

## ORIGINAL ARTICLE

# Albuminuria and Glomerular Filtration in Patients with Essential Hypertension

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### SUMMARY

**Background:** Essential hypertension (EH) is a widespread disease. One frequent complication of EH is Chronic Kidney Disease (CKD), whose diagnosis is delayed due to its asymptomatic course. The purpose of this study is to determine the involvement of the kidneys in patients with EH by biomarkers for kidney damage (albuminuria) and glomerular filtration rate (GFR) with creatinine and cystatin C.

**Methods:** We observed a control group of 153 healthy volunteers and a group of 150 patients with EH. The biomarkers we tested were urinary albumin, ACR, total protein, and PCR. The GFR was calculated by the CKD-EPI formula using creatinine simultaneously and by the combined formula CKD-EPI using creatinine and cystatin C.

**Results:** The obtained results for the studied biomarkers in the control group are similar to the ones reported in the literature. In the group of patients with EH (at the time of study none of which had been diagnosed with CKD) we observed albuminuria A2 in 59 of the patients (39.9%) and none with albuminuria A3; increased ACR in 60 patients (40%); PCR above reference range in 42 patients (28%). GFRR was  $< 60 \text{ mL/min/1.73 m}^2$  in 13 patients (8.6%).

**Conclusions:** These results show that albuminuria A2 and ACR are sensitive, while GFR is a specific biomarker for kidney damage. For patients with EH, a timely follow-up of these biomarkers is necessary in order to decrease the progression of the kidney damage to Chronic Kidney Failure, cardiac complications, and premature mortality. (Clin. Lab. 2015;61:677-685. DOI: 10.7754/Clin.Lab.2014.141121)

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#### KEY WORDS

essential hypertension, CKD, albuminuria, glomerular filtration rate, cystatin C, creatinine

#### INTRODUCTION

Essential hypertension (EH), also known as primary or idiopathic hypertension, is the most common type of hypertension representing 90 - 95% of all hypertension cases. It tends to be familial and is likely to be the consequence of an interaction between environmental factors and genetic factors (over 50) [1]. To date, hypertension affects over one billion people around the world. This significantly increases the risk of brain, cardiac, and kidney diseases.

Manuscript accepted December 18, 2014

*Original Research Article*

## Diagnostic value of homocysteine and albumin in dialysis patients

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**Abstract**

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Circulating homocysteine is often elevated in chronic kidney disease and end-stage renal disease (ESRD) patients. Hyperhomocysteinemia is a risk factor for cardiovascular disease (CVD). Serum albumin is usually decreased in these patients. **Methods:** We measured serum homocysteine and albumin concentration on a biochemistry auto analyser Cobas Integra 400 at the clinical laboratory of University Hospital – Pleven. To determine serum albumin and homocysteine we used the Roche assay test. Using ROC analysis we evaluated the sensitivity and specificity for each parameter - for homocysteine sensitivity - 62.5% and specificity - 55.8% for the albumin, the sensitivity is 69.2%, and specificity - 68.8%. The area under the ROC standard was defined too. (AUC) - coefficients for cardiovascular accident. Respectively AUC (homocysteine) is 0.632 and AUC (albumin) is 0.757. Using a statistical program we managed to compose the relation of cardiovascular disease by logistic regression. The results of our study show that serum albumin, and homocysteine may be considered as useful and important laboratory parameters for assessing the risk of vascular disease in patients on hemodialysis. Both indicators can be used as predictors of vascular risk in patients on dialysis.

**Keywords:** Albumin, Cardiovascular disease, Chronic Kidney Disease (CKD), Homocysteine

### INTRODUCTION

Homocysteine (Hcy) is a sulfur-containing amino acid and it is a mediate product in the metabolism of methionine. Methionine is a powerful antioxidant that neutralizes free radicals in the body that are formed by the action of a number of toxic or inflammatory agents and it has anti-sclerosis effect. Many studies suggest that this amino acid has a favorable effect on the lipid metabolism and it lowers cholesterol. For this transformation in the body are needed folic acid and vitamins B, vitamin B12 / cobalamin / vit. B6 / pyridoxine / vit. V2 and riboflavin. Violations in the balance of the formation and removal of homocysteine could lead to changes in its plasma concentrations.

In the overall population the slightly increased plasma levels of total homocysteine (tHcy) are associated with increased cardiovascular risk (Danesh and Lewington, 1998; Homocysteine Studies Collaboration, 2002; Wald et al., 2002). The normal range of tHcy is 3-15  $\mu\text{mol} / \text{l}$

but many factors can influence this level (Refsum et al., 2004). Except for nutritional vitamins deficiencies, genetic renal sparsity is one of the most common reasons for the clinical hyperhomocysteinemia. Patients with endstage of renal disease (ESRD) typically have 2-3 ways higher levels of tHcy. Pervasion of hyperhomocysteinemia in this exact patient group is over 90% (Suliman et al., 2002; Suliman et al., 2000; van Guldener et al., 1998). Although some processes may explain the correlation between renal function and higher plasma concentrations of tHcy, the exact mechanism is not yet fully clear.

Several studies have demonstrated the link between high levels of tHcy and the risk of vascular disease in the general population. Other studies have reported a link between high levels of tHcy in patients with chronic renal impairment and increased mortality or the risk of cardiovascular disease (Chauveau et al., 1993; Bachmann et al., 1995; Robinson et al., 1996; Jungers et

# The Role of Homocysteine and Other Clinical Laboratory Markers in Assessing Cardiovascular Risk in Patients on Hemodialysis

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**Abstract:** Cardiovascular diseases constitute approximately 50% of deaths among dialysis patients in the USA and Europe. The increase in traditional and nontraditional cardiovascular risk factors in determining the high mortality of patients with end-stage renal disease (ESRD) is complicated due to the high frequency of risk factors in these patients. Some laboratory markers like homocysteine, albumin, cholesterol, triglycerides, LDL-cholesterol, and creatinine could be efficient in marking the risk of cardiovascular disease in these patients. We use Roche assay tests, based on routinely principles to determine this laboratory parameters used in the clinical laboratory. All laboratory parameters we measured on a biochemistry auto analyser Cobas Integra 400 at the clinical laboratory of University Hospital—Pleven. Using a statistical program a research was done on the quantitative characteristics and prognostic capabilities of homocysteine and other biochemical parameters. We determined the diagnostic specificity and sensitivity of our lab performance against vascular disease (heart attack or stroke) by ROC curves. For each of the observed values of biochemical parameters we calculated the diagnostic sensitivity and specificity. The threshold values for which the parameters have the highest sensitivity and specificity have been concluded. Summary of diagnostic value of parameters to judge the coefficient AUC—area under the curve, for cholesterol, LDL, triglycerides, albumin, it was a significant ( $P < 0.05$ ). Homocysteine and the rest of the studied by us laboratory parameters can be regarded as laboratory markers of choice for assessing the risk of heart attack or stroke in patients on dialysis.

**Key words:** Homocysteine, albumin, end-stage renal disease, cardiovascular risk factors.

## 1. Introduction

Cardiovascular diseases form approximately 50% of deaths among dialysis patients in the USA and Europe [1]. The increase in traditional and nontraditional cardiovascular risk factors in determining the high mortality of patients with end-stage renal disease (ESRD) is complicated due to the high frequency of risk factors in these patients [2]. Hyperhomocysteinemia is seen as a cardiovascular risk factor in patients with chronic renal damage [3] and the issue is analyzed in several studies [4-12]. In relation to this, the observation that plasma homocysteine level (Hcy) is independently connected to the aortic injury [13], and left ventricular hypertrophy [14] are of particular interest. However,

with the exception of research Bostom et al. [15] and Moustapha et al. [16] in a total of 240 patients there is a lack of connection between hyperhomocysteinemia and cardiovascular mortality in hemodialysis patients. The issue is mainly important because a recent study probed that the reduced concentration of plasma homocysteine, but not hyperhomocysteinemia, predicts reducing of the risk of vascular events [17].

The elevated Hcy shows atherogenic and prothrombotic properties and histopathologic features of Hcy induced vascular damage. It is included thickening of the intimal disruption elastic layer vascular smooth muscle hypertrophy, marked accumulation of platelets and the formation of platelet-enriched blood clots. The role of homocysteine in coronary heart disease and stroke is not yet fully understood. In some randomized studies

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# Serum Adenosine Deaminase Values In Healthy People

Journal of Bioscience & Biomedical Engineering

Short Communication

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Submitted : 10 Jun 2020 ; Published : 29 Jun 2020

## Summary

The purpose of this study is to determine the activity of serum adenosine deaminase (ADA) in healthy people, in connection with significant differences in published reference ranges from different authors.

In our study, we examined 160 healthy subjects aged 18 to 84, of whom 64 were men and 96 women. We have determined serum adenosine deaminase levels using a method based on the ability of the enzyme adenosine deaminase to catalyze the deamination of adenosine to inosine and ammonia. The catalytic concentration is determined spectrophotometrically by the rate of reduction of NADH measured at 340 nm.

We found that normal serum ADA values among our healthy subjects are higher than the recommended reference range for the method we use, namely below 18 U / l. Using the percentile method, we worked out the following reference ranges: for women 14.53 - 25.73 U / l and for men 18.46 - 27.50 U / l. For women, the mean value is 21.07 U / l, and for men 21.30 U / l. At 95% CI, the serum ADA values of almost all subjects included in the study are within the recommended and other authors range of 11.50 - 25.00 U / l.

## Introduction

Adenosine deaminase (ADA) is an enzyme involved in purine metabolism. This enzyme is needed for the secretion of adenosine from food and for the exchange of nucleic acids in tissues. Its main function in people is the development and maintenance of the immune system. ADA is considered to be one of the major enzymes of purine metabolism. Adenosine deaminase deficiency leads to pulmonary fibrosis, suggesting that chronic exposure to high levels of adenosine may

exacerbate inflammatory reactions instead of suppress them [1,2].

Using the high activity of the enzyme in diseases with stimulated cellular immunity, such as tuberculosis, the study and report of elevated ADA values significantly above 20 U/L contributes to the diagnosis of tuberculosis and especially to tuberculous pleurisy and meningitis [3,4]. Serum ADA levels can be measured using high performance liquid chromatography, enzymatic or colorimetric techniques.

## Purpose

The aim of our study was to determine the activity of adenosine deaminase (ADA) in the serum of healthy individuals, due to the significant differences in the published reference ranges by different authors.

## Patients and Methods

In our study, we examined 160 healthy individuals aged 18 to 84 years, of whom 64 were men and 96 were women. Serum levels of adenosine deaminase were determined by a method, based on the enzyme's ability to catalyze the deamination of adenosine to inosine and ammonia. The catalytic concentration was determined spectrophotometrically by the NADH reduction rate measured at 340 nm.

## Discussion

We found that the normal serum ADA values in the healthy individuals we studied were higher than the recommended reference ranges for the method we used, namely below 18

# Laboratory Diagnosis of Bacterial Meningitis in a Patient with COVID-19

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**How to cite this paper:** Gencheva-Angelova, I.I. (2021) Laboratory Diagnosis of Bacterial Meningitis in a Patient with COVID-19. *Journal of Biosciences and Medicines*, 9, 110-115.

<https://doi.org/10.4236/jbm.2021.94008>

**Received:** March 17, 2021

**Accepted:** April 17, 2021

**Published:** April 20, 2021

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## Abstract

Against the background of a COVID-19 infection, the overlap of bacterial coinfection is associated with an increased risk of poor treatment outcomes. A 76-year-old man was treated for ischemic stroke in the period of one week. During his hospital stay, he showed symptoms of a viral infection, due to which a PCR sample was taken for SARS-CoV-2. The test result was positive. Meningoencephalitis is suspected on the basis of the clinical symptoms shown and the initial blood test. *K. pneumonia* was detected by a cerebrospinal fluid (CSF) microbiological examination. The risk of bacterial coinfection with COVID-19 remains unclear. Timely and rapid diagnosis and treatment of bacterial meningitis, in the context of a proven COVID-19 infection, require a variety of biological tests and a multidisciplinary approach. In the early stages of acute bacterial and viral meningitis, the signs and symptoms are often nonspecific and it is not always possible to make a differential diagnosis. Laboratory tests, characterizing COVID-19, should determine the type, prognosis, and outcome of a bacterial coinfection. Refining the laboratory diagnosis of a bacterial infection with COVID-19 is a new challenge for doctors.

