PERINATAL JOURNAL

Original Article

Perinatal Journal 2025; 33(2):522-527

https://doi.org/10.57239/prn.25.03320055

Measurement of IL-6 and renal function tests during the three pregnancy trimesters in Iraqi woman

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Abstract

Pregnancy is associated with changes in dynamic physiological, especially in kidney functions. Accurate evaluation of renal tests during gestation is important to distinguish between normal adaptation and early signs of pathology. To measure kidney function tests (including urea, uric acid, creatinine, and estimated glomerular filtration rate (eGFR)) during the three pregnancy trimesters and compare them with non-pregnant Iraqi women. This was a cross-sectional study with 48 members of healthy woman: 36 healthy pregnant women (12 in each trimester) and 12 non-pregnant serve as controls. The serum levels of urea, creatinine, and uric acidtests were assessed by the clinical chemistry analyzer IHeto AU240. The levels of IL-6 was measured by on Roche Cobas e 602 /Germany. Results: levels urea, uric acid and creatinine in healthy pregnant women within first and second trimester show significantly lowering ($p < 0.05$) than the third trimester and non-pregnant ladies. The eGFR levels showed the peak values through the second trimester and lower slightly in the third. A significant increase ($p < 0.05$) in serum IL-6 levels was observed in the second and third trimesters compared to non-pregnant controls ($p < 0.05$). It is valuable to know the variation in IL-6 and renal function parameters in pregnancy. These physiological changes must be considered in clinical practice to avoid misdiagnosis of renal dysfunction and inflammations.

Keywords: IL-6, Renal function Tests, eGFR, s.cr, Uric acid, Pregnancy

Introduction

During pregnancy several physiological changes were occur that effects on renal function, which must be understood when interpreting kidney function test in the pregnant women. The renal adjust to the increased metabolic demands crossing a normal pregnancy in order to maintain development of healthy fetal [**1**]. (IL-6) Interleukin-6 was a multi-functional cytokine include in regulate of immune system, hematopoiesis, and inflammation. In physiological pregnancy, IL-6 plays a dynamic physiological response, with the mild increases are particularly observed in the second and third trimesters underlying maternal immune adaption.IL-6 mediates trophoblast invasiveness, placental development and immune tolerance of the fetus. Regulated IL-6 expression is important for preventing complications, such as preeclampsia or preterm labor [**2**].

However, some researches have shown that increased IL-6 production was positively correlated with pregnancy complications including gestational hypertension, preeclampsia, as well as future renal function (around 2022) [**3**]. IL-6 has been related to the development of kidney injury due to its promoted pro-inflammatory pathways, like the JAK-STAT3 signaling pathway, which resulted in kidney glomerular damage, proteinuria, and decreased kidney glomerular filtration rate (GFR)[4]. It nesscessry to Understanding the healthy ranges of kidney function tests crossing pregnancy is important for early detections of kidney complications in order to ensuring mothers and fetals health**[5].** Close monitoring and accurate interpretation of these parameters help distinguish between physiological changes and pathological conditions [6]**.**

Emerging evidence also indicates that IL-6 might also play role in structural and functional changes in the mother's kidney in complicated pregnancies, likely affecting outcomes for both mother and fetus[7][8]. Nevertheless, more clinical studies are required to undertake the direct association of the interleukins levels with the renal function parameters in pregnant women, thereby new predictive markers for early prediction of renal complications in pregnancy may be provided.

The study aimed to:

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1. Measuring ofIL-6 in pregnant woman and compared it with non-pregnant.
2. To evaluate the association between serum Interleukin-6 (IL-6), and renal function tests in pregnant women.
3. To assess whether elevated interleukin levels can serve as early biomarkers of renal dysfunction during pregnancy.

Methods

2.1 Study design and sample selection

48 samples were collected from pregnant women who visited antenatal care at Abu-Ghraib Hospital General, through August of 2023 to March 2024. In this study, the pregnant women were classified into three groups depended on the semester of pregnancy. Among the 36 pregnant women, (12 members were in each trimester) and 12 healthy non-pregnant woman. The eGFR value calculated by CKD-EPI creatinine equation (2021). All members in the current study weren't getting oral contraception. In this study the weights of woman were varied. The mean of pregnant age of was matched with the non-pregnant age.

