KDIGO Controversies Conference on Women and Kidney Health

February 2-5, 2023

Athens, Greece

Scope of Work

Kidney Disease: Improving Global Outcomes (KDIGO) is an international organization whose mission is to improve the care and outcomes of kidney disease patients worldwide by promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines. Periodically, KDIGO hosts conferences on topics of importance to patients with kidney disease. These conferences are designed to review the state of the art on a focused subject and set priorities for improving patient care and outcomes. In addition to highlighting areas for which additional research is needed, sometimes the conferences can lead to KDIGO guideline developing or updating efforts.

CONFERENCE BACKGROUND AND RELEVANCE

Kidney diseases, like most chronic diseases, are biologically modulated by sex (i.e., the biological characteristics of the individual), and care may be culturally dependent upon gender (the socially expressed role of males, females, and gender-diverse people). For example, biological modulation affects prevalence and prognosis of some kidney diseases, such as lupus, and is associated with differential risks of mortality and rates of dialysis initiation in chronic kidney disease (CKD). Gender, which is modulated by social, economic, and cultural issues, affects access to healthcare, kidney donation within couples (women to men being more frequent), and recruitment and representation in randomized controlled trials in several fields, including nephrology.

Achieving health equity, defined as a state in which everyone has a fair and just opportunity to attain the highest level of health, is an ambitious goal that implies overcoming economic, social, and other obstacles to health and healthcare to eliminate preventable health disparities. Sex and gender differences in the presentation, diagnosis, and management of kidney diseases have long been recognized, and better characterization of sex and gender disparities in kidney care is essential to improving outcomes.
Reproductive health is also a challenge for women with kidney diseases, and pregnancy complications may exert a negative impact on kidney health of both women and their offspring.\textsuperscript{12-14}

Approximately 3\% of women of childbearing age have CKD, and the prevalence may be even higher in many developing countries.\textsuperscript{15,16} Preeclampsia affects approximately 3-5\% of pregnancies, and hypertensive disorders of pregnancy affect up to 10\% of pregnancies.\textsuperscript{17} CKD impacts all aspects of reproductive health. With advanced CKD, fertility is reduced, menopause may occur early, and the physical and psychological consequences of kidney disease may affect body image, sexual desire, and satisfaction.\textsuperscript{18,19} While kidney transplantation at least partially restores reproductive health, and intensive hemodialysis allows unprecedented success in pregnancy outcomes, these options are not universally available; several issues, including the optimal timing to start dialysis, dialysis access, and the role of peritoneal dialysis, remain unresolved.\textsuperscript{20-24}

Healthy kidney donors, who have reduced kidney tissue, have a higher risk of pregnancy complications even when kidney function is normal and hypertension and proteinuria are absent.\textsuperscript{25,26} Even in early CKD, there is an increased risk of pregnancy-related complications though its cause remains unclear\textsuperscript{27-29} and few follow-up programs are available for this population.\textsuperscript{30,31}

When women who develop hypertensive disorders of pregnancy, in particular preeclampsia or HELLP syndrome (Hemolysis, Elevated Liver enzymes and Low Platelets count), undergo a nephrology work-up, up to 20\% are diagnosed with CKD.\textsuperscript{32,33} Furthermore, regardless of the diagnosis, women with one or more episodes of preeclampsia have a 4 to 20-fold higher risk of developing kidney failure in their lifetime.\textsuperscript{34,35} Preeclampsia and pregnancy complications are the most common cause of acute kidney injury (AKI) in young women.\textsuperscript{36,37} Global disparities in healthcare are sadly evident, as women in low-resource regions have more pregnancy-related complications and less access to pregnancy-related healthcare and kidney replacement therapy.\textsuperscript{38,39}

Health risks are carried over in subsequent generations: children born small or small for gestational age have an increased risk of developing hypertension, CKD, and metabolic syndrome in adulthood\textsuperscript{40}; if a woman was born small or small for gestational age, her risk of developing preeclampsia or pregnancy-related complications is increased 4 to 10-fold.\textsuperscript{41}

Notwithstanding the growing acknowledgment of gender- and sex-related issues in kidney medicine, as well as the complex relationship between kidney and reproductive health, high-
quality care in those with CKD during pregnancy and hypertensive disorders is not available to all women. Given the high unmet need for shared guidance for reproductive health in patients with or at risk for developing CKD, this Controversies Conference will represent a major step forward in raising awareness and fostering dedicated programs.

