Need for pharmacotherapy and perinatal outcomes in gestational diabetes mellitus diagnosed by one abnormal value of IADPSG criteria

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Objective: To evaluate the need for pharmacotherapy (metformin or insulin), the maternal characteristics and perinatal outcomes of women with gestational diabetes mellitus (GDM) diagnosed by one abnormal value (OAV) on a 75-g oral glucose tolerance test (75-g OGTT) according of International Association of the Diabetes and Pregnancy Study Groups (IADPSG) criteria.

Methods: A retrospective cohort was performed by reviewing the electronic medical record of 8,738 pregnant women with 75-g OGTT between January 2018 and December 2022, attending their pregnancy at National Institute of Perinatology Isidro Espinosa de los Reyes, in Mexico City. Universal approach with 75-g OGTT was performed since the first prenatal visit. 687 women with a singleton pregnancy were included and the diagnosis of GDM was made with one abnormal value of glucose between 92-125 mg/dl on fasting, or 1h glucose >180 mg/dl or 2h glucose 153-199 mg/dL on a 75-g OGTT according of IADPSG criteria. Women with multiple pregnancies, with an incomplete medical record, with a diagnosis of pre-gestational diabetes, and with resolution of the pregnancy in another hospital, or with early pregnancy loss were excluded. After the exclusion, in 370 pregnant women medical nutritional therapy was started as part of the initial standard management. Only in women not meeting treatment targets (<95 mg/dL on fasting and <140 mg/dl after meals) or with abnormalities in fetal growth or excessive maternal weight gain, treatment was intensified to include pharmacotherapy as metformin to a maximum dose of 2.5 g daily or insulin.

The results were analyzed according 3 categories, abnormal fasting glucose, 1h and 2h post load. All data were analyzed using SPSS version 21.0 (SPSS Inc, Chicago, IL). Mean ± standard deviation (SD) was reported for continuous variables, and number and percentage were reported for categorical variables. ANOVA and Kruskal-Wallis test were used to compare continuous variables while Pearson's chi-square test and Fisher's exact test were used to analyze categorical variables.
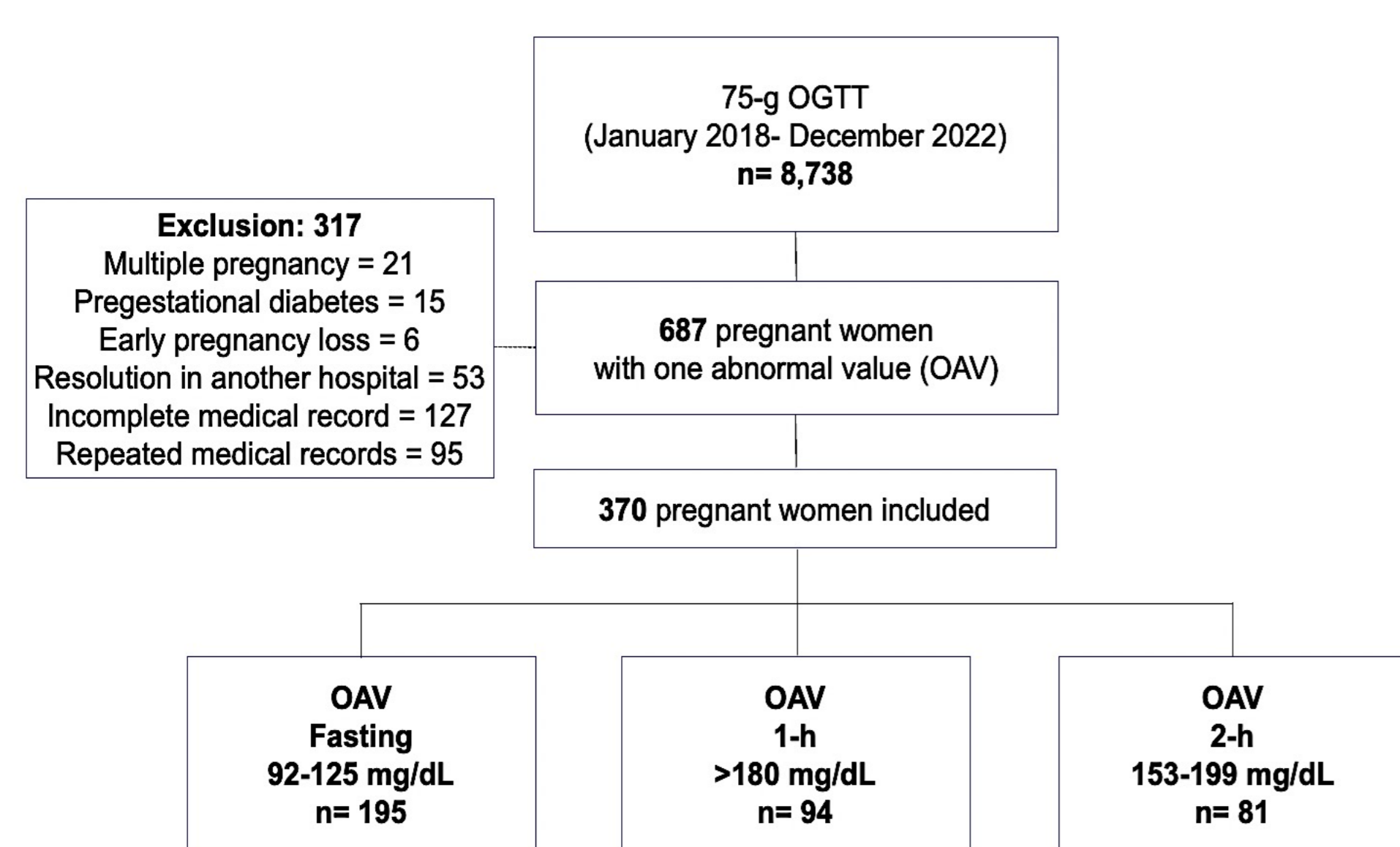