## Keywords

Meningitis, Laboratory, Prognosis, CSF, COVID-19

## 1. Introduction

With the spread of the COVID-19 pandemic, reports of bacterial coinfection in sick patients have become more frequent. Its manifestation can be considered as a direct impact of the virus on target organs and systems in humans. There have been reports of some patients developing meningitis due to various bacteria, such as *N. meningitides* [1] [2] [3]. Diagnosing and treating patients with a highly contagious infection, such as COVID-19, is not easy [4] [5].

# КОМПЮТЪРНО ИЗЧИСЛЕНА СКОРОСТ НА ГЛОМЕРУЛНАТА ФИЛТРАЦИЯ И ИНДЕКС НА ТЕЛЕСНА МАСА

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## COMPUTER – CALCULATED GLOMERULAR FILTRATION RATE AND BODILY MASS INDEX

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### ABSTRACT:

At the MDCL of UMHAT – Pleven the glomerular filtration rate (GFR) is being calculated by both the Cockcroft – Gault formula and the modified one regarding diet – MDRD.

The influence of changes in bodily mass as well as in GFR values is being studied. Through either of both calculators CFR has been calculated both for patients with normal BMI and such with a pathological one.

Among the studied groups a statistically significant difference is found in the group of men with a pathological BMI and with a serum creatinine above the referential rank ( $p=0.04$ ).

The data obtained so far confirm the higher predictability of the modified formula with patients indicative of kidney disease.

**Keywords:** GFR, serum creatinine, creatinine clearance, formulae Cockcroft-Gault, MDRD, BMI

За изчисляване скоростта на гломерулна филтрация /GFR/ се предлагат различни формули /5/. Класическата формула на Кокрофт-Гаулт за пресмятане на GFR е въз основа на серумния креатинин, пол, възраст и телесно тегло /5,8/.

В лабораторията на УМБАЛ Плевен от около година, бе въведена тази формула, като посредством софтуерен продукт се изчислява GFR чрез компютърен калкулатор /1/. Наред с това бе въведена и компютърно изчислена GFR по модифицирана формула MDRD /8/ при която се вземат допълнително стойностите на уреята и серумния албумин, като резултатът е приравнен към стандартната телесна повърхност. Последната е по-подходяща при болни с данни за хронично бъбречно заболяване, спазващи съответен хранително-диетичен режим. Рециди автори я препоръчват поради по-добрата и предиктивна стойност /4,11/.

Настоящата работа сравнява резултатите от изчислената GFR при използване на двата въведени калкулатора при пациенти с нормални и патологични стойности на телесната маса /BMI/

### МАТЕРИАЛ И МЕТОДИ

Изследвани са 240 хоспитализирани пациенти (120 мъже, 120 жени), разпределени по нивото на серумния креатинин в три групи съобразно литературни данни /7/.

# СРАВНИТЕЛНИ РЕЗУЛТАТИ ОТ КОМПЮТЪРНО ИЗЧИСЛЕНА СКОРОСТ НА ГЛОМЕРУЛНАТА ФИЛТРАЦИЯ

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## COMPARATIVE DATA OF COMPUTER – CALCULATED RATE OF GLOMERULAR FILTRATION

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### ABSTRACT:

The Cockroft- Goult formula for estimating the glomerular filtration ( GFR) and grading the gravity of kidney malfunction has been introduced and calculated by way of a computer calculator at the laboratory of UMHAT – Pleven for as long as a year.

Our suggestion concerns the introducing of a new way of GFR computerized MDRD formula, having since been recommended for patients indicative of chronic kidney disease and duly keeping to alimentary regimen.

The first data of GFR calculated by either of the two calculators introduced is available. There is no statistically significant difference between the respective patients' groups with serum creatinine of referential rank. Such a difference has been found in the group of men with a pathological level of creatinine, creatinine clearance.

**Keywords:** GFR, serum creatinine, creatinine clearance, formulae Cockroft-Goult, MDRD

Скоростта на гломерулната филтрация /GFR/ е показател, труден за измерване в рутинната практика. Много по удобно и достъпно е измерването на серумната и уринна концентрация на креатинина и съответно изчисляване на креатининовия клирънс.

Добре известни и проучени са факторите влияещи върху серумната коонцентрация на креатинин като възраст, пол, телесен хабитус, мускулна маса, медикаменти /9,10/ Освен това за определяне на креатининовия клирънс се изисква събиране на урина за време, което крие редица възможности за грешки. Наред с това са възможни и грешки в аналитичния етап на измерване на серумния и уринния креатинин /5/.

С цел избягване на възможните интерференции са разработени формули за изчисляване на креатининовия клирънс, каквато е тази на Кокрофт и Гаулт /2,7/ за възрастни, при която за изчисление на GFR се взема предвид телесното тегло а не ръста на пациента . Формулата е добре позната и използвана от клиницистите за оценка на бъбречната филтрация при начална бъбречна недостатъчност, при дозировка на медикаменти, както и при оценка ефективността на прогресивните бобречни заболявания. Наред с това са разработени и други модифицирани формули, включващи ниво на урея, албумин, телесното тегло и др. показатели, на фона на съответния хранително- диетичен режим, целящи максимално точно отразяване нивото на действителната гломерулна филтрация./4/

## СРАВНЕНИЕ НА КЛИНИЧНОЛАБОРАТОРНИ РЕЗУЛТАТИ, ПОЛУЧЕНИ ОТ ДВА БИОХИМИЧНИ АНАЛИЗАТОРА – ЗАТВОРЕНИ СИСТЕМИ

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## COMPARISON OF CLINICAL LABORATORY PARAMETERS PERFORMED BY TWO CLINICAL CHEMISTRY ANALYZERS

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<b>Резюме:</b>	Биохимичните изследвания на ензими – ASAT, ALAT, AP, GGT, CK и субстрати – урея, креатинин, общ белтък, албумин, холестерол, триглицериди, глюкоза и общ билирубин, извършени на биохимичен анализатор Pentra 400, се сравняват с тези, извършени на анализатор Cobas Integra 400. Изследвани са по 50 серума за всеки показател с реактиви и консумативи на фирмите производители на двете системи, съответно Horiba ABX и Roche. Представени са CV и Bias стойностите на използваните контролни материали при двата апарата за работния месец, в който е проведено проучването. Получените коефициенти на корелация за всички показатели показват значима корелация: $r > 0.9$ . Това прави възможно извършването и проследяването на лабораторните изследвания на всеки пациент независимо от използвания биохимичен анализатор.
<b>Ключови думи:</b>	клиничнолабораторни показатели: ензими, субстрати; биохимични анализатори: Pentra 400, Cobas Integra 400
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<b>Summary:</b>	Biochemical investigations of enzymes – ASAT, ALAT, AP, GGT, CK and substrates – urea, creatinine, total protein, albumin, cholesterol, triglycerides, glucose and total bilirubin, performed on biochemical analyser Pentra 400, are compared to those performed on the analyser Cobas Integra 400. Fifty serums for each parameter were assayed with reagents and materials provided by the producers of the two systems, respectively Horiba ABX and Roche Diagnostics. The CV and Bias values of the utilized control materials of both analysers for the month in which the analysis was performed are presented. The correlation coefficients for all parameters showed a significant correlation, $r > 0.9$ . This makes it possible to perform and observe the laboratory tests of each patient regardless of the biochemistry analyser used.
<b>Key words:</b>	clinical laboratory parameters: enzymes, substrates; biochemical analyzers: Pentra 400, Cobas Integra 400
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В клиничната лаборатория на УМБАЛ – Плевен, за рутинно изследване на биохимичните лабораторни показатели от една година се използва анализаторът Pentra 400 на фирма Horiba ABX. Това е първият работещ в страната анализатор

от този тип. Наред с това в лабораторията по клинична химия от 4 год. се използва и анализаторът Cobas Integra 400 на фирма Roche.

Двата анализатора са селективни, изследващи както стандартни клиничнолабораторни по-





ДРУЖЕСТВО НА  
КАРДИОЛОЗИТЕ В  
БЪЛГАРИЯ



## АНТИОКСИДАНТЕН КРЪВЕН СТАТУС И ОСНОВНИ МИКРОЕЛЕМЕНТИ (Cu, Zn, Se) ПРИ ПАЦИЕНТИ С АРТЕРИАЛНА ХИПЕРТОНИЯ

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### Резюме

Оксидативният стрес увеличава реактивните форми на кислорода (ROS) и играе важна роля в патогенезата на артериалната хипертония (АХ).

Цел: Да се потвърдят промени в активността на медно-цинковата супероксиддисмутаза (Cu/ZnSOD), глутатион-пероксидаза (GPx-I), тоталния антиоксидантен статус (ТАОС) и серумната концентрация на Zn, Cu и Se при пациенти с АХ.

Материал и методи: Изследването е проведено на 42 пациенти, разделени на три групи: Г1 - с АХ II ст. (n=15, средна възраст 61,0±3,57 г.), Г2 - с АХ I ст. (n=16, 55,7±5,1 г.) и Г3 - контрола (n=11, 56,6±2,87 г.). Серумните нива на Zn, Cu и Se са изследвани с атомно-абсорбционен спектро-фотометричен метод. Активността на Cu/ZnSOD е измерена в еритроцити с тест RANSOD, а активността на GPx-I - с тест RANSEL (RANDOX). ТАОС е определен с кит на същата фирма.

Резултати: Установи се статистически достоверно увеличаване (P<0,05) както на ТАОС в група Г3 (1,62±0,11) спрямо Г1 (0,91±0,07), така и на активността на Cu/ZnSOD в еритроцитите при Г3 (1512,09±93,7) спрямо Г2 (1303,18±42,1) и Г1 (1305,2±48,4), (P<0,05). Активността на GPx-I е повишена статистически достоверно при Г3 (13841,6±1994,11) спрямо Г1 (7361,36±487,7), (P<0,05). Серумната концентрация на Zn и Se е намалена при Г1 спрямо Г3, (P<0,05). Няма статистически достоверна разлика в серумната концентрация на Cu. HDL се повишават при Г3 (1,59±0,10) спрямо Г1 (1,26±0,06), (P<0,05), а LDL намаляват в контролната група.

Заключение: Проучването показва, че съществува връзка между антиоксидантния статус и серумната концентрация на микроелементи (Zn, Cu, Se), които могат да играят важна роля в патогенезата на АХ.

**Ключови думи:** оксидативен стрес, артериална хипертония, микроелементи, медно-цинкова супероксиддисмутаза (Cu/ZnSOD)

Българска кардиология 2007; 13: 211-217



Оксидативният стрес, т.е. дисбалансът между прооксидантите и антиоксидантите, е краен патогенетичен механизъм при много заболявания. Небалансираната продукция

на реактивни форми на кислорода (ROS) и увеличената антиоксидантна защита могат да доведат до развитието на възпалителни процеси, автоимунни заболявания, реакции на свръхчувствителност, канцерогенеза, сърдечно-съдови заболявания.

Последица от оксидативния стрес е възникването на ендотелна дисфункция, която се наблюдава в началните стадии на артериалната хипертония (АХ) и атеросклерозата. През последните години се натрупаха доказателства, че увеличаваният оксидативен стрес в ендотела на съдовата стена е важен рисков фактор (РФ) за развитието на сърдечно-съдовите заболявания.<sup>1</sup> Оксидативният стрес играе важна роля в патогенезата на АХ, тъй като води до много клетъчни събития като:

- инактивация на азотния оксид (NO<sup>•</sup>);
- оксидативна модификация на ДНК, протени и LDL;
- увеличена апоптоза на съдовите клетки;
- увеличена експресия и активация на чувствителни на оксидативен стрес гени.

