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Evaluation of Antithrombin-III Activity and Platelet Count in Pregnancy-Induced Hypertension among Pregnant Women attending Antenatal care in a Tertiary Health Facility in Southeast, Nigeria

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Abstract:

Background: Pregnancy-induced hypertension (PIH) is a significant health issue that affects maternal and fetal outcomes. Antithrombin-III (AT-III) and platelet count alterations could serve as pivotal indicators for the management and prognosis of PIH.

Objective: This study aimed to assess AT-III activity and platelet counts in pregnant women with and without PIH at the Federal Medical Centre (FMC), Owerri, Imo State, Nigeria.

Methods: A case-control cross-sectional analytical study design was employed, including 135 pregnant women with PIH and 135 age-matched normotensive pregnant women. Exclusion criteria comprised chronic hypertension, known thrombophilic disorders, or anticoagulant therapy before pregnancy. AT-III levels and platelet counts were compared between groups using SPSS version 20.0, with significance set at $p \leq 0.05$.

Results: AT-III activity was significantly lower in the PIH group (75.45±6.23%) compared to the normotensive group (96.84±9.64%, p=0.028). Similarly, platelet count was significantly reduced in the PIH group (170.90 ±8.78 x109/L) versus the normotensive group (191.56±6.54 x109/L, p=0.032). No significant differences were found in sociodemographic variables except for the trimester of antenatal care registration and history of preeclampsia in previous pregnancies.

Conclusion: This study highlights significant reductions in AT-III activity and platelet count among pregnant women with PIH, suggesting these parameters' potential role in PIH management and prognosis. These findings emphasize the importance of monitoring AT-III levels and platelet count as part of the antenatal care protocol in pregnant women, particularly those with or at risk for PIH.

Keywords: antenatal care; antithrombin-iii; platelet count; preeclampsia; pregnancy-induced hypertension

Introduction

Pregnancy-Induced Hypertension (PIH), also known as preeclampsia, is a complex hypertensive disorder affecting 2-8% of pregnancies worldwide and remains a leading cause of maternal and perinatal morbidity and mortality [1]. Characterized by high blood pressure and signs of damage to another organ system, most often the liver and kidneys, after 20 weeks of gestation in a woman previously diagnosed with normal blood pressure [2]. The pathophysiology of preeclampsia is not entirely understood, but it is believed to involve abnormal placental development leading to placental ischemia, oxidative stress, and endothelial dysfunction [3].

Antithrombin-III (AT-III) is a critical protein in the coagulation pathway, acting as a natural anticoagulant that helps regulate blood clot formation. Reduced AT-III levels have been associated with an increased risk of thrombosis and have been observed in various pregnancy complications, including preeclampsia [4].

Platelets play a crucial role in hemostasis, and thrombocytopenia (a low platelet count) is a common feature in preeclampsia, contributing to its complications [5]. Investigating the association between AT-III levels, platelet count, and preeclampsia can provide insights into the disease's pathophysiology and potential therapeutic targets.

The prevalence of PIH varies by geographical location, due to differences in genetic, environmental, and socio-economic factors. In Nigeria, and particularly in the Southeast region, the prevalence of PIH has been reported to be higher than in some other parts of the world. This variation can be attributed to factors such as dietary habits, access to healthcare, and awareness of PIH among pregnant women [6].

In Southeast Nigeria, antenatal care services play a crucial role in the early detection and management of PIH. However, there are challenges such as limited resources, inadequate healthcare infrastructure, and low patient literacy levels that may affect the effective monitoring and management of this condition [7].

Given the significant impact of PIH on maternal and fetal health, and the potential role of AT-III and platelet count in predicting and managing this condition, there is a need for more focused research in high-prevalence areas like Southeast Nigeria. Understanding the dynamics of AT-III activity and platelet count among pregnant women with PIH attending antenatal care in this region can provide insights necessary for developing targeted interventions to improve pregnancy outcomes.