CONFERENCE OVERVIEW

This KDIGO Controversies Conference will convene a global panel of individuals with multidisciplinary clinical and scientific expertise (i.e., nephrology, obstetrics, reproductive health, pediatrics/neonatology, etc.) and patients to identify key gender and sex issues in kidney care and to optimize reproductive care of women with CKD and women who have developed hypertensive disorders of pregnancy or pregnancy-related AKI.

With the support of an in-depth review of the most relevant literature, the goal of this conference is to describe current best practices and to identify areas of uncertainty, address ongoing controversial issues, and outline research needed to move the field forward.

Accepting that models of care will vary depending on the healthcare setting, the conference will focus on the essential elements that all models should include, with particular attention paid to challenges for caring aforementioned patients and addressing issues related to cultural diversity, religious needs, and health literacy.

Drs. Giorgina Piccoli (Centre Hospitalier Le Mans, France) and Christina Wyatt (Duke University, United States) will co-chair this conference. The format of the conference will involve topical plenary session presentations followed by focused discussion groups that will report back to the full group for consensus building. This highly interactive conference will invite key thought leaders and relevant stakeholders, including patients, in nephrology and other related disciplines who will comprehensively review the literature and current state of understanding in this area and address clinical issues as outlined in the Scope of Coverage (next page). The conference output will include publication of a position statement that will help guide KDIGO and others on therapeutic management and future research.
SCOPE OF COVERAGE

Breakout Group 1: Sex Differences in Prevalence, Incidence, and Outcomes in CKD

CKD Diagnosis and Progression
1. Are there sex and gender differences in the presentation, diagnosis, and access to care for CKD?
2. Are there sex and gender differences in progression, management, and monitoring of CKD?
3. Are there sex and gender differences in quality of life, values and preferences, and shared decision-making that impact care for advanced CKD?
4. Are there sex and gender differences in quality of life and mortality in kidney failure (conservative/supportive care, dialysis and transplant, end-of-life care)?
5. How can we reduce sex and gender disparities in CKD care?

Complications of CKD and Frequent Comorbid Conditions
6. Are there sex and gender differences in cardiovascular disease (CVD) presentation, access to diagnosis, and treatment?
7. Are there sex and gender differences in CVD risk and outcomes in kidney disease?
8. Are there sex and gender differences in metabolic bone disease (CKD-MBD) presentation, diagnosis, treatment, and outcomes?
9. Are there sex and gender differences in anemia presentation, diagnosis, treatment, and outcomes in kidney disease?
10. For non-sex specific cancers, for people with CKD, are there differences in access to screening, presentation, and diagnosis by sex and gender?
11. For non-sex specific cancers, for people with CKD, are there differences in access to treatment and outcomes (including side effects)?
12. How can we reduce sex and gender disparities in complications and comorbidities of CKD?
Sex versus Gender in CKD
13. Are there differences by sex or gender in quality of life and shared decision-making/values and preferences?

Representation by Sex and Gender Across the Research Lifecycle in CKD
15. What is the sex and gender representation in clinical trials?
16. Are sex- and gender-stratified results (benefits and harms/adverse effects) reported in clinical trials (or a core outcome requirement)?
17. Do patient-reported outcomes measures (PROMS) and patient-reported experience measures (PREMS) in nephrology research differ by sex and gender?
18. How can we ensure equity in gender representation in studies in nephrology?
Breakout Group 2: Reproductive Care of Women with CKD Not on Dialysis Therapy

Epidemiology and Outcomes in the Different CKD Stages

1. What is the prevalence of CKD among women starting or planning a pregnancy?
2. What are the best methods for detecting CKD in the pre-conception phase or pregnant women worldwide?
3. How do we define the key prognostic factors for fetomaternal outcomes in women with CKD starting or planning a pregnancy?
4. What impact does the specific underlying nephropathy have on pregnancy outcome in patients with CKD?
5. What is expected to change in the next decade(s)?

Care, Counseling, and Follow-up in Pregnancy in the Different CKD Stages

6. What is the optimal counselling strategy of women with CKD planning or starting a pregnancy, and how can it be adapted to different settings?
7. What is the approach to an unplanned pregnancy?
8. What is the optimal medical (nephrology, obstetric, neonatal medicine) follow-up of patients with CKD?
9. What is the best method for adapting the follow-up of pregnant women with CKD to local resources and system care?
10. What biomarkers are helpful for the follow-up of pregnant women with CKD?
11. When should early delivery be considered in pregnant women with CKD?
12. Are there specific considerations regarding pregnancy in women with CKD due to immunological disorders (e.g., glomerulonephritides and systemic diseases)?
13. What is the optimal blood pressure target in pregnant women with CKD?
14. What are the indications for drug prescription, including aspirin and heparin, and treatment modulation in women with CKD planning or starting a pregnancy?
15. What is the optimal nutritional care for pregnant women with CKD?
16. How should post-pregnancy follow-up be organized for the mother?
17. What are indications for the follow-up of the children?