Клетките на съдовата стена имат собствена антиоксидантна защитна система, изградена от различни ензими - GPx-I, каталаза, супероксиддисмутази (SOD), eNOS, затова редуцираният на антиоксидантния потенциал на съдовата стена е друг важен фактор в патогенезата на сърдечно-съдовите заболявания.

# Изчисляване скоростта на гломерулната филтрация по формулата на Cockcroft - Gault при деца в юношеска възраст

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**Ключови думи:** скорост на гломерулна филтрация, креатинин, формула на Cockcroft - Gault

Скоростта на гломерулната филтрация (GFR) е най-често използваният показател за оценка на бъбречната функция, който има важно значение за ранното диагностициране на бъбречните увреждания при деца (1,2,7,9). Като златен стандарт за определянето на GFR се използват екзогенните клирънси на йодгамата, на инсулина, 51Cr-ЕДТА и др. (3,4,5). В рутинната клиничната практика за скоростта на гломерулна филтрация се съди по серумния креатинин и респективно 24 часовия креатининов клирънс. Събирането на урина за 24 часа при определяне на креатининовия клирънс, особено при деца е свързано с грешки в преданалитичния етап, което се отразява върху достоверността на резултатите за GFR. По тази причина в практиката са въведени формули за изчисляване на клирънса респ. скоростта на гломерулна филтрация, при които освен серумния креатинин се вземат предвид и възраст, тегло, раса, телесна повърхност (3,8,10,11).

В педиатричната практика добре познати са формулите на Schwartz и Counahan-Barratt, основаващи се на пропорционалната зависимост между ръст и серумен креатинин. Редица проучвания по отношение на двете формули за изчисление на GFR дават данни за сравняването им със „златния стандарт“, като е известна средната разлика между изчисления GFR и измерения. Съществуват и проучвания относно приложението в детската възраст на формулата на Cockcroft-Gault, използвана при изчисление на GFR при възрастни (3,8). Последната има ограничено приложение в детската възраст предвид на големите отклонения в получаваните стойности за GFR (2,6,7,12). При тази формула за изчисление се използва серумния креатинин, възрастта на пациента и пола (3).

$$GFR = \frac{(140 - \text{age}(\text{years}) \times \text{weight}(\text{kg}) \times \text{constant})}{\text{Serum creatinin}(\text{mkmol/l})}$$

Двете формули на Schwartz и Counahan-Barratt използват ръста (пропорционален на мускулната маса), серумния креатинин и константна величина - К, различна за двете формули съобразно различните методи за определяне на креатинин.

В клиничната лабораторията на УМБАЛ - Плевен бе въведена формулата на Cockcroft-Gault за изчисляване на GFR при възрастни, като посредством софтуерен продукт последната бе компютърно адаптирана, кое-

то я прави лесна и удобна за използване в рутинната клинична практика.

Цел на настоящата работа е да проучи възможността за приложение на компютърно изчислената GFR и при деца в юношеска възраст (12 - 18 год.).

## МАТЕРИАЛ И МЕТОДИ

В условията на проведено скринингово проучване сред ученици в юношеска възраст са изследвани 50 момчета и 50 момичета без анамнестични данни за заболявания на възраст от 12-18 години.

Кръв за изследване на серумен креатинин е взимана сутрин на гладно преди началото на учебни занятия в затворена система. Биологичният материал - серум е отделен по приетите лабораторни правила. На всички изследвани юноши са измерени ръст и тегло.

Серумният креатинин е изследван на биохимичен анализатор Cobas Integra 400 и последващо изчисляване на GFR по трите посочени формули. За всеки изследван юноша е изчислен и индекс на телесна маса (BMI).

Резултатите са обработени чрез статистически анализ ANOVA с програмата SPSS V - 12,0.

## РЕЗУЛТАТИ И ОБСЪЖДАНЕ

На табл. 1 са представени резултатите за измерения серумен креатинин, изчислената скорост на гломерулна филтрация по трите формули и стойностите на BMI в двете групи момчета и момичета. Стойностите за серумния креатинин са в референтни граници, а изчислената и по трите формули GFR и при двете групи изследвани е в границите на приетата норма за запазена бъбречна функция - GFR над 60 мл/мин 1,73мл.

На фиг. 1 и фиг. 2 са представени стойностите на изчислената GFR при използване на трите формули.

Получените резултати показват, че стойностите на изчислената GFR по формулата на Schwartz съответстват на препоръките на Американската асоциация по педиатрия за деца на възраст от 12-23 год. (7), а именно GFR между 110 - 140 мл/мин. Прави впечатление, че стойностите при групата на момичетата са по-ниски от препоръчаните - 120 мл/мин, като достигат 90 - 110 мл/мин (фиг. 2). Това вероятно е свързано с по-тесния интервал (12-18год.) на проучваната от нас възрастова група.

Трябва да се отчете и по-високия BMI при момчетата, като в почти половината от изследваните (43%)

## РЕЗУЛТАТИ ОТ ИЗСЛЕДВАНЕ ЗА ГЛИКИРАН ХЕМОГЛОБИН A1c С ДВА БИОХИМИЧНИ АНАЛИЗАТОРА

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**Резюме.** Навлизането на гликирания хемоглобин A1c в рутинната клинична практика за контрол при пациенти със захарен диабет (ЗД) налага редица изисквания относно качеството на изследване и сравнимостта на резултатите, получавани от различни лаборатории и методи. В лабораторията на УМБАЛ – Плевен, съществува възможност за изследване на HbA1c с два биохимични анализатора – Pentra 400 (Horiba ABX) и Cobas Integra 400 (Roche), използващи имунотурбодиметричен метод, стандартизиран съответно по NGSP и IFCC. Сравняват се резултати на пациенти със ЗД за HbA1c, изследвани едновременно и на двата апарата. Проучват се различията в стойностите, получени от двата апарата, при резултати в референтен и патологичен диапазон. Установената значима разлика ( $p < 0.001$ ) в стойностите за HbA1c в диапазона до 7% е резултат от различията в стандартизацията на двата метода, с които работят анализаторите. Получените резултати за HbA1c от двата анализатора надеждно осигуряват контрол на ЗД, съобразно съответните диапазони на дадения анализатор.

**Ключови думи:** хемоглобин A1c, захарен диабет, гликемичен контрол

P. Yordanova-Laleva, A. Ruseva, M. Petkova and I. Gencheva. MEASUREMENT OF HEMOGLOBIN A1c WITH TWO BIOCHEMICAL ANALYZERS

**Summary.** The use of hemoglobin A1c for routine clinical control of diabetic patients necessitates a number of quality control requirements as well as comparability between results obtained by different laboratories and methods. The Clinical Laboratory of the University Hospital – Pleven has the capacity to perform HbA1c tests with an immunoturbidimetric method standardized by IFCC and NGSP with two biochemical analyzers – Pentra 400 (Horiba ABX) and Cobas Integra 400 (Roche). We compare the HbA1c results of patients with diabetes obtained simultaneously by the two analyzers. Furthermore, the differences between the values produced by the two analyzers for reference and pathological tests are studied. The statistically significant difference in the results for HbA1c up to 7% is a result of the differences in the standardization of the two methods which the two analyzers follow. The obtained measurements of HbA1c with the two analyzers provide reliable control for diabetes mellitus within the corresponding ranges for each analyzer, respectively.

**Key words:** hemoglobin A1c, diabetes mellitus, blood-glucose control

При болните със захарен диабет гликираният хемоглобин A1c (HbA1c) е един от най-важните показатели за мониторирането на степента на метаболитния контрол. Добре известно е, че този показател отразява средната концентрация на кръвната глюкоза през последните два до три месеца и представлява независим показател на въглехидратната обмяна за оценката на риска от развитие на късни усложнения при диабет [1, 2, 3].

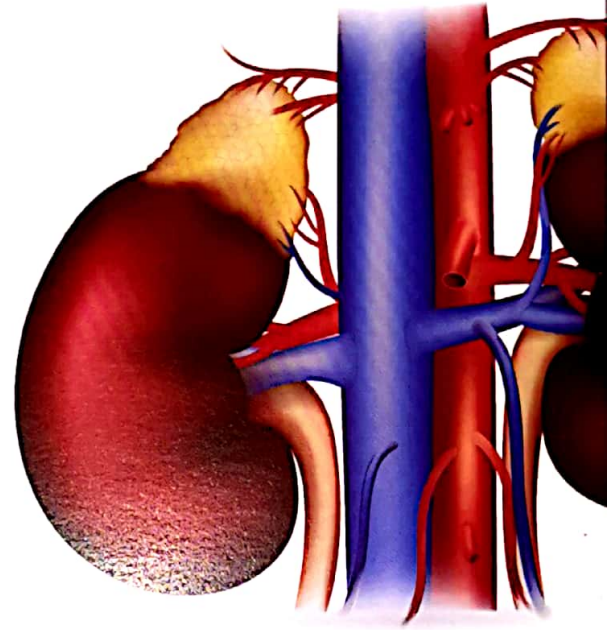
Понастоящем се използват различни методи за определянето на HbA1c, като: йонообменна хроматография, електрофореза, високоефективна течна хроматография, имунохимични методи и др. При едни от тях HbA1c се определя като

хемоглобин А, при други се определя „общия гликиран хемоглобин“, който наред с HbA1c включва и други гликирани съставки. Поради това резултатите, получени с различни методи, се различават помежду си. Това налага различните методи за определянето на гликиран хемоглобин HbA1c да бъдат стандартизирани спрямо един общ стандарт или референтен метод [3, 8, 9].

Основна задача на всяка лаборатория е да осигури качеството на даваните от нея резултати за HbA1c, като за целта е важно използването на стандартизирани методи с вариационен коефициент под 5%.

# ЦИСТАТИН С

## Нов надежден маркер за оценка на бъбречната функция



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**Х**роничната бъбречна болест е световен здравен проблем, засягащ повече от 50 млн. души. С непрекъснатото увеличаване на броя на лицата, страдащи от метаболитен синдром и захарен диабет, честотата на хроничната бъбречна недостатъчност (ХБН) постоянно се повишава. В САЩ тази честота се е удвоила през последните 10 години и продължава да нараства. Най-честите причини за хронична бъбречна недостатъчност

са съответно най-честите хронични двустранни нефропатии: хронични гломерулонефрити, хроничен пиелонефрит, бъбречна поликистозна болест, сателитни нефропатии, хипертонична болест и др. През последните 20 години етиологичното значение на захарния диабет нарасна неимоверно и диабетната нефропатия понастоящем е най-честата причина за хронична бъбречна недостатъчност в много страни по света. В България също се

наблюдава тенденция към повишаване броя на пациентите с хронична бъбречна недостатъчност, като това се свързва с действието на рисковите фактори: захарен диабет и хипертония. Терминалната ХБН се превръща в едно от социално-значимите заболявания за страната ни. Ето защо е важно да бъде установен най-ранният, достъпен и надежден маркер за хронична бъбречна увреда<sup>[1]</sup>.

Понастоящем, най-важният показател на бъбречната функция за изчистване на кръвта от различни вещества е скоростта на гломерулната филтрация. Познаването ѝ е от решаващо значение за предотвратяване и управление на хроничната бъбречна недостатъчност<sup>[2-3]</sup>. В клиничните лаборатории вече е въведен като лабораторен тест измерването на гломерулна филтрация (GFR), като мярка на бъбречната функция.

