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Prevalence and Correlates of Elevated NT-proBNP in Pregnant Women in the General U.S. Population

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Abstract

BACKGROUND—Physiologic changes in N-terminal pro-B-type natriuretic peptide (NT-proBNP) across trimesters of pregnancy have not been well studied.

OBJECTIVES—The authors aimed to measure NT-proBNP in adult women, by pregnancy status and trimester, in a nationally representative sample from the National Health and Nutrition Examination Survey 1999 to 2004.

METHODS—We conducted a cross-sectional analysis of 2,134 women (546 pregnant) aged 20 to 40 years without a history of cardiovascular disease.

RESULTS—Among pregnant women in the first trimester, the prevalence of elevated NT-proBNP (>125 pg/mL) was 20.0% (SE, 6.6%) compared to 2.4% (SE, 0.8%) among women in the

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APPENDIX For a supplemental figure, please see the online version of this paper.

third trimester and 8.0% among nonpregnant women. After adjustment for demographics and cardiovascular risk factors, NT-proBNP was 44% higher (absolute difference 26.4 [95% CI: 11.2–41.6] pg/mL) in the first trimester of pregnancy compared to nonpregnant women. Among pregnant women only, adjusted NT-proBNP was 46% lower (absolute difference −22.2 [95% CI: −36.9 to −7.5] pg/mL) in women in the third trimester compared to women in the first trimester. NT-proBNP was inversely associated with body mass index and with systolic blood pressure.

CONCLUSIONS—Women in the first trimester of pregnancy had significantly higher NT-proBNP than those in the third trimester and compared to similarly aged nonpregnant women. The dynamic nature of NT-proBNP should be taken into consideration when ordering NT-proBNP lab tests in pregnant women.

Keywords

biomarkers; heart failure; pregnancy; proBNP

Maternal morbidity and mortality from underlying cardiovascular causes, including heart failure and hypertensive disorders, are rising in the United States.[1] Pro-B-type natriuretic peptide (BNP) is a prohormone cleaved into biologically active BNP and N-terminal pro-BNP (NT-proBNP).[2] NT-proBNP is often used as an adjunct clinical measure when evaluating patients for heart failure.[3] While U.S. guidelines do not have specific recommendations on a cutoff value of NT-proBNP for suspected heart failure in ambulatory adults, guidelines from the European Society of Cardiology suggest that levels ≥125 pg/mL should be considered for additional investigation.[3,4] Other studies demonstrate that a value <100 pg/mL reduces the probability of ventricular dysfunction from a pretest probability of 18% to a post-test value of 6%.[5]

There are no currently recognized reference values for NT-proBNP in pregnant women, making it difficult to interpret NT-proBNP in this setting. Several physiologic adaptations during pregnancy may impact natriuretic peptide levels. Ventricular stretch stimulates secretion of BNP and NT-proBNP.[2,3] Pregnancy is characterized by several hemodynamic and cardiac structural changes, including an increase in left and right ventricular sizes.[6,7] In pregnancy, plasma volume and cardiac output increase by ~50%, red cell mass increases by ~30%, and overall hemoglobin concentration decreases due to hemodilution.[6,8,9] NT-proBNP is cleared through renal filtration, and glomerular filtration rate (GFR) increases during pregnancy. Additionally, sex hormones are known to affect the production of BNP.[10,11] Furthermore, BNP may be produced by fetal membranes and generate myometrial quiescence during pregnancy.[12] These cardiac, renal, hormonal, and fetal changes during pregnancy may all impact NT-proBNP levels.[13]

NT-proBNP is frequently measured in the work-up for heart failure in pregnant women. Studies also suggest that NT-proBNP levels in early pregnancy may be associated with the risk for the development of adverse pregnancy outcomes, including preeclampsia.[14] A recent analysis from Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-Be (nuMOM2B) demonstrated that low first trimester NT-proBNP levels were associated with a greater likelihood of developing of hypertensive disorders of pregnancy and that higher first trimester NT-proBNP may be a normal physiologic pattern.[14] Currently, expected

NT-proBNP levels during pregnancy, especially with concurrent comorbidities, are not well characterized. There is also a growing use of NT-proBNP outside the setting of clinical heart failure.[15–17] Studies in the general population have established NT-proBNP as an important predictor of cardiovascular morbidity and mortality—especially heart failure—across body mass index (BMI) categories.[18,19] Little is known about expected physiologic NT-proBNP levels in pregnancy and there have been no studies of NT-proBNP in a general population of pregnant women in the United States. As NT-proBNP is often used for its negative predictive value, it is important to understand its distribution in the general population.

