BM, et al. Effect of fetal and child health on kidney development and long-term risk of hypertension and kidney disease. *Lancet*. 2013; 382(9888): 273-283. doi: 10.1016/S0140-6736(13)60311-6
37. Luyckx VA, Brenner BM. Birth weight, malnutrition and kidney-associated outcomes--a global concern. *Nat Rev Nephrol*. 2015; 11(3): 135-149. doi: 10.1038/nrneph.2014.251
38. Davison JM, Lindheimer MD. Pregnancy and chronic kidney disease. *Semin Nephrol*. 2011; 31(1): 86-99. doi: 10.1136/bmj.39406.652986.BE
39. Hall M. Pregnancy in women with CKD: A success story. *Am J Kidney Dis*. 2016; 68(4): 633-639. doi: 10.1136/bmj.39406.652986.BE
40. Nevis IF, Reitsma A, Dominic A, et al. Pregnancy outcomes in women with chronic kidney disease: A systematic review. *Clin J Am Soc Nephrol*. 2011; 6(11): 2587-2598. doi: 10.2215/CJN.10841210
41. Cabiddu G, Castellino S, Gernone G, et al. A best practice position statement on pregnancy in chronic kidney disease: The Italian Study Group on Kidney and Pregnancy. *J Nephrol*. 2016; 29(3): 277-303. doi: 10.1007/s40620-016-0285-6
42. Garg AX, Nevis IF, McArthur E, et al. Gestational hypertension and preeclampsia in living kidney donors. *N Engl J Med*. 2015; 372(2): 124-133. doi: 10.1056/NEJMoa1408932
43. Josephson MA. Transplantation: Pregnancy after kidney donation: more questions than answers. *Nat Rev Nephrol*. 2009; 5(9): 495-497. doi: 10.1038/nrneph.2009.129
44. Gianfreda D, Quaglini S, Frontini G, Raffiotta F, Messa P, Moroni G. Does pregnancy have any impact on long term damage accrual and on the outcome of lupus nephritis? *J Autoimmun*. 2017; 84: 46-54. doi: 10.1016/j.jaut.2017.06.003
45. Blom K, Odutayo A, Bramham K, Hladunewich MA. Pregnancy and glomerular disease: A systematic review of the literature with management guidelines. *Clin J Am Soc Nephrol*. 2017; pii: CJN.00130117. doi: 10.2215/CJN.00130117