Точното определяне на GFR изисква употребата на инвазивни процедури,

Непрекъснатото нарастване на броя на пациентите с хронична бъбречна недостатъчност (ХБН), вследствие хипертония и захарен диабет, се превръща в световен здравен проблем. Поради социалната значимост на това заболяване е важно да бъде установен най-ранният, достъпен и надежден маркер за хронична бъбречна увреда. Редица проучвания доказват, че серумният цистатин С е по-добър показател за гломерулна филтрация (GFR) от серумния креатинин. Концентрацията на серумния цистатин С е постоянна и се определя главно чрез гломерулна филтрация, което го прави ендегенен маркер на GFR. Напълно автоматизирани тестове, на принципа на турбидиметрия или нефелометрия, са внедрени в клиничната лаборатория. Определени са референтни интервали за цистатин С при възрастни и деца над една година.

## ОЦЕНКА НА РИСКА ОТ ВЪЗНИКВАНЕ НА ЕПИДЕМИЧЕН ВЗРИВ ОТ МОРБИЛИ С ИЗПОЛЗВАНЕ НА ДАННИ ЗА КОЛЕКТИВНИЯ ИМУНИТЕТ

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## ASSESSMENT OF THE RISK OF AN OUTBREAK OF MEASLES USING DATA HERD IMMUNITY

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<p><b>Резюме:</b></p> <p><b>Ключови думи:</b></p> <p><b>Адрес за кореспонденция:</b></p>	<p>Морбили е високо контагиозно инфекциозно заболяване, причинено от вируса на морбили. Усложнения настъпват в около 30% от случаите и могат да включват слепота, енцефалит, тежка диария, отити, пневмония. Ваксината срещу морбили е ефективна и се прилага от 60-те години на миналия век. Заболяването се среща по-често през последните години в Европа въпреки наличието на високоефективна ваксина. <b>Целта</b> на нашето проучване е да се определи честотата на разпространение на морбилни IgG антитела при лица в активна възраст в гр. Плевен. <b>Материал и методи.</b> Извършено е проспективно сероепидемиологично проучване. За периода януари-юни 2014 г. са събрани и изследвани 194 серумни проби на лица от Плевен. Приложен е имуноензимен метод (ELISA) за откриване и количествено определяне на специфични IgG антитела срещу морбили в серум. <b>Резултати.</b> Анализирани са серумни проби от лица на възраст от 23 до 53 год. (средна възраст <math>35 \pm 0.871</math>). Разпределението на серумите по пол на проучените лица е, както следва: мъже – 146 (75%), и жени – 48 (25%). От проведеното изследване се установи, че 88% от проучената група лица са имунни по отношение на морбилни IgG антитела. Възприемчиви към инфекцията са лица от двата пола. Средната възраст на незащитените е 34 г. за мъже и 36 г. за жени. <b>Изводи.</b> Налице са възприемчиви към морбили групи от населението, спрямо които следва да се препоръчат и организират мероприятия за тяхното имунизирание.</p> <p>морбилни IgG антитела, разпространение, имунитет</p> <p><i>Доц. д-р Милена Карчева, дм, Сектор „Епидемиология“, МУ – Плевен, e-mail: milena_karcheva@abv.bg</i></p>
<p><b>Summary:</b></p>	<p>Measles is a highly contagious infection caused by the measles virus. Complications occur in about 30% and may include blindness, encephalitis, severe diarrhoea, ear infection and pneumonia. The vaccine is applied by the 60s of the last century. Measles is progressively occurring in Europe despite the availability of an effective vaccine. The aim of the study was to determine the prevalence of measles IgG antibodies in people in Pleven of working age. <b>Material and methods.</b> We performed a prospective seroepidemiological study. For the period January-June 2014 samples were collected and tested in 194 sera. Used is the enzyme immunoassay (ELISA) test for the detection and quantification of specific IgG antibodies in serum against measles. <b>Results.</b> Analyzed were serum samples from persons aged 23 to 53 years (mean age <math>35 \pm 0.871</math>). Distribution of serum sex of the studied individuals was as follows: men – 146 (75%) and women – 48 (25%). From the survey it was found that 88% of the studied group of persons are positive in terms of measles IgG</p>

## РАЗПРОСТРАНЕНИЕ НА ПАРОТИТНИ IgG АНТИТЕЛА – СЕРОЕПИДЕМИОЛОГИЧНО ПРОУЧВАНЕ

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## PREVALENCE OF MUMPS IgG ANTIBODIES – A SEROEPIDEMIOLOGICAL STUDY

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**Резюме.** Сероепидемиологичните проучвания са необходими за установяване на имунологичната структура на населението. Чрез събиране и изследване на кръвни проби от репрезентативна група се определя възприемчивостта и/или нееъзприемчивостта към конкретен инфекциозен причинител. Целта на проучването е да се определи честотата на разпространение на паротитни IgG антитела при лица в активна възраст. Извършено е проспективно сероепидемиологично проучване. За периода януари-юни 2014 г. са събрани и изследвани 194 серумни проби. Приложен е имуноензимен метод (ELISA) за откриване и количествено определяне на специфични IgG антитела срещу паротит в серум. Анализирани са серумни проби от лица на възраст от 23 до 53 години (средна възраст  $35 \pm 0.871$ ). Разпределение на серумите по пол на проучените лица е както следва: мъже – 146 (75%), и жени – 48 (25%). От проведеното изследване се установи, че 80% от проучената група лица са серопозитивни по отношение на паротитни IgG антитела. Във възрастови групи до 24 г. и над 43 г. всички изследвани серумни проби са позитивни. Във възрастови групи 25-29 г., 30-34 г., 35-39 г., 40-43 г. серопозитивните са съответно 32 (84%), 30 (75%), 47 (84%), 26 (65%). В контекста на епидемиологичен анализ, резултатите от тези проучвания дават оценка на изпълняваните имунизационни програми.

**Ключови думи:** паротитни IgG антитела, разпространение, имунитет

**Summary.** Seroepidemiological studies are needed to establish the immunological structure of the population. Through the collection and testing of blood samples from a representative group susceptibility and/or immunity to a specific infectious agent are determined. The aim of the study was to determine the prevalence of mumps IgG antibodies in people of working age. A prospective seroepidemiological study was made. For the period January-June 2014 there were collected and tested 194 sera samples. The enzyme immunoassay (ELISA) for the detection and quantification of specific IgG antibodies in serum against mumps was made. Serum samples from persons aged 23 to 53 years (mean age  $35 \pm 0.871$ ) were analyzed. Distribution of serum by gender of the studied individuals was as follows: men – 146 (75%) and women – 48 (25%). From the survey it was found that 80% of the studied group of persons is positive in terms of mumps IgG antibodies. In the age groups of over 43 years old and below 24 years old all examined serum samples were positive. In the age groups 25-29, 30-34, 35-39, 40-43, 32 (84%), 30 (75%), 47 (84%) and 26 (65%) were positive, respectively. **Conclusion:** In the context of epidemiological analysis, the results of these studies provide an assessment of the implemented immunization programs.

**Key words:** mumps IgG antibodies, prevalence, immunity



## ПРЕВАЛЕНС НА МОРБИЛНИ, ПАРОТИТНИ И РУБЕОЛНИ IGG АНТИТЕЛА ПРИ ЛИЦА В МЛАДА ВЪЗРАСТ

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### Резюме

Целта на проучването е да се установи честотата на разпространение на паротитни, морбилни и рубеолни IgG антитела при лица в млада възраст. Материал и методи. Извършено е проспективно сероепидемиологично проучване. За периода януари – май 2014 г. са събрани и изследвани 96 серумни проби от лица на възраст от 23 до 45 години (средна възраст 33.2±5.7). Съотношението мъже/жени е 1:1. Приложен е имуноензимен метод (ELISA) за откриване и количествено определяне на специфични IgG антитела срещу морбили, паротит и рубеола в серум. Използвани са китове на фирма IMMUNOLAB GmbH (Germany). Данните са обработени със статистически пакет Statgraphics Plus, Version 2.1. Извършен е тест на работна хипотеза Но - при ниво на значимост p<0,05. Резултати. Установи се серопозитивност към паротит при 80 (83%), към морбили при 80 (83%), към рубеола – в 92 (96%) от изследваните проби. Шест (6.2%) от изследваните серумни проби показаха липса на протективни антитела към две заболявания: морбили и паротит. Всички серумни проби отрицателни за специфични рубеолни антитела са на лица от женски пол (p<0.05). Заключение. Сероепидемиологичните проучвания са необходими за оценка на ваксиналните програми в страната.

**Ключови думи:** преваленс, морбили, паротит, рубеола

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## PREVALENCE OF MEASLES, MUMPS AND RUBELLA IGG AMONG YOUNG PEOPLE JENY STAYKOVA, ROSITSA CHILINGIROVA

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### Abstract

The purpose of this study is to determine the frequency distribution of mumps, measles and rubella IgG antibodies in young people. Material and Methods. It was done a prospective seroepidemiological study. Between January - May 2014 were collected and analyzed 96 serum samples from people, who are aged from 23 to 45 years (mean age 33.2 ± 5.7). Male / female ratio is 1:1. Serological tests were performed using enzyme-linked immunosorbent assays (ELISA) for the detection and quantification of specific IgG antibodies against measles, mumps and rubella in serum.

Reagents from IMMUNOLAB GmbH (Germany) were used. All analyses were conducted using Statgraphics Plus software, version 2.1. It was done a working hypothesis which significance level is p<0.05. Result. We found a seropositive to mumps at 80 (83%), at 80 to measles (83%), to rubella - 92 (96%) of the tested samples. Six (6.2%) of the tested serum samples showed a lack of protective antibodies to two diseases: measles and mumps. Serum samples that were negative for rubella antibodies were from women (p <0.05). Conclusion. Seroepidemiological studies are needed to evaluate the vaccine programs in the country.

**Key words:** prevalence, measles, mumps, rubella

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## ЕПИДЕМИОЛОГИЧНА ОЦЕНКА НА ТИТЪРА НА IgG АНТИТЕЛА ПО ВРЕМЕ НА ЕПИДЕМИЧЕН ВЗРИВ

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## EPIDEMIOLOGICAL ASSESSMENT OF IgG ANTIBODIES TITER DURING AN EPIDEMIOLOGICAL OUTBREAK

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**Резюме.** Значението на рубеолната инфекция като проблем на общественото здравеопазване се определя от тератогенния ефект на рубеоления вирус по време на бременността. Цел на настоящото проучване е да се установи честотата на разпространение на рубеолни IgG антитела при лица в млада възраст в град Плевен. Извършено е проспективно сероепидемиологично проучване. За периода януари–юни 2014 г. са събрани и изследвани 194 серумни проби от лица на възраст от 23 до 53 години (средна възраст  $35 \pm 0.871$ ). Приложен е имуноензимен метод (ELISA) за откриване и количествено определяне на специфични IgG антитела срещу рубеола в серум. Резултатите са представени в среда Microsoft Office Excel. От проведеното изследване се установи, че 188 (97%) от проучената група лица са серопозитивни по отношение на рубеолни IgG антитела и съответно 6 (3%) са серонегативни. При последните се установи, че преобладават жените – 4 (66%). Мъжете са съответно – 2-ма (44%). Серонегативните лица са на възраст 34 г. – 4 (66%), и на 36 г. – 2-ма (44%). Световната здравна организация цели в Европейския регион да се постигне елиминация на еродената рубеола. Необходимо е проследяване на възприемчивостта към рубеола сред жените в детеродна възраст.