We undertook this study to characterize NT-proBNP in a nationally representative sample of pregnant women without known cardiovascular disease in the United States. We conducted a cross-sectional analysis to compare NT-proBNP across trimesters of pregnancy and among nonpregnant women in the same age range in the National Health and Nutrition Examination Survey (NHANES) 1999 to 2004.

METHODS

STUDY POPULATION.

The NHANES is a nationally representative sample of the civilian, noninstitutionalized population in the United States. Participants are selected using a stratified, multistage probability-cluster sampling design utilizing both in-home interviews and mobile examination center visits.[20] Pregnant women were oversampled in the 1999 to 2004 survey. We measured NT-proBNP in all persons with available stored blood samples who participated in the 1999 to 2004 survey cycles, which included 546 pregnant women aged 20 to 40 years. We conducted comparisons with nonpregnant women in the same age range (n = 1,588). Participants with a self-reported history of cardiovascular disease or missing variables of interest were excluded (Supplemental Figure 1). Approval was obtained by the ethics board of the National Center for Health Statistics for this stored serum study.

MEASUREMENT OF NT-ProBNP.

NT-proBNP was measured in stored serum using a Roche e611 auto-analyzer (Roche Diagnostics), with upper and lower limits of detection of 5 and 35,000 pg/mL, respectively. Coefficients of variation are 3.1% (low, 46 pg/mL) and 2.7% (high, 32,805 pg/mL). Laboratory testing was performed between 2018 and 2020 at the University of Maryland School of Medicine (Baltimore, Maryland, USA).

OTHER VARIABLES.

Participant age, sex, race/ethnicity group (non-Hispanic White, non-Hispanic Black, Mexican American, or other Hispanic), education, smoking status, and physical activity level were self-reported. Gestational age during pregnancy and number of prior pregnancies (gravidity) were also assessed by self-report.

Diabetes was defined as a self-reported physician diagnosis outside of pregnancy. Hypertension was defined as a self-reported physician diagnosis. Standard hemoglobin A1c criteria for diabetes diagnosis and blood pressure for hypertension diagnosis were not

used for the definition of these conditions during pregnancy given the dynamic nature of both measures during gestation. In NHANES, blood pressure was measured by a physician certified in blood pressure measurement using mercury sphygmomanometry and appropriately sized arm cuffs after the participant rested for 5 minutes while seated.[21] Chronic kidney disease was defined as an estimated GFR (eGFR) ≤60 mL/min/1.73 m^2 or urine albumin to creatinine ratio ≥30 μg/mg.[22] Weight measured at the visit was used to calculate current BMI (kg/m^2).

STATISTICAL ANALYSES.

We compared demographic characteristics, cardiovascular risk factors, other clinical measurements, and NT-proBNP in pregnant and nonpregnant women. We evaluated differences across pregnancy trimesters using chi-squared tests (for categorical variables) and analysis of variance (for means).

We examined differences in NT-proBNP (log-transformed) with pregnancy status and trimester. Two sets of models were used. The first used the nonpregnant status as the reference and comparison was made to the first, second, and third trimesters. The second set of models used first trimester as the reference group and comparison was made to the second and third trimesters (ie, nonpregnant participants were excluded from these models). In both sets, Model 1 adjusted for age and race/ethnicity. Model 2 included all variables in Model 1 plus diabetes, systolic blood pressure (SBP), and eGFR (modeled as linear spline at 60 mL/min/1.73 m^2). Model 3 included all variables in Model 2 plus BMI (continuous). We calculated the adjusted absolute differences in NT-proBNP between pregnant and nonpregnant women, and among pregnant women, compared to the first trimester, using Models 1 to 3. We then calculated the percent difference as 100*(êBeta-1), with Beta as the coefficient from the linear regression model.

We also used multivariable linear regression to evaluate the associations of BMI and SBP with NT-proBNP in nonpregnant women and according to trimester of pregnancy. BMI and SBP were modeled using linear and restricted cubic splines with knots at 5th, 35th, 65th, and 95th percentiles, and were adjusted for age, race/ethnicity, SBP, diabetes, and eGFR (modeled as a linear spline with single knot at 60 mL/min/1.73 m^2). The spline models were overlaid on histograms of the distribution of BMI or SBP in the population.

All analyses were performed using Stata 17.0. Recommended NHANES sample weights and Taylor series linearization for variance estimation were used to account for the complex survey design and generate nationally representative estimates.

RESULTS

A total of 2,134 women (546 pregnant) were included. Overall, mean age was 30.2 ± 0.2 years and mean BMI was 27.6 ± 0.2 kg/m^2. Thirteen percent (1.2) women self-identified as non-Hispanic Black and 9.2% (1.1) as Mexican American. Ten percent (0.8) reported a history of hypertension and 1.8% (0.3) reported a history of diabetes outside of pregnancy. The distribution of race/ethnicity, hypertension, and diabetes were comparable across trimesters of pregnancy (Table 1).