Materials And Methods

Study Design

This is a case-control cross-sectional analytical study aimed to evaluate the association between Antithrombin-III levels and platelet count in pregnant women with and without pregnancy-induced hypertension (PIH) attending antenatal care at the Federal Medical Centre (FMC), Owerri, Imo State, Nigeria.

Inclusion Criteria: Pregnant women attending antenatal care at the teaching hospital, both with diagnosed pregnancy-induced hypertension (preeclampsia) and normotensive pregnant women as controls.

Exclusion Criteria: Women with chronic hypertension, known thrombophilic disorders, or on anticoagulant therapy prior to pregnancy.

Sample Size Determination

The sample size was determined based on the expected difference in Antithrombin-III levels and platelet counts between the two groups, considering the prevalence of preeclampsia in Nigeria.

It was determined using the Fisher's formula outlined by Ekeleme et al. [8]:

$n = (Z^2 (Pq))/e^2$

where n = minimum sample size

Z = 1.96 at 95% confidence level,

P = known prevalence of preeclampsia in Nigeria

e = error margin tolerated at 5% = 0.05

q = 1 - p

According to Musa et al. [9], the prevalence of preeclampsia in Nigeria is 8.8%.

P = 8.8% = 0.088

q = 1 – p

= 1 – 0.088

= 0.912

$n = ((1.96)^2 (0.088 \times 0.912))/ (0.05)^2$

$n = (0.3083114496)/ (0.0025) = 123.32$

The minimum sample size was 123 and was adjusted to 135 to account for non-response rate of 10 %.

Sampling Technique

Stratified random sampling was utilized for this study, with the strata being women with PIH and those without. Women were randomly selected from each stratum to participate in the study. Thus, one hundred and thirty-five (135) pregnant women with PIH and one hundred and thirty-five (135) age-matched normotensive pregnant women were recruited for the study.

Data Collection Methods

A structured questionnaire was utilized to collect the data. The questionnaire was composed of three sections: (1) Sociodemographic Details of Participants, (2) Obstetric History of Participants (3) Medical and Lifestyle Information of Participants. The questionnaire was developed and validated through extensive literature review and expert opinion, ensuring that it covered all pertinent information required for the study.

Determination of Anthropometric Indices and Blood Pressure

The body mass index for each participant was calculated from weight and height measurements obtained through the use of Hanson's weighing scale (capacity of 120 kg) and a meter rule attached to a wooden pole, respectively as described by Agu et al. [10]. Briefly, the participants were weighed in light clothing and reading was taken to the nearest 0.1 kg. Height to the nearest 0.1 cm was measured with the participants standing erect on a flat surface. Waist circumference was measured with a flexible non-stretch tape placed on the midpoint between the top of the iliac crest and the bottom of the rib cage where the last palpable rib is found [10]. The weighing scale was maintained at zero before taking the weight measurements.

Blood pressure was determined twice (a minimum of 3 mins interval was observed) by trained research assistants using Omron automatic sphygmomanometer (M2: HEM-7121-E, Vietnam) with the participant sitting comfortably and arm resting on a table at the same level with the heart as described by Ijioma et al. [11]. Average of the two readings was used in the analysis. Preeclampsia was diagnosed according to American college of Obstetrics and Gynaecology (ACOG) criteria [1]: a blood pressure higher than 140/90 mm Hg and proteinuria more than 300mg/24hr were observed on at least two occasions more than 6 hours apart after the 20th weeks of pregnancy.

Determination of Platelet Counts and AT-III

For platelet counts, blood samples were collected in EDTA tubes and plasma was separated after centrifugation for 5-10 minutes at 3000 rpm within one hour of the venepuncture. Haematological parameter (platelet counts) was performed on cell counter PCN-201(N) according to the method described by Chikezie et al. [12]. For Coagulation parameter (AT-III), blood was placed into test tubes containing 1 ml of 3.8% sodium-citrate. Centrifugation of these specimens was done for ten minutes at room temperature and at $2500^{\times}$ g. The level of AT-III was studied using the fully automatic Coagulometer equipment (Diagnostic Stago STA Compact; France).

