

Research Article**Association of D-Dimer Levels with Clinical and Laboratory Parameters in Gestational Hypertension: A Comparative Cross-Sectional Study of 80 Pregnant Women****B. P. Singh¹, Shahnaz Bano², Prashant Thakur³**

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Abstract**Introduction**

Gestational hypertension is associated with alterations in maternal hemostasis and can be a precursor of pre-eclampsia. D-dimer is a marker for fibrin formation and degradation and can be indicative of activation of the coagulation-fibrinolytic system. However, the extent of hemostatic alteration in the early stage of gestational hypertension is not well characterized.

Objective

To compare D-dimer and selected hematological and coagulation parameters in women with gestational hypertension and normotensive pregnant women at 20-28 weeks of gestation. To assess variation in D-dimer levels according to maternal age among women with gestational hypertension.

Methods

This comparative cross-sectional study was done in the Department of Pathology and Biochemistry in association with the Department of Obstetrics

and Gynecology, Chhattisgarh Institute of Medical Sciences, Bilaspur, India from January 2024 to June 2025. Eighty pregnant women were recruited. 40 with gestational hypertension and 40 normotensive controls. Clinical assessment and laboratory investigations were complete blood count, coagulation profile, D-dimer, liver and renal function tests. D-dimer was determined by latex-enhanced immunoturbidimetric assay. Student's t test was used for group comparisons, and $p < 0.05$ was considered to be statistically significant.

Results

The mean D-dimer level was significantly higher in women with gestational hypertension compared to normotensive controls (148.6 ± 49.7 versus 121.3 ± 53.2 ng/mL; $p = 0.02$). The gestational hypertension group had a significantly lower platelet count (22.41 ± 6.44 vs 27.20 ± 7.89 lakhs/ μ L; $p = 0.003$). Bleeding time was borderline shorter (3.32 ± 0.94 versus 3.70 ± 0.80 min; $p = 0.05$) while there was no significant difference in clotting time, prothrombin time and activated partial thromboplastin time. In women with gestational hypertension, D-dimer was higher in women of 31–40 years than in women

of 20–30 years (144.5 ± 37.5 vs 121.1 ± 29.4 ng/mL; $p=0.034$).

Conclusions:

Gestational hypertension between 20 and 28 weeks was associated with increased D-dimer levels and decreased platelet count indicating early activation of the coagulation-fibrinolytic system. Older women who developed gestational hypertension also had higher D-dimer levels. Further longitudinal studies are needed to establish whether these abnormalities predict progression to preeclampsia.

Keywords: D-dimer; gestational hypertension; coagulation; platelet count; pregnancy; preeclampsia

Introduction

Hypertensive disorders of pregnancy constitute one of the major causes of maternal and perinatal morbidity and mortality. Gestational hypertension is defined as new-onset hypertension after 20 weeks of gestation in a previously normotensive woman and may progress to preeclampsia, a multisystem disorder associated with endothelial dysfunction, platelet activation and coagulation abnormalities.

Pregnancy itself is a physiological hypercoagulable state. Progressive changes in coagulation and fibrinolysis take place in gestation to protect against hemorrhage at delivery. D-dimer is a breakdown product of cross-linked fibrin. It thus reflects activation of coagulation with subsequent fibrinolysis. Its concentration changes normally with increasing gestational age, so its interpretation in pregnancy is dependent on the gestational age and clinical setting. Normal pregnancy shows wide variation in D-dimer concentrations and further changes in hypertensive pregnancy have been observed. [1-4]

Hypertensive pregnancy Pathophysiology Endothelial dysfunction, platelet activation and disturbances in the coagulation-fibrinolytic system Therefore, increased platelet consumption and changes in markers of coagulation may occur before the clinical presentation of severe preeclampsia. Earlier studies have reported elevated D-dimer levels and platelet parameter abnormalities in pregnancy-induced hypertension and preeclampsia. [5-8]

Several studies have examined D-dimer in preeclampsia, but fewer studies have specifically examined D-dimer and routine coagulation parameters in women with gestational hypertension at an early gestational window of 20 to 28 weeks prior to the development of overt preeclampsia. Therefore, D-dimer, platelet and coagulation parameters were compared between women with gestational hypertension and normotensive pregnant women in this study. Age-related variation in D-dimer in women with gestational hypertension was also evaluated.

