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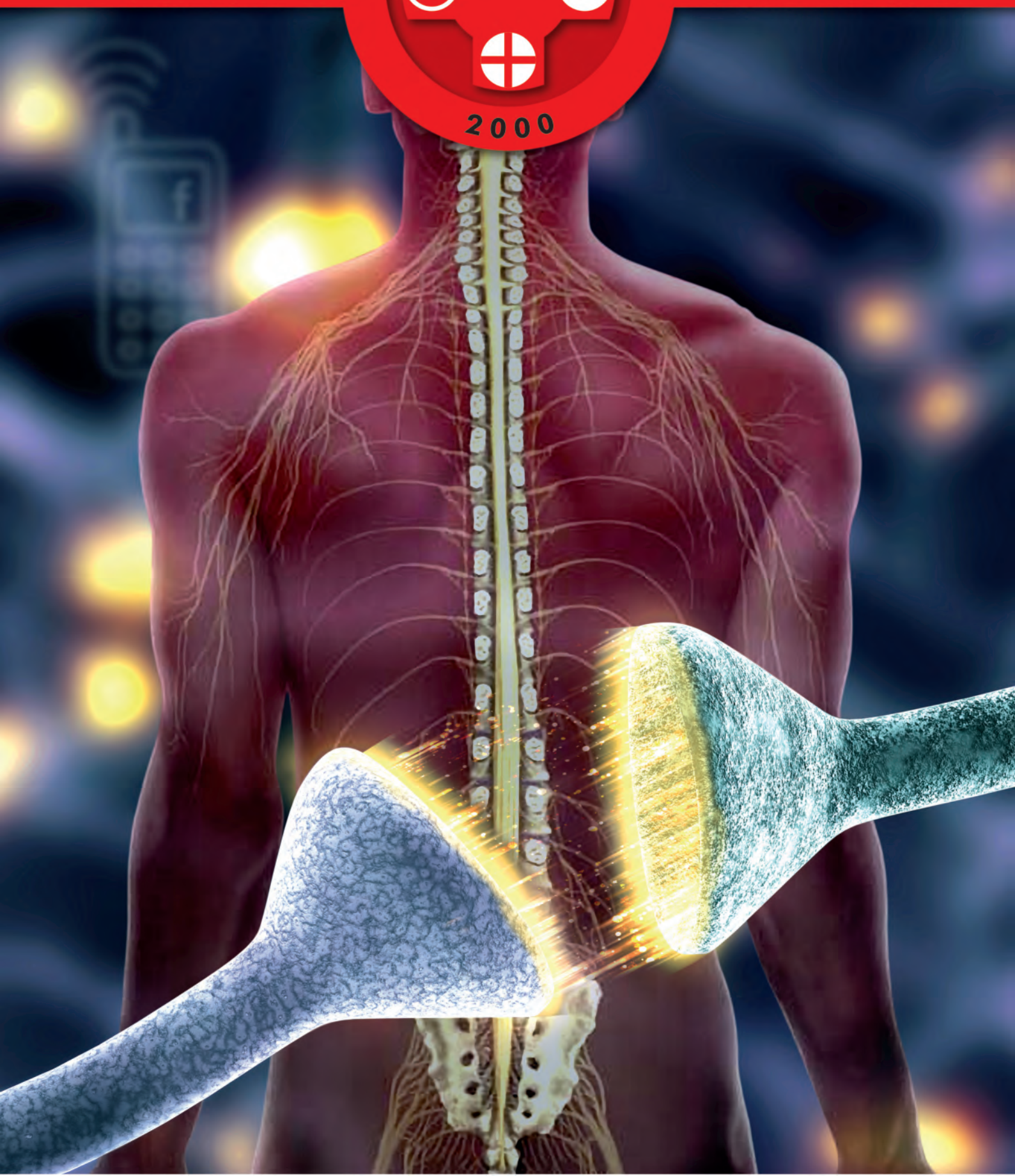

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EFFECTS OF A FACEBOOK PROFILE DEVOTED TO DRUG USE IN PREGNANCY ON THE DISCOVERY OF INAPPROPRIATE DRUG USE BY PREGNANT FEMALES IN THE FORMER YUGOSLAV REPUBLICS

Slobodan M. Jankovic[1], Marija Babic[1], Barudzic Nevena[1], Jelena Bogojevic[1], Obrad Vasic[1], Marija Vucicevic[1], Miona Dragojevic[1], Aleksadra Ivanovic[1], Aleksandra Ignjatovic[1], Ana Markovic[1], Jelena Milovanovic[1], Jovana Miloradovic[1], Sladjana Miladinovic[1], Milica Petrovic[1], Zora Pecelj[1], Jelena Radivojevic[1], Jelena Rajcic[2], Selena Rancic[1], Ana Ristic[1], Ivana Rudnjanin[1], Katarina Savic[1], Marija Spasic[1], Tatjana Stankovic[1], Stevan Stasevic[1], Milos Stevanovic[1], Sladjan Stojilkovic[1], Marina Trunic[1], Milica Scekic[1]

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DOPRINOS FEJSBUK PROFILA POSVEĆENOG KORIŠĆENJU LEKOVA U TRUDNOĆI OTKRIVANJU NEODGOVARAJUĆE UPOTREBE LEKOVA U BIVŠIM JUGOSLOVENSKIM REPUBLIKAMA

Slobodan M. Janković[1], Marija Babić[1], Barudžić Nevena[1], Jelena Bogojević[1], Obrad Vasić[1], Marija Vučićević[1], Miona Dragojević[1], Aleksadra Ivanović[1], Aleksandra Ignjatović[1], Ana Marković[1], Jelena Milovanović[1], Jovana Miloradović[1], Slađana Miladinović[1], Milica Petrović[1], Zora Pecelj[1], Jelena Radivojević[1], Jelena Rajčić[2], Selena Rančić[1], Ana Ristić[1], Ivana Rudnjanin[1], Katarina Savić[1], Marija Spasić[1], Tatjana Stanković[1], Stevan Stašević[1], Miloš Stevanović[1], Slađan Stojilković[1], Marina Trunić[1], Milica Šćekić[1]

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SHORT TITLE:
INAPPROPRIATE DRUG USE IN PREGNANCY AND FACEBOOK

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ABSTRACT

Background. *Although online social networking is increasingly used for medical purposes, studies investigating drug use among pregnant females by means of online networks are lacking.*

Objective. *The aim of our study was to investigate the extent of inappropriate drug use among pregnant women by creating a Facebook profile and using it as a tool for interacting with pregnant women.*

Methods. *A Facebook profile titled "Preserve babies from drugs" was created and maintained by a group of fourth-year pharmacy students for 3 months. Introductory educational material about the principles of drug use in pregnancy, information about health facilities offering counselling about pregnancy, information about a clinical pharmacology department that offered counselling and an open-ended questionnaire were posted in the "Notes" section of the Facebook profile.*

Results. *Of 239 registered pregnant "friends" of the profile who received the questionnaire from the investigators, 93 responded (39%). Among the respondents, 50 pregnant women (53.8%) reported taking medication(s) during their current pregnancy, and 42 of the respondents reported using one or more drugs improperly. The most frequently used drugs were multivitamin and multi-mineral preparations, oral antibiotics, parenteral progesterone and benzodiazepines.*

Conclusions. *The Facebook profile devoted to drug use in pregnancy could be a useful adjunct to efforts by official health care institutions to identify inappropriate drug use and educate pregnant women appropriately.*

Keywords. *Facebook, online social networking, drugs, pregnancy*

SAŽETAK

Uvod. *Iako se socijalno umrežavanje na internetu sve više koristi u medicinske svrhe, istraživačke studije putem internet mreža koje se bave upotrebom lekova kod trudnica nedostaju.*

Cilj. *Cilj našeg rada je bila analiza slučajeva neodgovarajuće upotrebe lekova među trudnicama koji mogu biti otkriveni stvaranjem fejsbuk profila sa odgovarajućim informacijama.*

Metode. *Grupa studenata četvrte godine farmacije formirala je fejsbuk profil pod nazivom „Čuvajmo bebe od lekova" koji je bio aktivan 3 meseca. U delu „Beleške" ovog profila unete su informacije o zdravstvenim ustanovama koje nude savetovanje trudnica, edukativni materijal o principima upotrebe lekova u trudnoći i otvoreni upitnik.*

Rezultati. *Od 239 prijavljenih trudnica, „prijatelja" našeg profila koje su dobile upitnik od istraživača, 93 (39%) njih je odgovorilo. Među ispitanicama bilo je 50 (53.8%) trudnica koje su uzimale lekove tokom trudnoće. Čak 42 trudnice koristile su jedan ili više lekova na neodgovarajuć način. Najčešće nepravilno korišćeni lekovi bili su multivitaminski i multi-mineralni preparati, oralno primenjeni antibiotici, parenteralno primenjeni preparati estrogena kao i benzodiazepini.*

Zaključak. *Fejsbuk profil posvećen upotrebi lekova u trudnoći može da bude korisna dodatna mera uz napore zvaničnih zdravstvenih ustanova za otkrivanje slučajeva nepravilog korišćenjag lekova kao i za informisanje trudnica.*

Ključne reči. *Fejsbuk, socijalno umrežavanje, lekovi, trudnoća*

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INTRODUCTION

Online social networking is increasingly being used for medical purposes. Patients with the same disorder or similar disorders frequently use online networks to exchange their experiences with new therapies or share emotional support [1]. Facebook is the most frequently used online network, followed by MySpace and Twitter [2]. Recently, Facebook has been used to investigate beliefs and attitudes associated with prescription drug misuse among students [3] and to increase spontaneous reporting of adverse drug reactions [4]. Such interventions are cheap and reasonably effective; just a few working days may reveal dozens of adverse drug reactions [4].

We are not aware of any previous studies investigating drug use among pregnant women by means of online networks. Pregnant women frequently use over-the-counter preparations, but, in the majority of cases, the safety of these preparations during pregnancy for both the mother and child is not supported by evidence [5]. Even when prescribed, drugs used in pregnancy may belong to categories with known teratogenic or toxic foetal effects in a significant percentage of the patients (up to 4%). Self-medication increases the likelihood of inappropriate drug use in pregnancy [6]. Appropriate information offered to pregnant women about the effects of drugs on pregnancy and the foetus and information gathered from pregnant women about drug use may help to identify or prevent inappropriate drug use.

The aim of our study was to investigate the extent of inappropriate drug use among pregnant women by creating a Facebook profile to interact with pregnant women.

METHOD

Building the profile

A Facebook profile titled "Preserve babies from drugs" (in the Serbian language) was created on February 24, 2011 by a group of fourth-year pharmacy students and their professor of clinical pharmacy (investigators: 26 students + professor) from the Medical Faculty, University of Kragujevac, Serbia (available at http://www.facebook.com/home.php#!/profile.php?id=100002117414536). The profile was active until June 5, 2011.

Introductory educational material about the principles of drug use in pregnancy (2 pages), information about health facilities offering pregnancy counselling (3 facilities), information about a clinical pharmacology department offering counselling for drug use in pregnancy and an open-ended questionnaire for pregnant women targeting their drug history during pregnancy were posted in the "Notes" section of the Facebook profile. All written materials were created by the investigators. An explanation of the purpose of the profile (identifying inappropriate drug use in pregnancy and providing information about counselling) was posted on the "Info" section of the profile. Motivating photographs and drawings about life during pregnancy and the mother-child relationship were posted in the "Photos" section of the profile.

Linking the profile

The profile "Preserve babies from drugs" was linked to the following Facebook profiles and groups dealing with pregnancy: Zdrava trudnoća, Klub trudnica i mladih mama, Trudnoća, YuMama, BEBAC.com, Super beba, Udruženje RODITELJ, Dnevnik bebe, Ringeraja porodični portal - www.Ringeraja.rs, Roditelji.hr, e-beba, Moje Dijete, BHBebe.com - Bosansko-hercegovački porodični portal, Yoga za trudnice, mame i bebe - Shakti mama, Mamino Sunce, NajboljaMamaNaSvetu.com, Škola za trudnice, & Mame & Bebe & Trudnice, KLUB MAMA SA FB-a, Moja trudnoća, MojaBeba, RoditeljSrbija, Dani beba, and djete i trudnica. Web pages devoted to pregnancy were also visited, and, after registration, information about the Facebook profile "Preserve babies from drugs" was left on these pages (http://www.trudnoca.net/forum/, http://www.ringeraja.rs/forum/tt.asp?forumID=204, http://mameibebe.biz.hr/phpBB2/viewforum.php?f=35).

Recruiting pregnant women

Pregnant women with their own profiles on Facebook were recruited by the investigators using both a joint profile ("Preserve babies from drugs") and the investigators' personal profiles. To reach as many pregnant women as possible, the information was spread by "friends" of the "Preserve babies from drugs" profile.

The recruitment of pregnant women was enhanced by posting flyers with information on the "Preserve babies from drugs" profile for patients of primary care health facilities that regularly offer pregnancy counselling in 11 Serbian towns (20 to 40 flyers posted on one occasion per town).

Establishing contact with pregnant women

The pregnant women who were recruited by the previously mentioned methods became "friends" of the "Preserve babies from drugs" profile. These women were then approached by investigators in three ways: by e-mail, by Facebook "Messenger" or by chat. The pregnant women were sent a questionnaire about their medical history before and during their pregnancy and about the ways they informed themselves about pregnancy. The subjects responded to the questionnaire by e-mail, Facebook "Messenger" or chat (with the help of the investigators).

