

# PRECONCEPTIONAL AMINO ACID PROFILING THROUGH NMR METABOLOMICS IN PREDICTION OF GESTATIONAL DIABETES MELLITUS

MD Kristiina Rönö 1, MD PhD Saira B Koivusalo 1, MD PhD Beata Stach-Lempinen 2, MSc PhD Hannu Kautiainen 3,4, Prof Johan G Eriksson 3,5

## 1. INTRODUCTION

Levels of branched chain (BCAA) and aromatic amino acids predict insulin resistance and type 2 diabetes (T2D). Findings from studies focusing upon the relationship between amino acids and risk of gestational diabetes mellitus (GDM) are inconsistent.

## 2. OBJECTIVE

To assess the relationship between amino acid levels before conception and development of GDM in high risk women.

## 4. RESULTS

Baseline characteristics of participants are presented in Table 1. Levels of glutamine, glycine, and tyrosine were higher, and valine and phenylalanine lower in the GDM group before pregnancy (Table 2).

**Table 1 Baseline prepregnancy characteristics of women with normal glucose tolerance (NGT) and gestational diabetes mellitus (GDM) in subsequent pregnancy**

	NGT (n=26)	GDM (n=39)	p
Age (years)	31.3 (4.5)	32.9 (3.9)	NS
BMI (kg/m <sup>2</sup> )	28.8 (6.2)	30.0 (6.2)	NS
History of GDM, n (%)			NS
No	5 (19)	3 (8)	
Yes	18 (69)	33 (85)	
Nulliparous	3 (11)	3 (8)	
Education years	14.2 (1.9)	14.5 (1.8)	NS
Current smoking, n (%)	2 (8)	3 (8)	NS
Fasting plasma glucose (mmol/L)	5.26 (0.34)	5.58 (0.48)	<0.05
Serum insulin (mU/L)	9.25 (10.10)	8.18 (6.45)	NS
HbA <sub>1c</sub> (mmol/mol)	34.5 (3.7)	35.5 (4.6)	NS
HOMA-IR	2.24 (2.59)	2.06 (1.74)	NS
ALAT	17.4 (5.6)	21.3 (15.9)	NS
HDL cholesterol (mmol/L)	1.53 (0.33)	1.40 (0.35)	NS
LDL cholesterol (mmol/L)	2.74 (0.60)	2.82 (0.75)	NS
Total cholesterol (mmol/L)	4.54 (0.64)	4.71 (0.79)	NS
Total triglycerides (mmol/L)	0.73 (0.19)	1.05 (0.55)	<0.05
Nutrition			
Energy, kJ/d	8386 (1913)	7657 (1273)	NS
Total fatty acid, E%	32 (8)	33 (5)	NS
Protein, E%	17 (4)	18 (4)	NS
Carbohydrates, E%	47 (7)	45 (7)	NS
Fiber, E%	2.74 (0.78)	2.90 (0.92)	NS
Saccharides, E%	10.32 (3.57)	9.67 (5.26)	NS
Physical activity, MET min/week	2283 (1889)	1655 (1236)	NS

Data are presented as mean (SD) or median (IQR) unless otherwise indicated  
HbA<sub>1c</sub> = hemoglobin A<sub>1c</sub>; HOMA-IR = Homeostasis model assessment for insulin resistance

## 3. METHODS

Out of sixty-five women with high GDM risk (BMI ≥ 30 kg m<sup>2</sup> and/or prior GDM) and planning pregnancy, 39 developed GDM, and were compared to 26 with normal glucose tolerance (NGT). GDM diagnosis was based on at least one pathologic value at 75 g OGTT performed around 13 and 26 weeks' of gestation (ADA 2008 criteria).

Targeted nuclear magnetic resonance spectroscopy was used to analyze the concentrations of nine amino acids from fasting serum samples at enrollment, on average 3.7 (95% CI 2.8 to 4.6) months before conception.

**Table 2 Serum concentrations (mmol/l) of amino acids in prepregnancy of women with normal glucose tolerance (NGT) and gestational diabetes mellitus (GDM) in subsequent pregnancy**

	NGT n=26	GDM n=39	p*
Alanine	0.339 (0.037)	0.357 (0.043)	0.087
Glutamine	0.432 (0.049)	0.473 (0.061)	0.007
Glycine	0.255 (0.038)	0.293 (0.057)	0.004
Histidine	0.063 (0.007)	0.066 (0.009)	0.23
Isoleucine	0.042 (0.009)	0.045 (0.011)	0.22
Leucine	0.065 (0.009)	0.067 (0.011)	0.51
Valine	0.175 (0.032)	0.160 (0.028)	0.049
Phenylalanine	0.070 (0.006)	0.067 (0.008)	0.045
Tyrosine	0.046 (0.009)	0.050 (0.009)	0.048

