DOI: https://doi.org/10.61841/hw728z53 Publication URL: https://nnpub.org/index.php/MHS/article/view/2065

THE SYSTEMATIC REVIEW OF THE ASSOCIATION OF PREGNANCY OUTCOMES AND CHRONIC KIDNEY DISEASE

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ABSTRACT

Background: *Pregnancy as a metabolic stress test that might reveal underlying endothelial dysfunction and vascular illness. Maternal cardiovascular disease risk is heightened in cases of adverse pregnancy outcomes, including hypertensive disorders of pregnancy, gestational diabetes, and premature birth.*

Aims : *This systematic review is to review the association of chronic kidney disease to its outcomes at pregnant women.*

Methods: *By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed and SCIENCE DIRECT, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.*

Result: *In the PubMed database, the results of our search brought up 661 articles, whereas the results of our search on SCIENCE DIRECT brought up 3.6314 articles. The results of the search conducted for the last year of 2014 yielded a total 12 articles for PubMed and 96 articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SCIENCE DIRECT. We included five research that met the criteria.*

Conclusion: *In summary, an increased risk of chronic kidney disease was linked to exposure to unfavorable pregnancy outcomes, such as hypertensive disorders of pregnancy, gestational diabetes, and premature birth. Preeclamptic women had the highest chance of developing ESKD. To identify women who are more likely to develop kidney disease, especially following hypertensive disorders during pregnancy, a systematic strategy may be necessary to maximize the patients' long-term follow-up.*

Keyword: *Chronic kidney disease, pregnancy*

INTRODUCTION

Long-standing research has addressed the topic of pregnancy in advanced chronic kidney disease (CKD). Early case series of hemodialysis patients who were pregnant were published by Herwing et al. in 1965 and Orme et al. in 1968. An Italian group study that reported the first successful pregnancies while receiving hemodialysis followed in 1971. Successful pregnancies among women receiving dialysis were further reported and defined by further research carried out in the United States and Europe. The pregnancy success rate in this patient population has increased by up to 90% between 1980 and the present, increasing in tandem with the data rise.[1]

For doctors, hemodialysis patients' pregnancies pose some of the trickiest clinical problems. Pregnant women have many physiological changes similar to those in the general population, such as an increase in blood volume, excretion of urine protein, cardiac output, and a roughly 50% rise in glomerular filtration rate (GFR). Hyperfiltration in the kidney lowers blood pressure, vascular resistance, and serum creatinine levels. Patients with chronic kidney disease (CKD), whether receiving dialysis or not, have a complicated range of coexisting conditions that can be challenging to manage, particularly in this situation. Pregnancy can be made more difficult by CKD alone, as well as by any of its concomitant conditions.[1]

As chronic kidney disease (CKD) becomes increasingly frequent in the general community, female patients with decreased kidney function who are fertile are becoming more prevalent. Pregnant individuals with chronic kidney disease (CKD) have been linked to worse pregnancy outcomes. When kidney problems persist for more than three months and have a negative impact on health, they are referred to be chronic kidney disease (CKD). In addition to the evident impairment of kidney excretory function caused by a reduction in glomerular filtration rate (GFR), additional kidney abnormalities such as tubular diseases, structural/congenital abnormalities, and proteinuria are also included in the term chronic kidney disease (CKD).[2]

Although their chances of becoming pregnant are reduced, female women with severe CKD can and frequently do conceive. There are also instances of end-stage renal disease (ESKD) people becoming pregnant. However, it is uncertain how common mild to moderate chronic kidney disease (CKD 1-3) is in pregnant people.[3]

Patients who are female and reproductive might have a wide range of renal problems. The most common ones would be hypertensive nephrosclerosis, diabetic nephropathy, and congenital anomalies of the kidney and urinary system. Additionally, a number of glomerulopathies are rather prevalent, including lupus nephritis (LN) and IgA nephropathy.[4]

