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Original Article

Association of Test Results for 33 Frequently Used Laboratory Tests with Body Mass Index (BMI)

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ABSTRACT

Once considered a problem only for high-income countries, obesity rates are now rising worldwide. When evaluating test results from obese patients it is important to be aware of the effect of obesity on individual laboratory test results. The aim of the present study was to study the association between body mass index (BMI) and a group of frequently requested laboratory tests to evaluate which of these analytes that are affected by BMI. We analyzed the association between body mass index (BMI) and Alanine aminotransaminase (ALT), Albumin, Alkaline phosphatase, Pancreatic amylase, Apolipoprotein A1, Apolipoprotein B, Apolipoprotein B/Apolipoprotein A1 ratio, Aspartate aminotransferase (AST), AST/ALT ratio, Bilirubin, Calcium, Calprotectin, Cholesterol, HDL-cholesterol, Creatinine kinase (CK), Creatinine, C-reactive protein, Cystatin C, Gamma-glutamyl transferase (GGT), Iron, Iron saturation, Lactate dehydrogenase (LDH), Magnesium, Phosphate, Transferrin, Triglycerides, Urate, Urea, Zink, Hemoglobin, Platelet count and White blood cell count in an 80-year old population (n=531, 266 females and 265 males). There were significant Spearman rank associations between BMI and laboratory test results for several of the studied markers in both females and males. The strongest associations with BMI were noted for ALT, Apolipoprotein A1, HDL-cholesterol, Hemoglobin, CRP, Cystatin C, Triglycerides and Urate. In conclusion, several of the most frequently used laboratory markers are significantly associated with BMI. To be able to correctly interpret a test result it is important to be aware of the effects of BMI on the test results.

Introduction

It is important to have appropriate reference intervals to correctly evaluate a laboratory test result. Reference intervals are based on healthy individuals and they are usually separated according to age and sex and sometimes according to ethnicity [1, 2]. We are not aware of any Swedish laboratory using body mass index (BMI) adjusted reference intervals or using BMI criteria when selecting individuals for establishing reference intervals. Obesity was originally considered as mainly a problem for high-income countries, but the obesity rates are now rising worldwide. The World Health Organization (WHO) defines overweight and obesity based on BMI. The obesity prevalence has increased over the last decades and in 2012 the prevalence of obesity among U.S. adults was 35% [3]. A recent study estimated that 2.1 billion people in the world are overweight [4]. This is a dramatic increase compared to the 857 million estimated in 1980. The increase will most likely continue over the coming years.

Obesity and overweight have many metabolic effects that could influence laboratory test results [5]. When BMI in the population increases, the increase will affect laboratory test results that show associations with BMI. For the doctor that sees an obese patient, it is important to be aware of which markers that are influenced by the obesity to avoid erroneous interpretations of the test results [6]. Such errors could otherwise lead to incorrect diagnosis and treatment.

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The aim of the present study was to study the association between body mass index (BMI) and a group of frequently requested laboratory tests to evaluate which of these analytes that are affected by BMI. The majority of patients seeking health care are elderly individuals. The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study was blood sampled at the age of 80 years and thus representative for an elderly group of individuals.

Methods

I Setting and Participants

The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study cohort consists of elderly individuals living in Uppsala, Sweden. They were originally enrolled when they were 70 years old [7]. The persons were chosen from the community register and invited to participate. The present data is from the reinvestigation of the cohort at the age of 80 years. In total 531 individuals (266 females and 265 males) provided blood samples for this study. Persons with a known diagnosis of diabetes or a fasting glucose value ≥7.0 mmol/L were excluded from this study. The study was approved by the ethics committee of the Faculty of Medicine, Uppsala University, and all participants gave informed consent prior to inclusion. The study was conducted according to the Declaration of Helsinki.

II Clinical and Biochemical Investigation

All blood samples were collected in the morning after an overnight fast. No medication or smoking was allowed after midnight. The whole blood samples were collected in K_2-EDTA tubes (Becton, Dickinson, Franklin Lakes, NJ, USA) and subsequently used for analysis of B-hemoglobin, B-white blood cell and B-platelet counts. The serum samples were collected in Vacutainer® tubes without additives (Becton, Dickinson). The serum samples were centrifuged at room temperature for 20 min at 2010 g. The serum was stored at –80 ° C until analysis.

