



EARLY WARNING SIGNS FOR METABOLIC SYNDROME

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Abstract — Chemometrics is the field of science covering the development and application of mathematical and statistical methods to identify important chemical information. It is indispensable in the evaluation of experimental results and suitable for exploration of large data sets. Within the Trans2Care project we intend to apply chemometrics methods in several areas related to the problems explored by the Project partners. In particular we shall investigate transmembrane protein transport mechanism with data-driven modelling approach and also applying biomolecular simulations. We'll combine our theoretical approach with experimental data provided by the Project partners, which will contribute to a better exploration of the available information in biomolecular systems studied, in the research of neurodegenerative diseases, in cardiovascular and pathohistological research. It will also intensify the collaboration, mobility of researchers and exchange of knowledge between partners.

Index Terms — chemometrics, data mining, predictive modelling, transmembrane proteins

1 BACKGROUND

Overweight and obesity are common conditions affecting health in all age and gender group and can lead to development of metabolic syndrome (MetS), a cluster of the medical disorders that increase risk of developing Type 2 Diabetes Mellitus and cardiovascular diseases (CVD). Obesity is associated with inflammation and accompanied by high oxidative status. Indeed, oxidative stress has been associated with adiposity, insulin resistance and MetS, suggesting that oxidative stress could be an early event in the pathology of these chronic diseases. Overweight can be considered as a pre-disease state that can compromise the antioxidant defence system on a long-term basis. From this perspective, low serum concentrations of endogenous antioxidants can be an early sign of disease-prone conditions in apparently healthy asymptomatic middle-aged individuals. Bilirubin, for example, the end product of heme metabolism, is an endogenous antioxidant with anti-inflammatory properties and it has been shown that high bilirubin serum concentrations are associated with increased total antioxidant

capacity, and confer protection against oxidative stress-induced diseases. Indeed, subjects with moderately elevated levels of serum bilirubin, such as those with Gilbert Syndrome, are at decreased risk of CVD.

Serum bilirubin is therefore gaining interest in preventive medicine, because higher serum bilirubin levels are correlated with the reduced cardiovascular disease risk. Thus, measuring serum bilirubin levels might become a predictive biomarker for indicating asymptomatic individuals at increased risk of developing MetS and other chronic oxidative stress induced pathologies.

2 OBJECTIVES

The objective of our study was therefore to evaluate the correlations between total and direct serum bilirubin levels and MetS components and inflammatory markers in asymptomatic healthy overweight individuals.

3 APPROACH & METHODS

General approach

1. Blood collection. 2. Serum preparation. 3. Measuring of total and direct serum bilirubin levels. 4. Perform correlation analysis.

Methods

This is a cross-sectional study involving 96 healthy adults aged 25-45 (64 women and 32 men). All participants underwent standard anthropometrical measurements of body composition, aerobic and anaerobic capabilities assessment, dietary intake evaluation, and fasting serological measurements of direct and total bilirubin, fasting glucose, insulin, total cholesterol, LDL cholesterol, HDL cholesterol, triacylglycerols, and C-reactive protein. Participants were divided in overweight and normal weight groups. Linear correlation analyses were used to examine the association between serum bilirubin levels with all metabolic syndrome risk factor changes.

4 RESULTS

Serum bilirubin levels were lower in healthy overweight individuals of both sexes (Figure 1).

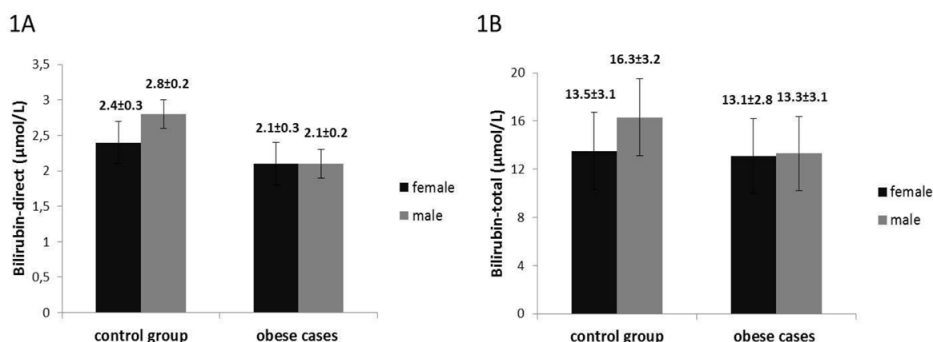


Figure 1: Serum bilirubin levels in normal weight and overweight group for male and female subjects. A direct bilirubin levels. B total bilirubin levels.

Moreover, serum bilirubin levels were negatively associated with abdominal obesity, insulin resistance, fasting glucose, fasting insulin, fasting triacylglycerols, fasting total cholesterol, LDL cholesterol, and C-reactive protein but positively associated with aerobic body capabilities (Figure 2).

