The Effect of Brain Natriuretic Peptide, and Prothrombin Biomarkers in Pregnant Women With Gestational And Chronic Hypertension

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Abstract

Background: Pregnancy complications, such as gestational hypertension (GH), affect around 5-8% of pregnancies, which may progress to more severe conditions like pre-eclampsia. It is essential to closely monitor various physiological and biochemical markers, including B-natriuretic peptide (BNP), prothrombin time, and iron levels, to detect and manage hypertensive disorders early on during pregnancy. Methods: Our study, conducted from July to October 2023, involved 96 women grouped into four categories: pregnant with GH, healthy pregnant, non-pregnant with chronic HT, and healthy non-pregnant individuals. We utilized techniques such as ELISA, coagulation analysis, and biochemical assays to measure physiological parameters like BNP, prothrombin time, and iron levels. Statistical analysis was performed using ANOVA and the Duncan multiple range test to derive meaningful insights from the data. Results: We observed significant increases in body mass index and blood pressure among pregnant individuals with GH and non-pregnant individuals with HT when compared to their respective control groups. BNP levels were notably elevated in both hypertensive groups, with pregnant individuals with GH exhibiting the highest levels. Furthermore, prothrombin time showed a significant increase in pregnant individuals with GH and non-pregnant individuals with HT. Conversely, iron levels decreased notably in pregnant individuals with GH and non-pregnant individuals with HT compared to their respective control groups. Conclusion: Elevated BNP levels may indicate cardiac stress, while increased prothrombin time suggests alterations in coagulation profiles in hypertensive pregnancies. Implementing routine screenings for pregnant women can help mitigate the risks associated with gestational hypertension and ultimately improve outcomes for both mothers and their babies.

Keywords: Pregnancy, Gestational hypertension, B-natriuretic peptide, Prothrombin, Iron.

Significance | A study of gestational hypertension (GH) and chronic hypertension (HT) impact pregnancy, emphasizing the importance of monitoring brain peptide and biomarkers.

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1. Introduction

Pregnancy is a series of changes in a woman's organs and tissues due to the embryo's development inside her uterus. Pregnancy begins after fertilization when the egg meets the uterine wall and is installed there. The entire pregnancy process, from fertilization to birth, takes between 266 and 270 days, which is about nine months. The pregnancy duration varies from woman to woman and may be slightly shorter or longer. During this period, a woman's body experiences many physiological and hormonal changes that support the growth of the fetus and prepare the body for childbirth and lactation. The fetus's organs are formed during this period,

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proliferating from a small mass to a complete human being capable of living outside the uterus after birth (Huffman, 2023). Pregnancy consists of stages, each with its features and importance, as these stages are integrated to reach a healthy birth (Dipietro et al., 2019). Signs of pregnancy also include increased blood volume, mood swings, increased heart rate, anxiety, constant sleepiness and increased hours of sleep, and a craving period where women frequently need to vomit (Kotaska, 2018). During pregnancy, the body undergoes normal physiological changes that may mimic disease symptoms, highlighting the importance of distinguishing between these and pathological symptoms. Pregnancy is divided into three stages, aiding in comprehending the development for both the mother and fetus throughout the process (Soma et al., 2016). Physiological changes in pregnancy encompass shifts in blood vessels, blood composition, and heart function, along with metabolic adjustments and alterations in lung and kidney functions. Increased cardiac output and respiratory rate, elevated blood sugar levels, and a cessation of menstruation result from heightened estrogen and progesterone levels. Hormonal interactions, particularly with progesterone, play a crucial role in regulating these changes, influencing the overall physical environment and impacting all organs and body systems (Zachariah et al., 2019)

High blood pressure, also known as arterial hypertension or essential hypertension, is a condition that occurs when the blood pressure in the arteries is above average for a long time (Fox, 2009; Iqbal and Jamal, 2023). Elevated blood pressure commonly emerges as a multifaceted quantitative trait affected by various genetic and environmental factors. This chronic, recurring condition is often associated with age-related issues and can lead to significant cardiovascular complications. Blood pressure assessments typically consider other cardiovascular risk factors. Additionally, the disorder involves contributions from the central nervous system, endocrine glands, large arteries, and microcirculation (Staessen et al., 2003 : Fuchs and Whelton, 2020).