Supervision and technical support were provided to trained research assistants throughout the study period to ensure study protocols were followed as planned. On the spot random checks of collected data were conducted and identified inconsistencies/missing data were fixed. Weight and blood pressure equipment were checked after each measurement to ensure continued functionality.

Data Analysis

The statistical package for the social science (SPSS) was used to analyze the collected data (version 20.0; SPSS, Chicago, IL). The mean, standard deviation and t-test were the statistical tests employed in this investigation. Simple tables containing frequencies, percentages, and mean values were used to display the obtained results. The threshold of statistical significance for group comparisons was set at P-value ≤ 0.05.

Ethical Consideration

The research was conducted in accordance with ethical principles, including informed consent, confidentiality, and data protection. Participants were informed of the purpose of the research and had the option to withdraw at any time without any consequences.

Results

In terms of sociodemographic details (Table 1), the age distribution among hypertensive and normotensive subjects did not show significant differences, with the majority being in the 30-39 age range for both groups (58.52% vs. 59.26%, p=0.494). Educational levels and marital status also did not significantly differ between the groups, with the largest proportion having secondary education (38.52% hypertensive vs. 52.59% normotensive, p=0.175) and being married (57.78% hypertensive vs. 86.67% normotensive, p=0.121).

Obstetric history (Table 2) revealed that gravidity and parity were not significantly different between the two groups. However, the timing of antenatal care registration and the history of preeclampsia showed significant differences. A smaller proportion of hypertensive women registered for antenatal care in the first trimester compared to normotensive subjects (14.81% vs. 25.19%, p=0.046), and a higher proportion of hypertensive women had a history of preeclampsia (46.67% vs. 16.30%, p=0.027).

Medical and lifestyle information (Table 3) indicated significant differences in previous diagnoses of hypertension or preeclampsia, family history of these conditions, smoking history, alcohol consumption, complications in previous pregnancies, pre-existing medical conditions, and physical activity levels. Notably, a higher proportion of hypertensive patients had a previous diagnosis (57.78% vs. 28.89%, p=0.009), a family history (60.00% vs. 32.59%, p=0.014), and reported experiencing complications in previous pregnancies (33.33% vs. 18.52%, p=0.004). Additionally, hypertensive patients were more likely to lead a sedentary lifestyle (61.48% vs. 26.67%, p=0.033).

Anthropometric parameters (Table 4) showed no significant difference in mean body mass index (BMI) or waist-hip ratio between the two groups. However, mean systolic and diastolic blood pressures were significantly higher in hypertensive patients (141.76 mmHg vs. 116.53 mmHg, p=0.007 for systolic; 98.43 mmHg vs. 76.82 mmHg, p=0.003 for diastolic).

Laboratory measures (Figures 1 and 2) revealed that hypertensive patients had significantly lower antithrombin-III activity (75.45% vs. 96.84%, p=0.028) and platelet count (170.90 x109/L vs. 191.56 x109/L, p=0.032) compared to normotensive subjects, indicating altered coagulation status

.

Variable	**Hypertensive Patients n (%)**	**Normotensive Subjects n (%)**	**p-value**
Age (in Years)			0.494
Less than 20	3 (2.22)	6 (4.44)	
20 – 29	22 (16.30)	20 (14.81)	
30 – 39	79 (58.52)	80 (59.26)	
40 and above	31 (22.96)	29 (21.48)	
Educational Level			0.175
No formal Education	21 (15.56)	11 (8.15)	
Primary Education	32 (23.70)	21 (15.56)	
Secondary Education	52 (38.52)	71 (52.59)	
Tertiary Education	30 (22.22)	32 (23.70)	
Marital Status			0.121
Single	39 (28.89)	7 (5.19)	
Married	78 (57.78)	117 (86.67)	
Divorced/Widowed	18 (13.33)	11 (8.15)	

Table 1: Sociodemographic Details of Participants

p-value ≤ 0.05 are statistically significant

Variable	**Hypertensive Patients n (%)**	**Normotensive Subjects n (%)**	**p-value**