**Ключови думи:** рубеолни IgG антитела, разпространение, имунитет

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**Summary.** The importance of rubella infection as a public health issue is determined by the teratogenic effect of the rubella virus during pregnancy. The goal of this study was to determine prevalence of rubella IgG antibodies in individuals at a young age in the city of Pleven. Material and methods. A prospective seroepidemiological study was performed. For the period of January–June 2014, 194 serum samples of 23- to 53-year-old (average age  $35 \pm 0.871$ ) individuals were collected and tested. The enzyme immunoassay (ELISA) for the detection and quantification of specific IgG antibodies against rubella in serum is attached. The results are presented in Microsoft Office Excel. Results. The survey found that 188 (97%) subjects from the studied group were seropositive in regards to rubella IgG antibodies and 6 (3%) subjects were seronegative, respectively. In the latter it was found that the majority were women – 4 (66%). The men were – 2 (44%), respectively. The seronegative subjects were 34-year-old – 4 (66%) and 36-year-old – 2 (44%). Conclusion. The goal of the World Health Organization is to eliminate the congenital rubella in the European region. It is necessary to monitor the susceptibility to rubella among women of childbearing age.

**Key words:** rubella IgG antibodies, prevalence, immunity

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*Original Contribution*

## MEASUREMENT OF C- REACTIVE PROTEIN BY TWO CLINICAL CHEMISTRY ANALYZERS

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### ABSTRACT

Clinical laboratory of the University Hospital, Pleven has the capacity to perform C-reactive protein (CRP) assay with high sensitivity tests by two biochemical analyzers closed type: Pentra 400 (Horiba ABX) and Cobas Integra 400 (Roche). This study is fulfilled to compare CRP- results obtained from the both analyzers with respect to investigate the possibility for interchangeability of these instruments. Both analyzers are based on the same method for determination of C-reactive protein - latex immunoturbidimetric. The analytical variation at different intervals of the referent range and outside is assayed. High correlation ( $r > 0.9$ ) between CRP values, obtained from the both analyzers has been shown for all investigated groups. However, a statistical significant difference in the mean values was established between the results from both instruments for some concentration groups. Analysis of the results obtained demonstrates that when CRP was used as a prognostic parameter despite, the high correlation between the results obtained from both analyzers, repeated measurements of CRP of a definite patient had to be made by one and the same analyzer.

**Key words:** CRP test, CRP assay with high sensitivity

### INTRODUCTION

Recent evidence has shown that inflammation plays a leading role in the inception and progression of atherosclerosis. In a number of studies has been concluded a strong and independent association between baseline concentrations of inflammatory biomarkers and future coronary events. In fact, the majority of individuals with coronary events are not in a high-risk group according to the Framingham risk assessment of traditional risk factors for coronary heart disease; half of those who suffer myocardial infarctions have normal lipid values. In view of that, measurement of inflammatory markers has been suggested as an addition to lipid testing to a better identification individuals at increased risk. According the evaluation of American Heart Association, only CRP met the analytical requirements for outpatient clinical use (1). More than 25 prospective epidemiological studies have shown that CRP is a strong and independent predictor of future myocardial infarction ischemic stroke, peripheral arterial disease, and sudden cardiac death in apparently healthy men and women. Physicians have become accustomed to use the terminology "high sensitivity CRP" when considering

measurement of CRP for vascular disease risk stratification (2). Concentrations less than 1.0 mg/l are considered as low risk, 1.0 – 3.0 mg/l – as average risk, and higher than 3.0 mg/l – as high-risk groups (3).

The goal of this study is to compare CRP-results obtained from two biochemical analyzers closed type: Pentra 400 (Horiba ABX) and Cobas Integra 400 (Roche) and to check the possibility for interchangeability of the two instruments.

### MATERIALS AND METHODS:

The principle of the method of CRP-assays by both analyzers – Pentra 400 and Cobas Integra 400, is identical: lateximmunoturbidimetric. Both analysers use 5-point calibration curve, have identical linearity range: 160 mg/l and reference range: < 5 mg/l. The two different reagents use different anti-CRP antibodies: rabbit and mouse respectively (4, 5)

For determination of CRP either by Pentra 400 or Cobas Integra 400 we have performed parallel tests of 105 sera. All necessary reagents, calibrators and controls were

## CLINICAL AND NEUROIMAGING STUDIES IN PATIENTS WITH ACUTE SPONTANEOUS INTRACEREBRAL HEMORRHAGE.

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### ABSTRACT

**Objective:** To define the prognostic value of clinical and neuroimaging parameters on the 30-th day mortality and clinical outcome after spontaneous intracerebral hemorrhage (sICH).

**Materials and methods:** we examined 88 patients with sICH admitted to Neurology Clinic, UMHAT Plevan within 48 hours after clinical symptoms onset. Glasgow Coma Scale (GCS) score was used to assess the primary stroke severity; neurological deficit on admission was assessed by National Institute of Health Stroke Scale (NIHSS); clinical outcome at discharge was evaluated by modified Rankin Scale (mRS) and by Glasgow Outcome Scale (GOS) on the 30-th day after sICH onset. Hematoma volume was measured by the formula of Kothari:  $A \times B \times C / 2$  in ml. The statistical analysis was performed by SPSS 19.0 and Statgraphics plus 4.1 for Windows.

**Results:** Initial assessment of primary stroke severity and neurological deficit by GCS  $\rightarrow$  NIHSS, hematoma localization and volume were found strongly correlated with the clinical outcome on the 30-th day after the sICH onset. Age and vascular risk factors did not correlate with the clinical outcome. Male patients had better survival on the 30-th day compared with the female ones.

**Discussion:** Neurological deficit on admission, hematoma localization and volume were found reliable predictors of the 30-th day clinical outcome that could serve for early stratification of patients and optimal choice of therapeutic approach.

**Key words:** CT, neurological deficit, sICH, clinical outcome.

### INTRODUCTION

Spontaneous intracerebral hemorrhage (sICH) is a type of stroke usually caused by a vessel rupture followed by spontaneous leakage of blood in the brain parenchyma [4]. sICH accounts for only 15-20% of all strokes but is associated with the highest mortality and disability rate [11, 22]. Despite the achievements of advanced neuroimaging methods and new therapeutic opportunities of neurovas-

cular intensive care the parameters of sICH morbidity and mortality remain unchanged [2, 8]. Almost 40% of the patients die before the 30-th day after sICH, 66% of the survivors are severely disabled and only 20% recover their functional independence on the 6-th month after the sICH [22].

According to the guidelines of AHA [American Heart Association] modern treatment of sICH is mainly supportive and is still one of the greatest challenges in the neurological practice [17]. The health and social policy of some countries, providing easy access to highly qualified medical professionals, effective primary prophylaxis and control of vascular risk factors, urgent admission to stroke units with modern intensive care equipment, results in stable reduction of sICH incidence during the last years [25, 26].

Unlike ischemic stroke sICH is less investigated in Bulgaria. There is a substantial lack of population-based studies on the problems of sICH in our country. No prospective studies, based on the hematoma volume measurement and correlative clinical and neuroimaging analyses of neurological deficit and clinical outcome are also conducted [3]. An urgent necessity for performing scientific investigations on sICH arises that could facilitate identification of patients with the highest mortality and disability risk and offer new therapeutic approaches.

The aim of the present study was to define the predictive value of some clinical and radiological parameters for the clinical outcome on the 30-th day after sICH.

### MATERIAL AND METHODS

#### Patients

Of the 337 patients with sICH, admitted to the Neurology Clinic, UMHAT "Dr. G. Stranski", Plevan from March 2005 to July 2010, only 88 (38 males, 50 females, median age  $63.8 \pm 11.7$  years) were selected on the grounds of strict exclusion and inclusion criteria. From the study were excluded patients with hemorrhage due to brain tumor, trauma, hemorrhagic transformation of ischemic infarction, rupture of an aneurysm or AVM. No individuals with intraventricular spread of blood or subarachnoidal hemorrhage,

## ALCOHOL ABUSE ENHANCES SYSTEMIC INFLAMMATORY RESPONSE IN PATIENTS AFTER SPONTANEOUS INTRACEREBRAL HAEMORRHAGE

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### SUMMARY

**OBJECTIVE:** The role of inflammation in the complex pathophysiology of spontaneous intracerebral hemorrhage (sICH) was studied by assessing the relationship between serum C-reactive protein (CRP) levels and some clinical and neuroradiological parameters. We also aimed to identify the effects of modifiable vascular risk factors on serum CRP levels.

**PATIENTS:** Forty six patients with sICH admitted to the Department of Neurology and Neurosurgery of the Pleven University Hospital, Bulgaria were examined. Serum CRP levels were measured within the first 48 hours of disease onset and analyzed in relation to neurological deficit severity and clinical outcome after sICH. The impact of some vascular risk factors on the inflammatory marker levels was also studied.

**RESULTS:** We found enhanced CRP levels in patients with severe neurological deficit as assessed by the National Institutes of Health Stroke Scale (NIHSS) score. Significantly higher CRP levels were measured in patients with progressive clinical deterioration and worse outcome. Serum CRP levels were also higher in patients with a history of alcohol abuse.

**CONCLUSIONS:** Our results suggest that inflammation plays a crucial role in the development of brain injury after sICH. They show that CRP, a nonspecific inflammatory marker, can serve as an additional diagnostic and prognostic test indicator in the acute stage of sICH thus providing an excellent opportunity for therapeutic interventions while the patient is still in clinic. Patients with a history of systemic alcohol abuse demonstrate stronger inflammatory response indicative for worse prognosis.

**Key words:** Intracerebral hemorrhage, inflammation, CRP, alcohol abuse, arterial hypertension.

### INTRODUCTION

Spontaneous intracerebral hemorrhage (sICH) is a devastating type of stroke characterized with severe

disability and the highest rate of mortality<sup>(1)</sup>. It accounts for 15-20 % of all strokes<sup>(2)</sup>. Despite the outstanding achievements in the modern diagnosis of sICH, the outcome after ICH has not been improved - its treatment is still symptomatic and the results achieved are very unsatisfactory<sup>(3,4)</sup>. The cerebral hemorrhage is considered to initiate a complex cascade of metabolic events causing neuronal damage and cellular death<sup>(5,6,7)</sup>. The inflammation plays a central role in the molecular mechanisms triggered after the hemorrhage onset<sup>(8)</sup>. There is data published on the role of C-reactive protein (CRP), an acute phase reactant, in the pathogenesis and prognosis of acute ischemic stroke<sup>(8)</sup>. Moreover increased CRP levels also indicate higher risk of future cerebrovascular events<sup>(9,10)</sup>. But the role of CRP in the pathogenesis of cerebral hemorrhage remains unresolved yet. It is not clear whether CRP only shows systemic inflammation, or is directly involved in the mechanisms of brain injury after sICH.

Obesity, alcohol consumption and smoking have been identified as risk factors for vascular events. They also play an essential role in the etiology and pathogenesis of atherosclerosis and arterial hypertension, which are considered the major causes for stroke<sup>(11,12)</sup>. There are a few scientific publications confirming that initiation of inflammatory reactions in the vascular endothelium causes cerebrovascular disorders<sup>(13)</sup>. CRP has been detected in atherosclerotic plaques and probably contributes to atherogenesis and initiates pro-coagulation state<sup>(13,14)</sup>. Furthermore, CRP levels are also correlated with arterial hypertension<sup>(12)</sup>. Evidence has been published showing that some risk factors as smoking, alcohol consumption and hyperglycemia cause increased CRP serum levels<sup>(15,16)</sup>. As CRP is frequently associated with cerebrovascular diseases and their prognosis it will be useful to investigate the relationship between CRP and the neurologic deficit severity after ICH in the context of risk factors for stroke.