For nonpregnant women, median (25th, 75th percentile) NT-proBNP was 48 ng/mL (27,77 ng/mL). Among pregnant women, median NT-proBNP was 68 (41,98) among women in the first trimester of pregnancy, 53 (30,80) among those in the second trimester, and 36 (25,60) among those in the third trimester (Table 1, Central Illustration). Elevated NT-proBNP (defined as ≥125 pg/mL) was present in 20.0% ± 6.6% of women in the first trimester compared to 2.4% ± 0.8% of women in the third trimester and 8.0% ± 0.7% of nonpregnant women.

After adjustment for cardiovascular risk factors, compared to nonpregnant women, NT-proBNP was consistently higher in the first trimester of pregnancy (Table 2). Among pregnant women, NT-proBNP was consistently lower among women in the third trimester compared to the first trimester across all models (Table 3).

BMI was inversely associated with NT-proBNP in the second and third trimesters (Figure 1). SBP was also inversely associated with NT-proBNP in the second and third trimesters (Figure 2).

DISCUSSION

In this nationally representative sample of pregnant women without cardiovascular disease, we found that NT-proBNP was highest in women in the first trimester of pregnancy. Additionally, NT-proBNP levels in the first trimester of pregnancy were significantly higher than average NT-proBNP levels among nonpregnant women in a similar age range. The finding of lower NT-proBNP levels among women in the third trimester of pregnancy than those in the first trimester persisted even after adjustment for demographics and cardiovascular risk factors. Additionally, we found that there was higher prevalence of elevated NT-proBNP (≥125 pg/mL) among pregnant women in the first trimester compared to pregnant women in the third trimester or nonpregnant women. We also observed inverse associations of NT-proBNP with BMI and SBP, particularly in the second and third trimesters.

Prior studies of NT-proBNP in pregnancy have had mixed results, with some reporting increasing NT-proBNP with longer duration of pregnancy while others reported a decline across trimesters.[15,23] In women free of pre-existing cardiovascular disease, studies by Dockree et al and Umazume et al showed lower NT-proBNP and BNP levels in the third trimester compared to the first trimester, while one by Furenäs et al showed no differences in NT-proBNP.[15,23,24] However, these were (N < 300), and in clinical populations that were not racially/ethnically diverse. On the other hand, a recent longitudinal of 307 pregnant women with existing cardiovascular disease showed stable NT-proBNP levels until labor and delivery, when a transient rise occurred, followed again by return to baseline NT-proBNP levels.[25]

Prior data suggest that in the first trimester of pregnancy, cardiac output rises steeply, secondary to an increase in heart rate and plasma volume, reaching an equilibrium near the end of the second trimester.[6] As estrogen levels rise in the first trimester, angiotensinogen production and aldosterone levels rise as well, resulting in salt and water retention.[26,27]

The surge in volume increases ventricular myocardial stretch, likely increasing NT-proBNP levels. Our results suggest that levels of NT-proBNP may be lower in the third trimester of pregnancy than the first or second. Left and right ventricular end-diastolic volume and mass are noted to be higher in the third trimester, suggesting a compensatory remodeling in response to preload changes.[28] These changes in ventricular sizes and remodeling may contribute to resolution of the initial rise in NT-proBNP to lower levels by the third trimester. It is also possible that an increase in BMI, as expected in normal pregnancy, may further lower NT-proBNP levels by the third trimester, similar to what is observed in nonpregnant individuals.[19,29] We observed inverse associations of BMI with NT-proBNP, consistent with findings in other nonpregnant populations.[19,29,30] Notably, multiple hormonal changes occur during pregnancy, including a rise in estrogen and progesterone which likely influence BNP production in part through the renin-aldosterone system.[10,11] It is also possible that BNP production by fetal membranes declines throughout pregnancy, particularly in the third trimester, to lower myometrial quiescence in preparation for delivery.[12] Lastly, NT-proBNP is cleared through renal filtration, and rising GFR during pregnancy may contribute to declining NT-proBNP through the trimesters (Central Illustration).