Gravidity (Number of pregnancies, including the current one)			0.082
1	40 (29.63)	55 (40.74)	
2	48 (35.56)	46 (34.07)	
3	27 (20.00)	15 (11.11)	
4	11 (8.15)	13 (9.63)	
More than 4	9 (6.67)	6 (4.44)	
Parity (Number of births after 28 weeks of gestation)			0.128
0	48 (35.56)	55 (40.74)	
1	51 (37.78)	46 (34.07)	
2	23 (17.04)	21 (15.56)	
3	8 (5.93)	10 (7.41)	
4	3 (2.22)	2 (1.48)	
More than 4	2 (1.48)	1 (0.74)	
What trimester did you register for antenatal care?			0.046*
First Trimester	20 (14.81)	34 (25.19)	
Second Trimester	104 (77.04)	89 (65.93)	
Third Trimester	11 (8.15)	12 (8.89)	
History of Preeclampsia in Previous Pregnancies			0.027*
Yes	63 (46.67)	22 (16.30)	
Not	32 (23.70)	58 (42.96)	
Not Applicable	40 (29.63)	55 (40.74)	
*Outcome of Previous Pregnancies (Check all that apply)			0.092
Live birth	82 (56.16)	70 (50.36)	
Stillbirth	7 (4.79)	3 (2.16)	
Miscarriage	12 (8.22)	9 (6.47)	
Premature birth	5 (11.64)	2 (1.44)	
Not Applicable	40 (27.40)	55 (39.57)	
*Experienced Symptoms during current pregnancy (Check all that apply)			0.048*
Swelling (hands/face/leg)	41 (25.31)	51 (30.54)	
Severe headache	56 (34.57)	39 (23.35)	
Vision problems (blurriness, light sensitivity)	4 (2.47)	00 (0.00)	
Upper abdominal pain	17 (10.49)	9 (5.39)	
None of the above	44 (27.16)	68 (40.72)	

Table 2: Obstetric History of Participants

p-value ≤ 0.05 are statistically significant

* = Multiple Response

Variable	**Hypertensive Patients n (%)**	**Normotensive Subjects n (%)**	**p-value**
Previous Diagnosis of Hypertension or Preeclampsia			0.009*
Yes	78 (57.78)	39 (28.89)	
No	57 (42.22)	96 (71.11)	
Family History of Hypertension or Preeclampsia			0.014*

Yes	81 (60.00)	44 (32.59)	
No	54 (40.00)	91 (67.41)	
Smoking History			0.036*
Current smoker	00 (0.00)	00 (0.00)	
Former smoker	28 (20.74)	11 (8.15)	
Never smoked	107 (79.26)	124 (91.85)	
Frequency of alcohol consumption			0.023*
Never	78 (57.78)	104 (77.04)	
Stopped alcohol	38 (28.15)	24 (17.78)	
Occasionally	19 (14.07)	7 (5.19)	
Regularly	00 (0.00)	00 (0.00)	
Have you experienced any complications in your previous pregnancies?			0.004*
Yes	45 (33.33)	25 (18.52)	
No	90 (66.67)	110 (81.48)	
Do you have any pre-existing medical conditions? (e.g., diabetes, kidney disease)			0.000*
Yes	56 (41.48)	8 (5.93)	
No	79 (58.52)	127 (94.07)	
Describe your daily physical activity level			0.033*
Sedentary (little or no exercise)	83 (61.48)	36 (26.67)	
Lightly active (light exercise/sports 1-3 days/week)	41 (30.37)	63 (46.67)	
Moderately active (moderate exercise/sports 3-5 days/week)	11 (8.15)	36 (26.67)	
Very active (hard exercise/sports 6-7 days a week)	00 (0.00)	00 (0.00)	
Extra active (very hard exercise/sports & physical job or 2x training)	00 (0.00)	00 (0.00)	