2.2 Blood Sample Collection

3ml of fresh blood was drawn from a both pregnant woman and non- pregnant woman to do HGB, and the remaining of blood were centrifuged to obtain serum and storage at -20C until assay urea, s.creatinine, uric acid. The levels of IL-6 was measured by on Roche Cobas e 602 (Germany) by electrochemiluminescence immunoassay (ECLIA). The serum of urea, creatinine, and uric acidtests were assessed by the clinical chemistry analyzer IHeto AU240, Fully Automated. All of this testes were done in the AL-Rahmah Laboratory for Medical and Hormonal Analysis in Abu-Ghraib.

2.3 Exclusion Criteria

The current study excluded with hypertension (HTN), and hyperglycemia that occur during pregnancy, in addition to smoker women.

2.4 Statistical Analysis

The parameters in this study were statistically analyzed by using SPSS and stated as (Mean±SD). One-way ANOVA was performed to compare between non-pregnant (healthy) and pregnant women in the first, second, and third trimesters. ($p>0.05$) expressed there are non-significant difference (NS) at a confidence interval (CI) of 95%. ($p<0.001$) considered a highly significant difference at a confidence interval (CI) of 99 %. P value of ($p<0.05$) was considered significant difference at a confidence interval (CI) of 95%.

3. Results

In the current study 12 members in each group, the mean ± SD of the age was non-significant difference ($P>0.05$), the age was matched in the pregnant and non-pregnant woman. Hemoglobin levels shown significant decrease ($P<0.05$) in three groups of pregnant woman as comparing with nonpregnant group, as shown in table (1).

Table (1): levels of age, and HG parameter

Variables	Non-pregnant (Mean ± SD) (n=12)	Pregnant (Mean± SD)		
		1st trimester 1,2,3 months (n=12)	2nd trimester 4,5,6 months (n=12)	3nd trimester 7,8,9months (n=12)
Age (years)	27.45 ± 5.95	27.81 ± 6.80	27.65 ± 7.85	27. 35 ± 5.02
p-value		(p>0.05) NS	(p>0.05) NS	(p>0.05) NS
HGB (g/dl)	12.65±0.62	10.04± 4.52	9.64±0.93	10.42± 1.47
p-value		P<0.05*	P<0.05*	P<0.05*

NS=non-significant * =there is significant difference (P<0.05)

There is highly significant lower (P< 0.01) in the concentration of urea in the first trimester of pregnant (17.73±2.06mg/dl) as compared with the mean value of urea of non-pregnant (32.05± 3.04 mg/dl). In the second trimester, the levels of urea show significant decrease (P<0.05) (21.166 ± 4.786mg/dl) as compared with the non-pregnant (32.05± 3.04 mg/dl). There is non-significant difference (p>0.05) in the level of urea **(**28.66±3.09mg/dl**)** in the third trimester as compare with the control (non-pregnant) as seen in table (2).

Table 2: Levels of serum RFTs in non-pregnant and pregnant women

Parameters	Non-pregnant (man ± SD) (n=12)	Pregnant (Mean± SD)		
		1st trimester 1,2,3 month (n=12)	2nd trimester 4,5,6 month (n=12)	3nd trimester 7,8,9month (n=12)
Urea (mg/dl)	32.05± 3.04	17.73±2.06	21.166 ± 4.786	28.66±3.09
p-value		P< 0.01**	P<0.05*	(p>0.05) NS
s. Cr(mg/dl)	0.82 ± 0.21	0.68± 0.10	0.61±0.62	0.79 ±0.04
p-value		P<0.05*	P<0.05*	(p>0.05) NS
U.A. (mg/dl)	4.97±0.03	4.01±0.93	4.25±0.21	4.72±0.58
p-value		P< 0.01**	P<0.05*	(p>0.05) NS
eGFR ml/min/1.73m^2	100±0.28	122 ±0.83	±0.62125	105±0. 91
p-value		P<0.05*	P<0.05*	(p>0.05) NS

NS=non-significant, *= there is significant difference (P<0.05), **= there is significant difference (P<0.01)

The level of s creatinine of pregnancy were significantly decrease (P<0.05) in the first trimester (0.68± 0.10mg/dl), and in the second trimester (0.61±0.62mg/dl)as comparing with the nonpregnant ladies (0.82 ± 0.21mg/dl). In the third trimester, there were non-significant difference (p>0.05) in the concentration of creatinine (0.79 ±0.04 mg/dl) as comparison to the control, as shown in table (2).

There are highly significant difference (P< 0.01) in the level of uric acid in the first trimester (4.01±0.93mg/dl) as compared with non-pregnant (4.97±0.03mg/dl). In the second trimester, there was significant decline (P<0.05) (4.25±0.21mg/dl) as compared with control (4.97±0.03mg/dl). There were non-significant difference (p>0.05) in the third trimester (4.72±0.58mg/dl), as shown in table (2).