Objectives

Primary objective:

To compare D-dimer and coagulation/haematological parameters between women with gestational hypertension and normotensive pregnant women at 20–28 weeks of gestation.

Secondary objective:

To compare D-dimer levels between younger and older age groups among women with gestational hypertension.

Material and Methods

Design and setting of the study

Comparative cross-sectional study Study area: Department of Pathology and Biochemistry in association with the Department of Obstetrics and

Gynecology, Chhattisgarh Institute of Medical Sciences (CIMS), Bilaspur, India. Study period: January 2024 to June 2025. Consecutive sampling was employed.

Population and sample size

The Study calculated the required sample size of about 80 using Epi Info with 80% power and 5% level of significance. The final analytical cohort presented in the Results and Summary consisted of 80 pregnant women equally divided between:

- 40 cases of gestational hypertension
- 40 normotensive pregnant controls

The study clearly indicated that each of the two groups had 40 participants.

Inclusion criteria

Pregnant women with gestational hypertension between 20 and 28 weeks of gestation were enrolled. Normotensive pregnant women at the same gestational window were recruited as controls.

Exclusion criteria included:

preeclampsia, age <18 years, known bleeding disorders, abruptio placentae, grade IV placenta previa, intrauterine death, established disseminated intravascular coagulation, known hypertension, gestational diabetes mellitus, twin pregnancy, liver disease, renal disease, deep-vein thrombosis or history of smoking or premature labor.

Clinical evaluation

The study was explained to the participants in their native language and written informed consent was obtained. Participants were consecutively enrolled. Information on demographic, obstetric, medical and life style

factors was obtained through a structured questionnaire.

Blood pressure was measured after a rest of at least 10 minutes in the sitting position with a standard mercury sphygmomanometer with a cuff of appropriate size. The average was taken after a gap of at least 4 hours between the two readings. Height, weight and body-mass index (BMI) were measured. Clinical examination included looking for signs suggestive of pre-eclampsia.

For the purpose of the study, the operational definition of gestational hypertension was persistent blood pressure $\geq 140/90$ mmHg on at least two occasions ≥ 4 hours apart after 20 weeks of pregnancy in a previously normotensive woman.

Laboratory investigations

The investigations performed at enrollment were:

- FBC (full blood count)
- Platelet count and mean platelet size
- Time to bleeding
- Clotting time of blood
- Prothrombin time (PT)
- Activated partial thromboplastin time (aPTT)
- Tests of hepatic function
- Tests for kidney function
- Uric acid in serum
- Serum Electrolytes
- Urine analysis/protein testing
- D-dimer

Proteinuria was assessed by 24-hour urine collection or spot urine protein/creatinine ratio. Dipstick testing was used for initial screening.

Coagulation tests and D-dimer

Venous blood (5 mL) was collected with minimal venous stasis into tubes containing 3.2% sodium citrate (blood:anticoagulant ratio, 9:1). Samples were processed within an hour. Platelet-poor plasma was prepared by centrifugation at 2500 rpm for 15 min at room temperature and analyzed immediately or stored at -80°C when needed.

PT and aPTT were measured with the use of semi-automatic coagulometer (Coagulable, Micro lab Instruments) with the use of Diagnostica Stago reagents. INR was established by:

$$\text{INR} = (\text{Patient PT} \div \text{Mean normal PT})^{\text{ISI}}$$

Fibrinogen was measured with modified Clauss method and platelet count was measured by an automated hematology analyzer (Sysmex XN-1000). D-dimer was measured using a latex-enhanced immunoturbidimetric assay (STA-Liatest D-Di, Diagnostica Stago) and expressed in ng/mL with a laboratory reference range <500 ng/mL.

Ethical considerations

The study protocol was submitted to and approved by the Institutional Ethics Committee of CIMS, Bilaspur, in accordance with the Declaration of Helsinki and its later amendments, as mentioned in the study. Informed consent was obtained in writing from participants.

Statistical analysis

The data were analyzed using the SPSS version 27 and Microsoft Excel. Continuous variables were described as mean $\pm$ standard deviation, and categorical variables were described as frequency and percentage. Significance was determined using two-tailed Student's t test between groups. A p value <0.05 was taken as statistically significant.

