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Pregnancy in immunoglobulin A nephropathy patients; an updated review

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ABSTRACT

Immunoglobulin A nephropathy (IgAN) is found as the most frequent primary glomerulonephritis worldwide, predominantly affecting the younger population. The peak incidence of this disease occurs between the second and third decades of life, thereby making pregnancy a significant concern for women diagnosed with IgAN. Extensive studies have demonstrated that pregnancy itself does not inherently pose a specific risk for the deterioration of kidney function in individuals with IgAN who are in the initial stages of chronic kidney disease. However, it is important to note that IgAN elevates the risk of preeclampsia, a condition that is a pivotal risk factor contributing to unfavorable outcomes during pregnancy. Consequently, healthcare providers should be attentive to the potential complications of preeclampsia in pregnant women with IgAN, as its presence holds substantial implications for maternal and fetal well-being.

Review

Implication for health policy/practice/research/medical education:
Immunoglobulin A nephropathy (IgAN) is a common primary glomerulonephritis, especially in young people. While pregnancy does not necessarily worsen kidney function in early IgAN stages, the risk of preeclampsia is heightened due to IgAN, potentially leading to adverse pregnancy outcomes.

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Introduction

Immunoglobulin A nephropathy (IgAN), also called Berger's disease, is the most frequent primary glomerulonephritis worldwide in younger people (1). The prevalence of IgAN differs broadly amongst the various races and ethnicities, with the highest frequency in individuals of East Asian descent, pursued by Caucasian persons. At the same time, it is comparatively rare in people of sub-Saharan African ancestry (2). This disease is a principal cause of chronic renal disease, which develops to end-stage kidney failure in about 40% of cases across twenty years of diagnosis. In addition, this disease is accompanied by significant mortality (2). IgA nephropathy (IgAN) displays several clinical courses, consisting of hematuria, ranging from microscopic to macroscopic hematuria, variable amount of proteinuria, comprising nephrotic syndrome; high blood pressure, and renal insufficiency as chronic kidney disease or acute kidney injury (3). This is an autoimmune disease, while IgA1-IgG immune complexes deposit on the glomerular mesangial area, followed by inflammation in the glomeruli. The immunogenicity of IgA1 is due to an IgA1 galactosylation defect (4). IgA nephropathy patients demonstrate substantial heterogeneity in the clinical manifestations, epidemiology, kidney progression, and long-term outcomes through their dissimilar racial and ethnic populations (2).

Since this disease is a common primary

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glomerulonephritis globally and has peaked in the second and third decades of living, pregnancy would be a main concern for female IgAN individuals (5). It is recognized that individuals with chronic renal failure have a considerably superior risk of adverse maternal and fetal consequences; therefore, pregnant women who have IgAN have elevated risks of preeclampsia, low-birth-weight infants, or preterm birth than pregnant cases without this disease. It is also possible that obstetric complications direct toward the progression of IgAN (6). For example, a previous systematic review showed that adverse pregnancy-associated outcomes, including gestational hypertension or preeclampsia, were tenfold greater in pregnancy with IgAN than in the normal population (7). Thereby, pregnancy would be a central concern for females with this glomerulopathy (6, 7), while the clinical management of IgAN cases with pregnancy-related complications is challenging. Little literature exists regarding IgAN management in pregnancy. Therefore, we aimed to review the most recent knowledge and concepts on IgAN in a pregnant woman.

Study method

This review collected materials by searching international databases such as PubMed/Medline, Directory of Open Access Journals, Web of Science, Google Scholar, EBSCO, Scopus, and EMBASE to obtain relevant information. The keywords of were conducted for this study were; IgA nephropathy, glomerulonephritis, Berger's disease, end-stage kidney disease, pregnancy, prognosis, chronic kidney disease, immunoglobulin A nephropathy, IgA deposition, glomerular disease, kidney function, hypertension, renal function, proteinuria and estimated glomerular filtration rate. This narrative review study contained papers published from 2010 to 2023.

Clinical and pathological presentations of IgAN

Immunoglobulin A nephropathy mostly involves young patients (8). A major finding of this disease is considerable heterogeneity in the clinical presentation along various peoples (9). They may present with various clinical syndromes, including microscopic hematuria and asymptomatic proteinuria, across episodes of macroscopic hematuria to nephrotic range proteinuria. This disease can present as an acute glomerulonephritis (acute kidney injury) or a rapidly progressive glomerulonephritis. Finally, around 50% of cases will develop end-stage kidney failure upon 20–30 years of follow-up (8).