Table 3: Medical and Lifestyle Information of Participants

p-value ≤ 0.05 are statistically significant

Anthropometric Parameters	**Hypertensive Patients**	**Normotensive Subjects**	**p-value**
Mean Body Mass Index (BMI) (kg/m^2)	23.38 ± 4.23	22.97 ± 3.92	0.846
Mean Waist Circumference (cm)	98.94±7.31	94.03±7.53	0.082
Mean Waist Hip Ratio	0.95±0.06	0.94±0.04	0.527
Mean Systolic Blood Pressure (mmHg)	141.76±11.82	116.53±11.31	0.007*
Mean Diastolic Blood Pressure (mmHg)	98.43±11.26	76.82±6.44	0.003*

Table 4: Anthropometric Parameters **of Pregnant Women**

p-value ≤ 0.05 are statistically significant

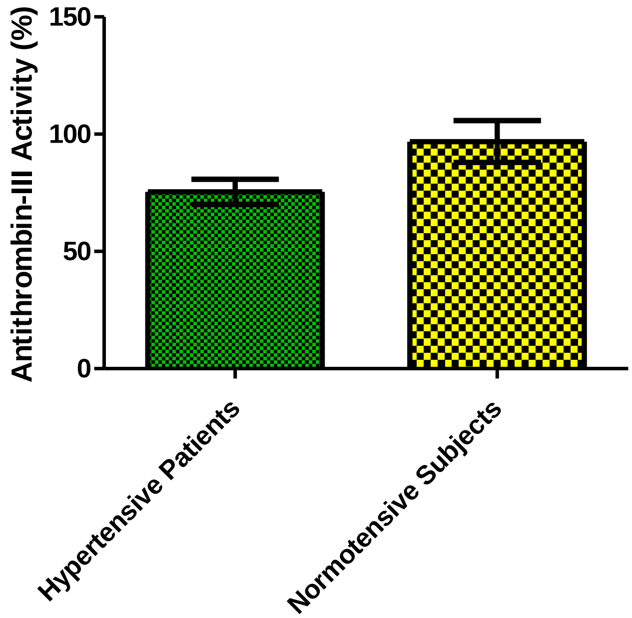

Figure 1: Antithrombin-III Activity of Hypertensive and Normotensive Pregnant Women

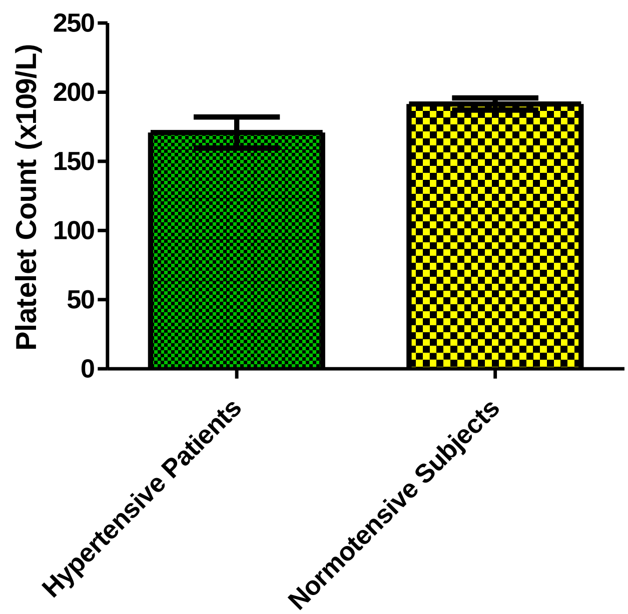

Figure 2: Platelet Count of Hypertensive and Normotensive Pregnant Women

Discussion

Pregnancy-induced hypertension (PIH) is a significant contributor to maternal and fetal morbidity and mortality, particularly in developing countries. Antithrombin-III (AT-III) activity and platelet count are critical parameters in assessing coagulation status and placental function in pregnant women. This study evaluates the association between AT-III levels and platelet counts in pregnant women with and without PIH attending antenatal care at the Federal Medical Centre (FMC), Owerri, Imo State, Nigeria.

The study observed no significant difference in gravidity and parity between hypertensive and normotensive pregnant women, with p-values of 0.082 and 0.128, respectively. This suggests that the number of pregnancies or births does not significantly influence the likelihood of developing PIH. Previous studies have offered mixed results on this matter. For example, a study by Bartsch, et al. [13] found that higher parity was associated with a reduced risk of preeclampsia, a specific form of PIH, in women with a history of the disease. The discrepancy between these findings may be due to differences in study populations, definitions of hypertension, or the inclusion of various risk factors.

