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Physiological impact of pregnancy on renal function; a prospective cohort study

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ABSTRACT

Introduction: Pregnancy induces substantial physiological adjustments that extend to renal function, driven by changes in blood volume, hormonal activity, and metabolic demands that alter the normal behavior of key biochemical markers. Understanding how these renal parameters evolve across gestation is essential for distinguishing healthy physiological adaptation from early signs of renal impairment.

Objectives: This study aimed to examine trimester-specific changes in renal function within a prospective cohort of pregnant women to clarify the expected trajectory of renal biomarkers during normal pregnancy.

Materials and Methods: The study employed a prospective cohort design conducted at a maternity teaching hospital in Nasiriyah, Iraq, enrolling 49 first-trimester singleton pregnant women who were followed from January 2024 to January 2025 to assess longitudinal renal changes. Eligible participants were singleton pregnant women who provided informed written consent. Demographic and obstetric data were collected at enrollment, and venous blood samples were obtained at the end of each trimester to measure blood urea and serum creatinine using standardized biochemical procedures. Renal biomarkers were compared across trimesters to evaluate alterations in kidney function during pregnancy.

Results: The study included 49 pregnant women with a mean age of 30.22 ± 8.25 years. The results demonstrated progressive alterations in renal biomarkers across pregnancy, with both blood urea and creatinine levels indicating a steady and statistically significant rise from the first to the third trimester ($P < 0.05$).

Conclusion: Pregnancy is associated with a steady and significant increase in renal biomarkers across trimesters. These findings highlight the importance of considering trimester-specific changes when evaluating maternal renal function.

Implication for health policy/practice/research/medical education:
In this study, we found that pregnancy produces a gradual and measurable shift in renal physiology, reflected in the steady rise of key biochemical markers as gestation progresses. The upward trajectory of these biomarkers signals a dynamic process of renal adaptation in which filtration and solute-handling mechanisms evolve in parallel with the physiological transformations of pregnancy. This pattern reinforces the concept that maternal kidney function is not static but undergoes a predictable, trimester-dependent modulation that must be considered when evaluating renal health during pregnancy.

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Introduction

Pregnancy induces profound physiological adaptations across multiple organ systems, including the kidneys, to support fetal development and maintain maternal homeostasis (1-3). Maternal renal function undergoes dynamic changes beginning early in gestation, driven by increased metabolic demands, plasma volume expansion, and hormonal modulation (1,4). These adaptations are essential for maintaining fluid and electrolyte balance, excreting metabolic waste, and supporting placental perfusion (1). Prior research has demonstrated that glomerular filtration rate (GFR) rises significantly during

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normal pregnancy, reflecting enhanced renal plasma flow and systemic vasodilation (5). Lopes van Balen et al reported that GFR increases by approximately 40–50% in early gestation, stabilizing through mid-pregnancy before gradually declining toward term, although remaining above pre-pregnancy levels throughout gestation (1).

Renal function during pregnancy is influenced by complex hemodynamic and hormonal factors, including relaxin-mediated vasodilation, activation of the renin–angiotensin–aldosterone system, and increased nitric oxide production. These mechanisms collectively reduce renal vascular resistance and promote hyperfiltration (6,7). Structural changes, such as kidney enlargement and dilation of the urinary tract, further contribute to altered renal physiology (8). Comprehensive reviews have highlighted that renal plasma flow may increase during pregnancy, underscoring the magnitude of these physiological shifts (6). Understanding these changes is essential for distinguishing normal gestational adaptations from early signs of renal pathology, particularly in women with pre-existing kidney disease or those at risk of hypertensive disorders of pregnancy.

The physiological impact of pregnancy on renal function has important clinical implications. Altered tubular handling of electrolytes, increased protein excretion, and changes in acid–base balance may complicate the assessment of renal health during gestation (9). The renal and urinary tract adaptations are integral to maintaining maternal–fetal equilibrium and can influence pregnancy outcomes when disrupted (10). Despite extensive characterization of these physiological processes, prospective cohort data remain essential for refining our understanding of renal functional trajectories across pregnancy and for improving clinical assessment frameworks. The present study aims to address this need by evaluating the physiological impact of pregnancy on renal function in a well-defined cohort.

Objectives

This study aimed to examine the physiological changes in renal function that occur throughout pregnancy by assessing trimester-specific variations in key biochemical markers within a prospective cohort of pregnant women, thereby distinguishing normal gestational adaptations from potential indicators of renal impairment.