On the other hand, the morphological findings also vary broadly, extending from mesangial proliferation/with matrix expansion to a considerable glomerular inflammation, accompanied by extracellular proliferation (crescents formation) (9), and sometimes as some morphologic lesions resemble focal segmental glomerulosclerosis (10). The pathological diagnosis of this disease requires significant IgA deposition in the mesangial area of the glomeruli. Additionally, staining for IgA is continuous across C3 deposits and sometimes with co-deposits of IgG. Nevertheless, IgG deposits are unnecessary to diagnose this disease (11). Conferring to the Oxford classification, five pathologic lesions (mesangial proliferation, endo-capillary hyper-cellularity, segmental glomerulosclerosis, and tubular atrophy/interstitial fibrosis and also crescent were detected as having prognostic implications (12).

A literature review on IgAN in pregnancy

Recently, Jarrick et al conducted a register-based investigation on a Swedish cohort of females with biopsy-proven IgAN. They considered the main outcome as preterm birth. Moreover, the secondary outcomes were the presence of gestational diabetes, development of preeclampsia, cesarean section, small for gestational age, low Apgar score, and fetal or infant loss. They found this glomerulonephritis was accompanied by an increased risk of preeclampsia, cesarean section, preterm birth, and small for gestational age birth. However, there were few total intrauterine or neonatal death risks, which did not vary from the reference study. Though furthermost females with this disease had an appropriate pregnancy outcome, these patients are at greater risk of preeclampsia, preterm birth, and small for gestational age birth (13).

Meanwhile, Limardo et al in an Italian multicenter investigation in a group of females of childbearing age with biopsy-confirmed IgAN and serum creatinine level ≤1.2 mg/dL at diagnosis across with a minimum follow-up of five years following biopsy, studied pregnancy and progression of IgA nephropathy. They concluded that pregnancy may not affect the long-term consequence of renal disease in females with IgAN and preserved renal function (14). In another study, Oki et al retrospectively studied the frequency of fetal and maternal complications in a group of renal transplant cases whose renal failure was due to the IgAN. Their study comprised 73 pregnancies in 64 renal transplant cases. They showed IgAN group had a more frequency of gestational hypertension than the non-IgAN group. This study also showed that the 20-year graft survival or prevention of chronic kidney disease stage five in a group with IgAN was lower versus patients with other primary glomerular disease (15). To find the renal and pregnancy outcomes in IgAN, Liu et al in a systematic review and meta-analysis, included pregnancies of 273 IgAN patients versus 241 IgAN without pregnancy. They showed that pregnancy in IgAN patients did not raise the risk of adverse kidney events, counting the doubling of plasma creatinine. There was no significant difference in the change in estimated glomerular filtration rate at the end of follow-up in the pregnant compared to non-pregnant cases.

However, females with IgAN had high rates of

preeclampsia, low birth weight, infant loss, and preterm delivery. This meta-analysis concluded that pregnancy in IgAN individuals with preserved renal function did not accelerate the worsening of kidney function. However, pregnant women with this disease are at greater risk of pregnancy complications (16). Recently Wang et al, in a systematic review and meta-analysis, studied the kidney outcomes of pregnant individuals with IgAN. Similar to the previous meta-analysis, they found no significant difference in kidney outcomes detected as a doubling of serum creatinine and a fifty-percent drop in glomerular filtration rate (GFR) of pregnant women versus non-pregnant individuals with IgAN. Wang et al showed that IgAN women had a superior pregnancy outcome probability compared to the normal Chinese populace (17). Pregnancy did not seem to accelerate renal deterioration in IgAN women in the primary stages of chronic kidney disease (17).

Pathophysiologic alterations of renal function and structure in IgAN women with pregnancy

During a normal pregnancy, several immunologic and hemodynamic alterations will occur. An increased systemic concentration of vasodilators, like relaxin and nitric oxide, and also resistance to vasoconstrictors, like angiotensin II, will lead to the main hemodynamic changes in pregnancy containing enhanced cardiac output, expanded blood volume, and decreased systemic vascular resistance. Therefore, a normal pregnancy will face a decrease in systemic blood pressure, across with an increase in GFR, around 50% of its baseline, which leads to a normal diminution in plasma creatinine concentration due to the hyperfiltration (18). Since IgA nephropathy is regarded as the most common primary glomerulonephritis globally and has a peak presentation in young people, pregnancy wounds are a general concern for females with this glomerulopathy. In general, the relationship of glomerulopathy with enhanced risk of adverse maternal and fetal outcomes, counting preeclampsia, accelerated drop in kidney function, preterm delivery and fetal death, and intrauterine growth retardation are well-detected complications (19). Pregnancy may impose several pathological alterations in IgAN patients. This disease can exacerbate kidney function and structure deterioration, leading to gestational hypertension (20). The main circumstances that imitate the prognosis are the quantity of proteinuria, renal function, and blood pressure level across morphologic lesions on renal biopsy (20). IgAN during pregnancy resembles the features of preeclampsia, which may be hard to discriminate from aspects of glomerulopathy (21). Gestational proteinuria is identified as new-onset proteinuria without high blood pressure after 20 weeks of pregnancy that dissolves by 12 weeks after delivery. Preeclampsia is delineated as new-onset high blood pressure with or without proteinuria from 20 weeks of pregnancy to 12 weeks after delivery (22). Pregnancy is not a specific risk for deterioration of kidney function in IgAN with primary stages of chronic renal failure (5,23).