We also found that NT-proBNP was inversely associated with SBP in the second and third trimesters of pregnancy. It has previously been shown that NT-proBNP rises with increases in SBP in a general nonpregnant population.[31] However, lower NT-proBNP in early pregnancy is associated with greater risk of hypertensive disorders of pregnancy and future hypertension 2 to 7 years after delivery.[14] A physiologic rise in BNP in early pregnancy in response to volume expansion may assist in lowering systemic vascular resistance. In early pregnancy, the association of lower NT-proBNP with higher SBP may represent poor cardiovascular adaptation to pregnancy.[14] Overall, these findings suggest that the relationship of NT-proBNP with SBP during pregnancy may be quite different than that in the nonpregnant state. Additionally, drastic changes in reproductive hormone changes during pregnancy may contribute to alterations in both blood pressure and BNP during gestation.[10,11,17]

Given the recent rise in cardiovascular-related mortality and morbidity during pregnancy in the United States, distinguishing expected from unexpected levels of NT-proBNP in healthy pregnant women is important.[32] Importantly, since NT-proBNP is often used as part of screening tools for evaluation of heart failure, it is critical to recognize that higher prevalence of NT-proBNP may be present in the first trimester of pregnancy independent of cardiovascular disease.[3,4] Our data help to further understanding of changes in NT-proBNP in healthy pregnancy, and consequently those that would be associated with disease states.[33–35] The increasing prevalence of obesity and hypertension among pregnant women in the United States, both well recognized risk factors for cardiovascular disease, also has implications for the interpretation of NT-proBNP during pregnancy.[36–38] Our findings suggest that the normal physiologic adaptations of pregnancy may have substantially effects on NT-proBNP. BMI, blood pressure, and pregnancy trimester appear to be major determinants of NT-proBNP levels in pregnancy and will need to be taken into consideration when using NT-proBNP to assess for clinical disease, such as peripartum cardiomyopathy or other forms of heart failure, in pregnant women.

STUDY LIMITATIONS.

The major limitation in the interpretation of these data was that we did not have longitudinal data on these women over time, that is, we do not have information on NT-proBNP on the same women throughout the course of their pregnancy. This limits our ability to interpret the differences we observed in NT-proBNP across trimesters as true physiologic changes. Despite rigorous adjustment for demographic and cardiovascular risk factors in our analyses, residual confounding remains a possible explanation for the observe differences. Furthermore, cardiac imaging studies were not available to correlate findings of NT-proBNP with structural and functional myocardial changes in pregnancy. We also were not able to identify women with pregnancy-induced hypertension, although this likely would affect only a very small number of women in our study as the mean SBP among pregnant women was well below 120 mms Hg. Strengths of this study included the large, nationally representative sample of diverse pregnant and nonpregnant women from across the United States and standardized measurements conducted by trained personnel. Women with clinically overt cardiovascular disease were excluded from this study to allow for observation of 'normal' NT-proBNP levels in pregnancy.

CONCLUSIONS

NT-proBNP levels were higher in women in the first trimester of pregnancy compared with nonpregnant women and women in later trimesters. Similarly, there was a higher prevalance of elevated NT-proBNP (≥125 pg/mL) in the first trimester compared to nonpregnant women and those in the later trimesters. BMI and SBP were associated with lower NT-proBNP across the second and third trimesters. These results suggest that NT-proBNP levels are dynamic throughout pregnancy and are different than in the nonpregnant state. Our data suggest that the interpretation of NT-proBNP in pregnant women without cardiovascular disease is complex. Trimester, BMI, and blood pressure may all need to be taken into consideration when assessing NT-proBNP in pregnant women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS AND ACRONYMS

BMI	body mass index
BNP	pro-B-type natriuretic peptide
eGFR	estimated glomerular filtration rate
NHANES	National Health and Nutrition Examination Survey
NT-proBNP	N-terminal pro-B-type natriuretic peptide
SBP	systolic blood pressure

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS:

Pregnancy is characterized by various physiologic and hormonal changes that result in dynamic alterations in NT-proBNP levels throughout pregnancy. Pregnant women may be more likely to have elevated NT-proBNP in the first trimester compared to nonpregnant women or pregnant women in later trimesters, independent of known cardiovascular disease.

TRANSLATIONAL OUTLOOK:

Clinicians should interpret NT-proBNP in pregnancy in the context of fluctuations in NT-proBNP throughout the trimesters of pregnancy. Pregnancy trimester, weight gain/BMI, and blood pressure should all be considered.