It has been shown that pregnant individuals with underlying CKD are more likely to experience fetal growth restriction (FGR), superimposed preeclampsia, and premature birth. The majority of patients with moderate chronic kidney disease (CKD 1-2) have good postpartum renal results. However, people with more severe kidney disease (CKD 3b-5) even at conception have been shown to have a significant decline in renal function throughout pregnancy.[4]

Increasing urine protein excretion and decreasing GFR are the two most widely utilized and recognized indicators of renal injury. Pregnant women should not utilize estimated GFR estimations since they routinely underestimate renal function. For these individuals, the sole accepted measure of renal function is still serum creatinine levels. An upper limit of 77 µmol/l (0.87 mg/dl) for serum creatinine should be considered during pregnancy.6. Protein excretion in the urine rises during a typical pregnancy, reaching up to 300 mg/day (protein/creatinine ratio up to 0.3 mg/mg) from less than 150 mg/day in non-pregnant persons.[5]

Women with a history of gestational diabetes (GDM), gestational hypertension, or preeclampsia are more likely to develop long-term cardiovascular disease. The long-term risk of end-stage kidney disease (ESKD) and chronic kidney disease (CKD) among women who have had unfavorable pregnancy outcomes is comparatively poorly understood. It is conceivable that compared to women with normotensive pregnancies, women with hypertensive disorders of pregnancy (HDP) may be more at risk for developing chronic kidney disease. Microalbuminuria is more common in women exposed to preeclampsia, and long-term renal damage may also be more likely in these individuals, according to longitudinal research. It's unclear if chronic hypertension and pregnant hypertension are related to the risk of renal disease in mothers.[6]

It is unknown if preterm delivery and the delivery of a low-birth-weight or growth-restricted newborn are linked to an increased risk of renal disease in the future, although they have been recognized as risk factors for maternal cardiovascular disease. These variables could function as a moderator in the relationship between CKD or ESKD and HDP or other pregnancy-related illnesses. GDM patients are more likely to experience chronic vascular endothelial dysfunction. Even if they never get type 2 diabetes, it's possible that this malfunction will raise their risk of kidney disease on its own. Women with GDM may have early renal impairment by the time they are 9 to 16 years postpartum, although it is unclear if they will develop clinically severe chronic kidney disease (CKD).[6]

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we review published literature contains the associations of chronic kidney disease with pregnancy. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

Weused"chronickidneydisease",“pregnancy and “outcome” as keywords.The search for studies to be included in the systematic review was carried out using the PubMed and SCIENCE DIRECT databases by inputting the words: *(("renal insufficiency, chronic"[MeSH Terms] OR ("renal"[All Fields] AND "insufficiency"[All Fields] AND "chronic"[All Fields]) OR "chronic renal insufficiency"[All Fields] OR ("chronic"[All Fields] AND "kidney"[All Fields] AND "disease"[All Fields]) OR "chronic kidney disease"[All Fields]) AND ("pregnancy"[MeSH Terms] OR "pregnancy"[All Fields] OR "pregnancies"[All Fields] OR "pregnancy s"[All Fields]) AND ("outcome"[All Fields] OR "outcomes"[All Fields])) AND ((clinicaltrial[Filter]) AND (2014:2024[pdat]))* used in searching the literature.