Figure 1. Flowchart of the 75-g OGTT performing universal screening, and the population selection
OAV: One abnormal value

Table 1: Clinical characteristics of pregnant women with one abnormal value (OAV) of IADPSG criteria according with the OGTT results.

	OAV Fasting 92-125 mg/dL n: 195 mean (SD)	OAV 1-h >180 mg/dL n: 94 mean (SD)	OAV 2-h 153-199 mg/dL n: 81 mean (SD)	p value
Maternal age (years)	30.7 (±6.8)	33.2 (±6.3)	33.4 (±6.3)	**0.002**
Pre pregnancy weight (kg)	73.8 (±16.04)	79.8(±85.4)	73.9 (±67.88)	0.657
Pre pregnancy BMI	29.7 (±7.2)	29.1 (±5.07)	27.5 (±5.2)	**0.039**
Gestational age at diagnosis (weeks)	20.8(±7.6)	22.1±6.9	24.5(±6.9)	**0.001**
Gestational weight gain (kg)	7.7 (±6.5)	6 (±6.0)	7.0 (±5.3)	0.481
Fasting glucose (mg/dL)	97.3 (±4.3)	82.8 (±5.9)	80.4 (±7.1)	0.000
1h glucose (mg/dL)	144.2 (±23.3)	191.2 (±11.8)	157.1(±20.7)	0.000
2h glucose (mg/dL)	117.6 (±23.3)	129.6 (±16)	165.9(±13.7)	0.000
HbA1C % 2T	5.26 (±0.38)	5.28 (±0.44)	5.26 (±0.50)	0.991
HbA1C % 3T	5.41 (±0.38)	5.30 (±0.43)	5.36 (±0.37)	0.366

Table 2: Need for pharmacotherapy (metformin or insulin) in women with GDM diagnosed by one abnormal value (OAV) of IADPSG criteria.

	OAV Fasting 92-125 mg/dL n: 195 number (%)	OAV 1-h >180 mg/dL n: 94 number (%)	OAV 2-h 153-199 mg/dL n: 81 number (%)	p value
MNT	156 (80)	70 (74.5)	57 (70.4)	0.198
MNT + Metformin	29 (14.9)	17 (18.1)	16 (19.8)	0.566
MNT + Insulin	2 (1)	2 (2.1)	2 (2.5)	0.622
MNT + Metformin + Insulin	0	2 (2.1)	0	0.052

Results: Women with one abnormal value on fasting were younger 30.7 ±6.8 years (p=0.002), with higher BMI before pregnancy 29.7 ±7.2 (p=0.039) and were diagnosed earlier 20.8±7.6 weeks (p=0.001). Between 70-80% of women diagnosed by one abnormal value of IADPSG criteria required medical nutrition therapy and only 2.1% insulin therapy. There were no differences in the need for pharmacological treatment between categories of abnormalities, however, when compared between those diagnosed before and after 22 weeks of pregnancy (mean 15±3.4 vs 28±3.7weeks) it was found that those diagnosed earlier required more pharmacological intervention with metformin 21.4% vs 12.8% (p=0.027). Regarding the perinatal outcomes, in the group with an abnormal value at 2 hrs, there was a statistically significant difference for a lower fetal weight (p= 0.016), a smaller abdominal circumference (p= 0.042), as well as a lower APGAR at 5 minutes (p= 0.006). In the abnormal fasting glucose group, there was a trend for more admissions to intermediate therapy as well as to the neonatal intensive care unit, without being a statistically significant difference (p= 0.71)

Table 3: Need for pharmacotherapy (metformin or insulin) in women with GDM diagnosed by one abnormal value of IADPSG criteria diagnosed before and after 22 weeks of pregnancy.