The Study shows aggregate rather than individual level observations, further correlation coefficients or multivariable models between D-dimer and individual clinical/laboratory parameters were not calculated in this manuscript.

Results

Participant characteristics

A total of 80 pregnant women were analysed: 40 with gestational hypertension and 40 normotensive controls. The groups were comparable in age and gestational age. Mean age was 28.63 ± 5.56 years in the gestational hypertension group and 29.50 ± 5.06 years in controls ($p=0.464$). Mean gestational age was 24.10 ± 2.41 and 24.83 ± 2.32 weeks, respectively ($p=0.174$).

Multigravida status was more frequent among women with gestational hypertension (90%) than controls (60%; $p=0.004$). Mean BMI was lower among women with gestational hypertension than controls (23.68 ± 3.41 vs 25.37 ± 3.76 kg/m²; $p=0.039$).

Table 1. Demographic and obstetric characteristics

Parameter	Normotensive (n=40)	Gestational HTN (n=40)	p value
Age, years	29.50 ± 5.06	28.63 ± 5.56	0.464
Gestational age, weeks	24.83 ± 2.32	24.10 ± 2.41	0.174
BMI, kg/m ²	25.37 ± 3.76	23.68 ± 3.41	0.039*

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Multigravida, n (%)	24 (60.0)	36 (90.0)	0.004*
Primigravida, n (%)	16 (40.0)	4 (10.0)	
Housewife, n (%)	23 (57.5)	25 (62.5)	0.648
Working, n (%)	17 (42.5)	15 (37.5)	

*Statistically significant at $p < 0.05$.

Blood pressure

As expected from the study-group definitions, both systolic and diastolic blood pressure were substantially higher in women with gestational hypertension.

Table 2. Comparison of blood pressure

Parameter	Normotensive (n=40)	Gestational HTN (n=40)	<i>p</i> value
Systolic BP, mmHg	113.05±5.89	142.75±3.03	<0.001*
Diastolic BP, mmHg	74.75±3.38	92.25±2.53	<0.001*

*Statistically significant.

Complete blood count

Platelet count was significantly lower in the gestational hypertension group than in controls (22.41±6.44 vs 27.20±7.89 lakhs/ μ L; $p=0.003$). No statistically significant differences were observed for haemoglobin, RBC count, WBC count, MPV, MCV, MCH, MCHC or PCV.

Table 3. Comparison of haematological parameters

Parameter	Normotensive	Gestational HTN	<i>p</i> value
Haemoglobin, g/dL	11.44±1.19	11.75±1.20	0.249
RBC, million/ μ L	4.48±0.65	4.49±0.63	0.972
WBC, cells/ μ L	10455.83±2264.23	10525.65±3151.42	0.910
Platelets, lakhs/ μ L	27.20±7.89	22.41±6.44	0.003*
MPV, fL	9.98±1.56	10.47±1.48	0.154
MCV, fL	88.98±5.96	89.13±6.01	0.911
MCH, pg	29.23±1.76	28.80±1.71	0.277

MCHC, g/dL	34.53±1.26	34.73±1.30	0.487
PCV, %	40.00±3.33	39.65±3.43	0.645

*Statistically significant.

Coagulation profile and D-dimer

The principal finding was a significant increase in D-dimer among women with gestational hypertension. Mean D-dimer was 148.6±49.7 ng/mL compared with 121.3±53.2 ng/mL in controls ($p=0.02$). Bleeding time was borderline shorter in the gestational hypertension group ($p=0.05$), while clotting time, PT and aPTT were not significantly different.

Table 4. Comparison of coagulation profile and D-dimer

Parameter	Normotensive (n=40)	Gestational HTN (n=40)	<i>p</i> value
Bleeding time, min	3.70±0.80	3.32±0.94	0.050
Clotting time, min	6.10±1.24	6.02±1.09	0.767
PT, sec	14.12±1.99	13.50±1.68	0.136
aPTT, sec	34.79±5.00	34.53±4.04	0.804
D-dimer, ng/mL	121.3±53.2	148.6±49.7	0.020*

*Statistically significant.

Liver function tests

No statistically significant differences were observed in total, direct or indirect bilirubin, SGOT, SGPT, alkaline phosphatase, total protein, albumin, globulin or albumin/globulin ratio.