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

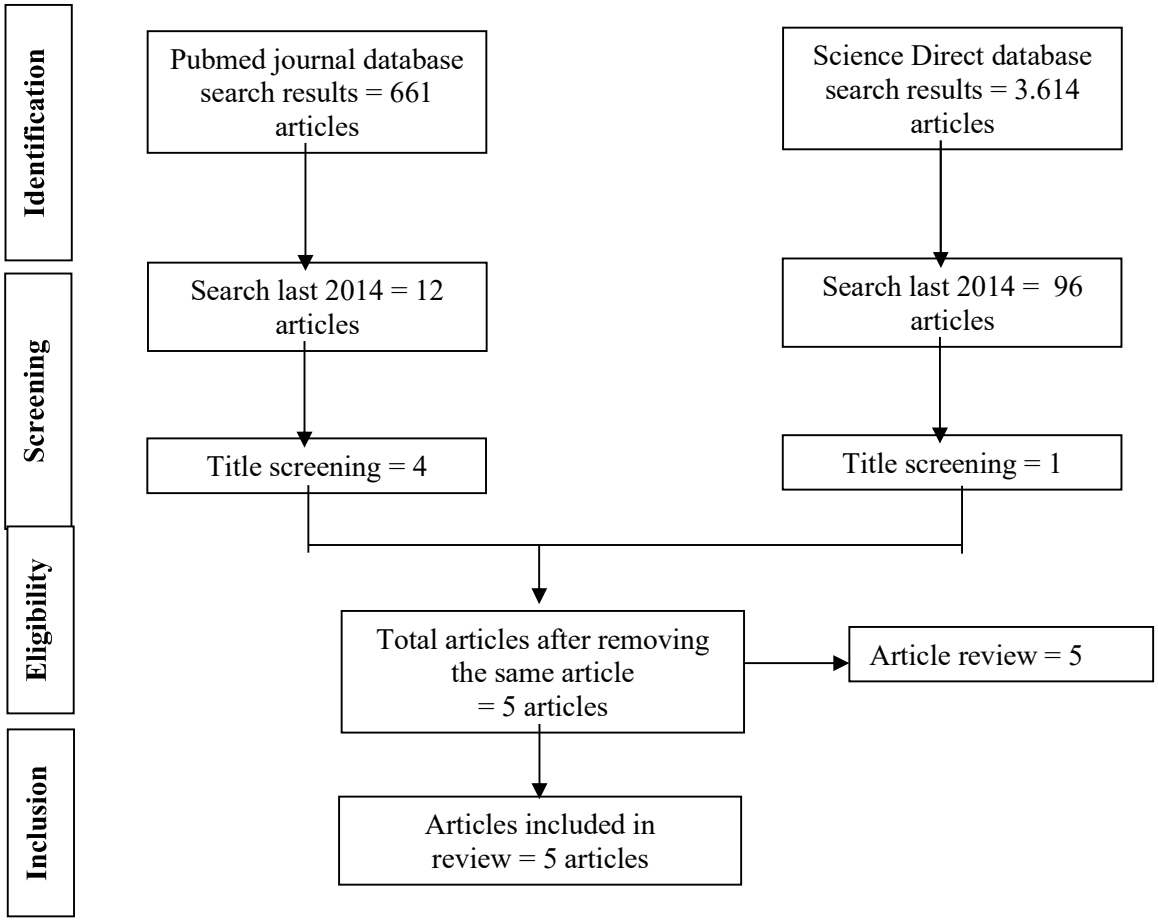

Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

This systematic review aims to review the association of chronic kidney disease to its outcomes at pregnant women.

RESULT

In the PubMed database, the results of our search brought up 661 articles, whereas the results of our search on SCIENCE DIRECT brought up 3.6314 articles. The results of the search conducted for the last year of 2014 yielded a total 12 articles for PubMed and 96 articles for SCIENCE DIRECT. In the end, we compiled a total of 5 papers, 4 of which came from PubMed and 1 of which came from SCIENCE DIRECT. We included five research that met the criteria.

Hewawasam, et al[7] (2023) showed that the needs of women with CKD for information and preconception counseling are now unmet. There is an urgent need for frameworks and tools to support patients and physicians, especially nephrologists, in initiating and carrying out sensitive, practical, and informed shared decision-making (SDM) regarding pregnancy.

