

Research Article

Comparison of Plasma Corin Levels in Gestational Hypertensive Patients, Normotensive Pregnant and Normotensive Non-Pregnant Women

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Abstract

Background: Multiple factors play role in gestational hypertension including vasopressin production and Renin-angiotensin-aldosterone system activation. Opposing these effects, corin plays an important role in mediating natriuretic peptide biosynthesis cascade which is an important factor in regulating fluid balance and blood pressure. Corin levels have been studied in relation to gestational hypertension and results were controversial.

Objective: This study aimed at comparing plasma corin levels in gestational hypertensive patients, normotensive pregnant women, and normotensive non-pregnant women.

Methods: This was a cross sectional comparative study conducted for one year at Shaikh Zayed Medical Complex. By convenient sampling, ninety women aged 18-45 years were included; thirty pregnant (primigravida and multigravida) with gestational hypertension, thirty pregnant (primigravida and multigravida) normotensive women, and thirty non-pregnant normotensive women. Patients with gestational diabetes, renal diseases, hypertension before pregnancy, and other cardiovascular diseases were excluded. Informed consent was taken and demographic data was recorded. Three ml of blood was taken from each participant and corin levels were measured using ELISA kit. Data were analysed using SPSS 24.

Results: A significant difference was found in BMI among the three groups with the gestational hypertensive patients having the highest BMI (p-value < 0.05). There was no significant difference in gravid and parity count between gestational hypertensive patients and pregnant normotensive women. No significant difference was found in corin levels among the three groups and there was no significant correlation between corin levels and age nor between corin levels and BMI.

Conclusion: There is no significant difference in plasma corin levels amongst gestational hypertensive patients, normotensive pregnant women, and normotensive non-pregnant women.

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Introduction

In pregnancy, vasodilatation leads to decrease vascular

resistance, blood pressure, and kidney blood flow. There is activation of the renin-angiotensin-aldosterone system and more vasopressin production. These mechanisms increase body water, cardiac output, and blood pressure.¹ Gestational hypertension is a systolic blood pressure of ≥ 140 mmHg and a diastolic blood pressure of ≥ 90 mmHg in pregnant women of 20 weeks gestational age or more. About 50% of gestational hypertension



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patients develop preeclampsia.²

Corin, a serine protease, has 1042 amino acids and contains several extracellular domains, one transmembrane domain, and a cytoplasmic tail. The extracellular domains are of different types, eight LDL receptor-like repeats, two domains that are frizzled-like, one trypsin-like protease domain, and one scavenger receptor-like domain. Corin is mainly expressed in cardiac myocytes. It activates pro-ANP and pro-BNP which in turn bind to the receptors of natriuretic peptide and promote cGMP synthesis. This process results in improved cardiac function, diuresis, natriuresis, vasodilation, and remodeling of uterus.³

Corin lack in mice causes hypertension by inhibiting the processing of natriuretic peptide.⁴ Atrial natriuretic peptide (ANP) promotes diuresis, natriuresis, and vasodilation, and therefore, it maintains blood pressure and heart function.⁵

Niu et al (2021) found that soluble corin injections in mice increased levels of atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), and cGMP; decreased pro-ANP levels, angiotensin II, and aldosterone levels; decreased hypertrophy of heart and fibrosis; and improved heart function.⁶ Gu et al (2023) stated that intestinal corin promotes sodium excretion via antagonizing intestinal aldosterone action.⁷ Chen et al (2022) reported higher corin levels to be a predicting factor for cardiovascular disease risk.⁸ Zhou et al (2016) stated corin as a prognostic marker of major adverse cardiac events.⁹ and its role in opposing cardiac hypertrophy in mice has been reported by Baird et al (2019).¹⁰

Corin levels were found to be higher in hypertensive patients as compared to normal individuals¹¹ and were suggested to have a role in hypertension.¹² During pregnancy, it is hypothesized that the syncytiotrophoblasts release corin¹³ which in turn plays a role in remodeling of spiral artery in the uterus.¹⁴

However, studies answering the question if corin levels relates to gestational hypertension have yielded controversial results with some studies suggesting its role^{15,16} and others stating no role.¹⁷ In our study, we compared plasma corin levels in gestational hypertensive patients, normotensive pregnant women, and normotensive non-pregnant women.

Methods

This cross-sectional comparative study was conducted for one year at Physiology Department and Gynaecology and Obstetrics Department, Shaikh Zayed Medical Complex after approval from the Institutional Review Board (IRB Ref No. F39/NHRC/Admin/IRB/167). Sample size was calculated using Power and Precision 3.0 and by convenient sampling, 90 women aged 18-45 years were included in which 30 pregnant (primigravida and multigravida) with hypertension (BP greater than 140/90 mmHg) after 20 weeks of gestation, 30 pregnant (primigravida and multigravida) with normal blood pressure, and 30 non-pregnant normotensive women. Patients with gestational diabetes, renal diseases, hypertension before pregnancy, and other cardiovascular diseases were excluded. After informed consent was taken from the participants, demographic data was recorded, history was taken, and clinical examination was conducted. Three consecutive readings of BP were taken with three minutes time interval and the mean was calculated. Under aseptic conditions, 3 mL of blood was taken from each participant. Blood was centrifuged and plasma corin levels were measured using ELISA kit (Glory Science Co. Ltd.). Data were analyzed using SPSS 24. A p value < 0.05 was considered significant.