Table 5. Liver function parameters

Parameter	Normotensive	Gestational HTN	<i>p</i> value
Total bilirubin, mg/dL	1.03±0.31	1.02±0.36	0.974
Direct bilirubin, mg/dL	0.31±0.12	0.32±0.13	0.901
Indirect bilirubin, mg/dL	0.71±0.22	0.71±0.26	0.911
SGOT, U/L	43.05±16.72	39.75±17.29	0.388
SGPT, U/L	43.48±19.88	42.10±19.42	0.755
ALP, U/L	167.63±50.23	171.25±49.26	0.745

Total protein, g/dL	7.14±0.56	7.16±0.63	0.881
Albumin, g/dL	4.01±0.46	3.91±0.49	0.350
Globulin, g/dL	3.13±0.72	3.25±0.67	0.442
A/G ratio	1.39±0.54	1.27±0.39	0.260

Renal function and electrolytes

Renal function and electrolyte parameters were comparable between the groups, with no statistically significant differences in blood urea, serum creatinine, uric acid, sodium or potassium.

Table 6. Renal function and electrolyte parameters

Parameter	Normotensive	Gestational HTN	<i>p</i> value
Blood urea, mg/dL	28.15±7.33	30.08±6.93	0.231
Creatinine, mg/dL	0.96±0.30	0.93±0.25	0.656
Uric acid, mg/dL	4.90±1.06	4.86±1.12	0.870
Sodium, mEq/L	139.88±2.90	140.38±2.98	0.450
Potassium, mEq/L	4.39±0.48	4.47±0.54	0.450

D-dimer according to maternal age

Within the gestational hypertension group, women aged 31–40 years had significantly higher D-dimer levels than women aged 20–30 years:

- **20–30 years:** 121.1±29.4 ng/mL
- **31–40 years:** 144.5±37.5 ng/mL
- *p*=0.034

Table 7. D-dimer according to age among gestational hypertension cases

Age group	D-dimer, ng/mL	<i>p</i> value
20–30 years	121.1±29.4	
31–40 years	144.5±37.5	0.034*

*Statistically significant.

Discussion.

We assessed hemostatic parameters in 80 pregnant women (40 with gestational hypertension and 40 normotensive pregnant controls) during the 20–28-week gestational window. The main findings were a significant increase of D-dimer and decrease of platelet count in women with gestational hypertension, while PT and aPTT were largely similar between groups.

Pregnancy induced hypertension and D-dimer

The most important finding was a significantly higher D-dimer concentration in women with gestational hypertension compared to normotensive pregnant women (148.6 ± 49.7 vs 121.3 ± 53.2 ng/mL; $p=0.02$).

D-dimer is a measure of the degradation of cross-linked fibrin, and thus is an indirect measure of activation of coagulation followed by fibrinolysis. Pregnancy itself is associated with progressive activation of hemostatic pathways, but the additional increase seen in gestational hypertension may reflect greater activation of the coagulation–fibrinolytic system.

The current finding is in line with the previous literature cited in the study. Sangeereni et al. found increased D-dimer levels in women with hypertensive pregnancy, with levels >500 ng/mL in approximately 54% of subjects. Liao et al. also showed differences in D-dimer between normotensive and preeclamptic pregnancy, especially in middle aged women.

It is important to point out that the current study is not aimed to define a predictive cut-off for preeclampsia. It was a cross-sectional study, and the data available did not allow for longitudinal analysis of outcomes. The study itself cites the lack of follow-up outcome data as a major limitation.

Platelet count and mean platelet volume (MPV)

The women with gestational hypertension had a significantly reduced platelet count (22.41 ± 6.44 vs 27.20 ± 7.89 lakhs/ μ L; $p=0.003$).

This finding supports the concept that platelet activation and consumption may be linked to the hemostatic changes associated with hypertensive pregnancy. The study also interpreted the lower platelet count as potentially reflecting increased platelet consumption.

MPV was a little higher in the gestational hypertension group but was not significant statistically (10.47 ± 1.48 vs 9.98 ± 1.56 fL; $p=0.154$). Therefore, although the platelet count differs between groups, the data available do not show an independent association between MPV and gestational hypertension.

Routine coagulation tests

Bleeding time was borderline shorter in the gestational hypertension group ($p=0.05$). Clotting time, PT and aPTT did not differ significantly.