The purpose of the present study was:

1. To investigate the relationship between serum CRP level and stroke severity and outcome in patients after acute

# COMPARISON OF AN AUTOMATED LEUKOCYTE DIFFERENTIAL COUNT TO THE MANUAL SLIDE REVIEW

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**Summary.** The WBC differential count is generally considered to yield clinically useful information in health and disease. This study was aimed to assess the performance of the ABX Pentra 80 leukocyte differential count by comparison with the microscopic technique. The differential count, performed on Pentra 80, is based on the technological principle: Double Hydrodynamic Sequential System "DHSS" (ABX DIAGNOSTICS patent) and includes: cytochemistry, Focused Flow Impedance and light absorbance. The DHSS principle defines two additional leukocyte populations: large immature cells (LIC) and atypical lymphocytes (ALY), in percentage and absolute count. Accuracy of the differential blood count was assessed by comparing results from the microscope examination (reference) to the test method (PENTRA 80). The differential parameters were analyzed by regression and correlation analysis and the mean difference between methods was calculated. The clinical performance of the parameters LIC and ALY was assessed through the determination of their clinical efficiency. 138 samples were analyzed on Pentra 80 for CBC plus leukocyte differential analyses in automatic mode and default settings. Blood smears were prepared from all samples. Our results show, that the correlation between the automated differential blood count and manual slide review was very high for neutrophils and lymphocytes and high - for eosinophils, monocytes and basophils. The priority alarms: LIC and ALY show excellent specificity: 97.34% and 93.75% respectively, and 100% sensitivity for both of them.

*Key words: blood cell count/instrumentation; hematology/instrumentation; automation (source: MeSH)*

**T**he WBC differential count has become widely accepted and used by clinicians, and is generally considered to yield clinically useful information in health and disease. The information derived from the WBC differential count has become a cornerstone in laboratory hematology and is used for screening, case finding, diagnosis and monitoring of hematological and non-

**REVIEW**

## Possibilities for Automated Detection of Abnormal White Blood Cells

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**SUMMARY:** The automated differential count has the advantage of precision, efficiency, safety and economy. Most of the new hematological analyzers give additional information about immaturity and the presence of atypical lymphocytes. More detailed characteristics of some cells can be investigated by means of flow cytometry. 21 K2EDTA blood samples with some abnormalities in the leukocyte population – lymphocytosis, presence of large immature cells (LIC), atypical lymphocytes (ALY) and Blasts, were detected with the automated hematology analyzer Pentra 80 (ABX, France), and were analyzed with a Flow Cytometer – (Becton Dickenson, USA). Three-color immunophenotype analyses of markers were performed on a FACSort flow cytometer using CellQuest Software for acquisition. The blood was stained with Fluorescein isothiocyanate (FITC), Phycoerythrin (PE) or Peridinin chlorophyll protein (PerCP)-labeled monoclonal antibodies (MoAbs). The aim of the study was to compare the information for WBC-abnormalities, obtained with a Pentra 80 and a Flow Cytometer. The presence of LIC, ALY, and Blasts alarms on Pentra are a high probability indicator for a haematological disease. The use of such a class of analyzers, followed by immunophenotyping with a Flow Cytometer, assists and accelerates the physician's work and is valuable for diagnosis of a greater number of patients.

**Key words:** ALY, LIC, Flow Cytometer, immunophenotyping

### Introduction

The information derived from the white blood cells (WBC) differential count has become a cornerstone in laboratory hematology and is used for screening, diagnosis, and the monitoring of hematological and non-hematological disorders. The traditional procedure for the differential WBC count by manual microscopy is time consuming and labor intensive. Also, the 100-cell differential count is often criticized for its statistical shortcomings. (1, 2) The automated differential counts have the advantage of precision, efficiency, safety, and economy. Most of the new hematological analyzers give additional information about immaturity and the presence of atypical lymphocytes. One of them is the Pentra 80 (Horiba ABX, France).

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The five-part differential count is based on the technological principle of the Double Hydrodynamic Sequential System "DHSS" (ABX DIAGNOSTICS patent). It includes: cytochemistry, focused flow impedance, and light absorbance. Each cell is individually analyzed by two different measurement principles: measurement of the cellular volume by the impedance variation principle, and analysis of the level of cellular complexity by measurement of the light transmitted. This analytical combination uses a high definition analysis of the transmitted signals, which allows for the quantification of 6 leukocyte populations on the LMNE matrix: Lymphocytes, Monocytes, Neutrophils, Eosinophils, large immature cells (LIC), and atypical lymphocytes (ALY). Basophils are counted by impedance on a specific channel. The differentiation is carried out by an analysis of the following criteria: cellular volume, shape of the nucleus (number of lobes), type and number of granules, aspect of nuclei chromatin, and intensity of staining. The immature granulocytic cells are detected by their larger volumes and

## LOW SERUM TOTAL ANTIOXIDANT STATUS MAY REFLECT THE SEVERITY OF NEUROLOGICAL IMPAIRMENT IN PATIENTS AFTER SPONTANEOUS INTRACEREBRAL HEMORRHAGE

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### ABSTRACT

The purpose of this study was to explore the relationship between the serum total antioxidant status (TAS) and the severity of neurological deficit in patients with acute spontaneous intracerebral hemorrhage (sICH). It was found that TAS correlated with the severity of neurological impairment, evaluated by both the NIHSS and the Mathew Stroke Scale. Furthermore, the parameter had the lowest values in patients who died, and the highest values were found in the group of patients who made a *good recovery* according to the Glasgow Outcome Scale. Future studies should show whether TAS may serve as a reliable predictor of outcome after sICH.

*Key words:* spontaneous intracerebral hemorrhage, oxidative stress, total antioxidant status, peripheral blood

### INTRODUCTION

Spontaneous intracerebral hemorrhage (sICH) accounts for only 15-20% of all strokes but in comparison with them it causes the highest degree of disability and lethality [7]. In contrast to ischemic stroke, the role of oxidative stress in hemorrhagic stroke-induced brain injury has been insufficiently investigated. Limited data have shown the presence of DNA and protein oxidative damage in the brain of experimental models [11]. Few data exist on increased lipid peroxidation level in erythrocytes and serum of sICH patients [13,14]. Furthermore, the level of serum lipid hydroperoxides predicts severe disability in hemorrhagic stroke survivors [2]. The published data on the antioxidant enzymes activity are contradictory [4,13]. To the best of our knowledge, there is no study published in which the serum total antioxidant status has been estimated as an indicator of the severity of neurological deficit after sICH.

The objective of the present study was to explore the possible relationship between the serum TAS level and the severity of neurological deficit in patients after acute spontaneous intracerebral hemorrhage.

### MATERIAL AND METHODS

#### *Patients*

Thirty nine patients, admitted within 48 hours of stroke onset to the Department of Neurology, University Hospital - Pleven, were selected. The study did not include individuals with a hemorrhage due to a brain tumor, trauma, hemorrhagic transformation of cerebral infarction, rupture of an aneurysm or arteriovenous malformation. No individuals with intraventricular spread of blood or subarachnoidal hemorrhage, acute or chronic infections, cancer, kidney and liver diseases or past surgical procedures were included. A detailed questionnaire assessing the medical history and physical state of the patients was filled out by an experienced neurologist. Data regarding demographic and risk factors, and clinical neurological symptoms of the study population were prospectively collected.

All experiments were conducted in accordance with the rules and regulations approved by the University Research Ethics Committee.

## ABNORMAL LEVELS OF INFLAMMATORY AND OXIDATIVE STRESS MARKERS IN PATIENTS WITH ARTERIAL HYPERTENSION AND DIABETES MELLITUS

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**Received:** November 17, 2013  
**Revision received:** December 5, 2013  
**Accepted:** December 27, 2013

### Summary

Individuals with hypertension and diabetes mellitus are at high risk of cerebrovascular and cardiovascular morbidity and mortality. Recent advances in the multifactorial pathophysiology of atherogenesis provide important information about the complex interrelations between traditional risk factors, inflammation and oxidative stress in mediating all stages of atherosclerosis. The objective of the study was to determine if some inflammatory and oxidative stress markers in patients with arterial hypertension and diabetes mellitus differ from those in healthy age-matched controls. Our results revealed a significant difference in blood pro/antioxidant activities in hypertensive diabetics and the controls. The investigation of inflammatory and oxidative stress markers along with traditional risk factors proves useful in complex assessment of vascular risk and primary prophylaxis of cerebrovascular and cardiovascular events.

**Key words:** diabetes, hypertension, inflammation, oxidative stress, C-reactive protein

### Introduction

Arterial hypertension and diabetes mellitus play a crucial role in the pathogenesis of atherosclerosis and atherosclerotic complications. The combination of arterial hypertension and diabetes mellitus accounts for a large proportion of cardiovascular and cerebrovascular morbidity and mortality. Recent investigations on the role of inflammation in mediating all stages of atherosclerosis provide important information about the complex interrelations between traditional vascular risk factors and atherogenesis [1, 2]. Persistent low-grade inflammation indicated by the levels of inflammatory markers predicts future coronary or cerebrovascular events, especially in patients with arterial hypertension and diabetes mellitus, and both conditions are recognized as pro-inflammatory conditions [3-7]. There is increasing experimental evidence that high-sensitivity C-reactive protein (hs-CRP) is a powerful and reliable marker for assessment of vascular risk. However, it is still not routinely measured in clinical practice [8]. During the last decades several studies have examined the

Original Article

## EFFECTS OF GLUCOSE AND BILIRUBIN ON THE KINETIC JAFFE'S AND THE ENZYMATIC METHODS FOR SERUM CREATININE ASSAY

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### Summary

The enzymatic method for the determination of serum creatinine is accepted as one of the most accurate methods in a clinical laboratory. This method was used on a biochemistry auto analyzer (Cobas Integra 400) to determine serum creatinine at the laboratory of University Hospital – Pleven. The characteristics and reliability of this enzymatic method for creatinine were compared with the Jaffe kinetic method. Effects of some interfering substances like bilirubin and glucose on the Jaffe kinetic method and the enzymatic method were compared. Glucose and bilirubin inhibit the reaction between creatinine and alkaline picrate. Glucose slowly reduces picric acid to picrate, while the bilirubin present in a sample is oxidized to biliverdin under alkaline conditions. This leads to a decrease in absorbance at 520 nm. We measured creatinine in serum samples with the enzymatic method and the Jaffe kinetic method in samples divided into four groups: group I – samples without bilirubin and glucose; group II – samples with high level of glucose; group III – samples with high level of bilirubin, group IV – all samples. For Group I, the correlation coefficient obtained by comparing the enzymatic creatinine method and Jaffe's kinetic method was  $R = 0.983$ . There was a very good agreement between the two methods in terms of correlation coefficient even in the samples with high levels of glucose or bilirubin.