However, IgAN is a risk for preeclampsia; this condition is a principal risk factor for adverse pregnancy outcomes. Likewise, a similar feature could be detected in IgAN (13). The importance of detection of early kidney disease in pregnancy is predominantly applicable for IgAN since its main presentation is at a young age. Individuals with IgAN should be informed about their disease and the related risk factors. In cases with preserved renal function, the risk of development of renal disturbance is low. Contrariwise, the hazard of developing preeclampsia and gestational hypertension is elevated.

In summary, the pregnancy outcomes of cases with IgAN are inconstant and depend on the blood pressure level, kidney function, amount of proteinuria, and pathologic lesions following renal biopsy. In some conditions, it is necessary to conduct a renal biopsy. Kidney biopsy is a routine procedure in detecting renal disease; however, in pregnancy, it carries potential adverse effects for both mother and child (24).

IgAN and pregnancy-induced complications

Pregnancy can stimulate several pathological alterations in IgA nephropathy patients. This disease can accelerate the deterioration of kidney function, which may result in pregnancy-induced hypertension, finally affects the prognosis of IgA nephropathy, and could also affect the fetus's life (20). Other factors, such as severe hypertension, inflammation, and immune imbalance, promote the progression of IgA nephropathy during pregnancy. A major point is treatment choices. However, inadequate data is mainly limited to case reports (14). The physicians have to balance the benefits of treatment versus the risks. In the case of deterioration of kidney function, a renal biopsy may be considered. Pregnancy, in the background of renal diseases, including IgA nephropathy, is concomitant with preterm delivery (23).

Conclusion

Diagnosis of IgA nephropathy in pregnancy and its treatment is challenging. The outcomes of these patients are variable and related to the level of blood pressure, kidney function, quantity of proteinuria, and the scores of Oxford classification on renal biopsy. Wealthy pregnancy is commonly feasible for these patients. However, it may portend high risks for both patient and fetus if the patient has a glomerular filtration rate below 70 mL/min or severe high blood pressure.

Authors' contribution

Conceptualization: Elham Saffarieh and Seyedeh Reyhaneh Yousefi Sharemi.

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Writing–original draft: Seyedeh Reyhaneh Yousefi Sharemi.
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Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