It is interesting that there were no significant differences in PT and aPTT despite increased D-dimer. D-dimer reflects fibrin turnover and therefore may indicate changes in coagulation–fibrinolysis earlier or more sensitively than conventional screening coagulation tests. The results are also in line with the study observation that the 20–28-week gestational window may anticipate more pronounced abnormalities in conventional coagulation parameters.

Variation in D-dimer with age

In a secondary analysis, D-dimer was significantly higher in women aged 31–40 years vs women aged 20–30 years in the gestational hypertension group (144.5 ± 37.5 vs 121.1 ± 29.4 ng/mL; $p=0.034$).

This finding is of potential importance because maternal age is known to be an important clinical characteristic in hypertensive pregnancy. However, the current age analysis was done in a relatively small subgroup and should be considered hypothesis-generating rather than evidence for an age-specific diagnostic threshold.

Kidney and liver parameters

Biochemical parameters of liver and renal function were not significantly different between

groups. Serum uric acid and electrolytes were not significantly different, likewise.

These results may suggest that no significant biochemical evidence of hepatic or renal end-organ dysfunction was present in this early gestational time frame. However, the cross-sectional design precludes the determination of whether or not the abnormalities would develop later in pregnancy.

Strengths and Limitations

Strengths

1. Study included both gestational hypertensive and normotensive pregnant controls.
2. Assessment of participants was at a specific gestational age between 20 and 28 weeks.
3. D-dimer was determined by a specific automated assay.
4. Hematological and coagulation parameters were simultaneously assessed.
5. Also, the variation in D-dimer was evaluated in gestational hypertension cases by age.

Limitations

The study was a single center study with a relatively small sample of 80 participants limiting generalizability. The cross-sectional design and assessment at a single gestational window do not allow determination of longitudinal changes or progression from gestational hypertension to preeclampsia. The study further stated that follow-up outcomes such as preeclampsia, eclampsia, HELLP syndrome, preterm birth and maternal/perinatal mortality were not available for analysis.

Figures

Potential confounders such as diet, physical activity, medication use and subclinical coagulation abnormalities were not fully controlled.

The study title/objective also refers to risk for development of preeclampsia, but the available dataset supports an association study rather than a predictive study. To establish predictive utility, a prospective cohort with serial D-dimer measurements and documented pregnancy outcomes would be required.

Conclusion:

Women with gestational hypertension at 20–28 weeks of gestation had significantly higher D-dimer levels and significantly lower platelet counts than normotensive pregnant women. Conventional coagulation parameters including PT and aPTT were generally similar between groups.

Our data suggest that in gestational hypertension, changes in the coagulation-fibrinolytic system may be measurable before biochemical abnormalities of hepatic or renal function become clinically evident. D-dimer was also significantly increased in older women with gestational hypertension.

However, these findings illustrate association and not prediction of progression to preeclampsia. More larger prospective studies with serial measurements and documented maternal and perinatal outcome are needed to identify whether D-dimer can be a clinically useful prognostic biomarker.