**Key words:** creatinine, enzymatic assay, Jaffe kinetic method, glucose, bilirubin

### Introduction

Several methods for estimation of serum and urinary concentrations of creatinine, most of which are based on the Jaffe's reactions are routinely used in clinical biochemistry laboratories. Using such methods is associated with problems concerning sample analysis, and this could be attributed to the Jaffe's reaction. Numerous chromogenic interfering substances have been documented. Usually, glucose and bilirubin are cited as interfering substances of the Jaffe's based methods [1-3]. Both substances inhibit the reaction between creatinine and alkaline picrate. Glucose slowly reduces picric acid to picramate, while bilirubin, under alkaline

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Received: March 30, 2015  
Revision received: April 03, 2015



## ХОМОЦИСТЕИН И ВИСОКОЧУВСТВИТЕЛЕН С-РЕАКТИВЕН ПРОТЕИН ПРИ ПАЦИЕНТИ НА ХЕМОДИАЛИЗА КАТО МАРКЕРИ ЗА КАРДИОВАСКУЛАРЕН РИСК

И. Генчева, А. Русева, П. Лалева и Ю. Пастухов

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## HOMOCYSTEINE AND HIGH SENSITIVE C-REACTIVE PROTEIN IN DIALYSIS PATIENTS AS MARKERS FOR CARDIOVASCULAR RISK

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<p><b>Резюме:</b></p> <p><b>Ключови думи:</b></p> <p><b>Адрес за кореспонденция:</b></p>	<p>Целта на изследването е определяне на серумен хомоцистеин (Hcy) и високочувствителен С-реактивен протеин (hsCRP) и оценка на тяхната ефективност като потенциални маркери за риск, свързан с кардиоваскуларно заболяване при пациенти на хемодиализа. За серумен хомоцистеин и високочувствителен CRP са изследвани 120 пациенти на хемодиализа. Те са проследени в рамките на една година след изследването за настъпване на кардиоваскуларно заболяване (инфаркт или инсулт) или смърт вследствие на него. Изчислени са положителната и отрицателната предиктивна стойност за хомоцистеина (PPV – 14,5%, NPV – 94,8%) и hsCRP (PPV – 18,3%, NPV – 93,7%). Използвайки ROC анализ, оценихме чувствителността и специфичността за всеки параметър – за хомоцистеина (чувствителност – 75%, специфичност – 50,96%) и hsCRP (чувствителност – 56,25%, специфичност – 72,12%). Определена е зоната под ROC кривата (AUC), съответно AUC (хомоцистеин) – 0,632 и AUC (hsCRP) – 0,623. Резултатите показват, че серумният хомоцистеин и hsCRP могат да бъдат разглеждани като полезни лабораторни показатели за оценка на риска от кардиоваскуларно заболяване при пациенти на хемодиализа.</p> <p>хомоцистеин, hsCRP, маркер, кардиоваскуларно заболяване, хемодиализа</p> <p><i>Д-р Ирена Генчева, Медико-диагностична клинична лаборатория, УМБАЛ „Д-р Георги Странски“, бул. „Георги Кочев“ № 8А, 5800 Плевен</i></p>
<p><b>Summary:</b></p> <p><b>Key words:</b></p> <p><b>Address for correspondence:</b></p>	<p>The aim of the stated study is to determine the serum homocysteine (Hcy) and high-sensitivity C-reactive protein (hsCRP), and to evaluate their effectiveness as potential markers of risk associated with cardiovascular disease in patients on hemodialysis. For serum homocysteine and hsCRP were examined 120 hemodialysis patients. They were followed within one year following the survey for the occurrence of cardiovascular disease (heart attack or stroke), or exitus due to such accident. Positive and negative predictive values were estimated for homocysteine (PPV – 14,5%, NPV – 94,8%) and hsCRP (PPV – 18,3%, NPV – 93,7%). Using ROC analysis the sensitivity and specificity were assessed for each parameter – for homocysteine (sensitivity – 75%, specificity – 50,96%) and for hsCRP (sensitivity – 56,25%, specificity – 72,12%). The area under the curve was determined (AUC), respectively for homocysteine – 0,632 and for hsCRP – 0,623. The results showed that serum homocysteine and hsCRP could be regarded as useful laboratory indicators to assess the risk of cardiovascular disease in patients on hemodialysis</p> <p>homocysteine, hsCRP, marker, cardiovascular disease, hemodialysis</p> <p><i>Irena Gencheva, M. D., Clinical Laboratory, University Hospital, 8A, G. Kotchev Blvd., Bg – 5800 Pleven</i></p>

## LABORATORY ASSESSMENT OF THYROID FUNCTION IN PATIENTS WITH PROTEINURIA

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Received: October 05, 2017

Revision received: January 16, 2018

Accepted: February 27, 2018

### Summary

Significant losses of functional proteins such as hormones and hormone-binding proteins are seen in patients suffering from proteinuria. Studies have reported loss of thyroid hormones and thyroxine-binding globulin in the urine. There is evidence that subclinical hypothyroidism is six times more common in patients with proteinuria than in healthy people. The parameters of the effect of proteinuria on thyroid function have not been fully studied yet. We investigated 74 patients with qualitatively established proteinuria, of whom 34 men and 40 women, without diagnosed thyroid disease. The average age of the patients was 60.9 years. We tested 20 free controls for free thyroxine (FT4), thyroid stimulating hormone (TSH), creatinine and albumin in serum, and the quantity of urine protein. The mean results found for TSH were higher in the patients with proteinuria than in those of the controls (2.719 mU/l vs 1.78 mU/l). For FT4, the mean result in the patients with proteinuria was 17.04 pmol/l vs 16.39 pmol/l in the controls. A correlation was sought between TSH and FT4 levels and all the laboratory parameters we tested. Patients with proteinuria had higher TSH levels, probably due to the loss of thyroid hormones in the urine. However, these losses cannot lead to clinically proven hypothyroidism.

**Key words:** proteinuria, TSH, FT4, hypothyroidism

### Introduction

Proteinuria is a sign of potential kidney disease. Proteinuria, hypoalbuminemia, edema and hyperlipidemia characterize nephrotic syndrome. The main protein in serum and urine in patients with nephrotic syndrome is albumin, which is being lost in the urine [1, 2]. Hypoalbuminemia, as a consequence of these losses, cannot be fully set off by increased liver albumin synthesis. In proteinuria patients, apart from albumin, other proteins are also lost with the urine [3]. Among them are some hormones.

The loss of thyroid hormones and thyroxine-binding globulin (TBG) in the urine in patients

# АКУШЕРСТВО И ГИНЕКОЛОГИЯ

## ОРИГИНАЛНИ СТАТИИ

### ДОКАЗВАНЕ НА ЧЕСТОТАТА НА ХЕРПЕСНИ ВИРУСИ В ЕНДОМЕТРИУМА ПРИ ЖЕНИ С РЕПРОДУКТИВНИ ПРОБЛЕМИ

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**Въведение:** Херпесните вируси могат да засегнат гениталния тракт и да доведат до хронично възпаление в половата система. Те са представени от над 100 различни вида, от които 8 засягат човека. След първоначалното инфектиране, всички херпесни вируси обикновено преминават в латентен стадий като интегрирана ДНК или като извън-хромозомна форма. Съществуват различни причини, които водят до реактивация на херпесните вируси в гениталния тракт като понижена имунна реактивност, циклични хормонални промени свързани с менструалния цикъл, телесна хипотермия или хипертермия, други инфекции, инвазивни гинекологични интервенции, нарушен психо-емоционален статус и др. Това може да доведе до развитие на трайни хронични инфекции в ендометриалната лигавица, което да е причина за репродуктивни неуспехи.

Благодарение на молекулярно-генетичните методи за доказване на херпесни инфекции е възможно да се проучи значението им в етиологията на хроничния ендометрит при жени с репродуктивни проблеми.

**Цел:** Да се проучи честотата на разпространение на херпесните вируси HSV-1,2, CMV и EBV в ендометриалната лигавица при жени с репродуктивни проблеми.

**Материали и Методи:** За период от 1 година (м. февруари 2018 г. – м. февруари 2019 г.) в Медицински център Клиничен институт за репродуктивна медицина в град Плевен са изследвани



## COMPARATIVE EVALUATION OF RISK FACTORS IN YOUNG AND MIDDLE-AGE PATIENTS WITH ACUTE ISCHEMIC STROKE

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### ABSTRACT

**Background:** Ischemic stroke (IS) in young adults has different etiologies and risk factors (RF). A better understanding of the contribution of potentially modifiable RF to the global burden of IS in young adults is crucial for successful prevention strategies.

**Objective:** To evaluate the incidence and prevalence of different RF in young and middle-age acute IS patients.

**Material and Methods:** In the study were included 63 patients with acute IS, admitted to the Neurology Clinic Pleven. They were classified in two groups: Group A (n=10) of young (18-44 y) and Group B (n=53) of middle-age (45-59 y) IS patients. Comparative evaluation of the following RF: age, sex, family history of stroke, arterial hypertension (AH), smoking, dyslipidemia, alcohol consumption, low physical activity, obesity and diabetes mellitus (DM) was done. The statistical analysis was performed with the Statistical Package for Social Sciences, version 24.0 (SPSS).

**Results:** Out of the 63 patients, 42 (66,7%) were males and 53 (84,1%) were 45-59 years old. No gender difference was found in group A, while in Group B, the prevalence of male patients (69,8%) was found, though statistically not significant (p=0,223). A first-degree family history of stroke had 30 (93,8%) of the middle-aged IS patients, as compared to only 2 of the young ones (6,3%), which was statistically significant (p=0,034). Group B showed prevalence of smoking (82,2%), alcohol consumption (83%), body overweight (90,5%), low physical activity (80%), AH (87,3%) and DM (87,3%).

**Conclusion:** The higher incidence of some RF in middle-age acute IS patients indicates that early identification and control of the RF is the best strategy for reducing stroke mortality and morbidity.

**Key words:** Ischemic stroke, risk factors, young and middle-age patients,

### INTRODUCTION

Stroke is a leading cause of death, physical and mental disability worldwide. Although stroke has been considered a privilege of the older population, recent data reveals the increasing number of "young" strokes [1, 2]. The incidence of IS in the age range 18-50 years is 10.8 to 100 000 population [3]. Approximately 10% of the young and middle-age IS patients remain severely disabled, half of them do not return to work with worsened quality of life thus causing serious economic consequences to their families and the society [4]. Annual expenses for treatment and rehabilitation of IS outpatients are assessed to 5.7 billion US dollars [4]. As the treatment of IS remains limited, the best approach to reduce stroke mortality and morbidity is the primary prevention through RF modification.

IS in young adults is considered a multifactorial disease involving genetic predisposition and a number of modifiable factors. The hypothesis that "young" stroke is associated only with rare RF is still under debate [1]. Regardless of the cumulating information that well-defined traditional RF are widely present in young male patients, undoubtedly IS in young adults has different etiologies and risk factors (RF) from the older population.

Although most of the RF for IS are potentially modifiable (smoking, low physical activity, irrational nutrition, alcohol consumption, dyslipidemia, hyperhomocysteinemia, asymptomatic carotid stenosis, AH, DM and others), their control and management are still a medical and social challenge.

For the purpose of primary stroke prevention in young adults, a multidisciplinary approach, integrating innovative screening and educational programs for early identification and control of the specific modifiable RF, is recommended [3, 4, 5].

The aim of the present study was to evaluate the incidence and prevalence of different RF in young (18-44 y) and middle-age (45-59 y) acute IS patients.

Original article



## SERUM LEVELS OF ADENOSINE DEAMINASE IN PATIENTS WITH TUBERCULOSIS AND INFLAMMATORY LUNG DISEASE

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### SUMMARY

**Introduction:** Serum adenosine deaminase (ADA) levels are used to diagnose tuberculosis and to monitor the condition of the patients during hospital treatment.

**Purpose:** The aim of the present study is to establish the diagnostic value of serum ADA in patients with inflammatory lung disease, including pulmonary tuberculosis.

**Materials and methods:** We measured ADA levels in 66 patients with lung disease, of whom 33 were men and 33 were women, all aged 18 to 86 years. Among the patients studied, 12 were diagnosed with tuberculosis, 34 with bacterial pneumonia and 20 with pleural effusion.

**Results:** We found that the serum ADA levels in our patients were higher than 18 U / l, which are the recommended upper limit in healthy people, according to the test performed by our laboratory. ADA levels were also higher than 21 U / l, the value we defined as the mean in healthy individuals in our previous study.

**Conclusion:** Based on our study, we can say that serum ADA levels in the patients we have studied with lung diseases, including pulmonary tuberculosis, have a high diagnostic value.

**Keywords:** ADA, diagnosis, tuberculosis,

### INTRODUCTION

Tuberculosis is one of the leading causes of death and morbidity worldwide. According to WHO, in 2018, the number of people globally suffering from tuberculosis is over 10 million, 1.5 million of whom died, and 484 thousand have developed resistant forms of the disease.

Various diagnostic methods are used to diagnose tuberculosis - microbiological detection of *Mycobacterium tuberculosis* and culture in Lowenstein-Jensen medium are the 'gold standards'. In the widely used Mantoux test after 72 hours, pass values above 15 mm are considered hyperergic. Isolating tuberculosis bacteria from sputum is the main and most trustworthy method. However, its disadvantage is the need for a significant number of bacteria in the test material. Another method used is the polymerase chain reaction (PCR). It is expensive, requires qualified staff and a lot of equipment. Many laboratories also use a relatively new automated diagnostic test that can identify *Mycobac-*

terium tuberculosis DNA and rifampicin resistance. There are also screening methods for detecting acid-fast bacilli, but their sensitivity is low. Therefore, there is a great demand recently for new microbiological, genetic, immunological and biomedical diagnostic methods for a rapid and accurate diagnosis of tuberculosis. Advances in immunological research have led to the introduction of new, significantly more sensitive methods than.

