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Pregnancy in Chronic Kidney Disease: questions and answers in a changing panorama

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Chronic kidney disease (CKD) is increasingly encountered in pregnancy because of greater diagnostic awareness, which is a reflection of the newer, broader definitions (i.e., any changes in blood or urine composition or at imaging, or a glomerular filtration rate (GFR) of <60 mL/min lasting at least 3 months) and of increased incidence (higher maternal age and better outcomes of several kidney diseases).

CKD is extremely heterogeneous and may be described by the degree of GFR reduction (CKD stages), the presence of proteinuria and hypertension and the type of kidney disease; the risk of adverse pregnancy-related events increases as GFR decreases and it is affected by proteinuria and hypertension. Specific risks are reported in various diseases such as lupus nephropathy or diabetic nephropathy. While transplantation at least partially restores fertility in end-stage kidney disease, pregnancy on dialysis is increasingly reported.

This chapter deals with the available evidence on the management of CKD patients in pregnancy.

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Introduction

Chronic kidney disease: a matter of definition

Almost 20 years ago, the National Kidney Foundation started a campaign entitled 'The Fight against the Silent Killers' [1]. These silent killers were chronic kidney diseases (CKD), and they were defined as 'silent' because they were frequently asymptomatic until renal failure occurred, and they were 'killers' as kidney disease affects survival [1–3]. Presently, after acknowledging the risks in elderly patients, the definition of 'silent killer' may be applied to CKD in pregnancy, as these often undiagnosed diseases are a main cause of morbidity in pregnancy [4,5].

CKD is currently broadly defined as any alteration in renal morphology, imaging or function, or by a glomerular filtration rate (GFR) <60 mL/min for at least 3 months [1,6,7]. Despite the revisions and criticisms, the advantage of this definition is that it focuses on the earlier CKD stages, when kidney function is still normal and the potential for recovery is higher [1].

Serum creatinine, which is derived from muscle mass, is physiologically lower in women and in small body size; furthermore, in pregnancy physiological hyperfiltration may mask an initial GFR reduction, thus leading to underestimation of CKD in pregnancy [6,7]. Changes in GFR are not an 'early' marker of disease, as it starts decreasing when >50% of the renal parenchyma is damaged; hence, it is important to identify CKD in stage 1, when kidney function is normal and CKD is revealed by proteinuria, haematuria, electrolyte derangements, tubulo-interstitial diseases, single kidney (including kidney donation) or even 'simple' kidney scars due to previous acute pyelonephritis [1].

On the basis of these broad definitions, the prevalence of CKD reaches 3% in women in childbearing age, a significant difference as compared to previous definitions, which were based upon high creatinine levels that probably identified <10% of cases [5,6].

Pregnancy is a very important opportunity to diagnose kidney disease in an apparently healthy woman. In our experience, CKD is diagnosed or acknowledged as a risk factor in pregnancy in at least 40% of cases [8]. The physiological increase in GFR, the lack of validated formulae for GFR assessment in pregnancy and the clinical and laboratory overlap with pre-eclampsia (PE) are important challenges for early diagnosis as discussed below [9–11]. We also discuss how CKD bears a risk of adverse pregnancy-related outcomes starting from the early stages, and even 'minor' signs of CKD should be taken into consideration [8,12–15].

In the following paragraphs, we summarise the available evidence and its limits, sharing our points of view on the diagnosis and care of CKD in pregnancy.

What is 'inside CKD'?

Regardless of how it is defined, CKD is a syndrome and not a disease; its main descriptors are kidney function, kidney disease, proteinuria and hypertension (Fig. 1).

Kidney function, which is subdivided by the Kidney Disease Outcomes Quality Initiative (K-DOQI) definition into five stages, is probably the most powerful descriptor of the severity of the disease and of the risk of complications [1,12–21].

As a rule, immunologic and systemic diseases (such as glomerulonephritis, or diabetic or lupus nephropathies) are more frequently associated with adverse pregnancy-related events; conversely, interstitial kidney diseases share a higher risk of upper urinary tract infection (UTI), unexplained oedema or stone disease [22–27].

Hypertension and proteinuria are independently correlated with CKD progression and with adverse pregnancy-related events, and, when present, PE may be difficult or impossible to diagnose [28,29].

Limits of the currently reported evidence

Despite the increased interest, evidence regarding CKD in pregnancy is scant and heterogeneous. There are several reasons for this, including fragmented literature that lacks a common language, the involvement of various diseases, the fact that it is subject to referral biases and that it is influenced by the study setting [12,13].