CURRENT RESEARCH TOPICS IN PHARMACY:
Pharmacology Debates

April 19th, 2023 10.00 AM ISTANBUL

FOR REGISTRATION:

First Session- *Moderator: Esra TATAR 10.00-11.30 AM*

Welcome- Prof. Hatice Kübra Elçioğlu
Marmara University, Istanbul, Türkiye

The roles of cheminformatics in natural product-based drug discovery-Prof.Long Chiau Ming
School of Medical and Life Sciences, Sunway University, Kuala Lumpur, Malaysia

Applications of machine learning to the lead discovery: Practical approaches – Dr.Said Moshawih
Universiti Brunei Darussalam, Gadong, Brunei Darussalam

Second Session – Moderator: Ayşe Nur HAZAR YAVUZ 12:00-13.30 PM

Can Vitamin C supplements prevent premature rupture of membranes and preterm birth- Assist. Prof. Ana V. Pejcic
University of Kragujevac, Kragujevac, Serbia

Drugs affecting newborn weight, length and head circumference at birth -Assist.Prof. Milos N. Milosavljevic
University of Kragujevac, Kragujevac, Serbia

From traditional medicine to brain tumor theraphy using Plectranthus diterpenes-Assoc.Prof.Patricia Rijo
Lusofona University, Lisbon, Portugal

Chair
Prof. Hatice Kübra ELÇİOĞLU

Vice Chairs
Prof. Levent KABASAKAL & Assoc. Prof. Esra TATAR

ORGANIZING & SCIENTIFIC COMMITTEE
Editorial Board of Journal of Research in Pharmacy
https://www.jrespharm.com/

JRP

Journal of Research in Pharmacy
An international open-access journal of pharmacy and pharmaceutical sciences
Formerly published as Marmara Pharmaceutical Journal

ONLINE SYMPOSIUM

CURRENT RESEARCH TOPICS IN PHARMACY:
Pharmacology Debates

April 19th, 2023 10.00 AM ISTANBUL

FOR REGISTRATION:

Third Session- *Moderator: Mehmet GÜMÜŞTAŞ 14.00-15.30 PM*

Side effects of COVID 19 vaccines and the contribution of graphenes- Assoc.Prof.Beril Anılanmert
Institute of Forensic Sciences and Legal Medicine, Istanbul University-Cerrahpaşa, Istanbul, Türkiye

Knowledge and behaviour of medical university students about drug store and use-Assist.Prof.Klodiola Dhamo
Aldent University, Tirana, Albania

The advancement of herbal-based treatments for hair loss- Dr.Oğuzhan Aydemir
Istinye University, Istanbul, Türkiye

Chair
Prof. Hatice Kübra ELÇİOĞLU

Vice Chairs
Prof. Levent KABASAKAL & Assoc. Prof. Esra TATAR

ORGANIZING & SCIENTIFIC COMMITTEE
Editorial Board of Journal of Research in Pharmacy
https://www.irespharm.com/

JRP
Journal of Research in Pharmacy
An international open-access journal of pharmacy and pharmaceutical sciences
Formerly published as Marmara Pharmaceutical Journal

ONLINE SYMPOSIUM

CURRENT RESEARCH TOPICS IN PHARMACY:
Pharmacology Debates

April 19th, 2023 10.00 AM ISTANBUL

ORGANIZING & SCIENTIFIC COMMITTEE
Editorial Board of Journal of Research in Pharmacy
https://www.jrespharm.com/

JRP
Journal of Research in Pharmacy
An international open-access journal of pharmacy and pharmaceutical sciences
Formerly published as Marmara Pharmaceutical Journal

ONLINE SYMPOSIUM

DRUGS AFFECTING NEWBORN WEIGHT, LENGTH AND HEAD CIRCUMFERENCE AT BIRTH

Miloš MILOSAVLJEVIĆ [1*] ⓘ**, Jovana MILOSAVLJEVIĆ [2]** ⓘ**, Ana PEJČIĆ [1]** ⓘ**, Petar ARSENIJEVIĆ [3]** ⓘ**, Ivana ŽIVANOVIĆ MAČUŽIĆ [2]** ⓘ**, Nevena FOLIĆ [4]** ⓘ**, Slobodan JANKOVIĆ [1]** ⓘ