The investigators did not advise the respondents about drug use during pregnancy, but they directed these women to the Clinical Pharmacology Department of the Clinical Center in Kragujevac to receive additional information.

Processing the data

After collecting the completed questionnaires, the responses were coded and entered in an SPSS workbook (version 18). Descriptive statistics were identified from the data using frequencies, measures of central tendency and measures of variability.

RESULTS

During the study period, 239 registered "friends" of the profile received the questionnaire from the investigators, and 93 pregnant women responded to the questionnaire (39% response rate). The characteristics of the respondents are shown in Table 1 . Among the respondents, 50 pregnant women took medication(s) during their current pregnancy (53.8%). The characteristics of the medications and therapeutic regimens are shown in Table 2. After comparing prescribed drugs and those used on the patient's own initiative with the respondents' stated reasons for taking drugs and current recommendations for drug use during pregnancy, two experts (clinical pharmacology specialists) from the Clinical Pharmacology Department of the Clinical Center in Kragujevac decided whether the drug use was justified. The results of their analysis are shown in Table 3.

DISCUSSION

In our study, a Facebook profile devoted to the use of drugs in pregnancy proved useful for identifying pregnant women who used drugs improperly. Of 50 pregnant women who reported using drugs, 42 used one or more drugs improperly. The drugs with the most frequent improper use were multivitamin and multi-mineral preparations (used for supplementation without a clear reason), oral antibiotics, parenteral progesterone and benzodiazepines. Although multivitamin and multi-mineral preparations (in recommended daily doses) do not cause harm to pregnant women (except for unnecessary costs), broad-spectrum antibiotics can cause diarrhoea. Progesterone is ineffective for treating threatened miscarriage [7], and both progesterone [8,9] and benzodiazepines are suspected to have teratogenic potential and are not recommended for use in pregnancy without clear indication [10,11].

The majority of pregnant women connected to our profile were inexperienced in drug use during pregnancy (68.8% of the respondents were in their first pregnancy). Only two of the respondents had a child with congenital anomalies in their families. However, 92% of the medications were prescribed by physicians, making physicians responsible for inappropriate prescribing in pregnancy. Visits to counselling services for pregnant women were not helpful for avoiding prescribing errors because more than 60% of the women visited such services regularly. The findings on inadequate prescribing and advising in pregnancy were further confirmed by the low percentage (24.7%) of pregnant women who were taking prophylactic doses of folic acid, an intervention that is considered a standard of care in pregnancy [12]. In addition to the obvious need for additional education of health workers regarding drug use in pregnancy, it seems that establishing and maintaining profiles devoted to drugs in pregnancy on social networks such as Facebook is a useful intervention that may not only help to identify inappropriate drug use during pregnancy but may also provide a communication channel through which pregnant women can receive important information about drugs and prevent the adverse consequences of inappropriate drug use.

CHARACTERISTIC	VALUE
Age of the respondents (mean ± standard deviation)	27.3 ± 5.0 years
Country of residence (Serbia/other ex-YU country/other European country)	83/7/3 **(89.2%/7.7%/3.3%)**
City or town of residence	32 different cities or towns
Level of education (elementary school/high school/higher vocational school/bachelor's/master's or specialist)	2/60/11/13/7 **(2.2%/64.5%/11.8%/14%/7.5%)**
Employed (yes/no)	34/59 **(36.6%/63.4%)**
Working during pregnancy (yes/no)	17/76 **(18.3%/81.7%)**
Marital status (married/widowed/single)	83/1/9 (89.2%/1.1%/9.7%)
Number of children (0/1/2)	66/20/7 **(71%/21.5%/7.5%)**
Order of current pregnancy (first/second/third/fourth)	64/17/8/4 (68.8%/18.3%/8.6%/4.3%)
Week of current pregnancy (mean ± standard deviation)	23.7 ± 8.9
Complications of pregnancy (yes/no)	14/79 **(15.1%/84.9%)**
Chronic disease (yes/no)	8/85 **(8.6%/91.4%)**
Allergies (yes/no)	24/69 **(25.8%/74.2%)**
Gestational diabetes (yes/no)	3/90 **(3.2%/96.8%)**
Taking medication during previous pregnancy (yes/no)	16/77 **(17.2%/82.8%)**
Previous spontaneous abortion (yes/no)	9/84 **(9.7%/90.3%)**
Cause of spontaneous abortion (trauma/anomaly/unknown)	3/5/1
Previous artificial abortion (yes/no)	6/87 **(6.5%/93.5%)**
Previous congenital anomalies in the family (yes/no)	2/91 **(2.2%/97.8%)**

Table 1. Characteristics of the pregnant women who responded to the questionnaire.

CHARACTERISTIC	VALUE
Reason for taking medication during pregnancy (hypertension/uterine contractions/common cold/anaemia/asthma/hormonal substitution/pain/antibiotic prophylaxis after amniocentesis/more than two reasons/no clear reason) (n=50)	2/12/9/3/3/3/3/3/4/8 (4%/24%/18%/6%/6%/6%/6%/6%/8%/16%)
Who advised or prescribed the medication (doctor/a friend/own decision) (n=50)	46/1/3 (92%/2%/6%)
Compliant with therapy regimen (yes/no) (n=50)	46/4 (92%/8%)
Gynaecological disorder (yes/no) (n=93)	6/87 (7%/93%)
Using vaginal preparation with St John's wort during pregnancy (n=93)	18/75 (19%/81%)
Using "natural" (herbal) drugs during pregnancy (no/honey-based preparations/herbal tea) (n=93)	66/4/23 (71%/4%/25%)
Using vitamins during pregnancy (no/hydrosoluble vitamins/liposoluble vitamins/multivitamin preparations) (n=93)	26/22/4/41 (28%/24%/4%/44%)
Experiencing side effects of medication during pregnancy (yes/no) (n=93)	3/90 (gastrointestinal complaints or rash) (3%/97%)
Source of information about pregnancy (Internet/TV/books/pregnancy counselling centre/other/multiple sources) (n=93)	6/8/1/3/2/73 (6.5%/8.6%/1.1%/3.2%/2.2%/78.5%)
Source of information about the Facebook profile (notice on the Facebook profile/recommended by a friend or relative/counselling service/other) (n=93)	19/53/8/13 (20.4%/57%/8.6%/14%)
Receiving antibiotics during pregnancy (yes/no) (n=93)	18/75 (19.4%/80.6%)
Receiving antihypertensive therapy during pregnancy (yes/no) (n=93)	6/87 (6.5%/93.5%)
Receiving anxiolytics during pregnancy (yes/no) (n=93)	2/91 (2.2%/97.8%)
Receiving sex hormones during pregnancy (yes/no) (n=93)	10/83 (10.8%/89.2%)
Receiving tocolytics during pregnancy (yes/no) (n=93)	13/80 (14%/86%)
Receiving multivitamins during pregnancy (yes/no) (n=93)	41/52 (44.1%/55.9%)
Receiving minerals during pregnancy (yes/no) (n=93)	20/73 (21.5%/78.5%)
Receiving analgesics during pregnancy (yes/no) (n=93)	9/84 (9.7%/90.3%)
Receiving folic acid during pregnancy (yes/no) (n=93)	23/70 (24.7%/75.3%)
Receiving drugs for anaemia during pregnancy (yes/no) (n=93)	4/89 (4.3%/95.7%)
Receiving antiepileptics during pregnancy (yes/no) (n=93)	1/92 (1.1%/98.9%)
Availability of counselling service (yes/no) (n=93)	83/10 (89.2%/10.8%)
Visiting counselling service (yes/no) (n=93)	56/37 (60.2%/39.8%)

Table 2. Characteristics of the medications and therapeutic regimens used by the pregnant women who responded to the questionnaire.

DRUG AND MODE OF ADMINISTRATION	NUMBER OF PREGNANT WOMEN USING THE DRUG	INDICATION	JUSTIFICATION
Amoxicillin, oral	6 (6.4%)	Common cold	Unjustified
Cephalexin, oral	4(4.3%)	Common cold	Unjustified
Erythromycin, oral	3 (3.2%)	Common cold	Unjustified
Amoxicillin, oral	2 (2.1%)	Antibiotic prophylaxis after amniocentesis	Justified
Progesterone, parenteral	8 (8.6%)	Threatening abortion	Unjustified
Diazepam, oral	2 (2.1%)	Nervousness	Unjustified
Folic acid, oral	23 (24.7%)	Supplementation	Justified
Multivitamin and multi-mineral preparations with recommended daily intake of vitamins and minerals, oral	32 (34.4%)	Supplementation	Unjustified
Iron, oral	12 (12.9%)	Anaemia	Justified
Tocolytic drugs (beta2 agonists), oral	12 (12.9%)	Premature contractions of uterus	Justified
Methyldopa, oral	4(4.3%)	Hypertension in pregnancy	Justified
Nystatin + nitrofurantoin, vaginal	4(4.3%)	Vaginal infection	Justified

Table 3. Justification of drug use during pregnancy in patients who participated in this survey.

Our study did not attempt to advise pregnant women because our group is not part of the health care system in Serbia, and legislation does not allow students to practice medicine, especially over social networks. Instead, we directed followers of our profile to official health care facilities that offer advice about drugs in pregnancy. However, none of the study participants followed this advice and went to an official facility. This study concludes that using Internet-based social networks may help to address certain health issues (such as inappropriate drug use in pregnancy) that cannot be addressed in official ways. This conclusion has been previously identified for other patient groups [1,13], but pregnant women are a particularly vulnerable group, and they may have difficulty visiting physicians.

There is also an issue about herbal drugs, which are frequently considered "safe" by patients without medical education [14]. As reported in a recent study, more than 50% of the pregnant women in Norway used herbal remedies during pregnancy, [14]. In our study, fewer pregnant women used herbal remedies (29%), but this number was almost one-third of the study sample. Because herbal remedies have received less investigation than registered drugs and their safety profiles have not been established with certainty [15], it is important to educate pregnant women about the possible risks of these remedies. A Facebook profile such as the one used in this study could be very useful for disseminating important information about herbal drug use in pregnancy.

Our results suggest that a Facebook profile devoted to drug use in pregnancy could be a useful adjunct to efforts by official health care institutions to educate pregnant women about potentially harmful drug use.

ACKNOWLEDGEMENTS

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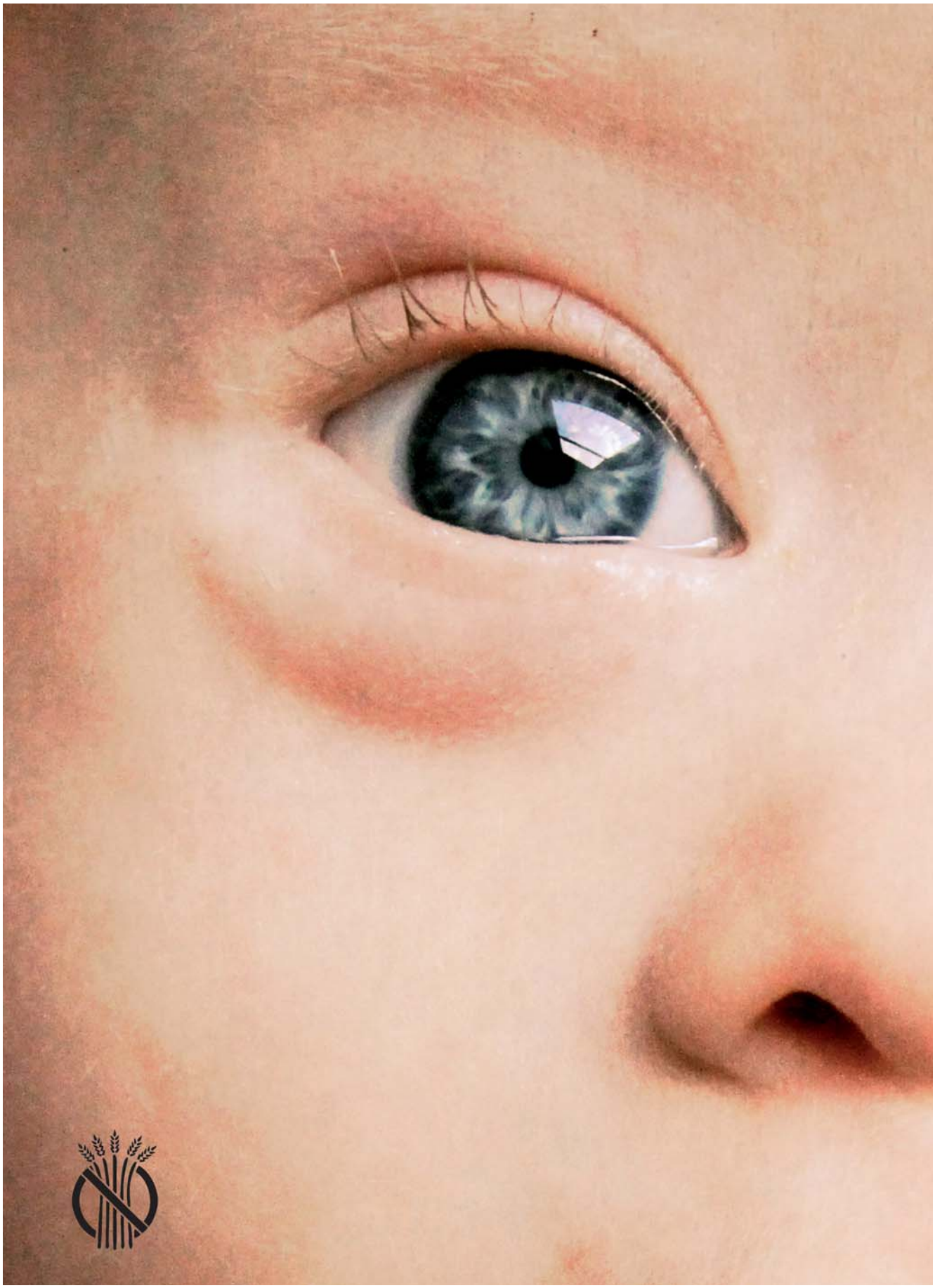