Hypertension affects one in three adults worldwide. Between 1990 and 2019, the number of infected people increased dramatically, rising from 650 million to 1.3 billion. It is linked to severe health risks such as strokes, heart attacks, heart failure, and kidney disease (WHO, 2023). While many individuals with high blood pressure may not show symptoms, it can lead to headaches, blurred vision, chest pain, and other indicators. Monitoring blood pressure remains the most effective method for identifying this issue. Severe hypertension, typically at 180/120 mm Hg or higher, may manifest symptoms like intense headache, chest pain, dizziness, breathlessness, nausea, vomiting, vision changes, anxiety, confusion, ringing in the ears, nosebleeds, and irregular heartbeat (Wall, 2010). In the context of high blood pressure during pregnancy, Gestational Hypertension can exhibit various symptoms. These may include persistent headaches, blurred vision, visual spots or changes, upper abdominal pain, nausea, vomiting, and swelling in the face or hands. Sudden weight gain and breathing difficulties are also potential indicators (Belayhun et al., 2021).

Pregnancy is associated with various pathological disorders, such as gestational hypertension (GH) during pregnancy and fetal development disorders, which increase the risk of cardiovascular disease and maternal death or cause fetal loss (Dipietro et al., 2019). Gestational hypertension is a blood pressure disorder that usually appears in the middle of pregnancy and occurs in approximately five to eight percent of pregnancies. Typically, this height returns to normal after childbirth. Gestational hypertension can develop into pre-eclampsia. Gestational hypertension is usually diagnosed when blood pressure readings go beyond 140/90 mm Hg after 20 weeks of pregnancy, following normal blood pressure (Stanford Healthcare, 2023). An important indicator in this study is the brain sodium diuretic peptide, also known as the type B-natriuretic peptide (BNP), which consists of 32 amino acids discovered in 1988 after being extracted from the brain. However, it was later found that its primary source is the heart, which is classified as a cardiac peptide, and BNP is secreted mainly from the ventricular heart muscle. It is the primary cardiac peptide that controls sodium levels in vertebrates, as it works to Increase urine output, reduce blood volume, and lower vascular pressure (Ando et al.,2021). Moreover, individuals with elevated blood pressure face a heightened susceptibility to clotting disorders, particularly those related to coronary artery and vascular conditions. Assessing prothrombin time in individuals with hypertension can yield valuable insights into the clotting process and identify potential issues with excessive clotting (Onyema et al., 2023). Following a sequence of chemical reactions, thrombin is generated, playing a crucial role in clotting at the injury site. Subsequently, thrombin transforms fibrinogen, a constant component in human blood, into fibrin. This fibrin forms a network around platelets and red blood cells, aiding in clotting and securing the damaged area tightly to prevent bleeding. The central purpose of the coagulation and fibrin systems is to uphold the integrity of blood vessels. Disruptions in either of these processes can give rise to primary health issues, such as bleeding or vessel blockage due to blood clots (Wojta, 2022 ; Al-Amer, 2022). The study sought to explore the correlation between hypertension and various physiological and biochemical factors both before and during pregnancy, aiming to understand their influence on essential bodily functions.

The research highlights how hypertension affects pregnancy and its level of severity, whether it exists as pre-existing chronic hypertension or arises during pregnancy. Implementing these tests as regular screenings for pregnant is intended to mitigate the risk of gestational hypertension.

2. Materials and methods

Study Design

The study was conducted from the beginning of July 2023 until the end of October 2023, and samples were collected from women visiting the (Children, Maternity, and Gynecology) Hospital in Kirkuk City. The study included (96) women, and the total number was divided into four groups as follows: (24) pregnant with gestational hypertension (in the third trimester), (24) healthy pregnant (in the third trimester), (24) non-pregnant with chronic hypertension, and (24) healthy non-pregnant females (control).

Physiological and biochemical tests

A set of physiological and biochemical parameters of the studied groups was measured.

Determination of B- natriuretic peptide

Through the use of a Kit from the German manufacturer Human by the use of ELISA device, and BNP was determined by immunoassays using antibodies directed to different carriers on antigen molecules (Clerico et al., 2015). The kit involves an ELISA test. The Test plate, pre-coated with the antibody specific to the BNP peptide, is equipped with 96 wells. Serum was added to the biologically treated antibody for human BNP, binding it to the BNP in the sample. Subsequently, Streptavidin-HRP was added, binding to the antibodies. After incubation, a reaction occurred between the serum and the original antigen. Excess Streptavidin-HRP was washed out to remove unreacted substances. Then, the Substrate was added, and the color turned blue proportionally to the amount of BNP in the sample. The color density, reflecting the reaction, was measured at a wavelength of 450 nm after adding the acidic Stop Solution.

