Original Article

Association of Maternal Renal Artery Resistive Index with Serum Uric Acid in Gestational Hypertension

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ABSTRACT

Objective: To quantitatively study the correlation between maternal renal artery resistive index (RARI) and levels of serum UA in Pregnancy Induced Hypertension.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Ziauddin Hospital from June-2017 to May-2018.

Materials and Methods: 90 females with PIH were included after ruling out conditions affecting renal artery flow other than PIH. Doppler ultrasound examinations were carried out at 36 weeks' gestation and maternal RARI and serum UA was noted. Regression analysis and Pearson's correlation were done to determine the relation of RARI and UA with each other.

Results: A highly significant (p=0.001) moderate (r=0.52) positive correlation between RARI and serum UA was observed.

Conclusion: We demonstrated that as RARI increases, so does the plasma level of UA. This can be directly attributed to decrease in blood flow to the renal arteries in PIH which has an inverse relation to RARI. This is the first study to our knowledge to quantify the relation of serum uric acid to RARI. We conclude that RARI could be a useful non-invasive and cost-effective tool in assessing the severity of PIH.

Key Words: Resistive Index, Uric Acid, Pregnancy Induced

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INTRODUCTION

Gestational hypertension for some reason has been increasing in incidence worldwide. It increases the risk of maternal as well as neonatal morbidity and mortality.[1] Its prevalence varies in different parts of the world with an average worldwide prevalence of 7.8%.[2] Different factors have been considered to be culprits developing GH at different points in time. Some of these factors are include hypoxia, diet, prostacyclin/ thromboxane ratio imbalance, intravascular volume contraction, endothelial injury and genetic predisposition.[3,4] Whatever the underlying cause, at the core of the changes occurring in these conditions lies a defective trophoblast invasion.[5]

Altered supply of blood to the placenta causes release of certain factors in maternal circulation causing altered metabolic pathways. All this ends up in increasing the maternal blood pressure.[6] *Studies have also shown that due to* hypoxia, soluble fms-like tyrosine kinase (sFlt-1) is released in greater amounts. This antagonizes vascular endothelial growth factor (VEGF) and placental growth factor (PlGF). Both of these are vasodilators as well as inducers of angiogenesis.[7] As these factors are antagonized, the trophoblast finds it difficult to invade the spiral arteries of the uterus, thus resulting in decreased fetoplacental circulation. Relationship between the rising levels of soluble endoglin and ratios of sFlt1: PlGF, and the onset of preeclampsia has also been demonstrated.[8] Elevated uric acid and diminished prostacyclin levels are also known to be related to hypertensive pregnancies. As a matter of fact, uric acid has been proven to be as important as proteinuria in identifying fetal outcomes in PIH.[9] Placental morphometric differences have been seen between normal and hypertensive pregnancies.[10,11,12]

Uric acid is produce breakdown of purine nucleotides. About 70% of uric acid in the body is excreted via urine. So any change in glomerular filtration rate (GFR) should directly influence the plasma uric acid level.[13]

The gold standard tool till date to pick variations in circulation is Doppler Ultrasound.[14,15] Studies done previously have proven that Doppler waveforms are important predictors of pregnancy outcome. The

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Resistive Index (RI) specifically shows the resistance to flow of blood through an artery.[16] Studies have shown higher values of RI in abnormal pregnancies as compared to normal and Doppler Indices overall have been shown to be a good tool in prediction of pregnancy outcome.[17,18,19] The study was a cross-sectional study. Written consent was taken from all participants. 90 patients were recruited.

Blood pressure readings of equal to or greater than 140/90mmHg at two separate points in time at least two weeks apart was defined as PIH.[20,21]

MATERIALS AND METHODS

The study was a cross-sectional study. Written consent was taken from all participants. 90 patients were recruited.

Blood pressure readings of equal to or greater than 140/90mmHg at two separate points in time at least two weeks apart was defined as PIH.[20,21]

Inclusion Criteria:

- Parity 1 to 3
- Confirmed gestational age (LMP + Ultrasound)
- Women registered at any campus of Ziauddin University Hospital before eighteenth week gestation
- Normotensive till twentieth week

Exclusion Criteria:

- Essential Hypertension
- Twin, Triplet or mor pregnancy
- Any surgery of uterus previously
- Placenta Praevia
- Leiomyoma
- Congenital uterine anomaly
- Abnormal vaginal discharge or bleeding
- Vascular Disorders
- Diabetes (Mellitus or Gestational)
- Fetus with congenital anomaly
- Previous delivery before term
- Use of any addictive drug

A single operator carried out Doppler ultrasound examinations noting down maternal Renal Artery Resistive Index. A mean of three values was recorded.

The study was approved by the Ethical Review Committee, Ziauddin University, Karachi.