COELIAC DISEASE IN CHILDREN WITH DOWN SYNDROME IN SERBIA

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CELIJAČNA BOLEST KOD DECE SA DAUNOVIM SINDROMOM U SRBIJI

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ABSTRACT

Introduction. *To determine the prevalence of coeliac disease (CD) in children with Down syndrome (DS) in Serbia and to analyse the clinical characteristics and laboratory data from patients with DS.*

Methods. *A total of 91 children (50 boys and 41 girls, mean age of 6.3 years) with DS were examined. The total levels of IgA and IgA transglutaminase (IgA tTG) antibodies were determined. The levels of IgG transglutaminase (IgG tTG) and IgG anti-endomysial (IgG EMA) antibodies were determined in cases of IgA immunodeficiency. Enterobiopsies were performed in patients with positive antibody titres.*

Results. *Of the children evaluated, 38 exhibited constipation (41.7%), 26 experienced vomiting and regurgitation (28.5%), 16 had anaemia (17.5%), and two had intermittent diarrhoea (2.2%). The DS-specific mean weight percentile was 15.2%±14.5% (range <5-75%). In four out of five of the children with positive levels of IgA tTG, an enterobiopsy showed the presence of CD (4.4%, 95% CI, 1.7%-10.7%). The levels of IgG tTG and IgG EMA were determined in five children with an IgA immunodeficiency. The IgG EMA was negative in all five of the children. Three of the children showed increased IgG tTG values and underwent an enterobiopsy, which showed a normal mucosa. Our analysis shows that the signs and symptoms of CD in children with DS are only of minor diagnostic value in the detection of the disease.*

Conclusion. *These results suggest the need for systematic screening for CD in children with DS because symptoms that are characteristic of both diseases may overlap.*

Keywords: *anti-endomysial antibodies; coeliac disease; Down syndrome; tissue transglutaminase antibodies*

SAŽETAK

Uvod. *Odrediti prevalenciju celijačne bolesti (CB) i analizirati kliničke karakteristike i laboratorijske nalaze kod dece sa Daunovim sindromom (DS) u Srbiji.*

Metode. *Ispitivano je devedeset jedno dete (50 dečaka i 41 devojčica, prosečne starosti 6,3 godine) određivanjem ukupnih vrednosti IgA i IgA transglutaminskih At (IgA TTG), a u slučajevima IgA imudodeficijencije i određivanjem IgG transglutaminskih At (IgG TTG) i IgG andiendomizijalnih At (IgG EMA). Kod seropozitivne dece je rađena enterobiopsija.*

Rezultati. *Četrdeset jedno dete je imalo konstipaciju (41,7%), 26 povraćanje i regurgitaciju (28,5%), 16 anemiju (17,5%), dok je dvoje dece imalo povremeni dijarealni poremećaj (2,2%). Prosečan percentil težine određivan tablicama za decu sa DS je iznosio 15.2%±14.5% (range <5-75%). Kod četvoro od petoro dece sa pozitivnim IgA TTG je enterobiopsijom dokazana CB (4,4%, 95% CI, 1.7%-10.7%). Kod petoro dece je utvrđena IgA imudodeficijencija i kod njih su određivana IgG TTG i IgG EMA. IgA EMA su bila negativna u svo petoro dece, dok su kod troje dobijene povišene vrednosti IgG TTG. Kod ovo troje je urađena enterobiopsija koja je ukazala na postojanje sluznice normalnih karakteristika. Znaci i simptomi koji su karakteristični za CB kod naše dece sa DS su imali malu dijagnostičku vrednost.*

Zaključak. *Naši rezultati ukaziju na potrebu za sistematskim skriningom za CB kod dece sa DS.*

Ključne reči: *antiendomizijalna antitela; celijačna bolest; Daunov sindrom; transglutaminska antitela*

Abbreviations: CD - coeliac disease, **DS** - Down syndrome, **IgA tTG** - immunoglobulin A transglutaminase antibodies, **IgG tTG** - immunoglobulin G transglutaminase antibodies, **IgG EMA** - immunoglobulin G anti-endomysial antibodies.

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INTRODUCTION

Down syndrome (DS) is a chromosomal disorder that results from trisomy and other aberrations of chromosome 21. With a prevalence of 1:700, DS represents the most common chromosomal disorder and is a leading cause of mental retardation (1). DS is characterised by multiple typical somatic and visceral malformations and an increased risk of infection, leukaemia, and autoimmune diseases, such as hypothyroidism, Hashimoto's thyroiditis, diabetes mellitus type 1 and coeliac disease (CD) (2).

The association between CD and DS was first described more than 30 years ago (3). Many papers published since then have reported the prevalence of CD in patients with DS to range from 2.5% to 18.6% (4-7). Several medical associations have concluded that serological screening for CD should be performed in all children with DS and have issued appropriate recommendations and guidelines in the light of the possibility that developing lymphoma is the most severe complication of CD (8,9). However, there are authors who believe that the consistent use of this approach might not be entirely justified, primarily for economic reasons (10).

The prevalence of CD in children with DS in Serbia has not yet been reported. The available data on the prevalence of CD in Serbia are from two studies. The first study was limited to children with a classic form of CD in the Province of Voyvodina (the north part of Serbia), which showed an incidence rate of 1 in 1715 live births (11). A recent article that included 121 children with type 1 diabetes mellitus in Serbia reported the prevalence of CD to be 5.8% (12).

The aim of the present study was to determine the prevalence of CD in children with DS in Serbia and to evaluate the clinical signs that might assist in the diagnosis of CD.

PATIENTS AND METHODS

Patients

A total of ninety-one children with DS were evaluated in the Pediatric Department at the General Hospital Subotica from October 2004 to January 2011. Children from all regions of Serbia were evaluated at the Facility for Children with Developmental Disorders "Kolevka" in Subotica. Trisomy of chromosome 21 was confirmed in all of the children by karyotype analysis. The age of the children with Down syndrome ranged from 8 months to 16 years (mean age of 6.3 years The male to female ratio was 1.2 (50 boys/41 girls). The body mass was determined based on the DS-specific mean weight percentile (13). Gastrointestinal functions that are specific to CD, such as chronic diarrhoea, constipation, vomiting, failure to thrive and associated anomalies that are characteristic of DS, were recorded. A complete blood count, serum iron, and hepatic transaminase levels were determined for all of the children.

Serologic Markers

After approval of the research by the Hospital Ethics Committee, all of the patients were tested to determine the immunoglobulin A (IgA) tissue transglutaminase (tTG) and total IgA levels. In cases of low total IgA levels, the immunoglobulin G (IgG) tTG and IgG anti-endomysial (EMA) levels were evaluated.

IgA tTG and IgG tTG were measured using a commercial enzyme-linked immunosorbent assay (Orgentec Diagnostika, Mainz, Germany). Values ≥10 U/mL were considered to be positive, as recommended by the manufacturer. Quantitative determinations of serum IgA levels were performed using a routine method.

In cases of IgA deficiency, sera were analysed for IgG EMA antibodies. IgG EMA antibodies were determined using an immunofluorescence method on a primate oesophagus substrate (IMMCO Diagnostics, Buffalo, New York).

Small Bowel Histology

The patients who were serologically positive for CD were scheduled for an upper endoscopy to biopsy the duodenum. Specimens of the mucosa were collected from the descendent duodenum and bulb (four biopsies) and sent for histopathological examination. Biopsies were evaluated by one pathologist who was unaware of the patients' identity. Biopsies were classified according to Marsh's (14) criteria, as revised by Oberhuber (15).

Statistical Analysis

Categorical variables are presented as absolute and relative frequencies, whereas continuous variables are summarised as the mean±SD. Student's t tests were used to evaluate the continuous data. Children with both DS and CD were compared to children without CD. The rejection of the null hypothesis was set at 5% ($P < 0.05$).

RESULTS

The Down syndrome-specific mean weight percentile of the 91 children evaluated was 15.2%±14.5% (range <5-75%). Out of 91 children with DS, 54 had malformations (59.3%). Forty of the children exhibited constipation (41.7%, 95% CI, 34.2%-54.2%), 27 experienced vomiting and regurgitation (28.5%, 95% CI, 21.2%-39.7%), 16 had sideropenic anaemia (17.5%, 95% CI, 10.3%-24.4%) and two had an intermittent diarrhoeal disorder (2.2%, 95% CI, 0.6%-7.6%).

IgA tTG and total IgA levels were determined for all of the children. Increased levels of IgA tTG were found in 5 of the children (5.5%) with DS. Three of the 5 were diagnosed with sideropenic anaemia, one had alopecia, and one was asymptomatic. In 4 out of 91 (4.4%) children (e.g., the three children with sideropenic anaemia and the child with alopecia), the pathohistological analysis of the duodenal mucosa sample showed that 2 of the patients had partial villous atrophy (Marsh 3a) and two had severe villous atrophy (Marsh 3b and Marsh 3c). In the asymptomatic child with increased levels of IgA tTG, the mucosa of the small intestine showed normal pathohistological characteristics (Table 1). Out of the four children with confirmed gluten

Patient	Sex	Age	Diseases	GI symptoms	IgA tTG levels	Biopsy
1	M	16 years, 2 months	Alopecia	Constipation	102.5 U/mL	Marsh 3a
2	M	6 years, 1 month	Sideropenic anaemia, AV septal defect	Vomiting	60 U/mL	Marsh 3b
3	M	6 years	Sideropenic anaemia	None	88 U/mL	Marsh 3c
4	F	7 years, 3 months	Sideropenic anaemia, AV canal	Constipation	45 U/mL	Marsh 3a
5	F	3 years, 8 months	None	None	17.7 U/mL	Normal

Table 1. Positive results of screening and the diseases associated with Down syndrome in children

	DS patients without CD (N=87)	DS patients with CD (N=4)	*P*
Weight, perc. (mean ± SD)	14.9 ±14.4	23.8 ± 18.9	0.233
Laboratory findings			
Haemoglobin (g/dL)	11.3± 1.3	9.3 ± 1.4	0.005
Mean corpuscular volume (fL)	84.6± 8.2	79.3± 4.2	0.197
Serum iron (μmol/L)	14.3± 6.2	11.4± 9.1	0.37
Alanine transaminase (UI/L)	23±7	24± 8	0.618
Aspartate transaminase (UI/L)	23±9	25± 8	0.765

Table 2. Clinical characteristics and laboratory test results for Down syndrome patients without coeliac disease (n=87) and Down syndrome patients with CD (n=4).

enteropathies, two of them had constipation and one intermittently suffered from vomiting and regurgitation. Gluten enteropathy was found in 4 out of 5 of the children with positive levels of IgA tTG antibodies (80%). The prevalence of CD in this population was 4.4%, with a confidence interval (95%) ranging from 1.7% to 10.7%.

Low levels of IgA (0.05-0.1 g/L) were found in 5 of the patients (5.49%). Due to the low levels of total IgA, these children were also tested for IgG tTG levels and IgG EMA antibodies. In all five of the children, the IgG EMA was negative. Increased levels of IgG tTG were found in three out of five of the children (28-36 U/mL). An enterobiopsy was performed and showed the presence of a normal mucosa.

A comparative analysis between the patients with diagnosed CD based on biopsy results and children without CD (Table 2) revealed that there were no statistically significant differences in the results of the aminotransferase and hematologic tests, except that patients with DS and CD tended to have significantly lower haemoglobin levels (P=0.005).

DISCUSSION

The prevalence of children with DS and CD in Serbia (4.4%), which is higher than in the general population, is in agreement with the rates observed in many other countries, including Europe (e.g., 2.6% in Germany, 4.5% in the Netherlands, 4.6% in Italy, 6.3% in Spain, and 6.4% in Turkey), North America (e.g., 2.6% to 6.6% in the USA), South America (e.g., 3.6% in Argentina and 5.6% in Brazil), the Middle East (e.g., 3.8% in Israel), and Australia (3.9%) (4-6,16-23). The reported rates are likely underestimated because most of authors from the other studies did not perform small bowel biopsies or additional confirmatory laboratory testing (EMA or HLA-DQ2 and HLA-DQ8 typing) in the patients with DS who had a positive serology. Differences in the type of antibody used for screening and cohort size may have influenced the variability in the rates of occurrence. A higher prevalence was reported in two smaller series from Sweden. Jansson and Johansson (24) screened 65 patients with DS and found a CD prevalence of 16.9%, while Carlsson et al. (7) reported a similar prevalence of 18.6% (8/43). These regional differences raise questions about geographic and ethnic influences on the development of CD in patients with DS (Table 3).