Alanine aminotransaminase (ALT) (8L92), Albumin (7D54), Alkaline phosphatase (7D55), Pancreatic amylase (6K22), Apolipoprotein A1 (9D92), Apolipoprotein B (9D93), Apolipoprotein B/Apolipoprotein A1 ratio, Aspartate aminotransferase (AST) (8L91), AST/ALT ratio, Bilirubin (6L45), Calcium (3L79), Calprotectin (Gentian, Moss, Norway), Cholesterol (7D62), HDL-cholesterol (3K33), Creatinine (8L24, enzymatic method), Creatinine kinase (7D63), CRP (6K26), Cystatin C (1101, Gentian, Moss, Norway), Gamma-glutamyltransferase (GGT) (7D65), Iron (6K95), Iron saturation, Lactate dehydrogenase (LDH) (2P56), Magnesium (3P68), Phosphate (7D71), Transferrin (1E04), Triglycerides (7D74), Urate (3P39), Urea (7D75), Zink (17255, Sentinel Diagnostics, Milan, Italy), were analyzed on a BS380 instrument (Mindray, Shenzhen, China). The reagents were from Abbott Laboratories, Abbott Park, IL, US if not otherwise specified. Hemoglobin, Platelet count and White blood cell count were analyzed with a CELL-DYN Sapphire Hematology System (Abbott Laboratories).

III Statistical Analysis

Spearman rank correlation was used for associations between BMI and individual markers (Statistica, StatSoft, Tulsa, USA). Mann-Whitney U-test was used to test for differences between individuals with BMI 20-25 and individuals with BMI >30. Considering the number of markers studied we used $p < 0.01$ to define statistically significant difference.

Table 1: Basic characteristics for the persons included in the study (n=531). DBP = diastolic blood pressure; SBP = systolic blood pressure.

	Females	Males
	median (IQR)	median (IQR)
Females/males (number)	266	265
Waist circumference (cm)	93 (86–101)	98 (90–103)
Waist/hip ratio	0.91 (0.86–0.96)	0.97 (0.93–1.01)
DBP (mmHg)	74 (68–78)	74 (68–80)
SBP (mmHg)	148 (136–162)	142 (132–156)
Height (cm)	159.5 (155.5-164)	174 (170-179)
Weight (kg)	67.8 (59.1-76.3)	79.7 (71.9-87.4)
BMI	26.3 (23.4-30.0)	26.4 (24.1-28.8)

Table 2: Spearman Rank associations between body mass index (BMI) and biomarkers for females (n=266).

Analyte	**Spearman R**	**p-value**
Albumin	0.038	0.542
Alkaline phosphatase	0.117	0.057
ALT	0.249	<0.001
Amylase (pancreas)	-0.193	<0.001
Apolipoprotein A1	-0.233	<0.001
Apolipoprotein B	0.084	0.174
Apolipoprotein B/Apolipoprotein A1	0.232	<0.001
AST	-0.06	0.329
AST/ALT ratio	-0.206	<0.001
Bilirubin	-0.062	0.318
Calcium	-0.05	0.419
Calprotectin	0.118	0.056
Cholesterol	-0.059	0.344
HDL-cholesterol	-0.361	<0.001
CK	0.028	0.656
Creatinine	0.167	0.007
CRP	0.21	<0.001
Cystatin C	0.274	<0.001
Gamma-GT	0.121	0.048
Iron	0.049	0.43
Iron saturation	-0.108	0.08
LDH	0.027	0.661
Mg	0.015	0.813
Phosphate	-0.125	0.041
Transferrin	0.031	0.62
Triglycerides	0.329	<0.001
Urate	0.33	<0.001
Urea	0.12	0.051
Zink	0.061	0.319
Hemoglobin	0.203	<0.001
Platelet count	0.046	0.457
White blood cell count	0.179	0.004

Table 3: Spearman Rank associations between body mass index (BMI) and biomarkers for males (n=265).

Analyte	Spearman R	p-value
Albumin	0.027	0.659
Alkaline phosphatase	0.117	0.057
ALT	0.249	<0.001
Amylase (pancreas)	-0.004	0.947
Apolipoprotein A1	-0.269	<0.001
Apolipoprotein B	0.084	0.174
Apolipoprotein B/Apolipoprotein A1	0.232	<0.001
AST	0.016	0.8
AST/ALT ratio	-0.206	<0.001
Bilirubin	0.039	0.527
Calcium	0.072	0.247
Calprotectin	0.143	0.02
Cholesterol	-0.059	0.3443
HDL-cholesterol	-0.361	<0.001
CK	0.136	0.027
Creatinine	0.142	0.022
CRP	0.118	0.056
Cystatin C	0.215	<0.001
Gamma-GT	0.15	0.015
Iron	-0.043	0.489
Iron saturation	-0.108	0.08
LDH	-0.026	0.677
Magnesium	-0.094	0.127
Phosphate	-0.117	0.059
Transferrin	0.135	0.029
Triglycerides	0.329	<0.001
Urate	0.253	<0.001
Urea	0.023	0.706
Zink	0.021	0.735
Hemoglobin	0.203	<0.001
Platelet count	0.046	0.458
White blood cell count	0.179	0.004

Results

I Description of the Study Population

Basic characteristics of the study population are presented in (Table 1). Cardiovascular disease was defined as myocardial infarction, stroke and heart failure.