Kattah, et al[8] (2017) showed that preeclampsia and ESRD are significantly correlated; however, obesity is a confounding factor that has not been thoroughly studied. Although prevalent, pre-existing renal illness was not always recognized or classified.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Hewawasam et al, 2023[7]	Australia	Cross sectional study	102 patients	Compared to nephrologists (26.7%), women (60.0%) started the majority of pregnancy-related conversations, with 14.7% starting them just after conception. Pregnancy-related conversations were seen satisfying (68.0%) and helpful (50.7%) by women, but they were also stressful (66.7%), and only 54.7% of them felt in control of the decision-making process. The effectiveness and results of counseling linked to pregnancy were influenced by information deficiencies and quality, preconceived decisions, the clinician-patient disconnect, and the stress of decision-making. Women were not given enough information on drug safety (40.9%), fetal problems (33.8%), the emotional and psychological effects of pregnancy (73.2%), or contraception (not given in

				35.2% of instances). Nephrologists (86.4%), in-person settings (79.5%), websites (72.7%), handouts (61.4%), and online support groups (46.6%) were the counseling sources that women favored. Peer assistance, psychological support, and high-quality, multiformat information from subject matter specialists were also highly requested.
Kattah et al, 2017[8]	USA	Case control study	132 patients	Prior to the first pregnancy, renal disease was present in 9 out of 44 cases (21%) and 1 out of 88 controls (<1%). Based on an examination of the charts, preeclamptic pregnancies were found in 8 of 44 (18%) cases and 4 of 88 controls (5%) (unadjusted OR, 4.0; 95% CI, 1.21–13.28). Following independent correction for race, education level, pre-pregnancy hypertension, or diabetes, the results were identical. After accounting for obesity, the link was reduced and stopped being significant (OR, 3.25; 95% CI, 0.93 −11.37).
Wu et al, 2014[9]	Taiwan	Case control study	13.633 patients	46 of the 13,633 pregnant women with hypertension conditions had end-stage renal disease. Pregnant women with hypertension disorders were 10.64 times more likely to have end-stage renal disease than non-hypertensive women (95% confidence interval [CI], 7.53-15.05). Women having a history of preeclampsia on top of chronic hypertension had the greatest risk (hazard ratio, 44.72; 95% CI, 22.59-88.51). Compared to women without hypertensive problems during pregnancy, women with gestational hypertension had a greater risk of end-stage renal disease (hazard ratio, 5.82; 95% CI, 2.15-15.77).
Paauw et al, 2018[10]	Netherlands	Cohort study	2.782 patients	None of the women experienced end-stage renal disease throughout the follow-up period, and the incidence of CKD was comparable for all HDP groups (HR, 1.04; 95% CI, 0.79-1.37; P=0.8). RAS blocker use increased following HDP on all visits. We found that both groups' eGFR decreased over a median

				of 11 years, with the HDP group seeing a somewhat more severe drop (98±15 to 88±16 vs. 99±17 to 91±15 mL/min/1.73 m2; Pgroup<0.01, Pgroup*visit<0.05). After controlling for mean arterial pressure, the group effect persisted, but it vanished when RAS blockage was taken into account. There was no difference in 24-hour albuminuria across the groups.
Ayansina et al, 2016	United Kingdom	Cross sectional	14.851 patients	Compared to 3.9% of women with normotension, 7.5% and 5.2% of women with a history of GH and PE, respectively, were diagnosed with CKD. In women with PE and GH, the adjusted chances ratio (95% confidence interval) of CKD was 1.93 (1.44, 2.57) and 1.36 (1.13, 1.63), respectively. The unadjusted odds ratio (95% confidence interval) of having CKD was 2.04 (1.53, 2.71) and that for GH was 1.37 (1.15, 1.65). Women with preeclampsia were more likely to experience renal function impairment sooner than those with gestational hypertension, according to Kaplan-Meier curves measuring survival times until the onset of chronic kidney disease.