CD can present as symptomatic and asymptomatic forms with clinical, serologic and pathohistological variations. In children with DS and symptomatic CD, growth failure, anaemia, intermittent diarrhoea, and constipation are described as the most common manifestations of the disease (7,8). The significance of these manifestations in clinical practice is not entirely obvious because the same signs can occur in children with DS that do not have CD (4).

The majority of children in this study with DS without CD presented with gastrointestinal symptoms that are typical for both diseases. Congenital heart defects, untreated CD and hypothyroidism might influence the growth and weight (between 0.5-2 kg) of children with DS (25). Growth

Country	Prevalence	Author (reference) *	No	Serologic markers	Biopsies in all **
Germany	2.6%	Storm (5)	78	IgA and IgG AGA	No
USA	3.2%	Mackey et al. (18)	93	IgA EMA,AGA and IgG AGA	No
Argentina	3.6%	Rumbo et al. (17)	56	IgA EMA,AGA,tTG and IgG AGA, tTG	Yes
Israel	3.8%	Shamaly et al. (16)	52	IgA EMA,AGA,tTG and IgG AGA, tTG	No
Australia	3.9%	Gale et al. (19)	55	IgA and IgG AGA	No
Netherlands	4.5%	Wouters et al. (20)	155	IgA EMA and IgA tTG	Yes
Italy	4.6%	Bonamico et al. (4)	1202	IgA EMA and IgA AGA	No
Brazil	5.6%	Nisihara et al. (21)	71	IgA EMA and IgA tTG	No
Spain	6.3%	Carnicer et al. (23)	284	IgA EMA,AGA and IgG EMA, AGA	Yes
Turkey	6.4%	Cogulu et al. (6)	47	IgA EMA and IgA AGA	No
USA	6.6%	Zachor et al. (22)	75	IgA EMA and IgA AGA	No
Sweden	16.9%	Jansson et al. (24)	65	IgA EMA and IgA AGA	No
Sweden	18.6%	Carlsson et al. (7)	43	IgA EMA and IgA AGA	No

Table 3. Prevalence of coeliac disease in children with Down syndrome
EMA, anti-endomysial antibodies; **AGA**, antigliadin antibodies; **tTG**, tissue transglutaminase antibodies; **IgA**, immunoglobulin A; **IgG** immunoglobulin G; * Author and the reference number; ** Biopsies were performed in all of the patients with positive serology.

failure as a manifestation of CD loses its significance in children with DS because some of the associated malformations (as observed in almost half of our patients, with a weight percentile of 15.2%) may also have the same effect.

We found that aminotransferases and hematologic tests did not predict the coexistence of CD in the children with DS. Although the patients with CD tended to have lower haemoglobin levels (P=0.005), CD was the cause of anaemia in only three out of 16 cases, and its value as an indicator of CD is clearly relative in children with DS.

Until recently, there has been a lack of standard evidence-based guidelines for the universal screening of children with DS for CD. The Healthcare Guidelines for Patients with DS, which was developed by the American Academy of Pediatrics, has not made any recommendations for CD screening (26). The Down's Syndrome Medical Interest Group recommends one screening between the ages of 2 to 3 years (9), while the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) has suggested that screening children with DS once in a lifetime is not enough and that periodic screening should be performed (8). The latest guidelines from the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) for the diagnosis of CD (27) state that human leukocyte antigen (HLA) testing should be performed in children with CD-associated conditions such as DS. If certain haplotypes are negative (e.g., HLA-DQ2 and HLA-DQ8), no further follow-ups with serological tests are necessary. If HLA testing is not available, the anti-TG2 IgA and the total IgA should be measured after the child is 2 years old. If titres of these antibodies are negative, then repeated testing for CD-specific antibodies is recommended. However, the recommended frequency of repeated testing has not been stated unequivocally.

Several antibody markers of CD can be used for screening. Due to their sensitivity and specificity, the tTG and EMA antibodies have been commonly used in recent years to screen children with DS and the general population for CD. In this study, out of the five patients that were IgA tTG positive, gluten enteropathies were identified in four of the children (80%). It is not surprising that the biopsy in one of the patients with a positive IgA tTG was normal because the elevation of IgA tTG in that case was mild (17.7 U/ml). Our findings are similar to Hansson et al. (28), who tested 52 patients with DS and reported a 98% sensitivity for IgA tTG, which is comparable to the results reported by Shamaly and colleagues (16). In contrast, Cerqueira et al. (29) screened 98 Portuguese patients with DS and diagnosed CD in only five out of the 10 (50%) patients who were IgA tTG positive. The study was performed both in children and adults, which could explain the difference in the results, and the author reported that the sensitivity of IgA tTG was lower in older patients.

According to the ESPGHAN guidelines, unnecessary biopsies in individuals with low CD-specific antibody levels could be avoided by using a more specific test for EMA. If the EMA test is positive, duodenal biopsies should be performed. If the EMA test is negative, repeated serological testing at 3 to 6 month intervals is sufficient (27).

Given that the incidence of IgA deficiency in patients with CD is 3% (30), IgA levels were determined for all of the children. IgA deficiencies were detected in 5 (5.5%) of the patients, which represents a high prevalence. In our small study, three out of five of the patients with IgA deficiencies showed increased IgG tTG values, but the mucosa showed normal histological char-

acteristics and the IgG EMA values were negative. Data from this study showed that the IgG EMA is a more reliable marker compared to the IgG tTG. Rumbo et al. (17) compared the efficiency of different serological markers and demonstrated the high diagnostic efficiency of IgA tTG and EMA with a large number of false positive IgG tTG results (9 out of 56 children with DS). However, EMA determination in children under 2 years of age is more difficult, expensive, and less accurate, and the results can vary depending on the investigator (31).

Our findings can be interpreted from the perspective that the normal mucosa in children with positive tTG antibody levels does not necessarily signify the absence of CD because it may be a prognostic sign of forthcoming mucosal villous atrophy (latent CD). A missed diagnosis can lead to the possibility of developing a malignancy as a late complication, such as enteropathy-associated T-cell lymphoma. Serological monitoring of these children can provide additional diagnostic data, but the frequency of screening remains questionable. We agree with Mackey et al. (18), who suggests yearly CD screenings for patients with DS who are serologically positive and biopsy negative.

The patients with CD in this study were treated with a strict gluten-free diet followed by an orally administered correction of any iron deficits for 3-4 months in the cases of children with anaemia. The levels of IgA tTG after 12 months were normal in all four patients. However, the issues with constipation did not resolve and additional dietetic therapeutic measures were undertaken, which moderately improved the common symptoms of constipation in the patients with DS. In patients with alopecia, the administration of a gluten-free diet had no effect on hair growth.

There are several limitations to this study. First, this study included a small sample size of patients who resided in a public health-care institution, many of whom had serious medical problems. Second, the prevalence of CD in the children with DS may have been underestimated because we did not perform IgA EMA screening for economic and ethical reasons (e.g., patients with a negative serology enterobiopsy). Finally, we did not perform HLA haplotyping analysis. HLA-DQ typing is planned in future studies, which could allow the exclusion of further investigations.

CONCLUSIONS

This prospective study shows that the prevalence of CD in children with DS in Serbia is 4.4%, which is similar to the findings of previous studies. Because children with DS who do not have villous atrophy but present with a positive serology may have latent CD, the prevalence of CD in these patients may be even higher. Our analysis shows that the signs and symptoms of CD in children with DS only have minor diagnostic value for detecting the disease and that systematic screening of children with DS for CD should be considered a routine evaluation, although the optimal frequency of the screening events need to be established in future studies.

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SECONDARY COMPLICATIONS AND ASSOCIATED INJURIES IN TRAUMATIC AND NON-TRAUMATIC SPINAL CORD INJURY PATIENTS

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SEKUNDARNE KOMPLIKACIJE I UDRUŽENE POVREDE KOD PACIJENATA SA TRAUMATSKIM I NETRAUMATSKIM POVREDAMA KIČMENE MOŽDINE

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ABSTRACT

Objective: *To assess the occurrence secondary complications and associated injury following spinal cord injury (SCI) during inpatient rehabilitation.*

Design*: retrospective study.*

Subjects*: A total of 441 persons with a spinal cord injury admitted to specialized rehabilitation center.*

Methods*: Clinic for rehabilitation "Dr M. Zotovic", Belgrade, Serbia, from January 2000 to December 2009.*

Results: *Complications during rehabilitation were reported in 368 (83.4%) patients. Complications during rehabilitation were experienced by 127 (78.4%) patients with non-traumatic SC I(NTSCI) and 241 (86.4%) patients with traumatic SCI (TSCI). The most common complications in both groups were urinary tract infections (47.5% in TSCI and 64.2% in NTSCI patients), spasticity (56.8% in NTSCI and 53.8% in TSCI patients) and decubital ulcers (9.9% in NTSCI and 17.6% in TSCI patients). Associated injuries were present in 110 (24.9%) patients and 331 (75.1%) patients were without them. The most common associated injuries were: head injuries (38.5%), followed by rib injuries (34.4%), injuries of upper and lower extremities (21.9%), injuries of internal organs (4, 4.2%) and pelvic injuries (1, 1%). Associated injuries were found only in traumatic group of patients.*

Conclusion: *Complications are common following spinal cord injury during rehabilitation. They need specific attention after discharge from inpatient rehabilitation.*

Key words: *Secondary complications, associated injury, spinal cord injury, rehabilitation*

SAŽETAK

Uvod : *sekundarne komplikacije i udružene povrede igraju veliku ulogu u funkcionalnom oporavku, morbiditetu, mortalitetu i dužini boravka kod pacijenata sa povredom kičmene moždine.*

Cilj: *utvrditi učestalost sekundarnih komplikacija i urduženih povreda kod pacijenatasa sa povredama kičmene moždine u toku rehabilitacije.*

Metod: *ovaj rad predstavlja retrospektivnu studija koja je obuhvatila 441 pacijenta sa povredom kičmene moždine koji su rehabilitovani u Klinici za rehabilitaciju "Dr M. Zotović" u Beogradu u periodu od januara 2000. do decembra 2009. godine.*

Rezultati: *komplikacije za vreme rehabilitacije je imalo 368 (83.4%) pacijenata. Od ukupnog broja pacijenata komplikacije je imalo 127 (78.4%) pacijenata sa netraumatskim i 241 (86.4%) pacijenata sa traumatskim povredama kičmene moždine. Najčešće koplikacija kod obe grupe pacijenata su bile: urinarne infekcije (47.5% kod traumatskih i 64.2% kod pacijenata sa netraumatskim povredama kičmene moždine), spasticitet (56.8% kod netraumatskih i 53.8% kod pacijenata sa traumatskim povedama) i dekubitalni ulkusi (9.9% kod netraumatskih 17.6% kod pacijenata sa traumatskim povredama). Od ukupnog broja pacijenata udružene povrede je imalo 110 (24.9%) pacijenata. Najčešće udružene povrede su bile: povrede glave (38.5%), povrede rebara (34.4%), povrede gornjih i donjih ekstremiteta (21.9%), povrede unutrašnjih organa (1.4%) i povrede karlice (1.1%). Udružene povrede su se javljale samo kod pacijenata sa traumatskim povredama kičmene moždine.*

Zaključak: *sekundarne komplikacije i udružene povrede su često kod pacijenata sa povredom kičmene moždine u toku rehabilitacije. Adekvatna nega u kućnim uslovima može smanjiti procenat komplikacija.*

Ključne reči : *sekundarne komplikacije, udružene povrede, povrede kičmene moždine, rehabilitacija*

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INTRODUCTION

Secondary complications and associated injuries have significant influence on health, quality of life and social participation in patients with spinal cord injury (SCI) (1–4). It has been estimated that approximately 11000 individuals have traumatic spinal cord injury in the United States each year and 262000 patients live with complications of spinal cord injury (1). With this in mind, an increased understanding of the clinical challenges associated with their care is very important (2). Increased morbidity as a result of secondary complications or associated medical conditions can play a significant role in their ongoing clinical management, functional outcomes, length of stay, and cost of care (3).

Complications have a considerable impact on those with SCI. A high incidence of complications is associated with a lower level of health-related aspects, such as physical capacity, activities and functional outcome (4). Complications may interfere with the start of active rehabilitation, can form a disappointing set-back during rehabilitation, and frequently lead to re-hospitalization (5). Diagnosis of secondary complications especially of infectious etiologies can be problematic in patients with SCI. Depending on the neurological level and completeness of injury, patients with SCI may present with diminished clinical signs and symptoms to assist in the diagnostic workup. Reasons for this include weakness of the abdominal muscles leading to diminished cough, and decreased sensation of painful symptoms (such as dysuria or discomfort from wound or bone infections (6). Additionally, complications are an important cause of mortality following SCI (7). Previous studies have investigated complications following SCI and their risk factors. They have illustrated the association between subject and lesion characteristics and the occurrence of complications (8, 9).

The aim of this study was to investigate and compare associated injuries and secondary complications during rehabilitation in traumatic and non-traumatic SCI patients (9).

MATERIAL AND METHODS

This is a retrospective study of 441 patients with the spinal cord injury treated in the Clinic for rehabilitation "Dr M. Zotovic", Belgrade, Serbia, from January 2000 to December 2009. For all patients, a detailed hospital history was taken. These hospital records were used to classify the following: age, gender, etiology of injury, neurological level of injury, associated injuries and secondary complications. The following criteria for conducting the study: 1st all patients diagnosed with spinal cord injuries, 2nd all patients with spinal cord injury that resolute gave signs of neurological lesions of spinal cord. Criteria for exclusion from the study: 1st any kind of deterioration in the underlying that resulted in termination of rehabilitation provided, 2nd patients younger than 18 years.