Materials and Methods

Study design and participants

The prospective cohort study was conducted at a major maternity teaching hospital in Nasiriyah, Iraq, over the period from January 2024 to January 2025, and enrolled a group of 49 pregnant women who were systematically followed throughout the course of their pregnancies to assess longitudinal changes in renal function.

Inclusion and exclusion criteria

The study enrolled singleton pregnant women in their first trimester who were receiving routine antenatal care and who provided informed written consent to participate in longitudinal follow-up throughout pregnancy. Eligibility required the absence of any known chronic kidney disease, hypertension, diabetes mellitus, or other systemic disorders with the potential to independently influence renal function. Women who developed pregnancy-related complications during the study period, as well as those using medications known to affect renal biomarkers, were excluded to minimize confounding influences. Participants with incomplete follow-up data or insufficient laboratory samples were also excluded to ensure the reliability and consistency of renal function assessments across all trimesters.

Kidney function tests assessment

Kidney function was evaluated through serial measurement of blood urea and serum creatinine concentrations at standardized time points across gestation. Venous blood samples were obtained from each participant at the end of every trimester to ensure consistency in physiological comparison and to capture trimester-specific renal adaptations. All samples were processed using routine biochemical analysis in the hospital laboratory, following standardized protocols and assessments throughout the study period.

Data collection

Data collection was conducted prospectively throughout the duration of pregnancy following the provision of informed written consent by all participants. At enrollment, comprehensive demographic and obstetric information, including maternal age, parity, and history of miscarriage, was obtained to characterize the study population. Venous blood samples were subsequently collected from each participant at the end of every trimester to enable standardized and temporally consistent assessment of renal function. Blood urea and serum creatinine concentrations were measured using validated biochemical laboratory procedures, and all results were systematically recorded to facilitate comparative analysis across the first, second, and third trimesters.

Outcome measurement

Outcome measurement was based on evaluating changes in renal function across gestation by comparing blood urea and serum creatinine concentrations at three defined time points corresponding to the end of each trimester. These biomarkers were selected as primary indicators of renal

function during pregnancy, and their serial assessment allowed for the identification of trimester-specific trends and the characterization of progressive alterations in kidney function over the course of gestation.

Statistical analysis

All statistical analyses were conducted using SPSS software, version 27 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize baseline maternal characteristics, including age, parity, and miscarriage history. Continuous variables such as blood urea and serum creatinine concentrations were expressed as means and standard deviations for each trimester. The normality of the distribution of quantitative data, including urea and creatinine, was assessed using the Shapiro–Wilk test; however, because the direction of the P values for both parametric and non-parametric tests was consistent, parametric tests were selected due to their greater statistical accuracy. To evaluate longitudinal changes in renal biomarkers across pregnancy, repeated-measures analysis was applied to test overall differences among the three trimesters. Pairwise comparisons between trimesters were subsequently performed using paired-samples t-tests to identify specific trimester-to-trimester differences. Statistical significance was defined as a two-tailed *P* value < 0.05.

Results

The study population consisted of 49 pregnant women with a mean age of 30.22 ± 8.25 years, reflecting a broad reproductive-age cohort. The distribution of parity indicated that most participants had previously given birth, whereas a smaller subset comprised women in their first pregnancy. A similar pattern emerged for pregnancy loss, as the majority of women reported no history of miscarriage, and only a limited number had experienced one or two prior losses (Table 1).

Blood urea levels demonstrated a clear upward pattern as pregnancy advanced, with values progressively increasing from the first through the third trimester. Statistical testing indicated that these changes were significant across all stages of gestation. Comparisons between trimesters showed that each subsequent stage was associated with a meaningful rise in urea levels relative to the previous one, reflecting the physiological adjustments in renal handling of nitrogenous waste that occur as pregnancy progresses (Table 2 and Figure 1).

Creatinine levels showed a consistent upward progression across pregnancy, reflecting the increasing physiological demands placed on maternal renal function as gestation advances. Each trimester was associated with a statistically significant rise compared with the preceding stage, indicating that renal filtration dynamics shift progressively throughout pregnancy. These trimester-to-trimester differences highlight the cumulative impact of gestational changes on creatinine handling, underscoring the importance of interpreting renal biomarkers within the context of normal physiological adaptation during pregnancy (Table 3 and Figure 2).