Measurement of the adenosine deaminase (ADA) activity is a biomedical method. ADA is essential for the proliferation and differentiation of lymphoid cells, especially T cells, and helps the maturation of monocytes to macrophages. The activity of this enzyme is increased in patients with tuberculosis. The level of ADA in sputum and serum is used to diagnose tuberculosis and is observed during the treatment of tuberculosis [1, 2, 3]. Enzyme testing is mainly used for pleural effusion, where microbiological testing often gives a negative result. Pleural ADA values above 20 U / l in combination with lymphocytic effusion are considered a positive result. However, testing for pleural effusion is not always possible, so it would be useful to take advantage of serum enzyme levels [4, 5, 6, 7].

Elevated ADA levels have been reported not only in tuberculosis and tuberculosis pleural effusion but also in some other inflammatory lung diseases, pulmonary fibrosis and cancer as adenosine levels are increased in cell damage, cell stress and hypoxia [8].

### PURPOSE

The aim of this study is to evaluate the diagnostic value of serum ADA levels in patients with inflammatory lung disease, including pulmonary tuberculosis.

### PATIENTS AND METHODS

In our study, we examined patients from the University Hospital "DrGeorgiStranski" Pleven with lung disease, who all have signed an informed consent during their admission. The studied patients were 66 aged 18 to 86 years, of which 33 men and 33 women. The average age for men is 54 years (18-86 years) and for women 49 years (22-77 years). Of the patients studied, 12 were diagnosed with tuberculosis, 34 had bacterial pneumonia, and 20 had pleural effusion in connection to other pulmonary diseases.

As a control group, we used the results of our previ-

## КЛИНИЧНОЛАБОРАТОРНИ ТЕСТОВЕ И ИНДЕКСИ ПРИ ПАЦИЕНТИ С ХРОНИЧЕН ХЕПАТИТ

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## CLINICAL LABORATORY TESTS AND INDICES IN PATIENTS WITH CHRONIC HEPATITIS

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**Резюме.** *Определени са средните стойности на важни лабораторни параметри при пациенти с хроничен хепатит В и хроничен хепатит С. Изчислени са индексите AST/ALT, APRI и FIB4. На базата на резултатите от чернодробна биопсия установихме, че FIB4 е индекс с добра надеждност, който може да се използва при пациенти с хроничен хепатит В или С за диференциране на тежка чернодробна фиброза.*

**Ключови думи:** *чернодробни тестове, индекси, FIB4, чернодробна биопсия*

**Abstract.** *Averages of important laboratory parameters are calculated in patients with chronic hepatitis B and chronic hepatitis C. The indices AST/ALT, APRI and FIB4 are calculated. Based on the results of a liver biopsy we found that FIB4 is an index with good reliability, which can be used in patients with chronic hepatitis B or C to differentiate severe hepatic fibrosis*

**Key words:** *liver tests, indices, FIB4, liver biopsy*

### ВЪВЕДЕНИЕ

Хроничните чернодробни заболявания са сред водещите причини за заболяемост и смъртност в световен мащаб. Те прогресират от леко възпаление до фиброза и цироза. Чернодробната фиброза се диагностицира основно на базата на чернодробна биопсия, образни методи и лабораторни тестове на серумни биомаркери. Чернодробната биопсия в момента все още е златният диагностичен инструмент за определяне на стадия на чернодробна фиброза [1]. Въпреки това много гастроентеролози избягват провеждането ѝ, позовавайки се на високия процент усложнения, свързани с лошо приемане от страна на пациента, сравнително висока цена,

ограничения в надеждността на хистологичните резултати, трудности при извършването на повторни оценки и др. [2]. Директните биомаркери (клас I) пряко корелират с фиброгенезата, те са обект на много нови изследвания. Биомаркери клас II (индиректни) отразяват фундаментални промени в чернодробната функция. Те са молекули, които се освобождават в кръвта вследствие на възпаление на черния дроб. Диагностичната точност на тези маркери се увеличава при комбинирането им в различни диагностични индекси: аспартат аминотрансфераза/аланин аминотрансфераза (AST/ALT), аспартатамино-трансфераза тромбоцитен индекс (APRI), FIB4 и др. [3, 4].



## COMPARATIVE ANALYSIS OF THE QUANTITATIVE AND QUALITATIVE METHOD FOR DETERMINATION OF D - DIMER

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### SUMMARY

**Introduction:** D - dimer is a product released during the process of blood clotting and degradation, which can be measured by blood sample analysis. There is usually the minimal activity of the pro/anticoagulant system in the human body, which generates low levels of D-dimer in healthy individuals. Normal values for plasma D-dimer are  $\leq 0.50$  mg / l.

**Aim:** The aim of the present study is to determine to what extent the quantitative and qualitative method for determination of D - dimer can be interchangeable and what is their diagnostic reliability in the normal and pathological area of measurement.

**Materials and methods:** We studied the levels of D-dimer by two methods - quantitative and qualitative, in 91 patients aged 25 to 86 years, of which 59 men and 32 women. To determine the D-dimer, we used venous blood taken in a vacuette containing sodium citrate. We used a Roche test for quantitative determination and a Latex agglutination test for qualitative determination.

**Results:** It was found that in positive samples above 0.5 mg/l, there is a very high percentage of coincidence. There is a discrepancy in the values obtained by the two methods at the negative values below 0.5 mg/l. We determined the sensitivity, specificity and accuracy of both methods.

**Conclusion:** The correlation in the results of the two methods is very good, but the quantification of D-dimer is more specific and accurate. We recommend that the value of 0.5 mg/l should be used as a cut off value for D-dimer.

**Keywords:** D-dimer, qualitative, quantitative, cut off

### INTRODUCTION

The D - dimer is a product released during the process of blood clotting and degradation, which can be measured by blood sample analysis. It is usually released when the blood clot begins to break down.

Thrombin converts fibrinogen to soluble fibrin by splitting of fibrin peptides A and B. Fibrin monomers polymerize spontaneously. Active factor XIII binds two D-domains and generates a solid fibrin clot. A new plasmin-resistant antigen determinant ("D-dimer") is obtained. During the degradation of the fibrin clot, fragments contain-

ing D-dimer are formed from plasmin, respectively. Most fibrin degradation products contain high molecular weight X-oligomers [1].

D-dimer testing is clinically relevant when deep vein thrombosis (DVT), pulmonary embolism (PE) or disseminated intravascular coagulation (DIC) are suspected [2, 3].

False negative and false positive results may occur in some cases. Due to the frequency of false-negative results, some authors recommend that D-dimer be used only at low probability of pulmonary embolism or deep vein thrombosis.

It should be noted that there are some physiological and medical conditions that can lead to elevated D-dimer in patients without pulmonary embolism, deep vein thrombosis, or DIC. These include, but are not limited to, pregnancy, malignancy, smoking, trauma, infection, or sepsis. In addition, elderly patients, immobilized patients, patients with autoimmune disorders, or those who have recently undergone surgery may have an elevated D-dimer [4].

In new studies, it is proposed to use corrected age limits for D-dimer, as D-dimer values may increase with age, even in the absence of pathology [5].

There is usually the minimal activity of the pro/anticoagulant system in the human body, which generates low levels of D-dimer in healthy individuals. The normal plasma D-dimer values are  $\leq 0.50$  mg/l. A D-dimer above 0.50 mg/l is considered positive [6].

The sensitivity and specificity of the D-dimer vary depending on the type of assay method. However, D-dimer tests generally have high sensitivity but low specificity. There are currently various methods for determining plasma D-dimer levels, both quantitative and qualitative [3, 7].

### PURPOSE

Our goal is to determine to what extent the quantitative and qualitative method for the determination of D - dimer can be interchangeable and what is their diagnostic reliability in the normal and pathological field of measurement.

### PATIENTS AND METHODS

In our study, we measured the levels of D-dimer in the plasma of patients at the University Hospital - Pleven. All of them have signed informed consent at the hospital



## DISTRIBUTION OF *MYCOPLASMA* SPP. AND *UREAPLASMA* SPP. AMONG PREGNANT WOMEN

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### SUMMARY:

The purpose of the present study is to determine the prevalence of genital mycoplasmas (*M. genitalium*, *M. hominis*, *U. parvum*, *U. urealyticum*) in pregnant women by molecular biological methods.

**Material/Methods:** A prospective epidemiological study of 107 pregnant women hospitalized in the Clinic of Obstetrics and Gynecology, University Hospital-Pleven, Bulgaria, was conducted. Vaginal secretion samples were taken from all 107 pregnant women. A Polymerase chain reaction (PCR) assay was used to detect the genomic DNA of the bacteria in pregnant women.

**Results:** The highest is the relative share of women in the age group from 20 to 35 years - 66 (64.68%), followed by women under 20 years - 27 (25.23%) and women over 35 years - 14 (13.08%). Detection of bacterial DNA was found in 85 (79.44%) of the cases, with present *Ureaplasma* spp. Colonization in 42 women (39.25%). Although no statistical dependence was found on open bacteria and age groups (p-value = 0.4688), it is noteworthy that the prevalence of *Mycoplasma* spp. and *Ureaplasma* spp. as a whole in the age group from 20 to 35 years, which has the highest birth rate, is more than twice higher than the group of up to 20 years and more than five times higher compared to the group over 35 years.

**Conclusions:** Studies on the incidence of *Mycoplasma* spp. and *Ureaplasma* spp. in pregnant women is important for controlling the pregnancy, predicting the risk of developing maternal-fetal infection and discussing the options for timely treatment.

**Keywords:** *Mycoplasma* spp., *Ureaplasma* spp., pregnant women, Polymerase chain reaction

### INTRODUCTION:

The bacteria of the genus *Mycoplasma* and the genus *Ureaplasma* are small free-living microorganisms that inhabit the mucous membranes of the respiratory and urogenital tracts in humans. They are conditionally pathogenic microorganisms and usually do not cause disease. Under adequate conditions, they can cause acute, chronic and latent infections. *M. pneumoniae*, *M. hominis*, *M. genitalium* and *U. urealyticum* are of the greatest importance for human pathology. In rare cases, mycoplasmas penetrate the submucosa and cause invasive diseases. The transmission of bacteria takes place through direct contact between people, including household and sexual contact. Children up to 5 years of age carry the infection subclinically. The most susceptible are young people. Significant colonization of *Mycoplasma* has been found predominantly in pregnant women compared to non-pregnant women [1]. The presence of *Mycoplasma* spp. and *Ureaplasma* spp. in the genitourinary tract of pregnant women is associated with miscarriages, premature birth, premature rupture of the amniotic membranes and birth of children at low gestational age. According to J. Hubenova (1982), *Mycoplasma* spp. can cause intrauterine infection of the fetus. Newborns are often colonized with *Mycoplasma* spp. and *Ureaplasma* spp. during birth, if the mothers are carriers without active infection.

*M. hominis* resides commensally in the cervix and vagina. The frequency of colonization in different studies varies between 20% and 50% [2, 3]. *M. hominis* can be isolated from the endometrium and fallopian tubes in about 10% of women with salpingitis. A number of studies have suggested that *M. hominis* is potentially pathogenic and has been linked to a variety of disorders: bacterial vaginosis, pyelonephritis, pelvic inflammatory disease, chorioamnionitis, endometritis, preterm birth, low birth, miscarriage, stillbirth, postpartum fever and perinatal mortality, and infertility [4, 5, 6]. *Ureaplasma* are directly as-