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PAPP-A predicts GDM in women under 35 but not in advanced maternal age: interaction analysis in7,487 pregnancies

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Objectives

This study aims to determine whether first-trimester PAPP-A predicts GDM differently across maternal age groups using formal interaction analysis, to quantify GDM cases identifiable at aneuploidy screening, and to assess PAPP-A's ability to detect OGCT-missed GDM.

Methods

Retrospective cohort, 7,487 singleton pregnancies at Bilkent City Hospital, Ankara, Turkey (2019–2024). PAPP-A (IU/L), free β-hCG, maternal age, AMA status (≥35 years), and 50g OGCT were analyzed. GDM diagnosis followed IADPSG criteria (75g OGTT). ROC analysis, Mann-Whitney U, logistic regression with PAPP-A×AMA interaction term, and subgroup analyses were performed. Ethical approval was obtained from the Institutional Review Board of Bilkent City Hospital (TABED 2-24-431).

Conclusion

PAPP-A prediction of GDM is formally age-dependent: significant in women <35 but nullified in AMA where age dominates risk. Beyond early detection, PAPP-A identified 85.7% of OGCT-missed GDMcases, demonstrating additive screening value. As this marker is already collected at aneuploidy screening,risk stratification is achievable at zero additional cost.

Results

- GDM prevalence was 4.0% (299/7,487).
- PAPP-A was significantly lower in GDM cases (median 2.10vs 2.59 IU/L; p<0.001).
- Age-stratified analysis revealed a critical interaction: in women <35 years PAPP-A was strongly predictive (GDM+ 2.00 vs GDM- 2.52 IU/L; p<0.001; AUC=0.600), whereas in AMA women (≥35) no predictive value was detected (2.19 vs 2.42 IU/L; p=0.84; AUC=0.507).
- Formal logistic regression confirmed a significant PAPP-A×AMA interaction (OR=1.199; 95%CI 1.044–1.377; p=0.010).
- Tertile analysis (T1: ≤1.89, T2:1.89–3.46, T3: >3.46 IU/L) showed a dose-response in <35 women (T1: 21.8%, T3: 10.0% GDM) but not in AMA (T1: 25.7%, T3: 24.3%).
- At cutoff ≤3.23 IU/L, 76.2% of all GDM cases were identifiable at 11–14 weeks.
- Among 56 women with false-negative 50g OGCT, 85.7% had PAPP-A ≤3.23 IU/L. Free β-hCG was not predictive (p=0.098).

Variable	GDM Diagnosis: No	GDM Diagnosis: Yes	p-value
Age (years)			
Mean ± SD	30.48 ± 5.21	32.66 ± 5.21	<0.001 ^a
Median (Min–Max)	30.00 (18.00–44.00)	33.00 (21.00–44.00)	
AMA status, n (%)			
<35 years	5579 (77.6)	186 (62.2)	<0.001 ^b
≥35 years (AMA)	1609 (22.4)	113 (37.8)	
PAPP-A (IU/L)			
Mean ± SD	3.31 ± 2.59	2.69 ± 2.14	<0.001 ^a
Median (Min–Max)	2.59 (0.11–19.70)	2.10 (0.18–16.20)	
Free β-hCG (IU/L)			
Mean ± SD	44.32 ± 33.66	41.56 ± 31.92	0.098 ^a
Median (Min–Max)	34.70 (4.30–462.00)	31.90 (5.47–287.00)	
50-g OGCT (mg/dL)			
Mean ± SD	115.39 ± 27.87	156.13 ± 27.61	<0.001 ^a
Median (Min–Max)	113.00 (50.00–359.00)	157.00 (71.00–254.00)	
OGCT status, n (%)			
<140 mg/dL	5943 (82.7)	61 (20.4)	<0.001 ^b
≥140 mg/dL	1245 (17.3)	238 (79.6)	
Fasting Glucose Proxy (mg/dL)			
Mean ± SD	73.33 ± 10.34	72.70 ± 11.58	0.220 ^a
Median (Min–Max)	73.00 (20.00–168.00)	72.00 (42.00–169.00)	