Figure 1. Comparison of D-dimer levels

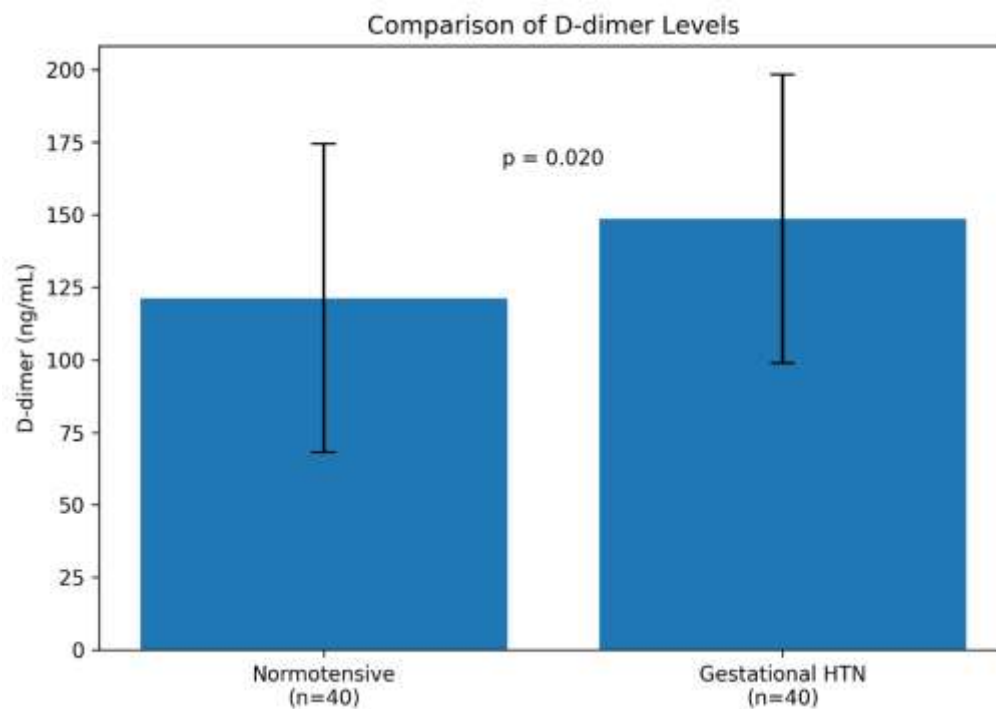


Figure 2. Comparison of platelet count

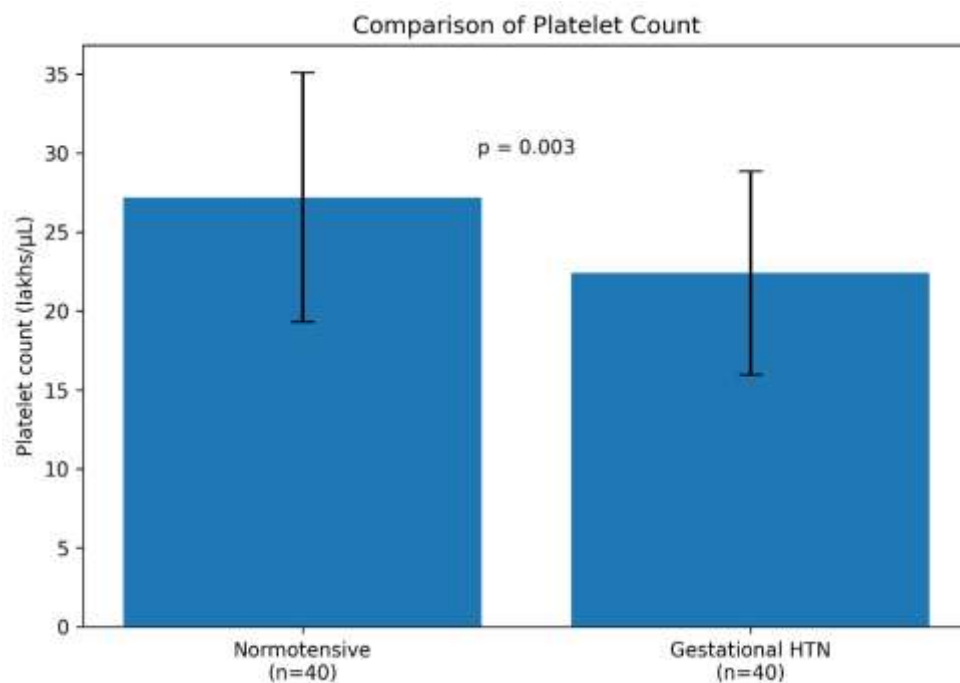


Figure 3. D-dimer according to age in gestational hypertension