A comparison of the results in the tests of kidney function in healthy pregnant women within first an trimester show that the levels urea, uric acid in pregnant ladies within the second trimester of gestation was slightly higher than the first stage but its statistically not significant; as shown in table (2).

As showing in table (2) the results of urea creatinine and uric acid in healthy pregnant ladies in the first and second trimesters show significantly lower levels than the third trimester and non-pregnant ladies.

There were significant increased (P<0.05) in the levels of GFR in the first trimester (122 ±0.83 ml/min/1.73m2), and in the second trimester (125± 0.62 ml/min/1.73m2)as compared with the non pregnant (100±0.28 ml/min/1.73m2). The level of GFR was non-significant difference (p>0.05) in the third trimester (105±0. 91 ml/min/1.73m2) as compare with non-pregnant ladies, as shown in table (2). As comparing of levels of GFR in the second and first trimester, there were significantly increased as compared with the third trimester and control(non-pregnant woman).

Table 3: IL-6 levels in pregnant and non-pregnant women

Parameters	**Non-pregnant** (man ± SD) (n=12)	**Pregnant (Mean± SD)**		
		1st trimester 1,2,3 month (n=12)	**2nd** trimester 4,5,6 month (n=12)	**3nd** trimester 7,8,9month (n=12)
IL-6 (Pg/ml)	2.523± 0.64	3.414±2.06	4.48 ± 4.786	5.136±3.09
p-value		(p>0.05) NS	P<0.05*	P< 0.001**

NS=non-significant, *= there is significant difference (P<0.05), **= there is significant difference (P<0.05)

There are non-significant difference **(**p>0.05) in the concentration of IL-6 in the first trimester (3.414±2.06Pg/ml) as compared with the control (2.523± 0.64Pg/ml). There are significant increased (P<0.05) in the level of IL-6 in the second trimester (4.48 ± 4.786 Pg/ml) as compared with the control (2.523± 0.64Pg/ml).In the third trimester, there were highly significant increased (P< 0.001) (5.136±3.09Pg/ml) as compared to control (1.523± 0.64Pg/ml) as shown in table (3).

IL-6 levels shows significant difference (P<0.05) in the first and second groups, also between first and third trimester groups. However, the comparison between second trimester and third trimester did not differ significantly (P>0.05).

4. Dissection:

The purpose of measuring RFTs in healthy pregnant woman to check the effect of pregnancy on renal function. RFTs values were measured for 36 healthy pregnant women and 12 as control, the age in this study was matched. Both group of pregnant and control (non-pregnant) not receive contraception. Understanding trimester-specific changes in renal biomarkers and IL-6 levels can help clinicians avoid misdiagnosis and better manage pregnancy-related complications.

The levels of urea, creatinine and uric acid levels in first and second trimesters of pregnancy were significantly dropper than control (non-pregnant) as shown in table (2). The current study agreement with [9] that found the creatinine, uric acid, and urea levels throughout the third trimester are greater than first and second trimester but statistically insignificant in contrast to the control group. Another studies found the lowing in levels of creatinine and urea through the pregnancy trimester, that demonstrating improved kidney clearance and metabolic adjustments to promote foetal growth [10][11].

The value of GFR will increased in the three trimester as comparison with non-pregnant (control), but the GFR were significant increase in both first and second trimesters and non-significant with third trimester as compared with non-significant. AL-Hamdani AH [9] found that the GFR begins to decline in third trimester, approaching to non-pregnant levels resulting in a small increased in the value of urea and s creatinine in the latter weeks of pregnancy. GFR begin to decrease in the 3rd trimester of pregnancy toward non-pregnant values [12], that strongly agreement with the current study.

The level of IL-6 in the current study was significantly increased in the second and third trimester as compared in the control, this agreement with Fu Y et al. [13] that found the IL-6 values in pregnant ladies are rise than non-pregnant ladies, and the values of IL-6 who are in the first is lower than in the second trimester and third trimester.