Results

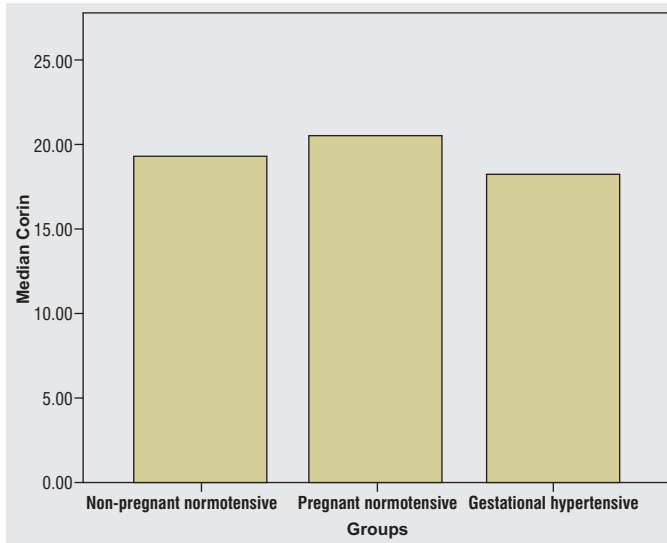
Mean±SD age of the pregnant women with gestational hypertension, pregnant normotensive, and non-pregnant normotensive groups were 28.8±4.4, 27.6±4.1, and 24.8 ± 6.8 years. There was a significant difference in BMI among the three groups with the group pregnant women with gestational hypertension having the highest BMI (p-value < 0.05). No significant difference in gravid and parity count was found between pregnant women with gestational hypertension and pregnant normotensive women (p-value > 0.05).

There was no significant difference in corin levels among the gestational hypertensive, pregnant normotensive, and non-pregnant normotensive groups (p-value= 0.398) (Table 1 and Figure 1). No significant correlation was found between corin levels and age nor between corin levels and BMI (p-values > 0.05) (Tables 2& 3).

Table 1: Comparison of corin levels in gestational hypertensive, pregnant normotensive, and non-pregnant normotensive groups using Kruskal-Wallis test

| Group | Corin levels (pg/ml) (Median (IQR)) | p-value |
|-----------------------------------|-------------------------------------|---------|
| Gestational hypertensive patients | 18.3 (13.7 - 20.6) | 0.398 |
| Pregnant normotensive women | 20.6 (13.5 - 27.7) | |
| Non-pregnant normotensive women | 19.3 (12.3-24.7) | |

*p-value <0.05 is significant
IQR= Interquartile range

**Figure 1:** Corin levels in gestational hypertensive, pregnant normotensive, and non-pregnant normotensive groups**Table 2:** Spearman's Correlation between age and corin levels

| Group | Correlation coefficient | p-value |
|-----------------------------------|-------------------------|---------|
| Gestational hypertensive patients | 0.115 | 0.544 |
| Pregnant normotensive women | -0.040 | 0.834 |
| Non-pregnant normotensive women | -0.160 | 0.398 |

*p-value <0.05 is significant

Table 3: Spearman's correlation between BMI and corin levels

| Group | Correlation coefficient | p-value |
|-----------------------------------|-------------------------|---------|
| Gestational hypertensive patients | -0.022 | 0.906 |
| Pregnant normotensive women | 0.024 | 0.901 |
| Non-pregnant normotensive women | 0.166 | 0.381 |

*p-value <0.05 is significant

Discussion

In our study, corin levels were compared in pregnant women with gestational hypertension, normotensive pregnant women, and normotensive non-pregnant women and no significant difference was found among the groups. Our results were different from the results of Badrovet al (2019) who found the change in levels of corin from the beginning of pregnancy to the end of it to be greater in women with gestational hypertension than women with normal pregnancy.¹⁸ However, their study included small sample size with eight participants having gestational hypertension. Moreover, Kumari et al (2019) found no significant difference in corin levels between preeclampsia patients and non-preeclampsia pregnant women.¹⁷

In studies conducted on mice, Zhou et al (2022) found that corin is required for normal blood pressure and it functions in the maintenance of salt-water balance in mice and Niu et al (2023) reported that corin may be used to suppress rennin-angiotensin-aldosterone system.^{19,20}

Liu et al (2015) reported corin levels during mid pregnancy to be associated with higher risk of pregnancy hypertensive disorders and suggested that increased corin could be used as an indicator for hypertensive disorders during pregnancy.¹⁵ Boron et al (2022) and Gu et al (2018) found corin levels to be higher in preeclampsia patients as compared to normal pregnant women.^{21,22}

One the other hand, Yavuz et al (2021) reported serum levels of corin to be lower in patients with hypertensive crisis and proposed that end organ damage may be predicted by low corin levels.²³ Li et al (2017) reported corin as a regulator of renal as well as cardiovascular functions. They proposed that corin defects might contribute to kidney disease, hypertension, preeclampsia, and heart failure.²⁴

Race might have an effect on corin levels as Khalil et al (2015) reported corin levels to be lower in Afro-Caribbean origin women as compared to Caucasian women.²⁵ The above controversial findings could have been due to the racial differences which calls for further studies.

Conclusion

This study investigated the role of corin in gestational hypertension. We found no significant difference in corin levels amongst gestational hypertensive patients,

pregnant normotensive women, and non-pregnant normotensive women. This may indicate no significant role of corin in gestational hypertension.

Ethical Approval: The Institutional Review Board, Federal Postgraduate Medical Institute, Lahore, Shaikh Zayed Hospital National Health Research Complex approved the study vide letter No. IRB-Number 1413.

Conflict of Interest: The authors declare no conflict of interest.

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Authors' Contribution:

HF: Acquisition of data, Conception & design, analysis & interpretation of data, drafting of article, final approval of the version

NHHA: Analysis & interpretation of data, drafting of article, critical review of content, final approval of the version.

SZ: Critical revision for important intellectual content, final approval

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