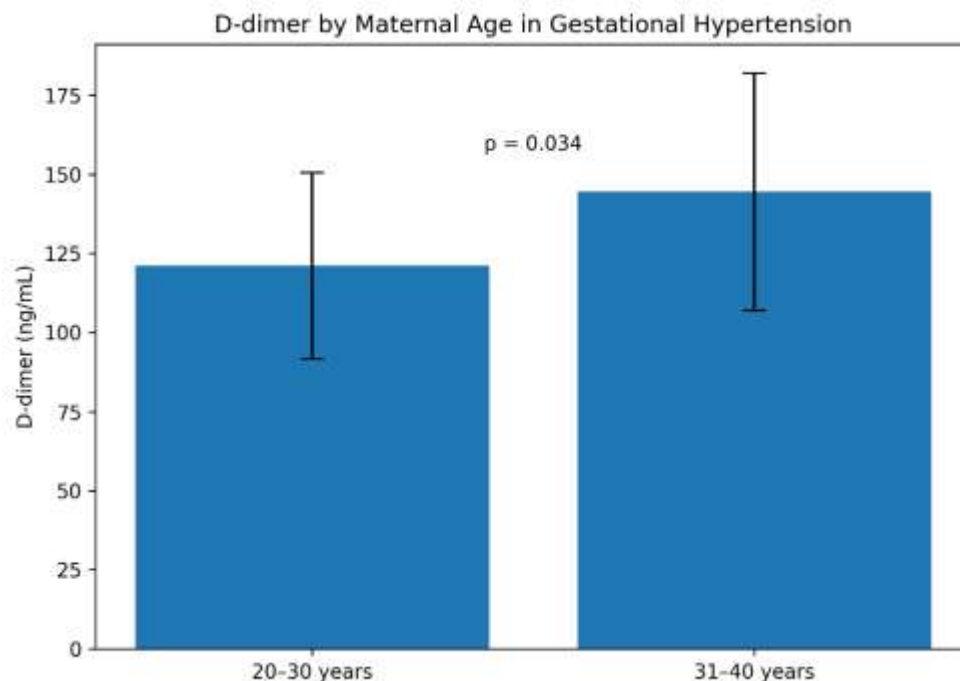
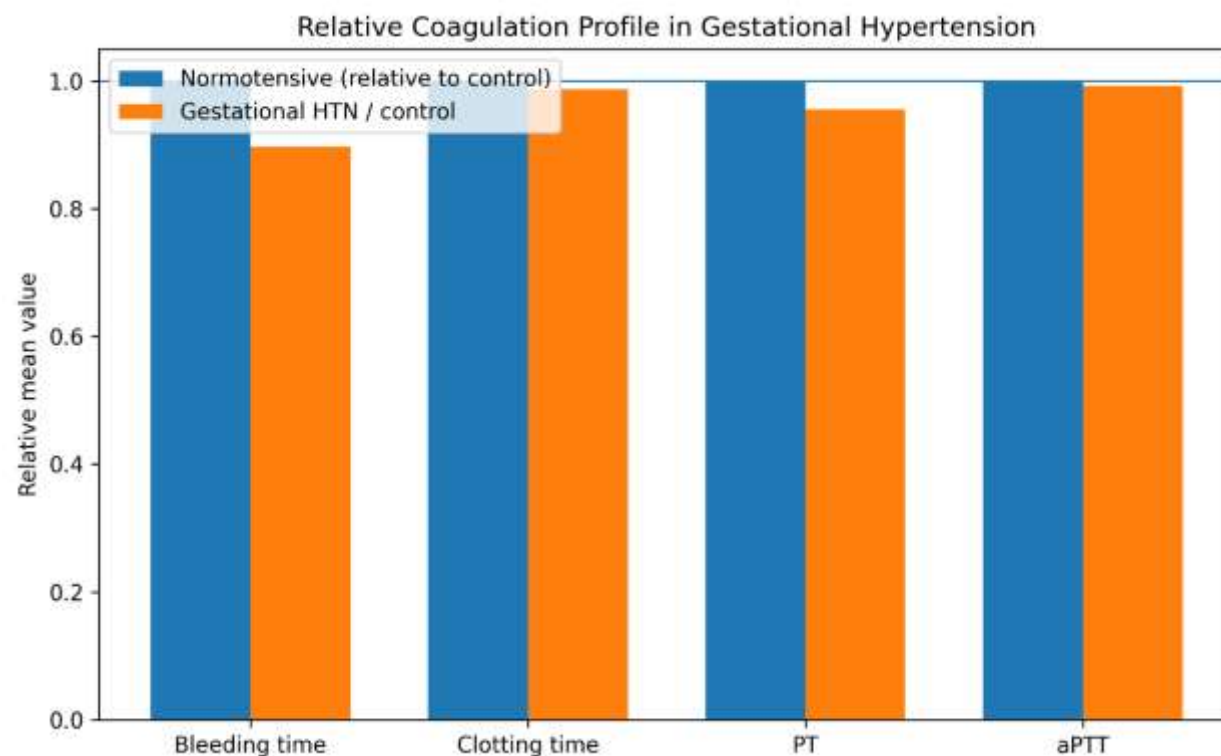


Figure 4. Coagulation profile comparison



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