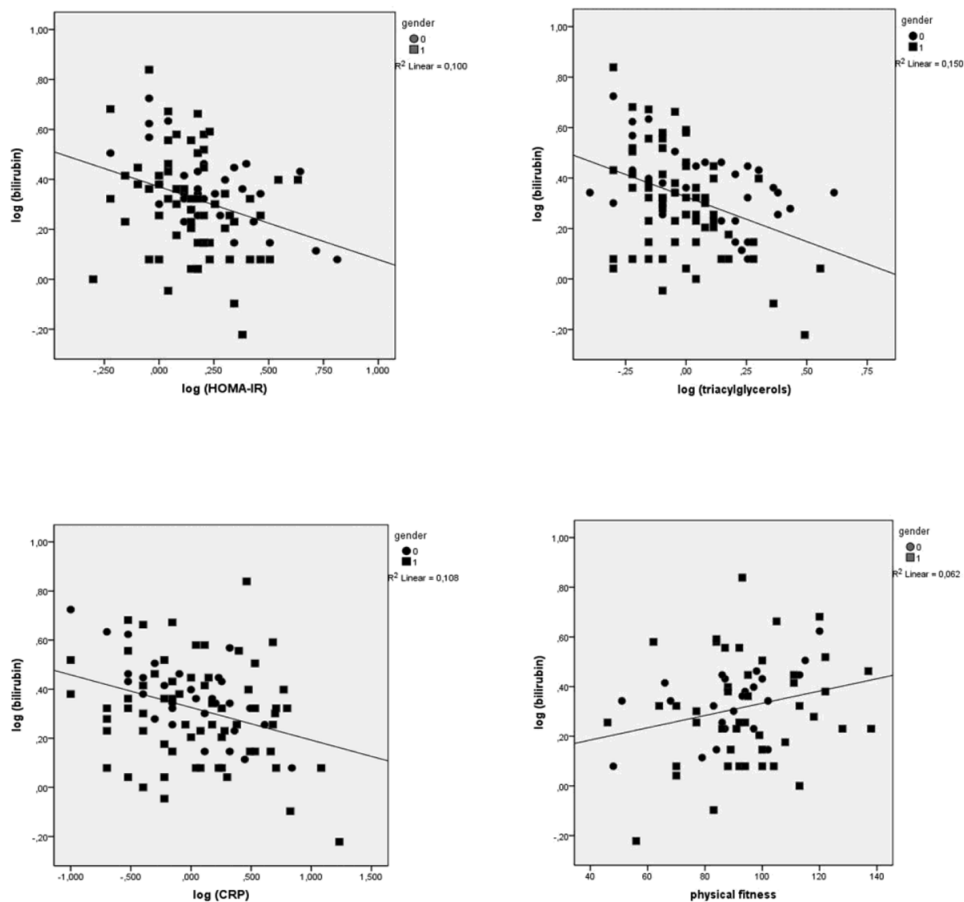


Figure 2: Correlations between total serum bilirubin levels and some of the metabolic syndrome components, CRP, and physical fitness.

Furthermore, the mean values for direct and total bilirubin values decreased with increasing numbers of metabolic syndrome components, in both men and women, as shown in Table 1.

Table 1: Relationship of serum bilirubin levels according to the number of metabolic syndrome components.

	n (%)	Bilirubin-direct	Bilirubin-total
Zero components of MetS			
Male	7 (22 %)	2.96 (0.36)	16.13 (2.10)
Female	24 (37 %)	2.49 (0.22)	14.00 (1.17)
One component of MetS			
Male	9 (28 %)	2.76 (0.38)	15.92 (2.35)
Female	26 (41 %)	2.16 (0.26)	13.16 (1.51)
Two components of MetS			
Male	9 (28 %)	2.21 (0.17)	13.22 (1.10)
Female	10 (16 %)	1.69 (0.27)	11.21 (1.22)
Three and more components of MetS			
Male	7 (22 %)	1.91 (0.23)	12.31 (1.30)
Female	4 (6 %)	1.55 (0.44)	10.20 (1.38)

5 POTENTIAL NEW PRODUCTS & SERVICES

Product: Analysis of serum bilirubin levels can be used as early biomarkers for indicating asymptomatic individuals at increased risk of developing MetS and other chronic oxidative stress induced pathologies.

Service: Analysis of serum bilirubin levels as an early biomarkers for indicating asymptomatic individuals at increased risk of developing MetS and other chronic oxidative stress induced pathologies can be utilized as service for customers such as medical institutions, scientific institutions, SMEs, as well as to general public, which enables highly-motivated individuals to check their blood antioxidant status.

6 CURRENT COLLABORATIONS

6.1 With other researchers

The University of Primorska, Faculty of Health Sciences (PP12, Trans2Care), Universities of Nova Gorica (PP3, Trans2Care), and Trieste (LP, Trans2Care) form a research consortium on bilirubin in biomedical research.

7 CONTACT OR COLLABORATIONS NEEDED

Future collaboration with clinical laboratories is needed.

8 COMMUNICATION TOOLS

This study has been presented to the biomedical community at the University of Primorska (<http://www.trans2care.eu/NewsData.aspx?IdNews=68&ViewType=Old&IdType=390>), University of Ferrara (<http://www.trans2care.eu/NewsData.aspx?IdNews=81&ViewType=Old&IdType=390>), Chemistry towards Biology on 10-13 September 2013 (Trieste, Italy), and 10th Congress of Slovenian Biochemical Society 2013 on 15-18 September 2013 (Ljubljana, Slovenia).

9 FUNDS NEEDED

9.1 For basic research (investigation of biological mechanisms): 25.000 €

9.2 For applied research (solutions for real-world problems): 50.000 €

9.2 For pilot & demonstrator activities (to develop a prototype): 90.000 €

10 CONCLUSION

Analysis of serum bilirubin levels have the potential to be used in the preventive medicine as early biomarker for indicating asymptomatic individuals at increased risk of developing MetS and other chronic oxidative stress pathologies.

ACKNOWLEDGEMENT

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