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# D-Dimer levels at different stages of pregnancy in Australian women: A single centre study using two different immunoturbidimetric assays ☆

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ABSTRACT

*Background:* To date there is minimal data available on D-Dimer levels at different stages of pregnancy.
*Patients and methods:* We prospectively measured D-Dimer levels in 632 consecutive pregnant women from March 2007 to January 2009. The median age of the participants was 31 years (range; 18–42) with a median weight of 78 kilograms (range; 46–137). All subjects were investigated during each trimester with two different immunoturbidimetric assays; D-Dimer PLUS and INNOVANCE D-Dimer. D-Dimer levels were determined using a Sysmex® CA 1500 analyser.
*Results:* Our data demonstrate that D-Dimer levels in pregnancy show different patterns of rise within the first trimester, depending on the assay used; D-Dimer PLUS = 0.88 (SD: mean ratio), INNOVANCE D-Dimer = 0.72 (SD: mean ratio). Furthermore, the rise in mean results was greater for the INNOVANCE D-Dimer assay compared to the D-Dimer PLUS assay as shown by the ratio of third to first trimester results of 3.68 and 1.96 respectively. Both D-Dimer assays demonstrated moderate levels of intra-subject variability, with overall mean CVs of 16.5% (D-Dimer PLUS) and 16.9% (INNOVANCE D-Dimer). Furthermore, we studied the association between D-Dimer levels and occurrence of diseases of pregnancy. For both assays, there was no consistently interpretable evidence of an association between raised mean D-Dimer levels or rising D-Dimer levels and any of the diseases or conditions associated with pregnancy.
*Conclusion:* Our data suggest that the INNOVANCE D-Dimer assay increases significantly with the advancement of pregnancy, and is more sensitive than D-Dimer PLUS assay in the pregnant population.


## Introduction

Pregnancy is a known hyper-coagulable state [1–3]. Fibrin is formed and degraded in many clinical scenarios including infections, tumours, surgery, trauma, burns, bruising, venous thromboembolism, inflammatory diseases, and pregnancy. Thus, a raised D-Dimer level cannot confirm a certain diagnosis due to its low specificity [4–6].

D-Dimer assays generally show variable sensitivity and specificity depending on both the technique and presence of disease. Several studies showed that D-Dimer tests using the turbidimetric technique are highly sensitive (93%), but only moderately specific (51%) for a particular disease [6,7]. While D-Dimer ELISA methods have a pooled similar sensitivity of 94% but with slightly less specificity of 45% in patients with suspected pulmonary embolism [8,9].

Different D-Dimer assays use their own, specific antibodies and standardization. Although this means a systematical difference of values determined within the different assays, method comparisons between assays have an acceptable correlation to VIDAS D-Dimer exclusion assay and to Stratus CS D-dimer assay [7–11]. The different antibodies, techniques or the method of standardization and calibration used in the D-Dimer assays may influence the numerical result of D-Dimer [4–11]. However, as long as the clinical cut-off for the different assays, to be compared, has been evaluated, the concordance of D-Dimer assays should be acceptable. Furthermore, such correlation may be achieved by aligning the standardization.

To date, there are no data available regarding the INNOVANCE assay reference range for pregnant women and its correlation with the D-Dimer PLUS assay. Both assays employ the immunoturbidimetric technique to measure the fibrin degradation end product (D-Dimers) with adequate sensitivity but less specificity [10]. However, the sensitivity and corresponding negative predictive value are generally high.

