

# Predictive Risk Factors for GDM in Mediterranean Women

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# Predictive Risk Factors for GDM in Mediterranean Women

## Rationale



# Prevalence of GDM by Criteria

plasma glucose	WHO	ADA	IADPSG Based on HAPO study
• Fasting	$\geq 7.0$ mmol/l	$\geq 5.3$ mmol/l	$\geq 5.1$ mmol/l
• 1-hour post load	-	$\geq 10.0$ mmol/l	$\geq 10.0$ mmol/l
• 2-hour post load	$\geq 7.8$ mmol/l	$\geq 8.6$ mmol/l	$\geq 8.5$ mmol/l
Study data: Prevalence GDM Population sample = 1368	N = 268 19.59%	N = 119 8.70%	N = 364 26.61%

- **Three-fold increase in identified patients from ADA → IADPSG criteria**

# Implications of using different criteria

- Specificity and sensitivity of the different criteria in correctly diagnosing GDM
- Potential differences in outcomes as a result of using the different criteria to establish a diagnosis of GDM
- Lack of cost-benefit analyses to determine the optimal diagnostic criteria
- Potential impact on healthcare budgets

Given regional differences in  
healthcare provision and variable  
access to OGTT

the identification of high  
risk/affected subjects by universally  
available means is crucial to ensure  
optimal outcomes



# Risk Factors & Outcome Indicators

Risk Factors	
<ul style="list-style-type: none"> <li>• <b>Maternal characteristics</b> <ul style="list-style-type: none"> <li>• Maternal Age</li> <li>• Pre-pregnancy BMI *</li> <li>• BMI in early 3<sup>rd</sup> trimester [at oGTT] *</li> <li>• Blood pressure [systolic/diastolic reading]</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Glycaemic indices</b> <ul style="list-style-type: none"> <li>• FBG &gt;5.0 mmol/l</li> <li>• Area under oGTT curve</li> <li>• HbA1c</li> <li>• Fasting insulin</li> <li>• HOMA-IR</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>• <b>Past Obstetric History</b> <ul style="list-style-type: none"> <li>• P/H macrosomia [BW &gt;4.0 kg]</li> <li>• Parity 4+</li> <li>• Miscarriages 3+</li> <li>• P/H Perinatal loss</li> <li>• P/H malformations</li> </ul> </li> </ul>	<h2>Outcome Indicators</h2>
<ul style="list-style-type: none"> <li>• <b>Family History</b> <ul style="list-style-type: none"> <li>• F/H DM mother</li> <li>• F/H DM father</li> <li>• F/H DM siblings</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Infant indicators</b> <ul style="list-style-type: none"> <li>• Birth weight of term infants &gt;37 weeks</li> <li>• Preterm infants &lt;=36 weeks</li> </ul> </li> </ul>
<ul style="list-style-type: none"> <li>• <b>Reproductive History</b> <ul style="list-style-type: none"> <li>• Irregular menses</li> <li>• Ovulation induction</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Maternal Indicators</b> <ul style="list-style-type: none"> <li>• Hypertensive disease</li> </ul> </li> </ul>

\* Maternal obesity defined as BMI pre-pregnancy >25 kg/m<sup>2</sup> or 3<sup>rd</sup> trimester BMI >30 kg/m<sup>2</sup>



# ADA-GDM Single Biological Risk Factors

Risk factor	Factor Prevalence	ADA GDM	Normal GT	p value	Specificity	Sensitivity
Age $\geq 30$ years	54.5	87	659	<0.0001*	47.2	73.1
pre-preg BMI >25	38.5	60	467	0.008*	62.6	50.4
BMI >30 at 3 <sup>rd</sup> trimester	31.4	56	373	<0.0001*	70.1	47.1
BP diastolic >80	15.6	34	179	<0.0001*	85.7	28.6
BP diastolic >90	2.0	9	19	<0.0001*	98.5	7.6
P/H macrosomia	3.8	11	41	0.004*	96.7	9.2
F/H DM mother	12.5	25	146	0.005*	88.3	21.0
F/H DM father	14.4	25	172	0.046*	86.2	21.0
F/H DM siblings	3.4	13	34	<0.0001*	97.3	10.9
irregular menses	13.2	16	164	0.966	86.9	13.4
ovulation induction	6.4	9	79	0.746	93.7	7.6
Parity 4+	3.9	5	49	0.927	96.1	4.2
Miscarriages 3+	2.0	3	24	0.921	98.1	2.5
P/H perinatal loss	2.9	1	38	0.280	97.0	0.8
P/H malformations	1.4	2	17	0.901	98.6	1.7
FBG >5.0 mmol/l	15.4	88	122	<0.0001*	90.2	73.9
<i>Statistical analysis using Chi Square test</i>	<b>1368</b>	<b>119</b>	<b>1249</b>			