Determination of Prothrombin in Plasma

Prothrombin time in plasma was measured using a kit from the French company (Biolabo) using the Quick and al. method (Quick, 1938). This test is based on the principle of the interaction between prothrombin, thromboplastin, and calcium to form a clot. The test measures the time it takes for blood to clot, recorded in seconds, expressed as Prothrombin Time (PT). The procedure involves the following steps. To perform the prothrombin time (PT) test, the Eppendorf tubes containing the plasma are first placed into the assigned slot of the Thrombo Genex coagulation analyzer. Next, 20 µl of plasma is added to the specified area on the device, followed by pressing Timer1 and allowing for a two-minute wait period. Subsequently, Optic 1 is pressed, and 40 µl of the Reagent is added. Finally, the result is promptly displayed in seconds on the screen, providing a timely assessment of PT.

Determination the level of Iron in serum

Iron was measured by the Ferene iron reagent method by kit from the French company (Biolabo) (Hennessy, 1984).

The iron concentration was determined using the Auto Chemistry Analyzer, measuring absorbance at a wavelength of 600 nm. This value is directly proportional to the amount of iron present in the sample.

Measurement of blood pressure and body mass index

Blood pressure was measured using a Sphygmomanometer after resting and sitting. A weighing scale and a height metric tape were used for each revision to compute body mass index (BMI) using the following formula:

Statistical Analysis

In this study, statistical analysis was conducted using the ANOVA test at a significant level of (0.05), specifically employing a one-way analysis of variance. The ANOVA test is utilized to assess whether there are any statistically significant differences between the means of three or more independent groups. Once significant differences were identified, the analysis delved deeper with applying the Duncan multiple range test. The Duncan multiple range test is a post hoc test applied after the initial ANOVA analysis. Its purpose is to compare all possible pairs of group means to determine where the significant differences lie. By doing so, researchers can identify which groups exhibit statistically distinct mean values. This process helps ensure a thorough data exploration, providing insights into the significance of differences between groups and contributing to a comprehensive understanding of the study's results.

3. Results

Table (1) shows the study participant's BMI and blood pressure levels. There was a statistically significant increase (P-Value ≤ 0.05) in the body mass index in the pregnant with GH at a rate of (33.52 ± 4.151), which is the highest rate compared to the three groups represented by the control group (22.936 ± 2.866), healthy pregnant (27.655 ± 3.004) and the group of non-pregnant with HT. With a significant increase in the group of non-pregnant with HT at a rate of (32.96 ± 5.658) compared to the control. When comparing the pregnant with GH and the non-pregnant with HT, we found that the was higher in the pregnant with GH.

As for blood pressure, a significant increase (P ≤ 0.05) in blood pressure (systolic and diastolic) was found in the group of non-pregnant with HT compared to the control group, with a significant increase in the group of pregnant with GH in comparison to both the control and healthy pregnant. Systolic pressure was found to be the highest in the pregnant with GH group (147.83 ± 6.365) compared to the control (121.00 ± 2.041) and the healthy pregnant (121.00 ± 2.041), followed by the group of non-pregnant with HT (146.52 ± 8.317), recording the second highest increase compared to control and with pregnant with GH. Diastolic pressure was higher in the non-pregnant with HT (94.78 ± 6.653) compared to the control (80.80 ± 1.871) and compared to the pregnant with GH, followed as the second highest significant increase in the pregnant

with GH (91.96 ± 4.94) compared to the control and the healthy pregnant group (81.4 ± 2.708).

Table (2) shows the studied aggregate's BNP, Prothrombin time, and iron levels. The concentration of BNP in non-pregnant with HT is the highest rate (620.739 ± 164.321) compared to the control group (40.801 ± 9.514), followed by the group of pregnant with GH (425.429 ± 84.138), which recorded the second highest significant increase in comparison to the control and the healthy pregnant (152.210 ± 22.682). When comparing pregnant with GH and non-pregnant with HT, it found that the height was higher in the non-pregnant with HT.