The diagnosis of associated injuries and secondary complications was based on both clinical features and relevant investigations when necessary. Secondary complications diagnosis was based on clinical and other diagnostic methods during hospitalization. Other specialists were consulted for treatment of secondary complications.

The patients in this study were divided into two groups based on the etiology of the injury as traumatic and non-traumatic SCI. During hospitalization the patients were assessed by the following tests: (1) ASIA scale (American Spinal Injury Association impairment scale) to assess motor and sensory levels of injury and completeness of injury and (2) MAS score (Modified Aschworth Score) to determine the level of spasticity (10,11). Data were analyzed for frequency. The data is presented in tables.

Statistical analysis: For the analysis of primary data descriptive statistical methods were used, as well as hypothesis testing methods. Among the descriptive statistical methods we have used were the central tendency (arithmetic mean, median), measures of variability (standard deviation) and relative numbers. To test hypothesis about the difference in frequency Chi – squared test and Fisher test were used. T-test and Mann-Whitney test of exact probability were used for testing hypothesis about difference of arithmetic means. The level of statistical significance in our study was set to 0.05.

RESULTS

A total of 441 patients were assessed. Of the total number of patients, 322 (73%) were male and 119 (27%) female. In the present study, 36.73% (n 163) of the SCI patients were in non-traumatic SCI patients and 63.27% (n 279) were in traumatic SCI group.

The proportion of paraplegic patients was 74.80% in the traumatic SCI group, and 82.53% in the non-traumatic SCI patients, and there was a significant difference between these two groups (p=0.005). The proportion of tetraplegic patients was 25.95% and 17.63% in traumatic SCI and non-traumatic SCI patients, respectively; and there was a significant difference between the two groups (p=0.04).

Associated injuries were present in 110 (24.9%) patients and 331 (75.1%) patients were without them. The most common associated injuries were: head injuries (n = 37, 38.5%), followed by rib injuries (n = 33, 34.4%), injuries of upper and lower extremities (n = 21, 21.9%), injuries of internal organs (n = 4, 4.2%) and pelvic injuries (n = 1, 1%). Associated injuries were found only in traumatic group of patients (Table 1).

Complications during rehabilitation were reported in 368 (83.4%) patients. Complications during rehabilitation were experienced by 127 (78.4%) patients with non-traumatic SCI and 241 (86.4%) patients with traumatic SCI. Most common complications during rehabilitation were presented in table 2.

Complications during rehabilitation were significantly more common in patients with traumatic SCI (p = 0.03). The most common complications in both groups were urinary tract infections (64.2% in traumatic and 47.5% in non-traumatic patients), spasticity (56.8% in non-traumatic and 53.8% in traumatic patients) and pressure ulcers (9.9% in non-traumatic and 17.6% in traumatic patients). Urinary tract infections and pressure ulcer were significantly higher in traumatic than in non-traumatic patients with SCI (p=0.001 and p=0.028).

Associated injury	Non-traumatic (n=162) n (%)	Traumatic (n=279) n (%)	p
Head	0 (0%)	37 (13,3%)	**<0,001**
Ribs	0 (0%)	33 (11,8%)	**<0,001**
Pelvic	0 (0%)	1 (0,4%)	1
Upper and lower extremities	0 (0%)	21 (7,5%)	**0,004**
Internal organs	0 (0%)	4 (1,4%)	0,302

Table 1. Associated injury

Complications during rehabilitation	Non-traumatic (n=162) n (%)	Traumatic (n=279) n (%)	p
Urinary tract infections	77 (47.5%)	179 (64.2%)	**0.001**
Pressure ulcer	16 (9.9%)	49 (17.6%)	**0.028**
Contactures	3 (1.9%)	12 (4.3%)	0.171
Calculosis	4 (2.5%)	13 (4.7%)	0.249
Autonomic dysreflexia	1 (0.6%)	3 (1.1%)	1
Respiratory complications	5 (3.1%)	8 (2.9%)	1
Wound dehiscence	0 (0%)	2 (0.7%)	0.534
Psychological complications	2 (1.2%)	5 (1.8%)	1
Spasticity	92 (56.8%)	150 (53.8%)	0.538
Deep venous thrombosis	0 (0%)	5 (1.8%)	0.163
Kardiovaculary complications	0 (0%)	4 (1.4%)	0.302
Syringomielia	3 (1,9%)	4 (1.4%)	0.711

Table 2. Complications during rehabilitation

DISCUSSION

In our study, the number of complications in the non-traumatic SCI patients was found to be less than the number of complications in the traumatic SCI group. In one study, it has been reported that complications such as spasticity, pressure ulcers, deep venous thrombosis, and autonomic dysreflexia in non-traumatic SCI patients had been found to be less often when compared to traumatic SCI patients (12, 13). In this study secondary complications of the patients have been compared and evaluated between non-traumatic and traumatic SCI patients.

In this study, urinary tract infection was the most common complication in the non-traumatic SCI patients (47.5%) and its ratio among complications in the traumatic SCI group was 64.2%. Urinary tract infection was found to occur in high rates in traumatic SCI. In another study, a frequency of 52.6% and 67.1% urinary tract infection has been reported in NT and traumatic SCI patients, respectively (14). New et al. evaluated the complications of rehabilitation patients only in the non-traumatic SCI patients and found that urinary tract infection was the most common complication (45.7%) (14,15).

Spasticity was the second most common complication in patients with SCI. In our study, the ratio of spasticity was found to be 56.8% in the non-traumatic SCI patients and 53.8% in the traumatic SCI group. In other studies, spasticity has been found in a ratio of 12.9% and 21.1% in the non-traumatic SCI patients and 32.2% and 44.3% in the traumatic SCI group (16).

The third most common complication in our study was pressure ulcer. Pressure ulcers was found in 9.9% of the non-traumatic SCI patients and in 17.6% of the traumatic SCI patients. Another study reported this ratio to be 31.3% in the non-traumatic SCI patients and in the traumatic SCI group, it has been reported to be 41.8% and 23.7% (17,18).

Deep venous thrombosis was another type of complication that was present in a 1.8% in the traumatic SCI patients. Other studies report a frequency of 7.9% (14) and 9.8% in non-traumatic SCI patients, and 22.8% in traumatic SCI patients. Deep venous thrombosis was diagnosed with clinical and Doppler ultrasonography findings (9,20).

In our study the most common associated injuries were: head injuries, followed by rib injuries, injuries of upper and lower extremities, injuries of internal organs and pelvic injuries. Associated injuries were found only in traumatic group of patients. Since the spinal cord injuries are often joined with head injuries or the injuries of other organs, even nowadays it happens that such injuries are overlooked when providing the first aid at the site of accident or during transportation (20). The development of spinal centers enables more successful taking care of, diagnosing and treatment of such injuries. Our findings about frequency of associated injuries are in accordance with previous study (20,21).

CONCLUSION

Secondary complications and associated injuries frequently occur in patients with spinal cord injury. Education, prevention and adequate curing of secondary complications may increase quality of life in persons with spinal cord injuries, their survival and functional outcomes. It also may have an important part in decreasing length of stay and cost of care of this patients.

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RISK FACTORS FOR BEHAVIOURAL AND EMOTIONAL DISORDERS IN CHILDREN WITH MILD INTELLECTUAL DISABILITY

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FAKTORI RIZIKA ZA BIHEJVIORALNE I EMOCIONALNE POREMEĆAJE KOD DECE SA LAKOM INTELEKTUALNOM OMETENOŠĆU

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ABSTRACT

Introduction: *The current study investigated the prevalence and characteristics of behavioural and emotional disorders in children with mild intellectual disability, as well as the predictive potential of personal and socio-demographic factors.*

Objective: *The main objective of this research was to determine the impact of socio-demographic and personal factors on the prevalence and types of emotional and behavioural disorders in children with mild intellectual disability.*

Methods: *Non-experimental research was conducted on 311 children with mild intellectual disability, aged 9-18 years, who attended 8 special primary schools in central and south-west Serbia. For the assessment of psychopathology, we used the Child Behaviour Checklist - Teacher Report Form (CBCL-TRF), a checklist of problem behaviours in children aged 6-18 years. To collect data on socio-demographic status, we created a questionnaire about socio-economic factors and demographic indicators. The informants were classroom teachers.*

Results: *An increased incidence of behavioural and emotional disorders was found in children with mild intellectual disability, compared to children of average intelligence. Both dimensions of psychopathology were significantly influenced by personal and socio-demographic variables, including child`s age, gender, academic achievement, placement type, parental educational level and employment, as well as the structure and socio-economic status of the families.*

Conclusion: *Children with intellectual disability are at increased risk of developing psychopathology, mostly within the dimension of adjustment and behavioural disorders. Risk factors include specific developmental and psychological characteristics and social learning difficulties, as well as a number of adverse socio-demographic factors.*

Keywords: *intellectual disability, internalizing disorders, externalizing disorders.*

SAŽETAK

Uvod: *U radu se razmatraju rasprostranjenost i karakteristike bihejvioralnih i emocionalnih poremećaja kod dece sa lakom intelektualnom ometenošću, kao i njihova veza sa personalnim i socio-demografskim činiocima kao potencijalnim faktorima rizika.*

Cilj rada: *Utvrditi uticaj socio-demografskih i personalnih faktora na rasprostranjenost i vrste emocionalnih smetnji i poremećaja ponašanja kod dece sa lakom intelektualnom ometenošću.*

Metod rada: *Sistematsko neeksperimentalno istraživanje obavljeno je na uzorku od 311 dece sa lakom intelektualnom ometenošću, učenika 8 specijalnih osnovnih škola centralne i jugozapadne Srbije, starosti od 9-18 godina. Za procenu psihopatologije korišćena je Skala poremećaja u ponašanju i emocionalnih smetnji kod dece uzrasta 6-18 godina, CBCL - TRF (Child Behaviour Checklist – Teacher Report Form). Za prikupljanje podataka o socio-demografskom statusu korišćena je Skala socio-ekonomskih faktora i demografskih pokazatelja, konstruisana za potrebe ove studije. Informanti su bili nastavnici-razredne starešine.*

Rezultati: *Utvrđena je povećana učestalost emocionalnih i bihejvioralnih poremećaja kod dece sa lakim intelektualnim smetnjama u odnosu na decu prosečne inteligencije. Oba pola psihopatologije nalaze se pod značajnim uticajem ispitivanih personalnih i socio-demografskih varijabli: uzrasta, pola, akademskog uspeha, vrste smeštaja deteta, nivoa obrazovanja i zaposlenja roditelja, kao i strukture, brojnosti i socio-ekonomskog statusa porodica.*

Zaključak: *Deca sa smetnjama u intelektualnom razvoju su pod pojačanim rizikom od ispoljavanja psihopatoloških fenomena, najčešće iz spektra problema ponašanja i prilagođavanja, što je posledica specifičnih razvojno-psiholoških karakteristika, ali i poteškoća socijalnog učenja, kao i delovanja niza nepovoljnih socio-demografskih faktora.*

Ključne reči: *laka intelektualna ometenost, internalizovane smetnje, eksternalizovane smetnje.*

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INTRODUCTION

Intellectual disability (ID) refers to significant limitations in intellectual functioning and in social, conceptual and practical adaptive skills. Deficits must occur during the developmental period before the age of 18 and be measurable using standardized methods of assessment, based on internationally accepted classification criteria. The most commonly used practical classification criteria is the level of intellectual functioning. For example, persons whose intelligence quotient (IQ) levels are below the accepted limit of 70 are diagnosed as intellectually disabled [1,2]. Many studies have shown an increased incidence of psychiatric disorders in children and adolescents with ID compared to those without disability. Although research findings vary depending on how the study variables are operationalized, i.e., the characteristics of the assessment instruments used and the populations studied, estimates suggest that 30-60% of children and youth with ID suffer from certain types of psychiatric disorder; this rate is three to four times more frequent than in children of average intelligence [3, 4]. As many as 36.8% of children with mild ID meet the DSM-IV criteria for comorbid disorders, which seriously impedes their education, social integration and functioning and reduces their adaptive capacities [3]. The types and clinical characteristics of the disorders depend on the level of ID because it is clear that the expression of certain behavioural and emotional problems requires a certain level of intelligence [5]. As shown by many studies, in children and adolescents with mild ID, patterns of psychopathology are similar to those in the general population. For this reason, during the diagnostic and treatment planning processes, procedures and instruments designed for children and youth without disability can be used [6, 7]. Mental disorders in children with mild ID can be classified roughly into one of two dimensions: *internalizing*, which refers to strong internal control and symptoms that include withdrawal, dysphoria, anxiety and depression, and *externalizing*, which includes lack of internal control and tendencies toward excessive aggression, destructiveness, hyperactivity, and antisocial behaviours. These disorders tend to occur early in childhood and continue throughout development [8, 9]. The question arises as to which personal, social or developmental factors enhance the risk of psychopathology in children with mild ID compared to children of the general population. Of note, children with mild ID usually do not have any genetic or neurological disorders that would lead to greater probability of mental disorders [10]. For this reason, the impact of certain socio-demographic factors, educational environments and living conditions of children with mild ID should be the focus of attention. In this respect, results of different studies show that, during childhood, such children often come from poverty, social and emotional deprivation, a broken and dysfunctional family life, and their parents are mostly unemployed with low levels of education [10, 11].