Table 1. Baseline characteristics of participating mothers in the study

Maternal demographic and obstetric information		Frequency	Percent
Parity (N)	0	10	20.4
	1	8	16.3
	2	15	30.6
	3	11	22.4
	4	5	10.3
	Total	49	100
Miscarriage (N)	0	38	77.6
	1	9	18.3
	2	2	4.1
	Total	49	100
Quantitative variable		**Mean**	**SD**
Maternal age (years)		30.22	8.25

N: Number, SD: Standard deviation.

Table 2. Changes in blood urea levels across pregnancy trimesters

Pregnancy time	Mean	SD	*P* value*
Blood urea (mg/dL)			
First trimester	41.81	13.27	<0.001
Second trimester	47.89	13.05	
Third trimester	53.77	20.08	
Between-trimesters comparison	**Mean difference (95% CI)**		***P* value****
Third vs first	+11.96 (5.08–18.83)		0.001
Second vs first	+6.08 (0.74–11.41)		0.026
Third vs second	+5.88 (1.61–10.14)		0.008

SD: Standard deviation. *Repeated measures, **Paired-samples t test.

Discussion

Our prospective cohort study demonstrated a steady and significant increase in renal biomarkers, specifically blood urea and creatinine, across the trimesters of pregnancy. This finding contrasts with the physiological adaptations typically observed in normal pregnancies, where renal function is characterized by GFR, leading to decreased serum levels of urea and creatinine (11,12). De Flamingh and van der Merwe investigated serum biochemical changes during uncomplicated pregnancy and reported a consistent downward trend in both urea and creatinine concentrations across gestation; their findings highlight the characteristic renal adaptations of pregnancy, in which increased glomerular filtration and expanded plasma volume enhance the clearance of nitrogenous waste products, resulting in notably lower circulating

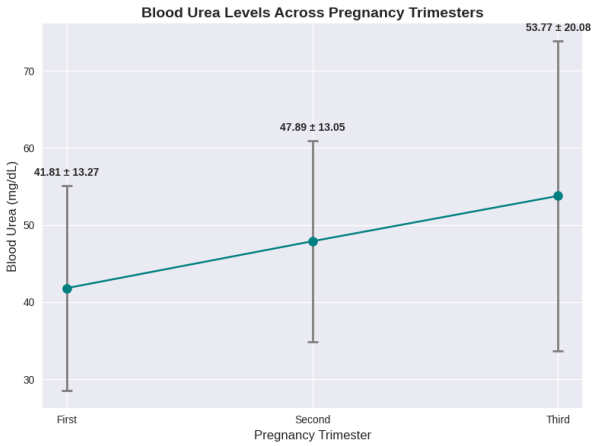

Figure 1. Mean blood urea concentrations comparison during the three trimesters of pregnancy.

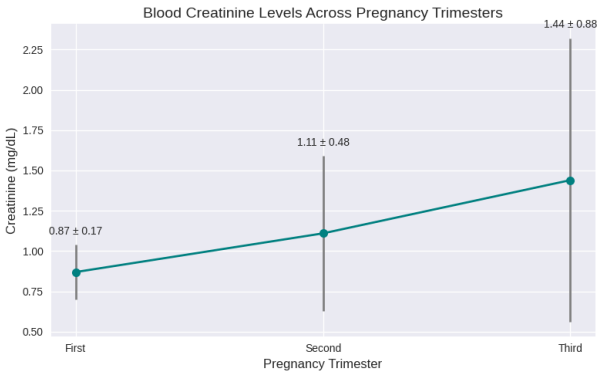

Figure 2. Mean blood creatinine concentrations comparison during the three trimesters of pregnancy.

levels of these markers as pregnancy progresses (12). Jin et al investigated establishing trimester-specific reference intervals for a broad range of biochemical, haematological, and haemostatic indices in healthy pregnant women. Their analysis demonstrated a pronounced reduction in blood urea nitrogen and creatinine concentrations from early to late gestation (11). These established patterns highlight increased renal clearance in uncomplicated pregnancies, underscoring the novelty of our observation of rising biomarker levels, which may indicate a deviation from typical physiological norms in our cohort and warrant scrutiny for potential underlying renal stress or subclinical impairment.

The observed steady increase in blood urea and creatinine across pregnancy trimesters suggests possible deviations from the expected hyperfiltration state, potentially reflecting early renal functional changes or cohort-specific factors such as subtle hemodynamic shifts, dietary influences, or unmeasured variables influencing biomarker accumulation (3,13). In normal pregnancy, renal physiology involves a 40%-65% rise in GFR by the first trimester, sustaining lower creatinine and urea concentrations despite increased plasma volume (1,3,14).