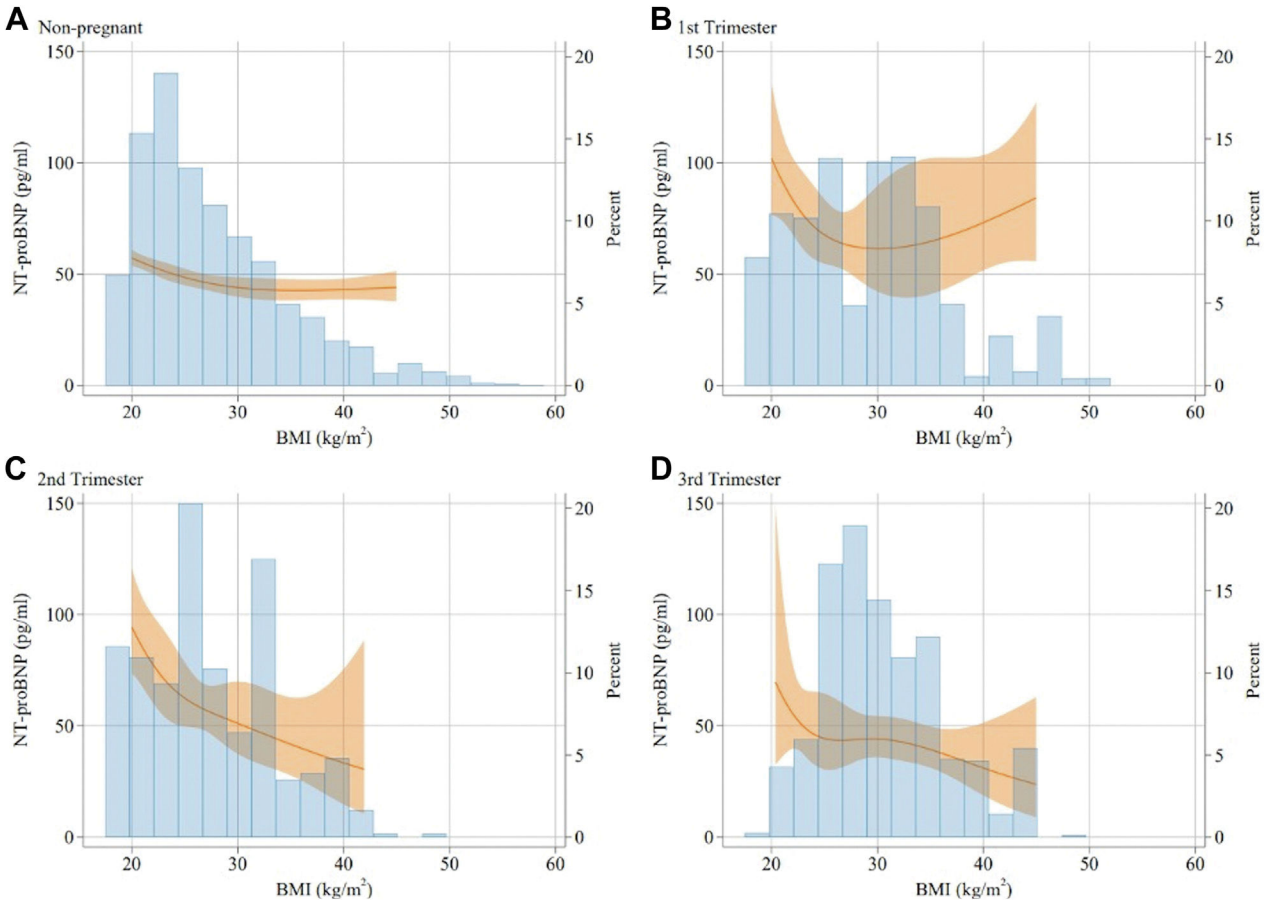


FIGURE 1. Associations of Body Mass Index With NT-proBNP in Nonpregnant Women and Pregnant Women According to Trimester, Aged 20 to 40 Years, NHANES 1999 to 2004

(A) Non-pregnant, **(B)** 1st trimester, **(C)** 2nd trimester, **(D)** 3rd trimester. BMI was modeled as a restricted cubic spline **(solid line)** with knots at the 5th, 35th, 65th, and 95th percentiles. The **orange shaded area** reflects the upper and lower 95% confidence interval for the restricted cubic spline. The models were adjusted for age, race/ethnicity, SBP, diabetes and eGFR. The **blue** histograms are the distribution (%) of BMI in each group. BMI = body mass index; eGFR = estimated glomerular filtration rate; NHANES = National Health and Nutrition Examination Survey; NT-proBNP = N-terminal pro-B-type natriuretic peptide; SBP = systolic blood pressure.