AIMS OF THE STUDY

The main goal of this study was to identify the characteristics and prevalence of internalizing and externalizing disorders in children with mild ID. An additional goal was to examine the impact of certain personal and socio-demographic predictors as potential risk factors for the manifestation of psychopathology in this population of children.

METHODS

A systematic, non-experimental study was conducted on 311 students from 8 primary schools for Serbian children with mild ID. Participants were from 9-18 years old, with no comorbid conditions. We used a questionnaire that was designed for this study to assess socio-economic factors and demographic indicators, together with the Child Behaviour Checklist - Teacher Report Form (TRF), a scale for behaviour and emotional disorders in children aged 6-18 years [12]. The informants were classroom teachers. From the TRF, we used the Problem Scale, which consists of 113 problem behaviours that are scored as 0 (not true), 1 (somewhat or sometimes true) or 2 (completely or often true). The TRF provides a *Total problem score*, scores for *Internalization* and *Externalization*, as well as scores for several syndrome subscales, including *anxious/depressed*, *withdrawn/depressed*, *somatic complaints*, *social problems*, *thought problems*, *attention problems*, *rule-breaking behaviour* and *aggressive behaviour*. The first three subscales are part of the broader dimension of *Internalization*, the last two belong to the *Externalization* dimension, and the subscales of *Social problems*, *Thought problems and Attention problems* have similar saturation on both of the broader dimensions. Clinically significant scores for total problems and internalizing and externalizing dimensions were considered to be $T \geq 63$, whereas clinical significance for syndrome subscales was set at $T \geq 70$ [12].

The socio-economic factors and demographic indicators questionnaire that was used included the following variables: gender, age, IQ, academic achievement, grade repetition, occupation and educational level of parents, social assistance, birth order, as well as family structure and size.

RESULTS

The average age of participants in this study was 13.21 years (SD = 2.24), and the average IQ was 62.18 (SD = 6.81). The sample had more boys (58.8%) than girls (41.2%), but the gender distribution among age groups was balanced ($\chi 2 = 4.678$, df = 9, p = 0.861). The largest number of children (60.8%) lived with both parents, more often in urban (79.7%) than in rural areas (20.3%). Only 31.5% of fathers and 9.3% of mothers were employed, and as many as 64.3% of families received some form of social assistance. As many as 60.8% of fathers and 74.5% of mothers had an in-

Figure 1

* anx/d.: *anxious/depressed*, with/d.: *withdrawn/depressed*, somat.: *somatic complaints*, soc.pr.: *social problems*, tho.pr: *thought problems*, att. pr.: *attention problems*, rule b.b.: *rule-breaking behaviour*, aggress.: *aggressive behaviour*).

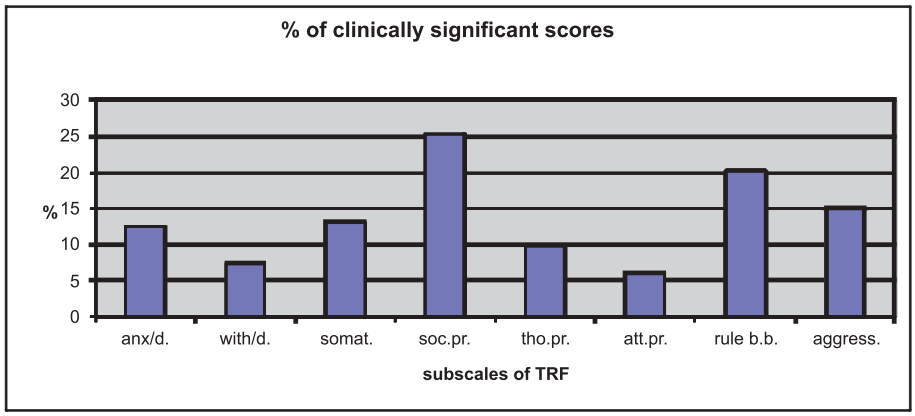
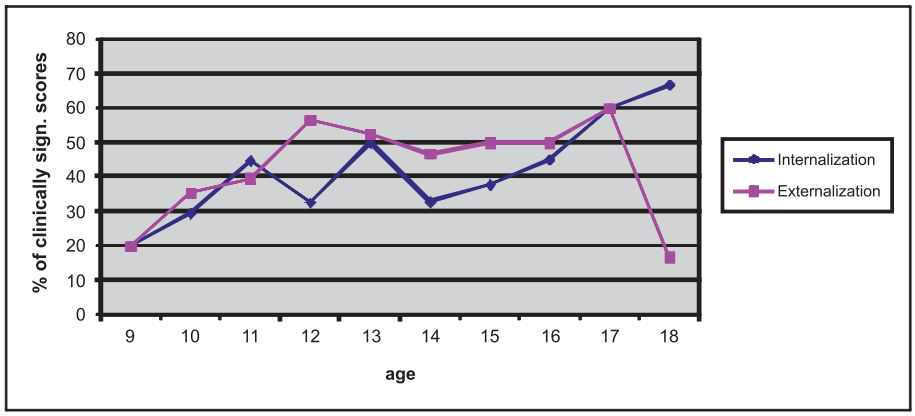


Figure 2



complete primary education, and only 3.2% of fathers and 3.9% of mothers had the highest levels of education (vocational college or university degree).

As many as 155 (49.8%) children in our sample had a *Total problem score* in the clinical range, whereas 122 (39.2%) had clinically significant *Internalization* scores and 145 (46.6%) had clinically significant *Externalization* scores. On individual subscales, the highest frequencies of clinical scores were obtained on the subscales of *Social problems* (25.4%) and *Rule-breaking behaviour* (20.26%), whereas the lowest were on the subscales of *Attention problems* (6.11%) and *Withdrawn/depressed* (7.40%)(Figure 1). Statistically significant correlations were found between scores on broad-band dimensions of *Internalization* and *Externalization* and *Social problems* scores, with stronger relations between *Internalization* and *Social problems* (r=0,638, p<0,0001) than between *Externalization* and *Social problems* (r=0,468, p<0,0001). Low frequency of clinical scores for *Attention problems* was a surprising result, because it was expected that there would be more significant problems in this domain of functioning, considering the developmental and cognitive characteristics of the tested population. We clearly observed a slight dominance of externalizing disorders, particularly *Rule-breaking behaviour*, which was expected.

Girls had higher average scores on *Total problems*, *Withdrawn/depressed* and *Attention problems* (p <0.0001), whereas significant differences for other scores were not obtained. Age had a weak, but statistically significant, correlation with scores for *Internalization* (r = 0.160, p = 0.005) and the subscales *Anxious/depressed* (r = 0.142, p = 0.012) and *Somatization* (r = 0.174, p = 0.002), but age was not correlated with the *Externalization* dimension. No statistically significant differences were found by comparing age groups on frequency of clinical scores for both broader dimensions (p> 0.05). Frequencies of clinically significant scores in different age groups are shown in Figure 2.

In all age groups, except for ages 11 to 18, clinically significant scores of *Externalization* dominated over *Internalization*. Contrary to expectations, frequencies of clinical *Externalizing* problems did not decrease with age, but instead, these frequencies increased, except for a slight decrease in the participants aged 13 and 14 years, as well as a serious decrease at the age of 18. The very low number of participants of that age (six) probably influenced this finding; notably, however, four of those six 18-year-old participants had clinically significant scores for *Internalization*, and only one for *Externalization*. Clinically significant behaviour problems, therefore, tended to be more pronounced with maturity, which was not expected. Clinical scores for Internalizing disorders showed consistent increase with the entry into early adolescence (age 14), which is consistent with previous studies.

Significant negative correlations were seen between IQ and *Total problems* (r =- 0.158, p = 0.005), *Internalization* (r =- 0.330, p <0.0001) and two of the subscales of that dimension, *Anxious/depressed* (r =- 0.346, p <0.0005) and *Withdrawn/depressed* (r =- 0.302, p <0.0005). IQ was positively correlated with *Externalization* (r = 0.121, p = 0.033). Children with lower academic achievement had higher average

Independent variables	B	S.E.	Wald	df	Sig.	Exp (B)	95% CI for Exp (B)
Gender (f)	0,698	0,304	5,265	1	0,022	**2,009**	1,107-3,646
School achievement	-0,531	0,145	13,354	1	0,0001	**0,588**	0,442-0,782
Birth order	-0,315	0,134	5,521	1	0,019	**0,730**	0,561-0,949
Father's education	0,609	0,234	6,785	1	0,009	**1,838**	1,163-2,905
Social assistance (not rec.)	1,234	0,426	8,414	1	0,004	**3,439**	1,493-7,924

Table 1. Predictors of clinically significant scores of Internalization

Independent variables	B	S.E.	Wald	df	Sig.	Exp (B)	95% CI for Exp (B)
Intelligence quotient	0,074	0,024	9,566	1	0,002	**1,076**	1,027-1,128
Number of children	0,374	0,176	4,539	1	0,033	**1,454**	1,030-2,050
Number of adults	-0,326	0,154	4,469	1	0,035	**0,722**	0,534-0,977
Residing in an orphanage	1,949	0,783	6,205	1	0,013	**7,024**	1,515-32,651

Table 2. Predictors of clinically significant scores of Externalization

scores on all scales, except for the aggregate *Externalization* scale and the *Aggression* subscale, whereas children with higher achievement had higher average scores ($\chi 2 = 12.652$, df = 4, p = 0.013). Birth order was also significantly negatively correlated with the dimension of *Internalization* (r =- 0.271, p <0.0001) and its subscales, *Social problems* and *Thought* and *Attention problems*, whereas no significant correlation with *Externalization* was observed. A total of 72 (59%) of the children within the *Clinically internalizing group* ($N_i = 122$) were first-borns. Educational level and employment of parents were also significantly related to the problems of children, with higher scores on all scales in children whose parents had higher education levels, except for the subscale of *Rule-breaking behaviour*, where children whose parents had lower education also had higher scores ($\chi 2 = 10.498$, df = 3, p = 0.015). Children of employed fathers had higher scores on all scales, except for *Rule-breaking behaviour*, whereas children of unemployed fathers had higher average scores (Z =- 2.487, p = 0.013). Children of employed mothers had higher scores for *Internalization*, but no differences were found for the dimension of *Externalization*. Family size was connected to *Internalizing* problems, with scores on the dimension of *Internalization* and its subscales increasing with decreasing numbers of children in the family (r =- 0.230, p <0.0001), and fewer family members in general (r =- 0.219, p <0.0005). Scores for *Externalization* were significantly correlated only with the number of children in the family (r = 0.134, p = 0.019).

To develop a predictive model for clinical scores on the dimensions of *Internalization* and *Externalization* ($T \geq 63$), i.e., to identify the particular characteristics of a child and his or her family as well as broader social environmental factors that significantly influence maladaptation and emotional difficulties of tested children, we used the stepwise binary logistic regression method. Potential outcomes included the dichotomous dependent variables *clinical internalization/ non-clinical internalization* and *clinical externalization/ non-clinical externalization*. The analysis separated out the effects of several important factors. It was found that clinically significant *Internalization* was influenced by gender, school performance, birth order, father's educational level and social assistance for the family (Table 1), whereas clinical *Externalization* was affected by intelligence quotient, the number of adult household members, the number of children in the family and placement in an orphanage (Table 2). The risk for the manifestation of clinically significant *Internalization* was increased by female sex (OR = 2.009), higher levels of education of the father (OR = 1.838) and no social assistance from the state (OR = 3.439), and this risk was reduced by better school achievement (OR = 0.588) and later birth order (OR = 0.730). Risk factors for clinical *Externalization* were higher IQ (OR = 1.076), more children in the family (OR = 1.454) and living in an orphanage (OR = 7.024), whereas the presence of more adult household members was a protective factor (OR = 0.722).

DISCUSSION

The results confirmed the hypothesis of a high prevalence of behavioural and emotional problems in children with mild ID. The obtained frequencies of clinically significant scores on the TRF scale were higher than expected; almost half of the sample (49.8%) had clinically significant *Total problems scores*. Behavioural problems were more frequent than internalizing disorders, which was expected considering the age of the respondents (70,4% were aged under 15 years) and the hypothesis that externalizing symptoms would be dominant in children with ID [13]. However, frequencies of clinically significant scores for behavioural problems remained stable in older children, too, which was slightly surprising, considering the expected decrease of externalizing symptoms with maturity. Similarly, a positive association was found between age and inter-

nalizing disorders. *Internalization* scores increased with age, meaning that a larger share of emotional problems in adolescents was found, which is consistent with previous studies [14]. Polarization of problems into *Internalization* and *Externalization* dimensions may underestimate these children`s behavioural issues; our study highlighted the subscale of *Social problems* (24,5% of clinical scores), suggesting that the items of that subscale could be more sensitive to the specific problems of this population, which include delayed development of social skills and poorer social relations [5, 12, 15]. Social problems are significantly related to emotional problems, especially depression, and also behavioural problems. Further research should place more emphasis on social skills in children with mild ID because it is clear that slower and impeded development of social skills and deficits of social cognition lead to considerable difficulties integrating into a social group and developing socially desirable behaviours, which can, in turn, result in pronounced maladaptation, aggression and internalizing problems. Surprisingly, girls had higher average scores for *Attention problems*, with no significant differences for broader dimensions of behaviour, in contrast to earlier findings that suggested more emotional and fewer behavioural problems in girls compared to boys [16]. A regression analysis did demonstrate a higher risk of emotional disorders in girls (OR = 2,009), but no significant gender differences for behavioural problems were found, which was unexpected. Considering the psychopathological profile of girls established in this study, we could point to a change in the accepted paradigm of sexual diversity and hypothesize that girls are more vulnerable when it comes to certain types of disorders, especially behaviour problems and attention difficulties. Statistically significant relationships between other socio-demographic factors and emotional and behavioural problems in children were also confirmed, with special emphasis on such factors as the economic standard of the family, housing conditions and family size. Higher scores on screening scales were related to poor academic performance, low standard of living, residing in rural areas as well as higher education and employment of parents. *Rule-breaking behaviour* was an exception in that lower levels of education in parents and parental unemployment were associated with greater problems. Employment and higher education levels of parents were significantly correlated only with the *Internalization* dimension. This finding suggests the possibility in higher educated parents of higher emotional pressure, higher expectations when it comes to the child`s development and more difficulty overall accepting the child`s disability. In addition, there may be a negative influence of parental business engagement and more frequent separations of the parents from their children. Children with better school achievement had higher average scores on the *Externalization* dimension. Together with the positive correlations found between IQ levels and *Externalization* scores, it could be concluded that intellectually and academically more successful children more often exhibit *Externalizing* problems. This finding is not consistent with previous findings, nor is it consistent with practical experience and common sense; it is simply hard to connect superior school performance and maladjusted behaviour.