Statistical Analysis: Data was fed and analyzed on SPSS ver20.0. General characteristics such as age, gestational age and weight are given as mean and standard deviation. Regression analysis and Pearson's correlation has been used to evaluate the correlation between renal artery resistive index and uric acid levels. In all analysis, a p-value <0.05 was considered as significant.

RESULTS

Table-1 shows the general characteristics of the subjects included in the study.

Table-2 shows a highly significant moderate positive correlation between RI and UA

Figure 1 graphically depicts the highly significant moderate positive correlation between renal artery RI and serum UA.

Table No.1: General Characteristic of the Subject

	Mean	SD
Age (Years)	24	± 3.57528
Gestational age at scan (Weeks)	36.6383	± 1.03052
Gestational Age at birth (Weeks)	39.1489	± 0.8335
Weight (kg)	65.234	± 5.42624

Table No.2: Highly significant moderate positive correlation between RI and UA

Model		Unstandardized Coefficients		Standardized Coefficients		
		B	Std. Error	Beta	T	Sig.
1	(Constant)	.406	.869		.467	.642
	RI	4.580	1.358	.344	3.372	.001

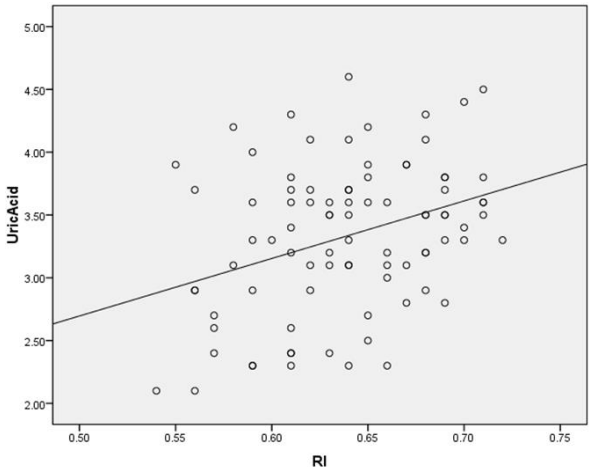

Figure No.1: Dependent Variable: Uric Acid

DISCUSSION

Numerous physiologic changes occur in the maternal body during pregnancy which include increase in blood volume with increased renal blood flow resulting in increased glomerular filtration rate. All these changes eventually decrease the uric acid concentration in serum. Similarly, uricosuric effect of estrogen also contributes significantly to the decline in UA levels in normal pregnancy.[22,23]

However, in gestational hypertension there is a reduction in renal blood flow and in glomerular filtration rate which is known to increase the levels of urea in serum.[24,25]

Our study demonstrates this effect using a non-invasive parameter called renal artery resistive index (RI). As the renal artery RI increases, so does the plasma level of UA. This can be directly attributed to the decrease in blood flow to the renal arteries in gestational hypertension which in our case is being represented by an increase in renal artery RI. As the flow to the kidneys decreases, the clearance of UA also decreases leading to its accumulation in blood. Similarly, there have been associations found in diseases with affect renal blood flow and serum uric acid but, none to our knowledge have been able to quantify it with relation to renal artery RI. [26]

Studies done in the past have shown an association of these parameters with hypertension.[27] Increased levels of UA have been shown to activate the renin-angiotensin-aldosterone system (RAAS). UA achieves this due to increased oxidative stress by increasing the levels of reactive oxygen species within certain cells like adipocytes. This in turn causes overexpression of the RAAS gene which ultimately leads to systemic hypertension.[28]

Gestational hypertension is also associated with placental ischemia.[29] Also reported in literature is that tissue ischemia results in increased conversion of adenosine triphosphate to adenosine and xanthine. Levels of xanthine oxidase are also increased in the ischemic tissue which further enhance the conversion of xanthine into uric acid and production of super oxide anions.[30,31,32]

The two mechanism stated above lead to a chicken and egg dilemma but none the less start a vicious cycle which contributes to the many complications associated with gestational hypertension.

These findings could prove UA to be a useful tool assessing the severity of gestational hypertension in a non-invasive manner ultimately helping in prevention of end organ damage.

CONCLUSION

The study shows that in women with gestational hypertension, the blood flow to the kidneys decreases, hence forth affecting the clearance of uric acid resulting in its accumulation in blood. The accumulated uric acid activates the rennin angiotensin system causing further hypertension. This starts a vicious cycle which, if not controlled can lead to further complications.

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Author's Contribution:

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Data Analysis:	Shazia Hashmat, Nuzhat Hassan, Syed Tousif Ahmed
Revisiting Critically:	Kevin Joseph Jerome Borges, Syed Nudrat Nawaid Shah
Final Approval of version:	Kevin Joseph Jerome Borges

Conflict of Interest: The study has no conflict of interest to declare by any author.

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