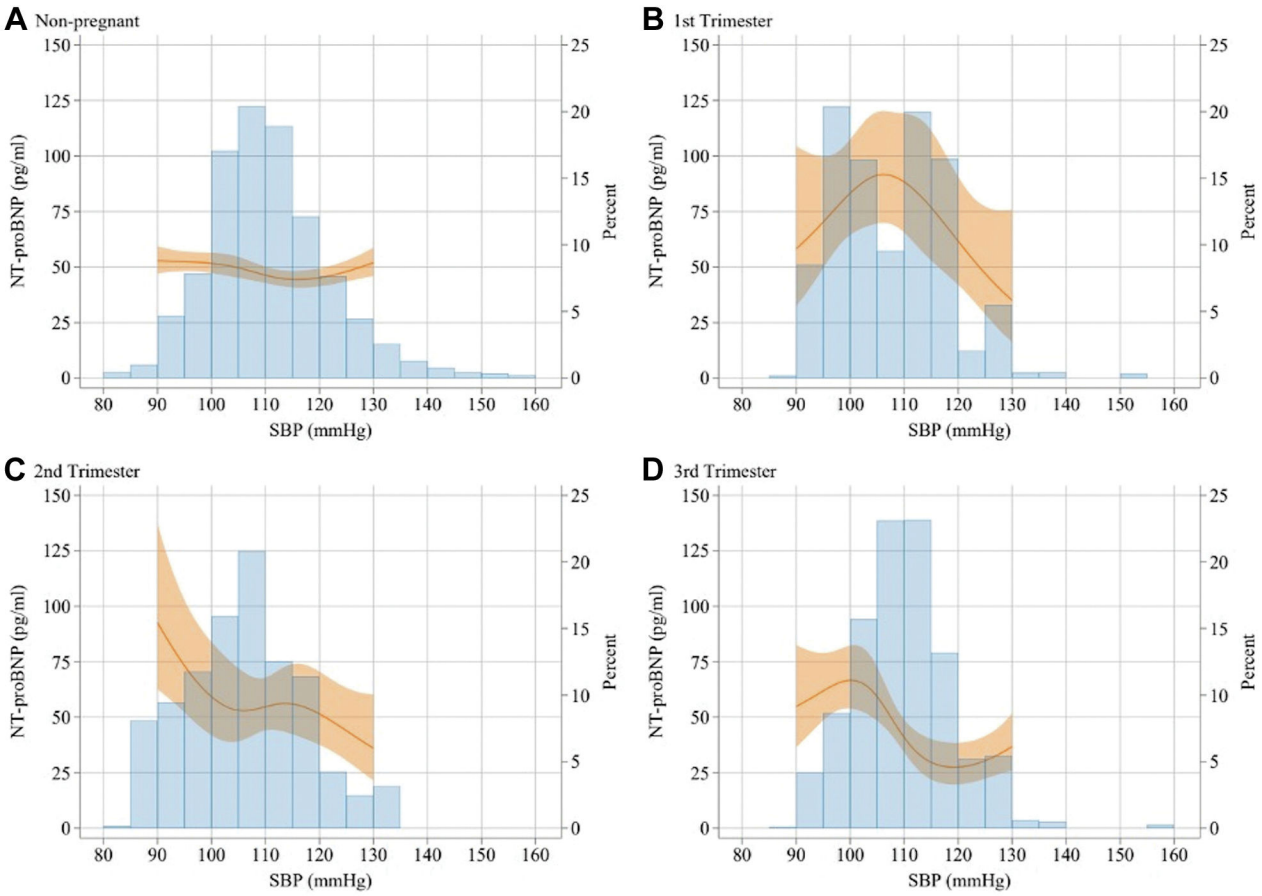
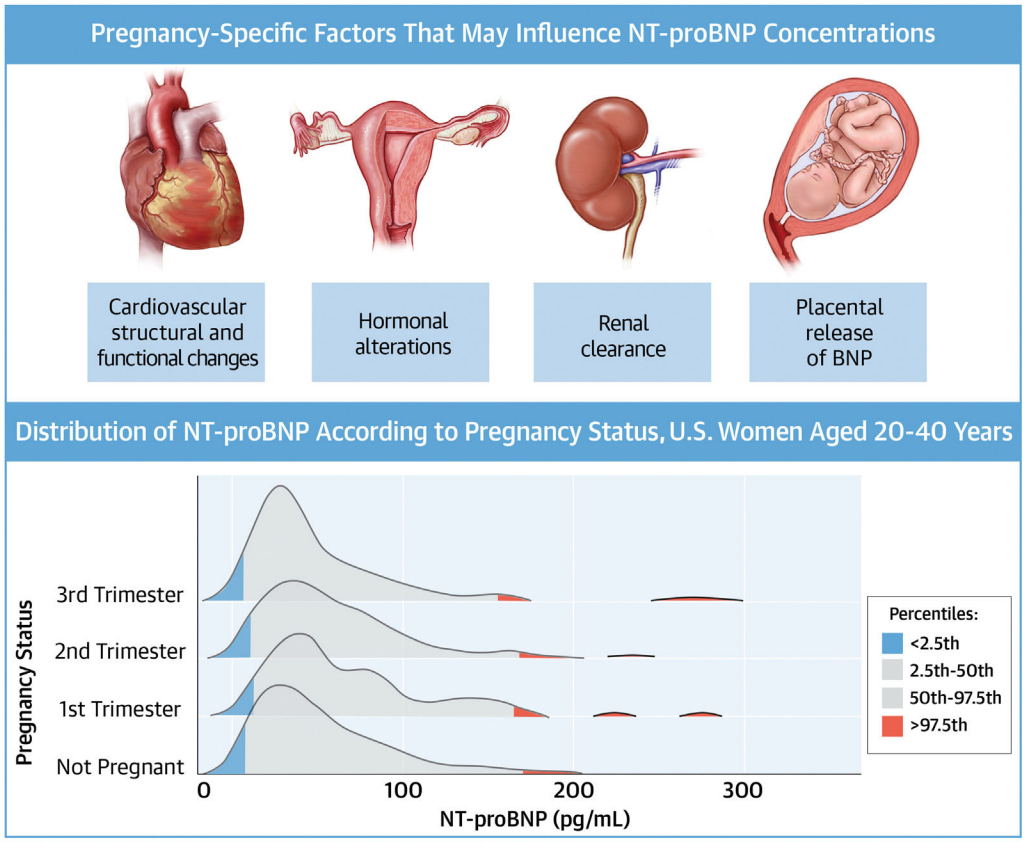