Family size and birth order were negatively related to internalizing disorders, supporting the hypothesis of greater social pressure on first born and only children with ID. In addition, there could be a dampening effect of large families containing more adults, which provide more opportunities, therefore, for positive identification. Children living without mothers had higher scores on *Internalization*, whereas children without fathers had higher risk of *Externalization,* suggesting the diverse importance of parental figures in development, with fathers being more important in effecting behaviours consistent with social norms. As a variable, a larger number of children in the family related negatively to *Externalization* scores, possibly because of diminished opportunities for children's behaviour monitoring, which is a well-known risk factor for conduct disorders and maladjustment [17, 18]. Moreover, residing in an orphanage significantly increased the risk of a behavioural disorder, which can again be explained by the lack of monitoring in these circumstances. In an orphanage, the typically disproportionate number of children to teachers causes reduced ability to establish close relationships and deeper emotional bonds, which are necessary for a child's positive identification and adoption of appropriate behaviour patterns. Other highly important questions include the consequences of early emotional deprivation, genetic-constitutional factors and potential abuse and neglect of children in foster care.

CONCLUSION

Children with mild ID are at increased risk for emotional and behavioural problems. Risk factors include developmental characteristics and specific socio-cultural and demographic factors, especially social deprivation, low standards of living, low parental education and employment, and changes in housing, family structure and size. More detailed research is needed considering the impact of certain socio-demographic factors on the mental health of these children. Such research could lead to better opportunities for prevention and early detection of risk factors that may lead to the manifestation of clinically significant emotional and behavioural disorders.

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INFLUENCE OF THE DIALYSIS MEMBRANE TYPE ON QUALITY OF LIFE, CLINICAL OUTCOMES AND LABORATORY PARAMETERS IN PATIENTS UNDERGOING HAEMODIALYSIS

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UTICAJ VRSTE DIJALIZNE MEMBRANE NA KVALITET ŽIVOTA, KLINIČKE ISHODE I LABORATORIJSKE PARAMETRE PACIJENATA NA HEMODIJALIZI

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ABSTRACT

Background: *High-flux haemodialysis uses dialysis membranes of significant porosity to permit the passage of larger molecules (ß2- microglobulin clirens >20 ml/min) and allows a higher coefficient of ultrafiltration (CUF >l5 ml/mmHg per hour). Preliminary results found that anaemia was more easily corrected among patients treated with high-flux membranes, while randomised trials failed to prove a significant effect. Total blood triglycerides, VLDL triglycerides and VLDL cholesterol decreased, and HDL cholesterol increased in the polysulphone high-flux group, while these variables remained unchanged in a group of patients treated with standard dialysers.*

Objective: *Comparisons were made between patients treated with high-flux membrane dialysers and patients treated with low-flux membrane dialysers with regard to quality of life, clinical outcomes and laboratory results.*

Methods: *The study was investigator-driven, cross-sectional and based on the intention-to-treat principle. The study population was composed of patients undergoing dialysis treatment (18 to 70 years of age) in the Studenica regional health centre in Kraljevo.*

The patients belonged to the low-flux haemodialysis group (n=33) or the high-flux haemodialysis (n=39) group. The patients were interviewed between December 2009 and January 2010. The results of laboratory tests and data on comorbidities were obtained from medical records. Information regarding quality of life and habits were obtained using the Comprehensive Quality of Life Scale – Adult.

Results: *Serum levels of urea were significantly different between patients who were treated with high-flux membrane dialysers and those who were treated with low-flux membrane dialysers (t=2, 094, p=0.040). No significant differences were found regarding other laboratory parameters, clinical symptoms, comorbidities, habits, or patients' quality of life.*

Conclusion: *Although high-porosity high-flux haemodialysis membranes remove waste solutes more efficiently than low-flux membranes with smaller pores, this fact did not translate into significant differences in patients' quality of life.*

Keywords: *Dialysers, quality of life, laboratory analysis*

SAŽETAK

Uvod : *U hemodijalizi visokog fluksa koriste se dijalizne membrane značajne poroznosti za veće molekule (klirens ß2- mikroglobulina >20 ml/min) i omogućen je koeficijent ultrafiltracije veći od l5ml/mmHg po satu. Preliminarni rezultati su ukazivali da se anemija lakše koriguje u pacijenata koji su na membranama visokog fluksa,dok randomizirane studije nisu uspele da dokažu značajan efekat. Ukupni krvni trigliceridi, trigliceridi i holesterol veoma male gustine (VLDL) su opali, a holesterol visoke gustine (HDL) je porastao u polisulfonskoj grupi visokog fluksa, dok su navedene varijable ostale neizmenjene u grupi pacijenata na standardnim dijalizatorima.*

Cilj: *Napravljeno je poređenje između pacijenata na hemodijalizi visokog i hemodijalizi niskog fluksa u pogledu kvaliteta života, kliničkog ishoda i laboratorijskih rezultata.*

Metod: *Studija je sprovedena kao studija preseka. Studijsku populaciju su sačinjavali pacijenti na dijaliznom tretmanu (u rasponu od 18 do 70 godina starosti) u regionalnom zdravstvenom centru „ Studenica “ u Kraljevu.*

Pacijenti su bili ili na hemodijalizi niskog fluksa (njih 33) ili hemodijalizi visokog fluksa (njih 39). Pacijenti su intervjuisani u periodu od decembra 2009. do januara 2010. Rezultati laboratorijskih testova i podaci o komorbiditetu su dobijeni iz zdravstvenih kartona. Informacije o kvalitetu života i navikama su dobijeni iz Comprehensive Quality of Life Scale – Adult “.

Rezultati: *Serumski nivoi uree su bili značajno različiti između pacijenata na dijalizatorima visokog fluksa i onih na dijalizatorima niskog fluksa (t= 2.094, p= 0.040). Za druge laboratorijske parametre, kliničke simptome, navike i kvalitet života- značajne razlike nisu nađene.*

Zaključak: *Mada visoka poroznost hemodijaliznih membrana omogućava uklanjanje raspadnih produkata efikasnije nego kod membrana niskog fluksa koje imaju manje pore, ta činjenica nije dovela do značajnih razlika u kvalitetu života pacijenata.*

Ključne reči: *Dijalizatori, kvalitet života, laboratorijske analize*

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INTRODUCTION

In patients with terminal renal insufficiency, toxins accumulate in the blood because the kidneys lose their ability to properly eliminate these substances. High-flux haemodialysis uses dialysis membranes of significant porosity to allow the passage of larger molecules, which allows a high coefficient of ultrafiltration (CUF >l5 ml/mmHg per hour).

Although the use of new haemodialysis modalities has grown, the clinical risks and benefits of these high-performance therapies are not well defined. In the literature published in the past ten years, definitions of high-efficiency and high-flux dialysis are confusing. At the moment, the quantity of dialysis treatment is defined not only by time, but also by dialysator characteristics, velocity of blood and dialysate circulation. In the past, when the efficiency of dialysis and the circulation had a tendency to be low, the quantity of dialysis treatment was well defined by time. Today, duration of dialysis treatment is not a useful expression of treatment quantity because the efficiency is highly variable.

Preliminary results found that there was an actual benefit in the correction of anaemia in patients treated with high-flux membranes, while randomised trials failed to prove a significant effect. Total blood triglycerides, VLDL triglycerides and VLDL cholesterol decreased, and HDL cholesterol increased in the polysulphone high-flux group, while these variables remained unchanged in group of patients treated with standard dialysers. (1)

A controlled prospective study investigated the change in lipid parameters from dialysis with cellulose membranes (which are low-flux membranes) to polysulphone membranes (which are high-flux membranes). Total serum triglycerides and VLDL cholesterol decreased, and the proportion of HDL cholesterol increased in the polysulphone high-flux group, while these variables remained unchanged in the control group. The LDL and total cholesterol, parathyroid hormone, albumin, and body weight remained unchanged. (2)

The HEMO study did not show a statistically significant effect of higher dialysis dose and high-flux membranes on survival and morbidity (3, 4), but it noted that chronic kidney insufficiency is a major reason for hospitalisation from cardiac diseases. The use of high- or low-flux membranes exhibited no difference in laboratory values in a study that investigated the effect of different synthetic membranes on laboratory parameters and survival in chronic haemodialysis patients. (4)

Though high-flux haemodialysis did not decrease mortality from all causes among those with cardiac diseases, it has been shown to improve other outcomes among patients with cardiac diseases. (5) Patients with diabetes have also shown a significant survival benefit when treated with high-flux haemodialysis. (6)

Due to their high porosity, high-flux membranes are able to remove waste solutes of higher molecular weight compared to low-flux membranes (7), which have smaller pores. However, it is not clear whether this amplified elimination of waste solutes confers a long-term benefit of long-term survival among patients treated with high-flux membranes.

The aim of our study was to investigate the influence of dialysator type on quality of life, clinical status and values of laboratory analyses among patients undergoing haemodialysis.

MATERIALS AND METHODS

Study type

This study was observational and cross-sectional and aimed to investigate the influence of dialysator type on quality of life, clinical status and laboratory analyses of patients undergoing haemodialysis.

The study population

This study was conducted in the Haemodialysis department of the Studenica Health Centre in Kraljevo, Serbia, from December 2009 to February 2010. The study population included all patients undergoing haemodialysis encountered during that period who agreed to participate in the study and who underwent haemodialysis for at least one year. The following patients were excluded from the study: those under age eighteen or over age seventy, patients with malignancy, patients undergoing chemotherapy, pregnant women, patients with portal hypertension and those who declined participation in the study.

The study groups

Patients were separated into two groups based on their exposure to high-efficacy haemodialysis during the year 2009. The patients belonged either to the low-flux haemodialysis (n=33) group or the high-flux haemodialysis (n=39) group. The patients were interviewed between December 2009 and January 2010. The results of laboratory tests and data on comorbidities were obtained from medical records. Information regarding quality of life and habits was obtained from the Comprehensive Quality of Life Scale – Adult. (8, 9, 10) All information was anonymous, patient consent was obtained, and the study was approved by the Ethical Committee of the Studenica Health Centre in Kraljevo.

The study variables

The following categorical variables were taken into account: symptoms of patients undergoing haemodialysis (headache, respiratory discomforts, and urinary discomforts), diagnosis of cardiac insufficiency, use of erythropoietin (more than six months), parenteral iron preparations (more than six months), presence of GIT bleeding, data about habits (cigarette smoking and alcohol), co-morbidities and the results of the life quality questionnaire. The following continuous variables were taken into account: serum values of urea, creatinine, sodium, potassium, calcium, phosphorus, proteins, cholesterol, alkaline phosphatase, iron, haematocrit, eryth-

rocytes, haemoglobin, leukocytes, thrombocytes, MCV (mean corpuscular volume), and body mass index.

Statistics

The prevalence of each characteristic during the study period was determined for both groups. Differences in the observed characteristics were assessed between patients who were treated with high-flux membrane dialysers and patients who were treated with low-flux membrane dialysers using an independent T-test for continuous variables and a Chi-squared test for frequencies. The differences were considered significant if the probability of the null hypothesis was less than 0.05. The statistical calculations were made using the SPSS statistical package (version 18).

RESULTS

Serum levels of urea were significantly different between patients who were treated with high-flux membrane dialysers and those who were treated with low-flux membrane dialysers (t=2, 094, p=0.040) No significant differences were found in other laboratory parameters, clinical symptoms, co-morbidities, habits, or quality of life (Table 1).

DISCUSSION

The different permeabilities of dialysis membranes lead to different removal capacities, particularly for uremic toxins of middle and large molecular weight. High-flux dialysers have been evaluated in clinical and epidemiological studies for their effects on mortality, morbidity, dialysis-related data and the preservation of residual renal function. However, many of these studies lack a prospective design and randomised treatment allocation, or they have too few patients and too short a period of follow-up. In this study, there was a significant difference in the serum urea levels among patients who were treated with different flux membranes, and it is believed that highly permeable dialysis membranes with a large pore size are more efficient than membranes with a small pore size for the removal of middle-sized molecules of uremic toxins.