II Associations Between BMI and Individual Markers in Females and Males

Several of the markers showed significant Spearman rank correlations with BMI (Table 2 & 3). At the p-level of 0.01, the following markers were significantly associated with BMI in females: ALT, pancreas amylase, apolipoprotein A1, Apolipoprotein B/Apolipoprotein A1, AST/ALT ratio, HDL-cholesterol, creatinine, CRP, cystatin C, triglycerides, urate, hemoglobin, and white blood cells. The corresponding Spearman rank correlations for males were: ALT, apolipoprotein A1, apolipoprotein B/apolipoprotein A1 ratio, AST/ALT ratio, HDL-cholesterol, cystatin C, triglycerides, urate, hemoglobin and white blood cells.

III Significant Differences in Laboratory Test Results between Individuals with BMI Over 30 Versus Individuals with BMI of 20-25

There were significant differences between males with BMI > 30 and males with BMI 20-25 for ALT (0.010), AST/ALT ratio (0.005), calprotectin (0.004), cholesterol-HDL (<0.001), creatinine (0.007), cystatin C (0.003), triglycerides (<0.001) and urate (0.008). The corresponding significant differences for females were pancreas amylase (0.009), apolipoprotein A1 (0.001), AST/ALT ratio (0.003), cholesterol-HDL (<0.001). CRP (0.009), cystatin C (<0.001), LPK (<0.001), triglycerides (<0.001) and urate (<0.001).

Discussion

In the present study the mean BMI in the PIVUS cohort at the age of 80 is just above 26. Several of the biomarkers in this study showed a significant association with BMI. During the past decades, the average BMI and the percentage of overweight and obese adults has increased markedly. Traditionally adipose tissue was considered a site for passive storage of triglycerides. Today the adipose tissue is increasingly recognized as an endocrine organ producing mainly proinflammatory cytokines [8, 9]. Adipose tissue may thus contribute to systemic inflammation. Adipose tissue has been reported to produce a large number of cytokines including IL-6 and TNF-alpha [10, 11]. These cytokines induce CRP synthesis in humans. We have previously shown that modest weight reduction in healthy individuals were associated with significant reduction in CRP levels further supporting the association between weight and CRP levels [12]. In this study we show a clear association between CRP levels and BMI, most likely mediated by adipose tissue cytokine production. CRP is an acute phase protein. Increased levels of CRP have been associated with cardiovascular disease (CVD) and atherosclerosis [13, 14].

A general atherosclerosis in the body, associated with increased cardiovascular mortality, also involves the kidneys leading to reduced glomerular filtration rate and increased levels of cystatin C [15, 16]. Chronic inflammation is also known to cause anemia. The inflammation interferes with the red blood cells ability to absorb and use iron efficiently. Also, the inflammatory process also inhibits the function of erythropoietin (EPO), a hormone that stimulates bone marrow to produce red blood cells. These effects will lead to reduced number of red blood cells and reduced hemoglobin values. ALT is a marker for liver damage and is often used as a surrogate marker for nonalcoholic fatty liver disease. Previous studies have found an association between obesity and elevated ALT levels [6]. Elevated urate is associated with the metabolic syndrome and obesity [17]. There are also reports on associations between BMI, triglycerides, Apolipoprotein A1, and HDL-cholesterol. Previous studies have mainly focused on the relationship between BMI and laboratory test results in younger individuals (< 75 years of age). In this study we show clear associations between BMI and laboratory test results in a fairly large elderly population (80 years of age). The included patients are representative for elderly people. In the

present study the mean BMI in the PIVUS cohort at the age of 80 is just above 26. Several of the biomarkers in this study showed a significant association with BMI and significant differences between individuals with BMI 20-25 and >30.

Conclusion

During the past decades, the average BMI and the percentage of overweight and obese adults has increased markedly. This will lead to increased number of patients with skewed test results due to the association between BMI and lab results. It is important that the doctor is aware of these associations when reviewing laboratory test results.

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Conflicts of Interest

None.

Competing Interests

None

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Ethical Approval

The ethics committee of the Faculty of Medicine, Uppsala University approved the study. Ethical approval 01-367.

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