Significantly, more normotensive subjects registered for antenatal care in the first trimester compared to hypertensive patients ($p = 0.046$). Early antenatal registration may contribute to better monitoring and management of potential hypertensive disorders. This is in line with literature suggesting that early and regular antenatal care can help in early detection and management of preeclampsia and other hypertensive disorders of pregnancy [14].

The study found a significant association between a history of preeclampsia in previous pregnancies and the development of hypertension in the current pregnancy (p = 0.027). This corroborates with previous research indicating that a history of preeclampsia is a strong predictor for recurrence in subsequent pregnancies [15].

Although not statistically significant for the outcome of previous pregnancies, there was a trend towards more adverse outcomes in hypertensive patients. Notably, experienced symptoms during the current pregnancy, such as swelling, severe headache, and vision problems, were more common in hypertensive patients, with a significant difference in vision problems (p = 0.048). This aligns with the known clinical manifestations of PIH and preeclampsia [1].

The study notes a statistically significant difference (p=0.009) between hypertensive patients and normotensive subjects concerning previous diagnoses of hypertension or preeclampsia, with 57.78% of hypertensive patients having a history compared to 28.89% of normotensive subjects. This aligns with findings by Brown et al. [16], who reported that a history of hypertension or preeclampsia increases the risk of PIH in subsequent pregnancies, emphasizing the need for closer monitoring of these patients.

Similarly, a significant difference (p=0.014) was observed in the family history of hypertension or preeclampsia between the two groups, suggesting a genetic predisposition or familial risk factor. This finding is consistent with the literature, which indicates that a family history of these conditions significantly elevates the risk for PIH [17].

The study also found significant differences in the history of smoking and alcohol consumption. Although no current smokers were reported, former smokers constituted a higher percentage in the hypertensive group than in the normotensive group (p=0.036). For alcohol consumption, those who never consumed alcohol were significantly higher in the normotensive group. These results suggest lifestyle modifications as potential interventions for reducing PIH risk. The negative impact of smoking on pregnancy outcomes is well-documented, but its specific role in PIH is complex and multifactorial [18].

A significant correlation was found between complications in previous pregnancies (p=0.004) and pre-existing medical conditions (p=0.000) with PIH. These factors underscore the importance of comprehensive prenatal screening and management of women with such histories to mitigate the risk of PIH.

Physical activity levels showed significant variation, with a sedentary lifestyle being more common among hypertensive patients (p=0.033). This finding suggests that increased physical activity could potentially lower the risk of PIH, supporting the recommendations for moderate exercise during pregnancy [19].

The study reports no significant difference in the mean Body Mass Index (BMI) between hypertensive and normotensive pregnant women, with values of 23.38 ± 4.23 kg/m2 and 22.97 ± 3.92 kg/m2, respectively (p=0.846). This suggests that BMI may not be a distinguishing factor for PIH in this population, aligning with the findings of some studies while contrasting with others that have identified a higher BMI as a risk factor for the development of PIH [20,21]. For instance, Spradley's meta-analysis indicated a correlation between higher pre-pregnancy BMI and an increased risk of developing PIH, suggesting a complex interaction between maternal adiposity and blood pressure regulation during pregnancy.

In terms of waist circumference, the study found a slightly higher mean waist circumference in hypertensive patients (98.94±7.31 cm) compared to normotensive subjects (94.03±7.53 cm), with a p-value of 0.082. Although not statistically significant, this trend towards higher waist circumferences in hypertensive pregnant women could reflect central adiposity's role in PIH pathogenesis. This is supported by evidence suggesting that central obesity may contribute more significantly to cardiovascular risk factors, including hypertension, than total body fat [22].