A promising biochemical parameter with excellent specificity and sensitivity, IL-6 serves as both an early warning system for certain common foetal illnesses and an early assessment of infection. Changes in serum IL-6 levels throughout pregnancy must be monitored since IL-6 play important role in the health of both the foetus and the pregnant woman. The primary role of immune system in the mothers through the pregnancy are to simultaneously defend the mother against illness and also produced a semi-allogeneous foetus [13]. This procedure illustrates how the inflammatory immune system is positively regulated throughout pregnancy to guarantee particular tolerance to alien foetal antigens [14]. One possible explanation for the rise of levels of IL-6

during pregnancy is that pregnancy is an inflammatory process induced by the embryo in the endometrium, which progressively gets stronger as the pregnancy goes on [13]. It's critical to fully comprehend how IL-6 changes throughout pregnancy. The alterations in IL-6 that occur throughout pregnancy have been detailed in our work, along with the associated reference periods. This will make it easier for doctors to diagnose pregnant women medically.

Conclusion: Being the major players in immunity, ILs have a significant impact by influencing the physiological adaptations and complications in pregnancy. Dynamic cytokine profiles, including increase of some pro-inflammatory and anti-inflammatory interleukins, are directly related to maternal immune tolerance towards the fetus development. Simultaneously, pregnancy brings about major alterations in renal function, including an elevated GFR, decreased serum creatinine, and lower urea, all of which are marks of the kidneys system adapting for the additional metabolic requirements.

Recommended: It is advisable to routinely measure interleukin with renal function in pregnancy, particularly in women with high risk of developing complications like preeclampsia or gestational hypertension.

Acknowledgments; The author would like to thank all the contributors and personnel in AL-Rahmah laboratory for medical and hormonal analysis, and al staff of general Abu-Ghraib hospital for collaboration and assistances in performing this experiment. Special thanks are extended to my family who supported me throughout the preparation of this study.

Conflicts of interest statement: Conflicts of interest the author states that they have no conflict of interest.

References

1. Cheung KL, Lafayette RA. Renal physiology of pregnancy. Adv Chronic Kidney Dis. 2013;20(3):209–14.
2. Romero R, Gotsch F, Pineles B, Kusanovic JP. Inflammation in pregnancy: its roles in reproductive physiology, obstetrical complications, and fetal injury. Nutr Rev. 2007;65(12 Pt 2):S194–202.
3. Gu C, et al. Interleukin-6 and its correlation with maternal characteristics in preeclampsia and gestational hypertension. Pregnancy Hypertens. 2022.
4. Zhang Y, et al. Targeting interleukin-6 for renoprotection: recent advances and future directions. Front Immunol. 2024.
5. Mohammed HJ, AL-Owaidi MN. Liver function tests in Iraqi pregnant women. Int J Sci Res. 2025;14(4):2046–9.

DOI:https://www.doi.org/10.21275/SR25407004847
6. Kattah AG, Garovic VD. The management of hypertension in pregnancy. Adv Chronic Kidney Dis. 2013;20(3):229–39.
7. Kovács N, et al. The effect of maternal inflammation on fetal renal development: an animal model study. BMC Pregnancy Childbirth. 2022.
8. Gregg LP, Richardson PA, Akeroyd J, Matheny ME, Virani SS, Navaneethan SD. Effects of the 2021 CKD-EPI creatinine eGFR equation among a national US veteran cohort. Clin J Am Soc Nephrol. 2022;17(2):283–5.
9. AL-Hamdani AH. Physiological effect of pregnancy on some renal function tests. Frontline Med Sci Pharm J. 2022;2(5):5–15.
10. Purru Kanakaiah M, Kumar PR, Venu SV, Raju G, Jameema MA. A comprehensive analysis of biochemical changes across trimesters and the puerperium period. Int J Acad Med Pharm. 2023;5(6):1350-5.
11. Cheung KL, Lafayette RA. Renal Physiology of Pregnancy. Adv Chronic Kidney Dis. 2013 May;20(3):209–14.
12. Biswajit D, Manidipa C, Asif M, Debasish P, Dipak K. A Study on Serum Urea, Creatinine and Uric Acid Levels in Normal Pregnancy (First and Third Trimester) in Rohilkhand Region, Uttar Pradesh. Scholars Journal of

Applied Medical Sciences (SJAMS). 2016;4(9A):3236-41.

13. Fu Y, Tang L, Hu M, Xiang Z, Hu Y. Changes of serum interleukin-6 in healthy pregnant women and establishment of relevant reference intervals. Clinica chimica acta. 2020 Mar 1;502:116-9.

14. Song H, Lim H. Evidence for heterodimeric association of leukemia inhibitory factor receptor and gp130 in the mouse uterus for LIF signaling during blastocyst implantation. Reproduction. 2006;131(2):341–9. https://doi.org/10. 1530/rep.1.00956.