As for the prothrombin time, it was found that there a significant increase in the pregnant with GH at a rate of (15.413 ± 1.352), which is the highest compared to the other groups represented by the control group (11.604 ± 0.486) and the group of healthy pregnant (11.124 ± 0.492). Then comes the second highest significant increase in the non-pregnant with HT at a rate of (14.673 ± 1.058) compared to the control group. When comparing the pregnant with GH and the group of non-pregnant with HT, we note the significantly higher in pregnant with GH.

A significant decrease in iron levels was found in the pregnant with GH. They were the least significant at a rate of (44.787 ± 4.468) compared to the control group (110.76 ± 15.645) and healthy pregnant (77.196 ± 13.476), in addition to a decrease in the group of non-pregnant with HT at a rate of (62.904 ± 4.102) in comparison to the control. When comparing the pregnant with GH with the group of non-pregnant with HT, we note that the infected pregnant group recorded a significant decrease compared to the non-pregnant group.

4. Discussion

The current study showed a significant increase in systolic and diastolic blood pressure in pregnant with gestational hypertension and those with chronic hypertension compared to the control. Hypertension is a significant factor that leads to clinical and preclinical damage to the heart, brain, retina, kidneys, and arterial vessels, the effects of this damage are usually manifested by several diseases such as angina, heart failure, strokes, and other cardiovascular diseases, in addition to reducing kidney function or renal failure at the end of the stage (Mensah, 2016). This increase in pressure has many reasons, as an association was found between the increase in the body mass standard and high blood pressure in both pregnant with GH as well as non-pregnant with chorionic HT in comparison to both the control and the healthy pregnant, as overweight and obesity are very important risk factors for gestational hypertension in women who are pregnant for the first time and pregnant women in general (Moftakhar et al., 2018). An increase in BMI leads to the development of high blood pressure. It plays a major role in causing the disease (Sullivan et al., 2015), average systolic and diastolic blood pressure increases significantly and progressively as BMI levels increase. There is a close association between increased BMI levels and blood pressure, which aligns with the present research findings (Landi et al., 2018). It's established that obesity contributes to 65-78% of cases of primary high blood pressure. The ways involve increased activity of sympathetic nervous system, activation of the renin-angiotensin-aldosterone system, alteration in cytokines derived from lipid, insulin resistance, and structural and functional changes in the kidneys (Shariq and McKenzie, 2020). Wuehl (2019), emphasized that weight gain is associated with elevated blood pressure, increasing the risk of heart and cardiovascular diseases. Early diagnosis and treatment are crucial for blood pressure control and weight reduction, aiming to prevent diseases and reduce mortality related to these conditions. The connection between visceral fat and high blood pressure is attributed to the significant role of inflammatory processes in the mechanisms leading to elevated blood pressure (Caillon et al., 2019).

It was found that there was an increase in BNP levels in pregnant with GH and non-pregnant with chronic HT as well as in healthy pregnant compared to the control group. These results agreed with the study of Unurjargal et al. (2023), as there was increase in BNP concentration in participants with hypertension. In addition to the study of Yu et al. (2018), it has been shown that in pregnancies complicated by pregnancy-induced hypertension, especially pre-eclampsia, the contractile function of the heart is impaired and BNP levels are higher compared to a normal pregnancy. This could be due to the essential role BNP plays in maintaining the body's fluid and mineral balance and helping the heart deal with various stresses and pressures Once excreted in the blood, it moves to the kidneys where it affects the tiny blood vessels in the renal glomeruli and works to expand them, which increases blood flow to the kidneys and this leads to increased urine production and relieve pressure inside the blood vessels, and the expansion of venous vessels, which reduces the traffic return of blood to the heart and thus reduces of the burden on the heart and its pressure and reduces contractions of the heart (Dohi, 2022).

The prothrombin time (PT) showed a significant increase in pregnant with GH and non-pregnant with chronic HT in comparison to both the control and healthy pregnant, the results of the study are consistent with the study of Bawore et al. (2021), and Shekar et al.(2022), as there was an increase in PT in pregnant women who suffer from high blood pressure during pregnancy compared to the healthy pregnant group, and this indicates significant changes in the coagulation profile in women with high pressure during pregnancy. The current study is also consistent with that of Nnenna Adaeze et al. (2014), The results showed an increase in PT in hypertensive patients compared to standard blood pressure patients, and this increase can be explained by the presence

Table 1. BMI and blood pressure in the studied groups. * The values in the table indicate to (Mean ± S.D). *Different letters vertically indicate significant differences at (P ≤ 0.05).