Other issues

18. Which birth control policies are indicated in CKD patients and how best to adapt them according to the presence of systemic diseases, severity of CKD, hypertension, and proteinuria?
Breakout Group 3: Reproductive Care of Women on Dialysis Therapy (Hemodialysis [HD], Peritoneal Dialysis [PD], Home Dialysis) or with Kidney Transplant

Epidemiology and Outcomes on Dialysis and After Transplant

1. What are the key trends in birth rates for individuals on kidney replacement therapy across countries?
2. What are the expected pregnancy outcomes, and which are the main differences between countries?
3. What are the key clinical and health system factors that determine pregnancy and maternal kidney outcomes, and how do these differ between countries?
4. What is expected to change in the next decade(s)?

Care, Counseling, and Follow-up in Pregnancies on KRT

5. What is the optimal counselling strategy of women on kidney replacement therapy planning or starting a pregnancy, and how can it be adapted to different settings?
6. In considering whether to have a pregnancy on dialysis versus after transplant, what are the competing risks, and what is the best window of opportunity?
7. What is the approach to an unplanned pregnancy?
8. How much of an issue is rejection in transplant pregnancies, and how should immunosuppressive drugs be managed?
9. How should residual kidney function and patient factors be used to determine dialysis schedules in pregnancy?
10. What is the best approach for dialysis access for hemodialysis starting in pregnancy?
11. Should patients who become pregnant while undergoing peritoneal dialysis be switched to HD, and if so, when?
12. What is the best timing and plan for delivery in dialysis and transplant patients?
13. How should available biomarkers be incorporated into the clinical follow-up of women undergoing dialysis and transplant recipients?
14. What are the indications for drug care and modulation, including aspirin and heparin, in women on kidney replacement therapy planning or starting a pregnancy?

15. How should post-pregnancy follow-up be organized for the mother?

16. Which indications require follow-up of the children?

Other issues

17. What is the role of fertility treatments, and what are specific risks? What is the approach to menopause?
Breakout Group 4: Preeclampsia and AKI and Future Maternal-Child Health

Epidemiology and Outcomes of Preeclampsia and Related Hypertensive Disorders of Pregnancy and Acute Kidney Injury (AKI) in Pregnancy

1. What is the epidemiology of pregnancy-related AKI and preeclampsia, and how does it vary worldwide?
2. What are the strengths and weaknesses of currently available measures to identify AKI in pregnancy?
3. Should gestational-age stratification be included in the definition of AKI in pregnancy?
4. Which new tests and biomarkers that have been developed for AKI have potential use in early recognition of AKI in pregnancy?
5. What is the epidemiology of kidney diseases in pregnancies complicated by AKI or preeclampsia?
6. What is the risk of developing CKD, and what is the association between CKD, preeclampsia, and pregnancy-related AKI?
7. What is the epidemiology of kidney disease in offspring from pregnancies complicated by preeclampsia, pregnancy-related AKI, and other hypertensive disorders of pregnancy?

Care, Counseling, and Follow-up During and After Pregnancies Complicated by AKI and Preeclampsia

8. Does every woman require determination of kidney function before or during pregnancy?
9. Which are the key gaps in diagnosis and management of CKD after preeclampsia or pregnancy-related AKI?
10. Can we better predict the risk for future CKD in women with preeclampsia or pregnancy-related AKI and identify patients at higher risk of progressive CKD?
11. How should follow-up after preeclampsia or pregnancy related AKI be organized (including follow-up of future pregnancies)?
12. What is the role of kidney biopsy in pregnancy and in the post-partum period?

Other Issues

13. What are the key gaps in diagnosis and management of kidney diseases in the offspring of high-risk pregnancies (and more broadly of small babies and of infants with intrauterine growth restriction)?
14. Which follow-up protocols should be suggested?
15. Should approaches to these children differ by preeclampsia type (severe vs mild; early vs late; with and without preterm or intrauterine growth restriction)?
REFERENCES