FIGURE 2. Adjusted Associations of Systolic Blood Pressure With NT-proBNP in Nonpregnant Women and Pregnant Women According to Trimester Aged 20 to 40 Years, NHANES 1999 to 2004

SBP was modeled as a restricted cubic spline **(solid line)** with knots at the 5th, 35th, 65th, and 95th percentiles. The **orange shaded area** reflects the upper and lower 95% confidence interval for the restricted cubic spline. The models were adjusted for age, race/ethnicity, BMI, diabetes and eGFR. The **blue** histograms are the distribution (%) of SBP in each group. BMI = body mass index; eGFR = estimated glomerular filtration rate; NHANES = National Health and Nutrition Examination Survey; NT-proBNP = N-terminal pro-B-type natriuretic peptide; SBP = systolic blood pressure.



Minhas AS, et al. JACC Adv. 2023;2(2):100265.

CENTRAL ILLUSTRATION. Pregnancy-Specific Factors That May Influence NT-proBNP Levels

NT-proBNP = N-terminal pro-B-type natriuretic peptide.

TABLE 1

Characteristics of U.S. Women 20 to 40 Years of Age, According to Pregnancy Status and Trimester, NHANES 1999 to 2004

		Pregnant			
	Nonpregnant (n = 1,588)	**First Trimester (n = 105)**	**Second Trimester (n = 233)**	**Third Trimester (n = 208)**	***P* Value[a]**
Age, y	30.4 (0.2)	28.6 (0.8)	26.8 (0.7)	28.7 (0.6)	0.07
Race 0.08					
Non-Hispanic White	67.0 (2.0)	68.5 (8.4)	61.4 (5.8)	49.5 (7.0)	
Non-Hispanic Black	12.8 (1.2)	5.0 (2.2)	14.6 (4.4)	14.9 (5.2)	
Mexican American	8.8 (1.1)	16.5 (4.8)	13.8 (2.8)	10.8 (2.8)	
Other Hispanic	11.4 (1.7)	10.0 (6.5)	10.2 (3.2)	24.8 (6.6)	
Education					
≤High school	15.9 (1.1)	30.7 (7.2)	16.8 (3.7)	12.3 (2.9)	
High school	24.5 (1.5)	11.8 (5.8)	23.5 (5.0)	15.0 (3.9)	0.20
Some college	35.2 (1.3)	30.1 (7.5)	31.2 (6.6)	35.8 (6.1)	
≥College graduate	24.3 (1.6)	27.5 (6.3)	28.5 (5.1)	36.9 (6.6)	
Smoking					
Never	59.1 (1.7)	52.3 (9.2)	59.7 (5.6)	59.5 (5.6)	0.68
Former	12.3 (1.1)	29.3 (6.0)	28.6 (6.2)	30.8 (6.0)	
Current	28.6 (1.4)	18.5 (6.5)	11.7 (3.7)	9.7 (3.7)	
Gravidity					
0	29.6 (1.6)				
1	15.5 (1.1)	11.3 (5.4)	32.8 (5.0)	22.8 (5.3)	0.029
2+	54.9 (1.9)	88.7 (5.4)	67.2 (5.0)	77.2 (5.3)	
Body mass index, kg/m^2	27.5 (0.2)	28.9 (1.3)	27.5 (0.9)	30.7 (0.6)	0.002
Diabetes (self-report)	1.8 (0.2)	0.8 (0.6)	1.2 (0.6)	2.6 (1.7)	0.39
Anemia (hemoglobin <12 g/dL)	6.0 (0.8)	9.6 (5.1)	33.6 (5.3)	38.0 (7.0)	0.014
History of hypertension	9.8 (0.8)	12.0 (5.7)	10.6 (3.6)	5.5 (1.3)	0.33
Systolic blood pressure (mmHg)	110.4 (0.4)	107.1 (2.0)	105.7 (1.4)	109.5 (1.1)	0.11
Chronic kidney disease	5.9 (0.8)	4.0 (2.3)	1.0 (0.7)	3.7 (1.5)	0.24
NT-proBNP (pg/mL)	48 (27, 77)	68 (41, 98)	53 (30, 80)	36 (25, 60)	0.001