Wu, et al[9] (2014) showed that regardless of the kind of hypertension condition, women who experience it during pregnancy are more likely to develop postpartum end-stage renal disease. Regular postpartum examinations are advised for women with a history of hypertensive problems during pregnancy, particularly for renal function.

Paauw, et al[10] (2018) showed that the incidence of CKD was not noticeably increased by HDPs. After controlling for the use of RAS blockers, we saw a slightly decreased eGFR following HDP that was no longer statistically significant. However, we did not find any variations in albuminuria throughout follow-up. We were unable to find a meaningful risk of decrease in kidney function in this sample following patient-reported HDP.

Ayansina, et al[11] (2016) showed that preeclamptic women seem to have a little but considerable increased chance of developing chronic kidney disease (CKD). This suggests that long-term renal function needs to be taken into account in addition to controlling the risk of cardiovascular disease in women with PE and GH. The same changes to lifestyle and risk factors should be made: eating a balanced diet, getting regular exercise, keeping a healthy weight, quitting smoking, lowering cholesterol, and controlling blood pressure.

DISCUSSION

The kidneys experience a number of physiological changes during pregnancy. In the second trimester, the glomerular filtration rate increases by 50%. In the third trimester, there is a relative reduction in creatinine clearance. Pregnancy was once thought to impair kidney function in those with underlying chronic kidney disease (CKD). Glomerular disorders, particularly IgA nephropathy and lupus nephritis, might decrease kidney function and hence be risk factors for unfavorable pregnancy-related outcomes. Given the connection between kidney function and the morbidity of the mother and fetus, women with chronic kidney disease (CKD) were formerly recommended against getting pregnant until after a renal transplant and after stabilizing their kidney function. But new information has caused this idea to change.[12,13]

Multifactorial etiopathogenesis is a prevalent cause of infertility in women receiving dialysis. Women with end-stage kidney disease (ESKD) have changes in their hormonal balance. The hypothalamic-pituitary axis is activated by the

estradiol-stimulated luteinizing hormone surge, which is absent in patients with chronic kidney disease (CKD). Prolactin levels may rise as a result of CKD, altering ovulatory cycles. The association between low anti-Müllerian hormone concentrations and infertility in women with CKD needs further investigation, however low anti-Müllerian hormone concentrations at advanced stages of the disease can be utilized to predict infertility in CKD women. Infertility may also result from other reasons including diminished libido, problems with body image, depression, the effects of uremic toxins, and pharmacologic adverse effects from immunosuppressants or antihypertensive drugs.[14,15]

Reproductive counseling should ideally start in the early stages of chronic kidney disease (CKD) and continue through subsequent follow-up visits with regular reevaluations until the time of conception. Reproductive counseling should take into account the woman's wish to get pregnant or not, and it should include topics such as fertility, the dangers associated with a potential pregnancy, and how to use contraceptives. The age, medical history, and stage of chronic kidney disease (CKD) of the woman can all affect the hazards to the mother, the child, and the transplant. For this reason, risk assessment and customized counseling are crucial for CKD women who wish to become pregnant.[16]

Pregnancies in CKD-afflicted women necessitate intensive monitoring and a multidisciplinary approach. Pregnant dialysis patients and KTR patients both require special attention; in either case, the prescription for dialysis and its accompanying drugs should be reassessed. Materno-fetal outcomes may be significantly impacted by obstetric follow-up, which includes serial monitoring of the amniotic fluid index, Doppler ultrasonography of the uterine and umbilical arteries, and the interpretation of the biomarkers sFlt-1/PIGF. These measures may help discover predictive indicators.

CONCLUSION

In summary, an increased risk of chronic kidney disease was linked to exposure to unfavorable pregnancy outcomes, such as hypertensive disorders of pregnancy, gestational diabetes, and premature birth. Preeclamptic women had the highest chance of developing ESKD. To identify women who are more likely to develop kidney disease, especially following hypertensive disorders during pregnancy, a systematic strategy may be necessary to maximize the patients' long-term follow-up.

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