ADA criteria: F  $\geq 5.3$  – 1hr  $\geq 10.0$  – 2hr  $\geq 8.6$  mmol/l  
Two values abnormal

# ADA-GDM Combined Risk Factors

Risk factor	Factor Prevalence	ADA GDM	Normal GT	p value	Specificity	Sensitivity
Maternal obesity: <i>BMI pre-preg &gt;25 or 3<sup>rd</sup> trimester &gt;30</i>	41.9	70	503	<0.0001 *	59.7%	58.8%
Maternal obesity + maternal age >30 years	24.6	50	287	<0.0001 *	77.0%	42.0%
FBG >5.0 mmol/l or Maternal obesity	48.4	97	565	<0.0001 *	54.8%	81.5%
FBG >5.0 mmol/l or (Maternal obesity + maternal age >30 yrs)	34.1	96	370	<0.0001 *	70.4%	80.7%
<b>Total cases</b>	<b>1368</b>	<b>119</b>	<b>1249</b>			

*Statistical analysis using Chi Square test*

ADA criteria: F  $\geq 5.3$  – 1hr  $\geq 10.0$  – 2hr  $\geq 8.6$  mmol/l  
Two values abnormal

## COST-EFFECTIVE SCREENING PROTOCOL

- FBG:  $\geq 5.1$  mmol/l → consider as GDM and manage as such with dietary, physical activity advice & metabolic follow-up [*identifies 74.0% of GDM cases*]
- FBG:  $\leq 5.0$  mmol/l → Aged  $\geq 30$  years and pre-pregnancy BMI  $\geq 25$  kg/m<sup>2</sup> or 3<sup>rd</sup> trimester BMI  $\geq 30$  kg/m<sup>2</sup>
  - Perform a 75 g oGTT [*would be required in 18.7% of population*]
  - Abnormal oGTT managed as GDM [*identifies 6.7% of GDM cases*]
  - Normal oGTT → consider as normal with dietary advice.
- Aged <30 years and pre-pregnancy BMI <25 kg/m<sup>2</sup> or 3<sup>rd</sup> trimester BMI <30 kg/m<sup>2</sup>
  - Consider as normal [*includes 19.3% of GDM cases*]



# Antenatal & Intrapartum Data

Outcomes	Prevalence	GDM	%	Normal GT	%	p value
• Recurrent [x2] fasting glycosuria	3.0	12	10.7	25	2.2	<0.0001*
• Polyhydramnios	1.9	2	1.8	22	1.9	0.92
• Multiple pregnancy	0.8	-	-	10	0.9	0.32
• Hypertension	6.2	10	8.9	68	6.0	0.22
• Premature delivery ≤36wks	9.2	17	15.2	99	8.7	0.04*
• Planned delivery	40.0	52	46.4	451	39.4	0.18
• Mode of delivery						
○ Spontaneous	46.2	50	44.6	530	46.3	
○ Operative vaginal	17.8	16	14.3	208	18.2	
○ Operative abdominal	36.0	46	41.1	406	35.5	0.41
• Shoulder dystocia	0.2	Nil	-	3	0.3	-
Total cases	1251	112		1139		