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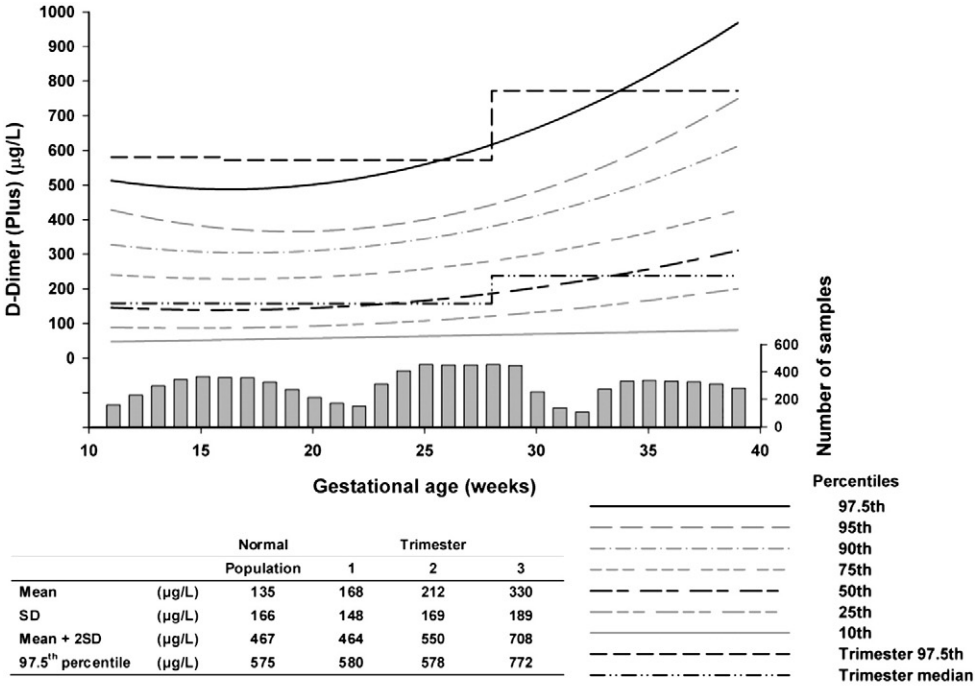
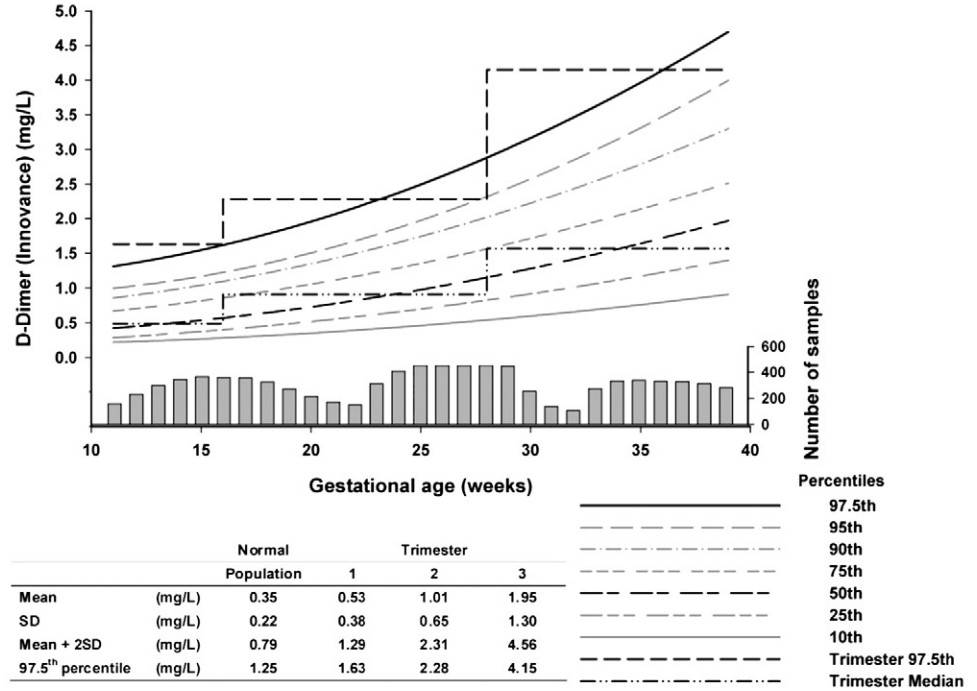



| | | Normal Population | Trimester 1 | 2 | 3 |
|---|---|---|---|---|---|
| Mean | (µg/L) | 135 | 168 | 212 | 330 |
| SD | (µg/L) | 166 | 148 | 169 | 189 |
| Mean + 2SD | (µg/L) | 467 | 464 | 550 | 708 |
| 97.5th percentile | (µg/L) | 575 | 580 | 578 | 772 |




| | | Normal Population | Trimester 1 | 2 | 3 |
|---|---|---|---|---|---|
| Mean | (mg/L) | 0.35 | 0.53 | 1.01 | 1.95 |
| SD | (mg/L) | 0.22 | 0.38 | 0.65 | 1.30 |
| Mean + 2SD | (mg/L) | 0.79 | 1.29 | 2.31 | 4.56 |
| 97.5th percentile | (mg/L) | 1.25 | 1.63 | 2.28 | 4.15 |

**Fig. 1.** Distribution of D-Dimer (DD PLUS and INNOVANCE DD) values during pregnancy.

The test can therefore be used to exclude the presence of venous thromboembolism (VTE) [10–12].

The INNOVANCE D-Dimer assay (Siemens, Marburg Germany) uses a monoclonal antibody (8D3) specific for epitopes contained on the cross linked D-domains of fibrin derivatives [13]. The antibody is covalently linked to polystyrene particles. The reagent also contains a blocking agent to heterophilic antibodies. On reaction with D-Dimer molecules aggregation occurs which can be accurately measured by turbidimetry [14]. The results are given in mg/L FEU (fibrinogen equivalent units). A value of 0.50 mg/L FEU is intended as the decision threshold for exclusion of venous thromboembolism [15].

**Table 1**
Characteristics of patients.

| Variable | Mean (SD) | Range |
|---|---|---|
| Age at recruitment (years) | 28.8 (5.4) | (15.2 - 45.5) |
| Gestation at delivery (weeks) | 39.5 (2.5) | (18.3 - 45.1) |
| Mother's weight at recruitment (kg) | 76.3 (18.3) | (42.0 - 169.0) |
| BMI at recruitment ($kg.m^{-2}$) | 27.1 (6.4) | (17.0 - 55.0) |
| Multiple pregnancies | 6 of 580 | |

The D-Dimer PLUS assay (Siemens, Marburg Germany) employs the same principle as described above but utilises a different monoclonal antibody that targets a different portion (DD5 domain) of the same molecule. The cut-off value for the test is 130 µg/L. The reagent contains no blocking agent to heterophilic antibodies [16].