	GDM Before 22 weeks n: 173 number (%)	GDM After 22 weeks n:1 97 number (%)	p value
MNT	127 (73.4)	155 (79.1)	0.200
MNT + Metformin	37 (21.4)	25 (12.8)	**0.027**
MNT + Insulin	3 (46.9)	3 (53.1)	0.877
MNT + Metformin + Insulin	1(0.6)	1 (0.5)	0.929

Table 4: Perinatal outcomes of women with GDM diagnosed by one abnormal value of IADPSG criteria.

	Abnormal value Fasting 92-125 mg/dL n: 195	Abnormal value 1h >180 mg/dL n: 94	Abnormal value 2h 153-199 mg/dL n: 81	p value
Fetal weight, Mean (SD)	2440 (718)	2530 (643)	2230 (733)	**0.0163**
Fetal weight percentile, Mean (SD)	44.1 (26.0)	47.8 (27.5)	42.8 (23.7)	0.391
Fetal abdominal circumference, Mean (SD)	298 (53.9)	309 (36.7)	290 (54.2)	**0.0422**
>75th percentile	53 (27.2%)	30 (31.9%)	13 (16.0%)	0.229
Abnormal amniotic fluid	6 (3.1%)	8 (8.5%)	4 (4.9%)	0.141
Large for gestational age	16 (8.2%)	10 (10.6%)	2 (2.5%)	0.372
Gestational age at resolution, Mean (SD)	37.6 (2.27)	37.6 (2.02)	37.5 (2.09)	0.813
Mode of birth				0.186
Vaginal birth	49 (25.1%)	14 (14.9%)	24 (29.6%)	
Forceps	4 (2.1%)	3 (3.2%)	1 (1.2%)	
C-section	142 (72.8%)	76 (80.9%)	56 (69.1%)	
Birth weight, Mean (SD)	2960 (633)	2930 (534)	2830 (620)	0.283
Percentile, Mean (SD)	49.1 (29.7)	53.7 (68.4)	45.0 (29.9)	0.413
Z-score, Mean (SD)	0.497 (7.13)	-0.0220 (1.14)	-0.170 (1.06)	0.553
Newborn Size, Mean (SD)	48.7 (3.48)	48.2 (2.94)	48.1 (3.23)	0.312
APGAR 1 minute, Mean (SD)	7.62 (1.49)	8.02 (0.642)	7.89 (5.16)	0.458
APGAR 5 minute, Mean (SD)	8.88 (0.553)	8.95 (0.308)	8.63 (1.15)	**0.00612**
Silverman Anderson, Mean (SD)	1.13 (0.792)	1.22 (0.912)	1.37 (1.33)	0.191
Permanence of newborn				0.071
Stays with mother	143 (73.3%)	75 (79.8%)	60 (74.1%)	
Neonatal intermediate therapy	29 (14.9%)	6 (6.4%)	8 (9.9%)	
Intermediate care unit	10 (5.1%)	12 (12.8%)	8 (9.9%)	
Neonatal intensive care unit	**11 (5.6%)**	0 (0%)	4 (4.9%)	
Transfer to another hospital	0 (0%)	1 (1.1%)	0 (0%)	
Death	1 (0.5%)	0 (0%)	1 (1.2%)	
Neonatal asphyxia	3 (1.5%)	2 (2.1%)	2 (2.5%)	0.878
Neonatal malformations	7 (3.6%)	4 (4.3%)	4 (4.9%)	0.873
Neonatal hypoglycemia	4 (2.1%)	2 (2.1%)	3 (3.7%)	0.705
Neonatal hyperbilirubinemia	23 (11.8%)	18 (19.1%)	8 (9.9%)	0.137
Mechanic ventilation	13 (6.7%)	1 (1.1%)	3 (3.7%)	0.092
Respiratory distress syndrome	13 (6.7%)	3 (3.2%)	4 (4.9%)	0.456
Transient tachypnea	8 (4.1%)	5 (5.3%)	6 (7.4%)	0.530
Intraventricular hemorrhage	1 (0.5%)	0 (0%)	0 (0%)	0.636
Necrotizing enterocolitis	1 (0.5%)	0 (0%)	1 (1.2%)	0.539
Retinopathy or prematurity	1 (0.5%)	0 (0%)	0 (0%)	0.636
Neonatal death	3 (1.5%)	1 (1.1%)	1 (1.2%)	0.941
Hospitalized days, Mean (SD)	4.70 (9.29)	4.91 (9.64)	7.68 (17.6)	0.143

Conclusion: One abnormal value on fasting is related to a higher pre pregnancy BMI and younger maternal age. No differences were found between categories of OAV on the need of pharmacotherapy. A tendency to a lower fetal weight, a smaller abdominal circumference, as well as a lower APGAR at 5 minutes was observed in the group with an abnormal value at 2 hrs. Those women diagnosed before 22 weeks of pregnancy required more pharmacological intervention with metformin. With earlier triage of patients with GDM, even in the milder form of hyperglycemia, probability-based treatment pathways or requiring pharmacotherapy may optimize patient models of care while reducing unnecessary interventions.

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