# Infant Outcomes

	Prevalence	GDM	%	Normal GT	%	p value
• Gender						
○ Male	54.7	70	62.5	619	53.9	
○ Female	45.3	42	37.5	529	46.1	0.10
• Birth weight						
○ <2500 g	6.4	13	11.6	67	5.8	
○ 2500-3999 g	86.0	88	78.6	996	86.8	
○ >4000 g	6.9	11	9.8	76	6.6	
○ unrecorded	0.7	-	-	9	0.8	0.04*
• Congenital malformations	0.8	Nil	-	10	0.9	-
• Low Apgar score 1-6	0.8	Nil	-	10	0.9	-
• Respiratory distress [RDS]	5.0	8	7.1	55	4.8	0.39
• Sepsis	1.4	2	1.8	16	1.4	0.94
• Jaundice	10.2	8	7.2	120	10.5	0.35
• SCBU admission	4.3	8	7.2	46	4.0	0.19
• Infant outcome						
○ Antepartum death	0.5	Nil	-	6	0.5	
○ Neonatal death	0.3	Nil	-	4	0.3	
○ Still alive	99.2	112	100	1139	99.2	0.61
Total infants born	1261	112		1149		

# IADPSG-GDM Single Biological Risk Factors

Risk factor	Factor Prevalence	IADPSG GDM	Normal GT	p value	Specificity	Sensitivity
Age $\geq$ 30 years	54.5	238	508	<0.0001 *	49.4%	65.4%
pre-preg BMI >25	38.5	172	355	0.0001 *	64.6%	47.3%
BMI >30 at 3 <sup>rd</sup> trimester	31.4	155	274	<0.0001 *	72.7%	42.6%
BP diastolic >80	15.6	91	122	<0.0001 *	87.8%	25.0%
BP diastolic >90	2.0	15	13	0.001 *	98.7%	4.1%
P/H macrosomia	3.8	21	31	0.02 *	96.9%	5.8%
F/H DM mother	12.5	71	104	<0.0001 *	89.6%	19.5%
F/H DM father	14.4	76	125	0.0001 *	87.5%	20.9%
F/H DM siblings	3.4	26	21	<0.0001 *	97.9%	7.1%
irregular menses	13.2	61	119	0.02 *	88.1%	16.8%
ovulation induction	6.4	26	62	0.52	93.8%	7.1%
Parity 4+	3.9	17	37	0.41	97.3%	4.7%
Miscarriages 3+	2.0	9	18	0.43	98.2%	2.5%
P/H perinatal loss	2.9	6	33	0.11	96.7%	1.6%
P/H malformations	1.4	6	13	0.62	98.7%	1.6%
FBG >5.0 mmol/l	15.4	210	Nil	<0.0001 *	100.0%	57.7%
<i>Statistical analysis using Chi Square test</i>	1368	364	1004			

IADPSG criteria: F  $\geq$ 5.1 – 1hr  $\geq$ 10.0 – 2hr  $\geq$ 8.5 mmol/l  
Any one value abnormal

# IADPSG-GDM Combined Risk Factors

Risk factor	Factor Prevalence	IADPSG GDM	Normal GT	p value	Specificity	Sensitivity
<b>Maternal obesity:</b> <i>BMI pre-preg &gt;25 or 3<sup>rd</sup> trimester &gt;30</i>	41.9	195	378	<0.0001 *	62.4%	53.6%
<b>Maternal obesity + maternal age &gt;30 years</b>	24.6	134	203	<0.0001 *	79.8%	36.8%
<b>FBG &gt;5.0 mmol/l or Maternal obesity</b>	48.4	285	377	<0.0001 *	62.5%	78.3%
<b>FBG &gt;5.0 mmol/l or (Maternal obesity + maternal age &gt;30 yrs)</b>	34.1	263	203	<0.0001 *	79.8%	72.3%
<b>Total cases</b>	1368	364	1004			