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References

1. Pattrapornpisut P, Avila-Casado C, Reich HN. IgA Nephropathy: Core Curriculum 2021. Am J Kidney Dis. 2021;78:429-441. doi: 10.1053/j.ajkd.2021.01.024.
2. Rajasekaran A, Julian BA, Rizk DV. IgA Nephropathy: An Interesting Autoimmune Kidney Disease. Am J Med Sci. 2021;361:176-194. doi: 10.1016/j.amjms.2020.10.003.
3. Prasad N, Khurana M, Behera M, Yaccha M, Bhadauria D, Agarwal V, et al. Clinicopathologic Manifestations of Immunoglobulin A Nephropathy in a Northern Indian Cohort: A Mute Assassin with Delayed Diagnosis. Indian J Nephrol. 2023;33:12-21. doi: 10.4103/ijn.ijn_351_21.
4. Segawa Y, Ishida R, Kanehisa F, Nakai K, Morimoto M, Seno M, et al. IgA nephropathy in a patient receiving infliximab for generalized pustular psoriasis. BMC Nephrol. 2020;21:366. doi: 10.1186/s12882-020-02015-0.
5. Carosso A, Zonca M, Colla L, Borella F, Daniele L, Benedetto C. Pregnancy in a woman with recurrent immunoglobulin a nephropathy: A case report. Case Rep Womens Health. 2018;20:e00074. doi: 10.1016/j.crwh.2018.e00074.
6. Tang C, Si FL, Yao YX, Lv JC, Shi SF, Chen YQ, et al. The efficacy and safety of hydroxychloroquine in pregnant patients with IgA nephropathy: A retrospective cohort study. Nephrology (Carlton). 2022;27:155-161. doi: 10.1111/nep.13991.
7. Piccoli GB, Kooij IA, Attini R, Montersino B, Fassio F, Gerbino M, et al. A Systematic Review on Materno-Foetal Outcomes in Pregnant Women with IgA Nephropathy: A Case of "Late-Maternal" Preeclampsia? J Clin Med. 2018 Aug 11;7:212. doi: 10.3390/jcm7080212.
8. Gutiérrez E, Praga M, Rivera F, Sevillano A, Yuste C, Goicoechea M, et al; all members of the Spanish Registry of Glomerulonephritis. Changes in the clinical presentation of immunoglobulin A nephropathy: data from the Spanish Registry of Glomerulonephritis. Nephrol Dial Transplant. 2018;33:472-477. doi: 10.1093/ndt/gfx058.
9. Yeo SC, Goh SM, Barratt J. Is immunoglobulin A nephropathy different in different ethnic populations? Nephrology (Carlton). 2019;24:885-895. doi: 10.1111/nep.13592.
10. Roberts IS. Pathology of IgA nephropathy. Nat Rev Nephrol. 2014;10:445-54. doi: 10.1038/nrneph.2014.92.
11. Ştefan G, Ismail G, Stancu S, Zugravu A, Andronesi A, Mandache E, et al. Validation study of Oxford Classification of IgA Nephropathy: the significance of extracapillary hypercellularity and mesangial IgG immunostaining. Pathol Int. 2016;66:453-9. doi: 10.1111/pin.12442.
12. Coppo R, Peruzzi L. IgA Nephropathy. In: Schaefer F, Greenbaum LA, eds. Pediatric Kidney Disease. Cham: Springer; 2023. doi: 10.1007/978-3-031-11665-0_17.
13. Jarrick S, Lundberg S, Stephansson O, Symreng A, Bottai M, Höijer J, et al. Pregnancy outcomes in women with immunoglobulin A nephropathy: a nationwide population-based cohort study. J Nephrol. 2021;34:1591-1598. doi: 10.1007/s40620-021-00979-2.
14. Limardo M, Imbasciati E, Ravani P, Surian M, Torres D, Gregorini G, et al; Rene e Gravidanza Collaborative Group of the Italian Society of Nephrology. Pregnancy and progression of IgA nephropathy: results of an Italian multicenter study. Am J Kidney Dis. 2010;56:506-12. doi: 10.1053/j.ajkd.2010.03.033.
15. Oki R, Unagami K, Kakogawa J, Beppu H, Banno T, Yagisawa T, et al. Pregnancy Complications and Impact on Kidney Allograft After Kidney Transplantation in IgA Nephropathy. Transpl Int. 202336:11220. doi: 10.3389/ti.2023.11220.
16. Liu Y, Ma X, Zheng J, Liu X, Yan T. A Systematic Review and Meta-Analysis of Kidney and Pregnancy Outcomes in IgA Nephropathy. Am J Nephrol. 2016;44:187-93. doi: 10.1159/000446354.
17. Wang F, Lu JD, Zhu Y, Wang TT, Xue J. Renal Outcomes of Pregnant Patients with Immunoglobulin A Nephropathy: A Systematic Review and Meta-Analysis. Am J Nephrol. 2019;49:214-224. doi: 10.1159/000496410.
18. Gonzalez Suarez ML, Kattah A, Grande JP, Garovic V. Renal Disorders in Pregnancy: Core Curriculum 2019. Am J Kidney Dis. 2019;73:119-130. doi: 10.1053/j.ajkd.2018.06.006.
19. Kendrick J, Sharma S, Holmen J, Palit S, Nuccio E, Chonchol M. Kidney disease and maternal and fetal outcomes in pregnancy. Am J Kidney Dis. 2015;66:55-9. doi: 10.1053/j.ajkd.2014.11.019.
20. Chen H, Li X, Wu Y, Fan L, Tian G. Pregnancy-induced complications in IgA nephropathy: A case report. Medicine (Baltimore). 2018;97:e0470. doi: 10.1097/MD.0000000000010470.
21. Oliverio AL, Zee J, Mariani LH, Reynolds ML, O'Shaughnessy M, Hendren EM, et al. Renal Complications in Pregnancy Preceding Glomerulonephropathy Diagnosis. Kidney Int Rep. 2018 Oct 25;4:159-162. doi:

10.1016/j.ekir.2018.10.012.
22. Koda N, Matsumoto K, Maruyama Y, Ishikawa N, Tsuboi N, Kawamura T, et al. A Pregnant Woman with IgA Nephropathy Showing Histological Preeclampsia Findings without Hypertension Treated with Steroids: A Case Report and Literature Review. Intern Med. 2023;62:1195-1202. doi: 10.2169/internalmedicine.9146-21.
23. Podymow T, August P. Stage 1 chronic kidney disease in pregnancy. Obstet Med. 2012;5:141-146. doi: 10.1258/om.2012.120009.
24. Moguel González B, Garcia Nava M, Orozco Guillén OA, Soto Abraham V, Vasquez Jimenez E, Rodriguez Iturbe B, et al. Kidney biopsy during pregnancy: a difficult decision. A case series reporting on 20 patients from Mexico. J Nephrol. 2022;35:2293-2300. doi: 10.1007/s40620-022-01366-1.