		Pregnant			
	Nonpregnant (n = 1,588)	**First Trimester (n = 105)**	**Second Trimester (n = 233)**	**Third Trimester (n = 208)**	***P* Value[a]**
Elevated NT-proBNP (≥quartile 3 of nonpregnant, race/ethnicity specific)	25.0 (1.2)	36.1 (7.0)	29.8 (6.1)	18.5 (5.4)	0.14
Elevated NT-proBNP (≥125 pg/mL)	8.0 (0.7)	20.0 (6.6)	7.9 (3.2)	2.4 (0.8)	0.003

Values are n (%) or median (25th, 75th percentile).

[a] *P* value for differences across pregnancy trimesters (pregnant women only).

NHANES = National Health and Nutrition Examination Survey; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

TABLE 2

Crude and Adjusted Means and Absolute and Percent Differences in Mean NT-proBNP (pg/mL) According to Pregnancy Status

	Mean NT-proBNP, pg/mL				First Trimester vs Nonpregnant		Second Trimester vs Nonpregnant		Third Trimester vs Nonpregnant	
	Nonpregnant	First Trimester	Second Trimester	Third Trimester	Absolute Difference (95% CI)	% Difference	Absolute Difference (95% CI)	% Difference	Absolute Difference (95% CI)	% Difference
Crude	44.8	63.0	45.5	35.2	18.2 (4.8, 31.5)[b]	34%	0.7 (−9.4, 10.8)	2%	−9.6 (−16.4, −2.8)[a]	24%
Model 1	46.3	64.0	49.3	39.2	17.7 (3.5, 32.0)[b]	32%	3.0 (−6.5, 12.5)	6%	−7.1 (−13.7, −0.5)[a]	17%
Model 2	46.5	69.5	55.1	39.5	23.0 (8.5, 37.5)[b]	40%	8.6 (−4.1, 21.3)	17%	−7.0 (−13.1, −0.8)[a]	16%
Model 3	47.2	73.6	57.6	42.0	26.4 (11.2, 41.6)[b]	44%	10.4 (−2.2, 23.1)	1%	−5.2 (−11.9, 1.5)	12%

Model 1 included age and race/ethnicity. Model 2 included all variables in Model 1 plus hypertension (self-report), systolic blood pressure, diabetes (self-report), and eGFR. Model 3 included all variables in Model 2 plus BMI (continuous).

[a] $P \leq 0.05$.

[b] $P < 0.001$.

BMI = body mass index; eGFR = estimated glomerular filtration rate; NT-proBNP = N-terminal pro-B-type natriuretic peptide.

TABLE 3

Crude and Adjusted Mean and Mean Difference in NT-proBNP (pg/mL) According to Pregnancy Trimester

	Mean NT-proBNP, pg/mL			Second vs First Trimester		Third vs First Trimester	
	First Trimester	Second Trimester	Third Trimester	Absolute Difference (95% CI)	% Difference	Absolute Difference (95% CI)	% Difference
Crude	63.0	45.5	35.2	−17.5 (−34.8, −0.2)[a]	32%	−27.8 (−13.2, −42.4)[b]	57%
Model 1	58.3	46.2	36.3	−12.0 (−27.6, 3.5)	23%	−22.0 (−7.5, −36.4)[b]	46%
Model 2	58.3	46.0	36.5	−12.4 (−25.6, 0.8)	24%	−21.8 (−36.3, −7.3)[b]	46%
Model 3	58.9	45.4	36.7	−13.5 (−25.5, −1.4)[a]	22%	−22.2 (−36.9, −7.5)[b]	46%

Model 1 included age and race/ethnicity. Model 2 included all variables in Model 1 plus hypertension (self-report), systolic blood pressure, diabetes (self-report), and eGFR. Model 3 included all variables in Model 2 plus BMI (continuous).

[a] $P < 0.05$.

[b] $P < 0.00$.

BMI = body mass index; eGFR = estimated glomerular filtration rate; NT-proBNP = N-terminal pro-B-type natriuretic peptide.