Statistical analysis using Chi Square test

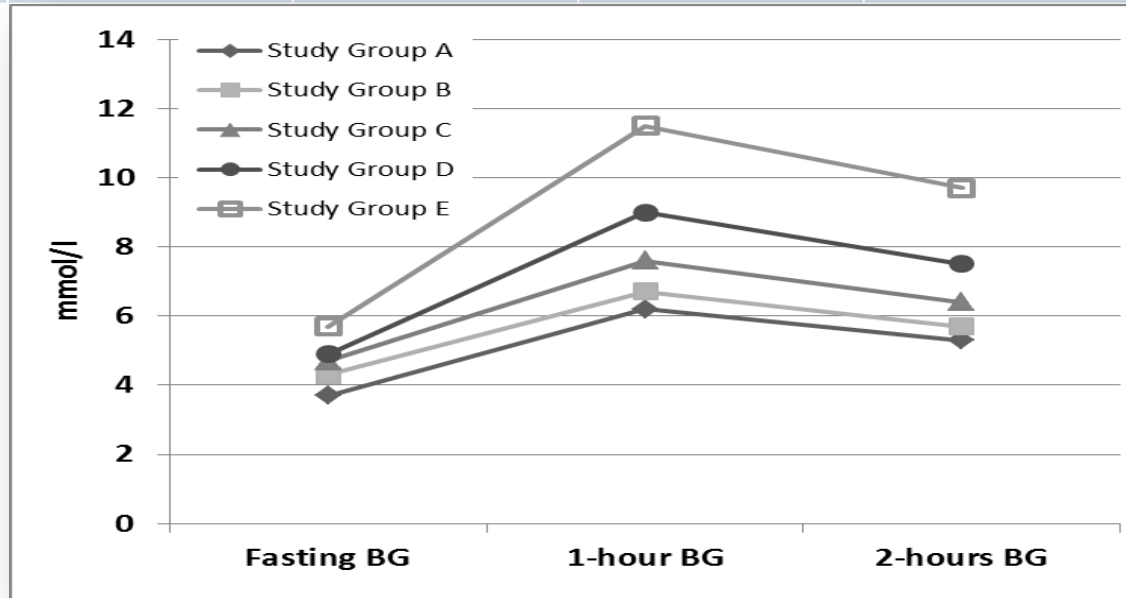
IADPSG criteria: F  $\geq$ 5.1 – 1hr  $\geq$ 10.0 – 2hr  $\geq$ 8.5 mmol/l  
Any one value abnormal

## COST-EFFECTIVE SCREENING PROTOCOL

- FBG:  $\geq$ 5.1 mmol/l → consider as GDM and manage as such with dietary, physical activity advice & metabolic follow-up [*identifies 57.7% of GDM cases*]
- FBG:  $\leq$ 5.0 mmol/l → Aged  $\geq$ 30 years and pre-pregnancy BMI  $\geq$ 25 kg/m<sup>2</sup> or 3<sup>rd</sup> trimester BMI  $\geq$ 30 kg/m<sup>2</sup>
  - Perform a 75 g oGTT [*would be required in 18.7% of population*]
  - Abnormal oGTT managed as GDM [*identifies 14.6% of GDM cases*]
  - Normal oGTT → consider as normal with dietary advice.
- Aged <30 years and pre-pregnancy BMI <25 kg/m<sup>2</sup> or 3<sup>rd</sup> trimester BMI <30 kg/m<sup>2</sup>
  - Consider as normal [*includes 27.7% of GDM cases*]

# Glycaemic subdivisions:

	A	B	C	D	E
<b>FBG</b>	$\leq 4.0$ mmol/l	4.1-4.5 mmol/l	4.6-5.0 mmol/l	$\geq 5.1$ mmol/l	$\geq 5.3$ mmol/l
<b>1hr BG</b>	$\leq 8.9$ mmol/l	9.0-9.4 mmol/l	9.5-9.9 mmol/l	$\geq 10.0$ mmol/l	$\geq 10.0$ mmol/l
<b>2hr BG</b>	$\leq 7.2$ mmol/l	7.3-7.7 mmol/l	7.8-8.4 mmol/l	$\geq 8.5$ mmol/l	$\geq 8.6$ mmol/l
	n = 272 19.9%	n = 418 30.6%	n = 314 23.0%	n = 245 17.9%	n = 199 8.7%
	Low normal GT by IADPSG criteria with all blood glucose values being below the arbitrary set levels	Medium normal GT by IADPSG criteria with all blood glucose values being within the defined range	High normal GT by IADPSG criteria with all blood glucose values being within the define range	Abnormal GT by IADPSG criteria but normal by ADA criteria	Abnormal GT by the ADA criteria with at least two blood glucose values above the defined range