Table 3. Changes in blood creatinine levels across pregnancy trimesters

Pregnancy time	Mean	SD	*P* value*
Creatinine (mg/dL)			
First trimester	0.87	0.17	<0.001
Second trimester	1.11	0.48	
Third trimester	1.44	0.88	
Between-trimesters comparison	**Mean difference (95% CI)**		***P* value****
Third vs first	+ 0.57 (0.31 – 0.81)		<0.001
Second vs first	+ 0.24 (0.08 – 0.37)		0.002
Third vs second	+ 0.33 (0.13 – 0.53)		0.002

SD: Standard deviation. *Repeated measures, **Paired-samples t test.

Our results, however, imply a progressive accumulation rather than dilution or clearance, which could signal attenuated renal reserve in some pregnant individuals, aligning with reviews noting that while most women adapt well, certain populations experience challenges in maintaining homeostasis (15). This discrepancy with prior longitudinal studies in healthy cohorts (11,14) highlights the importance of prospective monitoring in diverse settings, as our findings challenge the universality of decreased biomarker profiles and suggest that pregnancy may unmask vulnerabilities in renal handling of nitrogenous waste. Practically, these elevations could inform refined clinical thresholds for renal assessment, prompting earlier interventions to mitigate risks like hypertension or preeclampsia, where such biomarkers are further deranged (16,17).

Overall, our study reveals that pregnancy can be associated with a significant and progressive rise in blood urea and creatinine, diverging from the predominant literature documenting declines in normal gestation. These findings emphasize the need for pregnancy-specific reference ranges tailored to cohort characteristics and advocate for routine serial monitoring of renal biomarkers to detect atypical trajectories early. Future research should explore mechanistic drivers, such as longitudinal GFR measurements or correlations with proteinuria, to elucidate whether these changes represent adaptive variations or precursors to pathology. Clinically, integrating such profiles could enhance risk stratification, optimizing maternal care and outcomes in prospective cohorts.

Conclusion

This prospective cohort study shows that pregnancy is accompanied by progressive changes in renal function, evidenced by consistent increases in blood urea and creatinine levels across trimesters. These findings underscore the importance of interpreting renal biomarkers

within the context of normal gestational physiology to avoid misclassification of healthy adaptive changes as pathological. Recognizing these trimester-dependent patterns can support more accurate clinical assessment and enhance monitoring strategies for maternal kidney health during pregnancy.

Limitations of the study

The study is subject to several limitations that should be considered when interpreting the findings. The sample size was relatively small, with 49 participants, which may limit the generalizability of the results to broader populations. Renal function assessment relied solely on blood urea and serum creatinine measurements, without inclusion of additional biomarkers or GFR estimations that could provide a more comprehensive evaluation. The study also excluded women with pregnancy-related complications and those with incomplete follow-up, which, while necessary for methodological consistency, may reduce the applicability of the findings to more diverse clinical scenarios. Finally, although samples were collected at standardized trimester endpoints, unmeasured confounding factors, such as dietary intake, hydration status, or inter-laboratory variability, may have influenced biomarker levels.

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Authors' contribution

Conceptualization: Saad Mashkoor Waleed and Saba Sabeeh Hussain.
Data curation: Abdul-Hassan Mahdi Salih and Saad Mashkoor Waleed.
Formal analysis: Abdul-Hassan Mahdi Salih.
Investigation: Saba Sabeeh Hussain.
Methodology: Abdul-Hassan Mahdi Salih and Saba Sabeeh Hussain.
Project management: Saad Mashkoor Waleed.
Resources: All authors.
Supervision: All authors.
Validation: Abdul-Hassan Mahdi Salih.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Conflicts of interest

The authors declare no conflict of interest.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

While preparing this work, the authors utilized AI (Grammarly, https://app.scinito.ai/, and Copilot) to refine grammar points and language style. Subsequently, they thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

Ethical issues

The research was conducted in accordance with the principles outlined in the Declaration of Helsinki. Informed written consent was taken from all participants. This study was conducted at the maternity teaching hospital in Nasiriyah, Iraq, and approved by the ethics committee of the University of Alkafeel, Iraq, under the registration number 1425. Besides, the authors have ultimately observed ethical issues (including plagiarism, data fabrication, and double publication).

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