Haemodialysis with high-flux membrane dialysers and haemodiafiltration were both connected to reductions of the pretreatment beta 2 microglobulin level, but the reduction was much greater in haemodiafiltration. Haemodialysis with high-flux membrane dialysers and haemodiafiltration of renal replacement therapy modes led to better nutritional status and to a better response to rHu EPO in patients with anaemia. Regarding sodium and energy balance, haemodiafiltration resulted in a much lower number of hypotensive episodes and an improvement in the quality of life (11).

Removal of small solutes (urea and creatinine) and larger solutes, such as b2-microglobulin and complement factor D, is much better with haemodiafiltration than with haemodialysis with high-flux membranes. Concentrations of pretreatment plasma complement factor D decreased more greatly with time among patients undergoing haemodiafiltration than among patients undergoing haemodialysis with high-flux membrane dialysers.(12)

During the beginning of dialysis treatment, serum potassium concentrations tend to decrease rapidly in the dialysate and to cause lower systolic and mean blood pressure by altering peripheral resistance. It has been concluded that the risk for developing intra-dialysis hypotension is strongly correlated with the dialysate potassium concentration.(13)

High-flux membranes showed a benefit in the lowering of plasma triglyceride, which has been confirmed elsewhere. (14)

Previous studies have reported controversial information. However, a study that investigated the effect of different synthetic membranes on laboratory parameters and survival among patients with ESRD (end-stage renal disease) found no differences in laboratory parameters between patients treated with high- or low-flux membranes.

A secondary study, the HEMO Study, aimed to examine the changes in health-related quality of life. It offered the specific hypotheses that study interventions would have a large impact on physical functioning, vitality, Short Form-36 Health Survey (SF-36) scores of physical and mental component summaries, kidney disease symptoms and problems and sleep quality. In that trial, among patients undergoing haemodialysis three times a week, the SF-36 physical component summary score and pain scale showed a benefit in the clinical status with higher dialysis dose, especially among patients who underwent dialysis treatment three times per week. Dose or flux interventions showed no benefit that was clinically meaningful, especially regarding other indices of health-related quality of life.(5)

A study that examined middle-sized molecules, high-flux membranes, and optimal dialysis (15), and a randomised trial of high-flux vs. low-flux haemodialysis on the effects on homocysteine and lipids (16), showed that highly permeable dialysis membranes with a large pore size are more efficient in the removal of middle-sized molecules such as homocysteine and lipids. Regarding the removal of urea (Kt/V) and phosphate, greater removal was observed with online haemodiafiltration than in haemodialysis. In a study that investigated dialysis dose and membrane flux impact on parameters of nutrition, neither mean serum albumin levels nor mean post-dialysis weight were significantly affected (17). The mean erythrocyte sedimentation rate declined more significantly in patients treated with high-flux membrane dialysers compared to patients treated with low-flux membrane dialysers.

Nutritional parameters can be altered subtly by interventions targeting the dose and flux, but nothing has been shown to prevent deterioration in nutritional status over time. (2)

Higher dialysis dose or high-flux membrane dialysers have not been shown to improve survival or reduce morbidity among patients undergoing maintenance haemodialysis, which is in contrast to the results of observational

Table 1. Values of measured variables in the study groups.

	HDF (mean±SD) */ n (%)†	Non-HDF (mean±SD) */ n (%)†	Values of independent samples T-test	Values of Chisquared test	p Value
Urea	17,761±3,469	20,309±6,604	2,094		0,04
Creatinine	640,161±118,521	591,705±159,29	−1,478		0,144
Sodium	136,518±1,987	136,161±1,951	0,767		0,446
Potassium	4,466±0,432	4,315±0,727	1,045		0,3
Calcium	2,403±0,155	2,382±0,191	−0,506		0,615
Phosphorus	1,628±0,325	1,694±0,369	0,807		0,422
Proteins	67,713±4,635	67,365±5,61	0,286		0,776
Cholesterol	4,419±0,938	4,712±0, 871	−1,355		0,18
Alkaline phosphatase	92,441± 46,749	82,720± 32,298	−0,997		0,322
Iron	12,994±5,978	11,497±3,613	1,256		0,213
Haematocrit	288,634±50,923	281,280±38,486	−0,681		0,498
Haemoglobin	97,456±9,928	93,132±12,304	−1,650		0,103
Erythrocytes	3,075±0,379	2,965±0, 459	−1,108		0,272
Leukocytes	6,333±1,740	7,010±1,888	1,582		0,118
Thrombocytes	199,346±73,119	218,303±62,108	−1,173		0,245
MCV	95,779±5,297	94,465±3,685	−1,200		0,234
BMI	24,019 ±4,407	24,184±4,317	−0,152		0,88
Headache	23 (58,974%)	23 (69,697%)		0,345	0,461
Respiratory discomfort	25 (64,103 %)	17 (51,515%)		0,28	0,341
Urea	17,761±3,469	20,309±6,604	2,094		0,04
Urinary discomfort	3 (7,692%)	6 (18,182)		0,194	0,287
Cardiac insufficiency	6 (15,385%)	7 (21,212 %)		0,522	0,554
GIT bleeding				0,992	1
Alcohol	3 (7,692)	4 (12,121)		0,527	0,695
Smoking	18 (46,154)	19 (57,576)		0,751	0,814
ComQuol				0,153	0,163

* Mean±SD- For non-categorical variables; † n (%)- For categorical variables; ‡ The HDF study group has 39 patients, and the non-HDF study group has 33 patients.

studies that have reported reductions in mortality with the use of high-flux membrane dialysers.

A benefit of high-flux membranes for patients who are on dialysis treatment for more than 3.7 years was shown in a study that investigated the dialysis dose and membrane flux among haemodialysis patients. Regarding total mortality, no significant decrease was observed in the patients who were treated with high-flux membrane dialysers. (17)

This study showed no significant differences between patients who were treated with high-flux membrane dialysers and those who were treated with standard dialysers, though this does not mean that there were no true differences between them, considering the relatively small number of study subjects and the low power of the study. We should also not forget that specific conditions in the Serbian health system may have influenced the results; these include the limited number of dialysis centres, the fact that a high number of patients travel more than two hours for dialysis treatment, which affects their quality of life, the limited number of available high-flux dialysers and the high average age of haemodialysis patients in the examined sample of patients (57,3056 ±12,64314).

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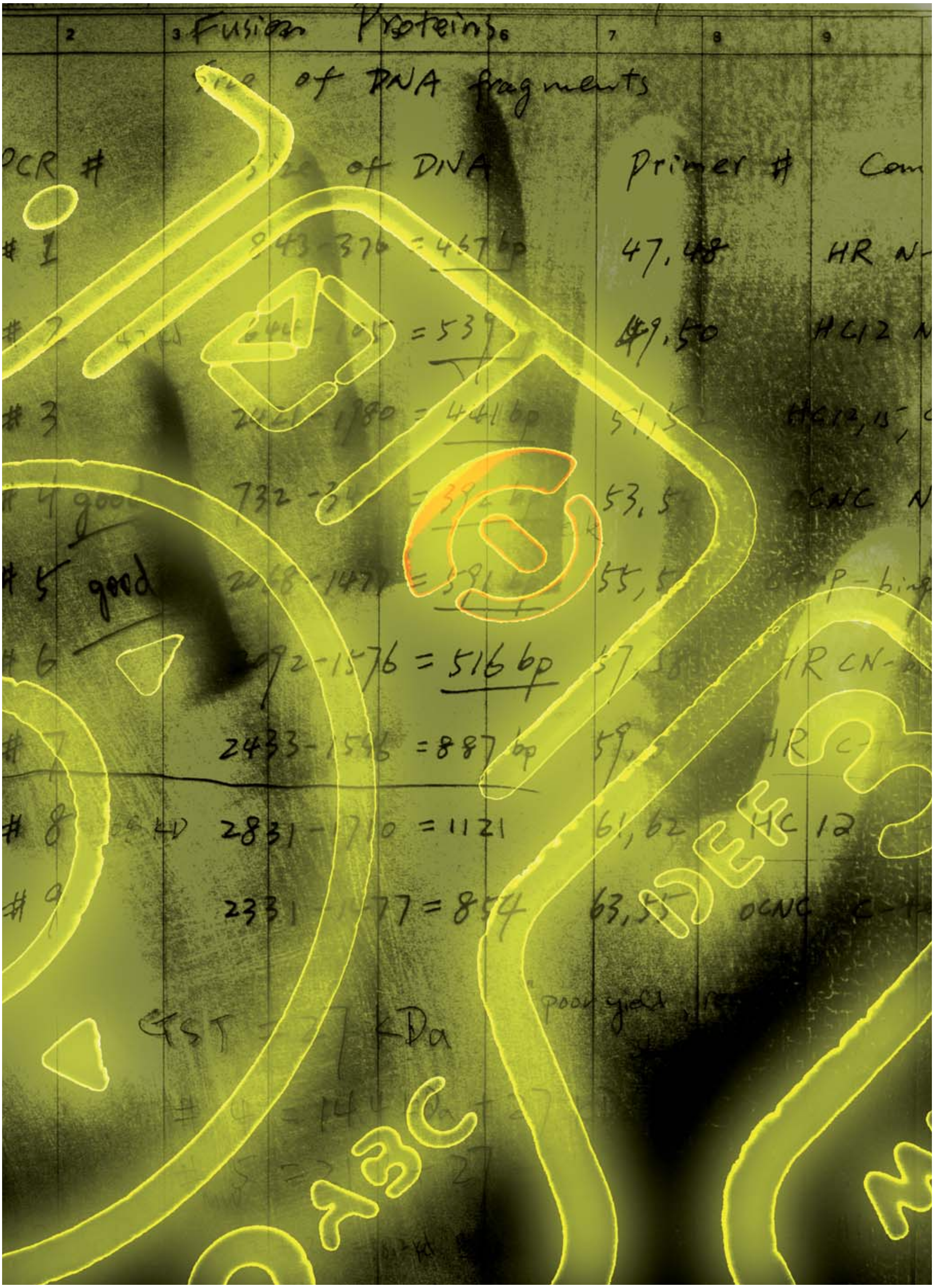
Fusion Proteins
of DNA fragments
PCR #
of DNA
Primer #
47, 48
49, 50
516 bp
887 bp
= 1121
61, 62
HC 12
GST
kDa
DEF
A3C

MOBILE PHONE RADIATION SIMULATOR COULD BE USED FOR TESTING THE EFFECTS OF MICROWAVES ON BIOLOGICAL SYSTEMS

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SIMULATOR ZRAČENJA MOBILNOG TELEFONA MOŽE SE KORISTITI ZA ISPITIVANJE UTICAJA MIKROTALASA NA BIOLOŠKE SISTEME

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A question that has repeatedly drawn the attention in recent years not only of the scientific community, but also of the general public is the potentially harmful effect of mobile phones on users' health. This concern especially applies to long-term use and use by children (1). It is necessary to perform a large number of studies because the effects microwave radiation from cell phones have on human organisms are still unclear (2,3,4). To understand the mechanisms of action of microwave radiation from mobile phones on biological systems, a simulator of mobile phone radiation (SZMT-QUAD 2010) was created. This simulator is actually a computer-controlled mobile phone (Figure 1A).

SZMT–QUAD 2010 was purchased from the manufacturer: the Innovation Center of Belgrade's Faculty of Electrical Engineering Ltd. (ICEF) 11120 Belgrade, 73 Boulevard of King Aleksandar. It was constructed by Dipl. Ing. Nikola Rajovic. The characteristics of the SZMT-QUAD 2010 radiation correspond to the characteristics of the original mobile phone working on the GSM-900 MHz (Global System for Mobile communications: originally from Groupe Spécial Mobile), GSM-1800 MHz and DCS-1800 MHz (Digital Cellular System 1800 MHz) frequencies. The antenna of SZMT-QUAD 2010 is located in the box and fully corresponds to the frequency bands of GSM-900 MHz, GSM-1800 MHz and DCS-1800 MHz GSM by power and radiation bands.

Adhesive foil marking the field of radiation of the SZMT-QUAD 2010 antenna was affixed on the cover of the box to mark the areas where the testing samples were placed (Figure 1B). For each batch of samples irradiated, the amount of energy radiated was calculated through the signal, which was automatically depicted on the computer monitor and expressed in dBm.

SZMT-QUAD 2010 consists of the following parts: box, power supply, circuit board, GSM module, antenna, GSM module control button, light indicators, and PC software (Figure 1B).

The GSM module is used to provide registration, identification and voice communication over the GSM network. The functionality of the module is independent of the chosen network provider.

Figures 1A and B. SZMT- QUAD 2010

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A special software application called “Radiation Simulator” was developed for Microsoft Windows to manage SZMT-QUAD 2010.

The application has the following functionalities:

- Checking the SZMT - QUAD 2010 registration with the network provider
- identifying the service provider and frequency range
- continuously presenting the signal strength from the base station of the network operator
- selecting the type of work - sleep or conversation
- measuring the duration of each type of simulation

These qualities make the SZMT–QUAD 2010 simulator a useful piece of equipment for testing the biological effects of microwave radiation from mobile phones. We used the simulator to test the effect of microwave radiation on the growth of bacterial cultures in vitro. SZMT–QUAD 2010 should be increasingly used in various experimental preclinical models to broaden our knowledge about the potentially harmful effects of microwave radiation from mobile phones.

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