# Glycaemic Indices in the Various Subgroups

Glycaemic indices Mean + s.d. Statistical significance <sup>1</sup>	A	B Significance <sup>2</sup>	C Significance <sup>2</sup>	D Significance <sup>2</sup>	E Significance <sup>2</sup>
<b>Fasting (mmol/l)</b> 4.5 + 0.8; N= 1362 P<0.0001	3.7 ± 0.3 N = 272	4.3 ± 0.2 N = 416 ***	4.7 ± 0.3 N = 314 ***	4.9 ± 0.6 N = 245 ***	5.7 ± 1.5 N = 115 ***
Fasting glucose >5.0 mmol/l	Nil	Nil	Nil	122 49.8%	88 74.0%
<b>1 hour (mmol/l)</b> 7.6 + 2.1; N = 1360 P<0.0001	6.2 ± 1.3 N = 271	6.7 ± 1.3 N = 416 ***	7.6 ± 1.4 N = 314 ***	9.0 ± 1.5 N = 244 ***	11.5 ± 1.8 N = 115 ***
1 hour glucose >9.9 mmol/l	Nil	Nil	Nil	71 29.0%	104 89.4%
<b>2 hour (mmol/l)</b> 6.5 + 1.9; N = 1360 P<0.0001	5.3 ± 1.0 N = 272	5.7 ± 1.1 N = 418 ***	6.4 ± 1.2 N = 314 ***	7.5 ± 1.6 N = 244 ***	9.7 ± 2.6 N = 112 ***
2 hour glucose >8.4 mmol/l	Nil	Nil	Nil	77 31.4%	89 74.8%
<b>Area under the curve</b> 786.7 + 180.3; N = 1354 P<0.0001	639.9 ± 101.2 N = 271	705.1 ± 100.4 N = 414 ***	789.6 ± 102.8 N = 314 ***	914.0 ± 100.6 N = 243 ***	1146.5 ± 190.6 N = 112 ***
<b>HbA1c (%)</b> 5.1 + 0.6; N = 1303 P<0.0001	4.8 ± 0.5 N = 245	4.9 ± 0.5 N = 399 ns	5.1 ± 0.5 N = 304 ***	5.1 ± 0.5 N = 242 ***	5.5 ± 0.9 N = 113 ***
<b>Fasting insulin (uIU/ml)</b> 6.2 + 8.9; N = 1292 P<0.0001	4.7 ± 8.1 <sup>3</sup> N = 246	4.6 ± 4.3 N = 385 ns	6.8 ± 9.6 N = 305 **	7.5 ± 1.7 N = 239 ***	8.7 ± 7.2 N = 116 ***
<b>HOMA-IR (mmol/mIU)</b> 1.3 + 1.8; N = 1290 P<0.0001	0.9 ± 2.4 N = 247	0.9 ± 0.9 N = 383 ns	1.4 ± 2.1 N = 305 **	1.7 ± 1.7 N = 239 ***	2.3 ± 2.0 N = 116 ***

<sup>1</sup> ANOVA One-way analysis of variance; <sup>2</sup> Bonferroni's Multiple Comparison test [ns = not significant, \* = significant, \*\* = very significant, \*\*\* very highly significant]

<sup>3</sup> Excluding one extremely high insulin reading of 177.0 uIU/ml – inclusion of this gives a mean value of 5.4 + 13.6 uIU/ml