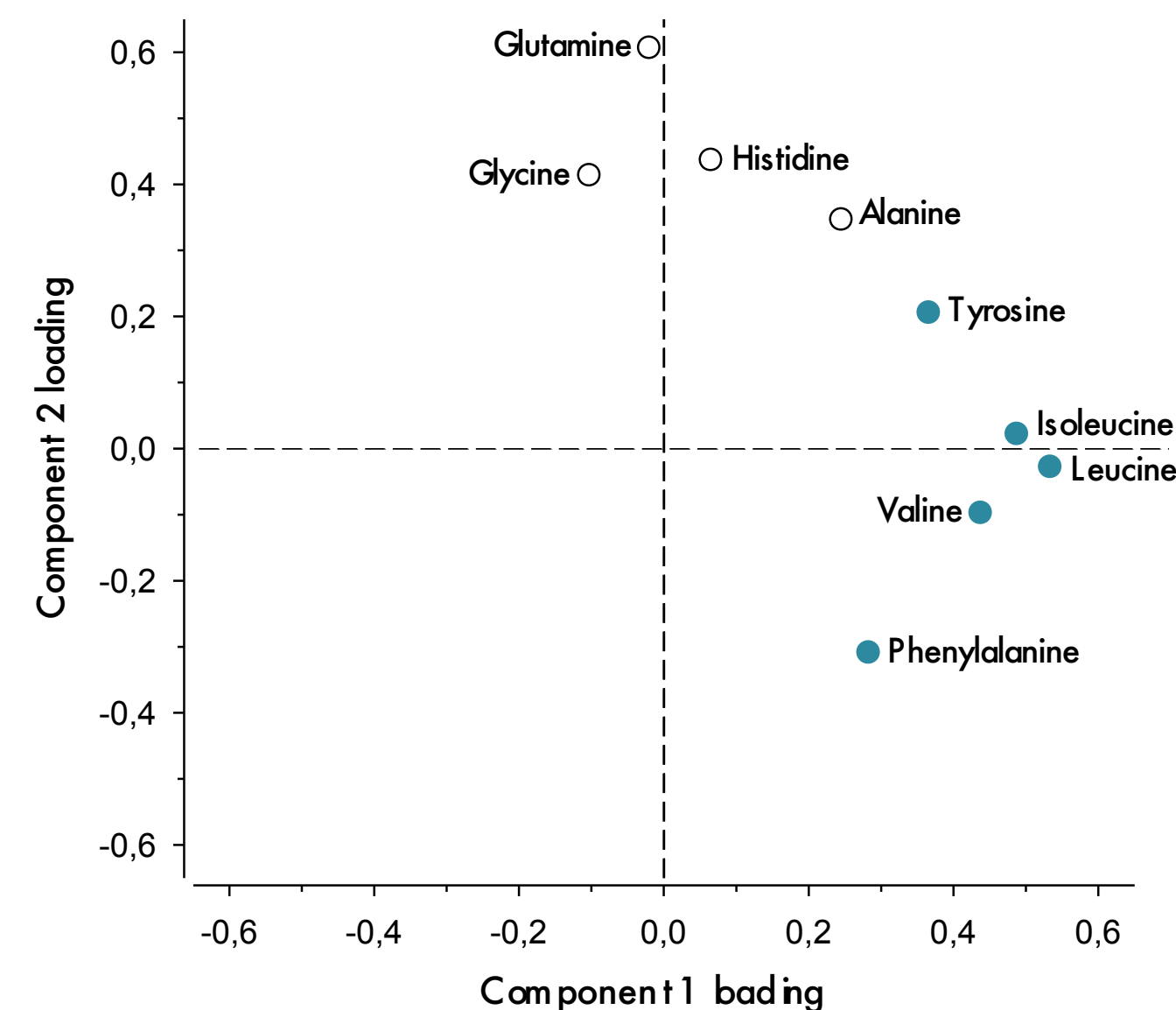
\*permutation type t-test

We performed principal component analysis where component 1 (PC1) included BCAA and aromatic amino acids (isoleucine, leucine, valine, phenylalanine, and tyrosine) and component 2 (PC2) other assessed amino acids (alanine, glutamine, glycine, histidine) (Figure 1).

Adjusted (age, BMI, fasting glucose, and prior GDM) risk for GDM was 5.1 (OR per 1-SD change [95% CI 1.8 to 14.2]) for PC2 and 0.7 (OR per 1-SD change [95% CI 0.3 to 1.7]) for PC1.

1 Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland  
2 Obstetrics and Gynecology, South Karelia Central Hospital, Lappeenranta, Finland  
3 General Practice and Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki, Finland  
4 General Practice and Primary Health Care, University of Eastern Finland, Kuopio, Finland  
5 Folkhälsan Research Centre, Helsinki, Finland

Correspondence:  
MD Kristiina Rönö  
Helsinki University Hospital/Womens Hospital  
P.O. Box 140  
00029 HUS, Finland  
kristiina.rono@helsinki.fi



**Figure 1 Component loadings for Component 1 (teal circles) including branched chain and aromatic amino acids and Component 2 (open circles) including other amino acids.**

## 5. CONCLUSION

In preconception PC2 (alanine, glutamine, glycine, and histidine) but not PC1 (BCAA and aromatic amino acids) is related to higher risk of GDM.