Group	BMI	Systolic (mmHg)	Diastolic (mmHg)
Gestational hypertension	33.52 ± 4.151 a	147.83 ± 6.365 a	91.96 ± 4.468 b
Chronic hypertension (Non-pregnant)	32.96 ± 5.658 a	146.52 ± 8.31 a	94.78 ± 4.102 a
Healthy pregnant	27.655 ± 3.004 b	121.00 ± 2.041 b	81.4 ± 2.708 c
Control	22.936 ± 2.866 c	121.00 ± 2.041 b	80.80 ± 1.871 c

Table 2. BNP, Prothrombin time, and iron levels in the studied groups. * The values in the table indicate to (Mean ± S.D). *Different letters vertically indicate significant differences at (P ≤ 0.05).

Group	BNP (pg / ml)	Prothrombin Time	Iron (µg/dL)
Gestational hypertension	425.429 ± 84.138 b	15.413 ± 1.352 a	44.787 ± 4.468 d
Chronic hypertension (Non-pregnant)	620.739 ± 164.321 a	14.673 ± 1.058 b	62.904 ± 4.102 c
Healthy pregnant	152.210 ± 22.682 c	11.124 ± 0.492 c	77.196 ± 13.476 b
Control	40.801 ± 9.514 d	11.604 ± 0.486 c	110.76 ± 15.645 a

of damage to the lining of blood vessels as a result of atherosclerosis caused by HT in these patients. This may be because the coagulation activities, anticoagulants, fibrinolysis, and antifibrinolytic activities are further enhanced during pregnancy. A change in the hemodynamics of the uterine artery and umbilical artery occurs during this period, including an increase in blood flow and a decrease in resistance, to meet the needs of the fetus (Hui et al., 2012), and HT can lead to changes in platelets, vascular lining, and coagulation system (Nadar, 2003). This may explain the increase in PT in women with gestational stress and chronic hypertension.

The study showed a decrease in iron levels in pregnant with GH and non-pregnant with chronic HT compared to the control group, this aligns with study of Rohilla et al. (2010), where it was observed that there is a relationship between iron deficiency and hypertension gestational and the occurrence of disorders down to the occurrence of pre-eclampsia. Gestational hypertension may interfere with iron metabolism in the placenta, which may increase the risk of anemia in children (An et al., 2022). During pregnancy, iron deficiency negatively affects the health of the mother and fetus, as it is associated with increased rates of disease and fetal death, and infected mothers often suffer from breathing difficulties, fainting, fatigue, palpitations, and sleep difficulties. This deficiency may be that many mothers can go through pregnancy without meeting their body's needs for iron through food (Abu-Ouf and Jan, 2015). This may be because iron deficiency can increase the production of reactive oxygens, causing an increase in oxidative stress and inflammation, and negatively affecting mitochondrial function, leading to increased hypertension (Ames et al., 2005). These results underscore the crucial importance of integrating these tests as fundamental assessments for pregnant women, not only to mitigate the risk of elevated blood pressure but also to proactively address potential complications. Early detection and management of hypertensive conditions during pregnancy are vital for preventing pre-eclampsia and reducing the overall health risks for both the mother and the developing fetus. Regular monitoring and intervention based on these tests contribute significantly to ensuring a healthier outcome for expectant mothers and their babies.

5. Conclusion

In this study, we observed a higher concentration of BNP and prothrombin time in pregnant with gestational hypertension compared to non-pregnant with chronic hypertension. The increase was higher than in the control group and pregnant women with normal pressure, so we suggest that this increase is associated with an increase in blood pressure and might be a predictive sign before pre-eclampsia and eclampsia. It was found that the decrease in iron levels is inversely proportional to blood pressure, as its low levels in Infected groups are associated with hypertension compared to both the control and healthy pregnant. We conclude from the current research that high blood pressure is more dangerous in pregnant women than in non-pregnant women and can develop to cause pre-eclampsia or continue after childbirth to become chronic hypertension. Based on these findings, it is essential to incorporate these tests as primary evaluations for pregnant women to minimize the risk of high blood pressure. This proactive approach aims to decrease the chances of pre-eclampsia or heightened severity, thereby safeguarding the health of both the mother and the fetus.

Author contribution

S.A.D.M.K. and W.I.A.A. conceptualized, curated data, analyzed data, processed the grant, and wrote the article.

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Competing financial interests

The authors have no conflict of interest.

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