# Biological Characteristics by Glycaemic Levels

F  $\geq$ 4.6 – 1hr  $\geq$ 9.5 – 2hr  $\geq$ 7.8 mmol/l

Biological characteristics Mean + s.d. Statistical significance <sup>1</sup>	A	B Significance <sup>2</sup>	C Significance <sup>2</sup>	D Significance <sup>2</sup>	E Significance <sup>2</sup>
Maternal age P<0.0001	28.9 ± 5.6 N = 272	29.5 ± 5.6 N = 418 ns	30.4 ± 5.4 N = 314 **	31.2 ± 5.7 N = 245 ***	32.0 ± 5.0 N = 119 ***
Pre-pregnancy BMI P<0.0001	23.6 ± 4.1 N = 268	24.0 ± 4.4 N = 409 ns	25.1 ± 5.3 N = 304 ***	25.6 ± 5.3 N = 240 ***	26.8 ± 5.8 N = 116 ***
BMI at oGTT in early 3 <sup>rd</sup> trimester P<0.0001	26.5 ± 4.3 N = 271	27.4 ± 4.7 N = 413 ns	28.8 ± 5.2 N = 313 ***	29.5 ± 5.4 N = 244 ***	30.5 ± 5.6 N = 119 ***
Systolic BP P=0.0014	109.9 ± 12.4 N = 271	110.1 ± 12.2 N = 417 ns	111.1 ± 12.3 N = 314 ns	112.9 ± 12.0 N = 244 *	114.2 ± 13.9 N = 119 **
Diastolic BP P<0.0001	64.5 ± 10.3 N = 271	65.8 ± 8.5 N = 417 ns	66.8 ± 8.7 N = 314 *	69.1 ± 9.7 N = 244 ***	71.7 ± 10.2 N = 119 ***
Birth weight of singleton term infants $\geq$ 37 weeks P=0.03	3234.9 ± 435.7 N = 229	3288.9 ± 469.2 N = 351 ns	3350.4 ± 492.5 N = 258 *	3352.2 ± 470.5 N = 195 *	3348.1 ± 515.1 N = 93 ns
Preterm infants $\leq$ 36 weeks	32 12.3%	27 7.1%	18 6.5%	21 9.7%	18 16.2%

<sup>1</sup> ANOVA One-way analysis of variance; <sup>2</sup> Bonferroni's Multiple Comparison test [ns = not significant, \* = significant, \*\* = very significant, \*\*\* very highly significant]

# Biochemical Correlations



	Fasting blood glucose	1-hour blood glucose	2-hour blood glucose	Area under glucose curve
<b>Pre-pregnancy BMI</b>	P = 0.08 R = 0.19 N = 1336	<b>P &lt; 0.0001 *</b> R = 0.21 N = 1332	P = 0.34 R = 0.14 N = 1336	P = 0.91 R = 0.21 N = 1329
<b>HbA1c</b>	<b>P=0.016 *</b> R = 0.37 N = 1305	P = 0.83 R = 0.33 N = 1302	P = 0.59 R = 0.31 N = 1286	P = 0.64 R = 0.36 N = 1299
<b>Fasting insulin</b>	<b>P = 0.001 *</b> R = 0.14 N = 1290	<b>P &lt; 0.0001 *</b> R = 0.14 N = 1286	<b>P &lt; 0.0001 *</b> R = 0.10 N = 1291	P = 0.28 R = 0.14 N = 1284
<b>HOMA-IR</b>	<b>P &lt; 0.0001 *</b> R = 0.27 N = 1290	<b>P &lt; 0.0001 *</b> R = 0.21 N = 1284	<b>P &lt; 0.0001 *</b> R = 0.06 N = 1289	<b>P = 0.002 *</b> R = 0.23 N = 1284
<b>Infant birth weight</b>	P = 0.79 R = 0.05 N = 1239	<b>P &lt; 0.0001 *</b> R = 0.04 N = 1235	P = 0.15 R = 0.07 N = 1239	P = 0.70 R = 0.05 N = 1232

*P = statistical probability; R = Pearson coefficient; N = number of observations*



# Conclusions

The progressive relationship of increasing glycaemia to adverse characteristics suggests that the new IADPSG criteria are reasonable provided that dietary advice is given to all pregnant women.

In situations of economic restraints, it appears possible to screen Mediterranean women for GDM risk by means of a composite model using FBG  $>5.0$  mmol/l combined with the performance of an oGTT in women with a low FBG but who are overweight and aged  $>30$  years.

# Acknowledgements

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*Thank you*