The waist-hip ratio (WHR), a measure of fat distribution, showed no significant difference between the two groups (0.95±0.06 in hypertensive patients vs. 0.94±0.04 in normotensive subjects; p=0.527). This finding indicates that WHR may not be a critical marker for PIH in this specific population, which could reflect the multifactorial nature of PIH where genetic, environmental, and other metabolic factors play a role beyond simple anthropometric measures.

Significantly, the study found marked differences in mean systolic and diastolic blood pressures between hypertensive and normotensive pregnant women. The hypertensive group had a mean systolic blood pressure of 141.76±11.82 mmHg and a mean diastolic blood pressure of 98.43±11.26 mmHg, significantly higher than the normotensive group (116.53±11.31 mmHg systolic and 76.82±6.44 mmHg diastolic, with p-values of 0.007 and 0.003, respectively). These findings are consistent with the diagnostic criteria for PIH and underscore the condition's impact on cardiovascular strain during pregnancy [23].

The current study's findings on BMI and PIH are consistent with those of Buhimschi et al. [24], who found no significant difference in BMI between women with and without PIH in a cohort study. However, the evidence regarding waist circumference and WHR as predictors of PIH remains mixed. Some studies have suggested that these measures of central adiposity may be more closely linked to metabolic syndromes and cardiovascular disease than to PIH specifically [25].

Regarding blood pressure differences, the results align with the established understanding that PIH is characterized by significantly elevated blood pressure levels. These findings are in line with the broader literature, which consistently shows elevated systolic and diastolic blood pressures in PIH cases [26].

Antithrombin-III, a key anticoagulant, plays a critical role in maintaining hemostatic balance. Its reduced activity in PIH suggests an increased risk of thrombosis, which is a concern given the hypercoagulable state of pregnancy [27]. The observed mean AT-III activity of 75.45±6.23% in hypertensive patients versus 96.84±9.64% in normotensive subjects aligns with earlier studies indicating that AT-III activity decreases as pregnancy progresses and this reduction is more pronounced in women with PIH [28]. For instance, a study by Sharma and colleagues [29] found similar reductions in AT-III levels among women with PIH, reinforcing the association between decreased AT-III activity and the pathogenesis of PIH.

The platelet count findings from the study further illuminate the altered coagulation landscape in PIH. With hypertensive patients showing a mean platelet count of 170.90±8.78 x109/L compared to 191.56±6.54 x109/L in normotensive subjects, there's evidence of thrombocytopenia associated with PIH. This is consistent with the literature, where PIH has been linked to a reduction in platelet count, reflecting increased consumption or destruction of platelets, potentially leading to complications like HELLP syndrome (Hemolysis, Elevated Liver enzymes, and Low Platelet count) [30]. A meta-analysis by Haase et al. [31] corroborated these findings, suggesting that thrombocytopenia could serve as an early marker for PIH diagnosis and severity assessment.

When comparing the current study's findings with previous literature, it is evident that the reduced AT-III activity and platelet count in hypertensive pregnant women are consistent with the broader research narrative. However, the magnitudes of these changes and their clinical implications may vary across populations due to genetic, dietary, and environmental factors. For example, studies in different geographical locations have reported varying degrees of reduction in AT-III activity and platelet count among PIH patients [32], indicating the influence of ethnic and regional differences on the hematological manifestations of PIH.

Conclusion

Reduced AT-III activity and lower platelet counts are associated with pregnancy-induced hypertension, suggesting that these parameters could serve as useful markers in the early detection and management of PIH. The study highlights the importance of comprehensive antenatal care and the potential for targeted interventions to mitigate the risks associated with PIH.

Implications And Future Directions

The findings from this study underscore the importance of monitoring AT-III activity and platelet count in pregnant women, particularly those with or at risk of developing PIH. They suggest that targeted interventions aimed at stabilizing these parameters could mitigate the risk of thrombotic events and improve maternal and fetal outcomes. Future research should explore the underlying mechanisms driving the reduction in AT-III activity and platelet count in PIH, with an eye towards developing predictive models for early identification of women at risk. Additionally, longitudinal studies examining the recovery of these parameters postpartum and their long-term health implications would provide valuable insights into the overall impact of PIH on women's health.

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