[1] Department of Pharmacology and Toxicology, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
[2] Department of Anatomy, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
[3] Department of Gynecology and Obstetrics, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia
[4] Department of Pediatrics, Faculty of Medical Sciences, University of Kragujevac, Kragujevac, Serbia

milosavljevicmilos91@gmail.com

*Presenting and corresponding author

The weight, length, and head circumference of newborns at birth are important markers of neonatal health, infant survival, and childhood morbidity [1,2]. It is known that infants with smaller body sizes at birth have a higher mortality rate and a higher risk of developing various somatic and cognitive-behavioral disorders in childhood and adulthood compared to children with normal body sizes at birth [2,3]. Numerous factors have so far been found to play a role in the birth of newborns with small birth sizes. However, there are controversies regarding the influence of certain groups of drugs on newborn birth size. So, for instance, while calcium channel blocker use during pregnancy has not been associated statistically significantly with low-birth-weight infants in one study [4], the use of these antihypertensive drugs has been identified as a predictor for the birth of small for gestational age newborns in another study [5]. Because of this and similar controversies, we conducted research with the aim of identifying drugs and other socio-demographic and clinical factors that significantly affect the values of parameters of the body size of newborns at birth.

We designed our research as an ambidirectional cohort study that was conducted on the population of pregnant women whose pregnancy was monitored at the Clinic for Gynecology and Obstetrics of the University Clinical Centre Kragujevac, Serbia. All pregnant women with pregnancies confirmed by a gynecology specialist were taken into account, with the exception of pregnant women under the age of 18, functionally illiterate pregnant women and those with a confirmed high risk of genetic abnormalities

of the fetus by a combination of ultrasound and biochemical examination during the 12th week of pregnancy. Our major outcome measures were body weight, body length and head circumference of newborns at birth. We examined the potential impact of the following variables to the newborn body size: demographic factors, presence of acute or chronic diseases during pregnancy, medications used during pregnancy, pregnancy factors, presence of uterine or placental abnormalities and maternal nutrition. For the assessment of the nutritional status of pregnant women, we previously developed and validated a special questionnaire that we named Balkan Food Quality and Diversity in Pregnancy Questionnaire-18 (BFQDPQ-18) [6]. We used the method of multiple linear regression analysis to evaluate the influence of potential factors on birth weight, length, and head circumference.

The study included 320 pregnant women with an average age of 30.35±5.50 years and 332 newborns (12 pairs of twins). At least one acute or chronic disease was diagnosed in 247 pregnant women (75.3%). The most frequently diagnosed diseases were thrombophilia (22.2%), colpitis (19.1%), hypertension (18.4%), anemia (12.2%), diabetes mellitus (11.3%), proteinuria (10.6%), and hypothyroidism (9.7%). The most commonly used drugs among our participants were antibiotic drugs (34.7%), progesterone, (28.1%), anticoagulant drugs (24.1%), calcium channel blockers (17.5%), antifungal drugs (16.6%), methyldopa (15.9%) and corticosteroids (11.9%). Four factors had a significant negative effect on birth weight: smoking (B= –196.647;p=0.002), twin pregnancy (B= –434.109;p=0.000), use of methyldopa (B= –145.561;p=0.033) and corticosteroids during pregnancy (B= –287.921;p=0.001). Smoking (B= –0.813;p=0.028), twin pregnancy (B= –1.719;p=0.005) and corticosteroid use during pregnancy (B= –1.818;p=0.000) also had a significant negative effect on birth length. Negative effect on fetal head circumference at birth had smoking (B= –0.585;p=0.011), use of corticosteroids (B= –0.961;p=0.003) and antibiotics during pregnancy (B= –0.547;p=0.009). Maternal height and gestational age at birth showed a positive influence on weight, length and head circumference of newborns, while pregnant women age was another factor in positive correlation with head circumference at birth.

Corticosteroids are widely used in pregnancy [7]. However, the negative effects of corticosteroids on cell growth and deoxyribonucleic acid replication are well known and described [8]. The results of a large population study conducted in Finland showed that fetuses exposed to antenatal corticosteroids during pregnancy had significantly lower body weight, body length, body mass index, and head circumference at birth compared to newborns that were not exposed to the effects of these drugs [9]. The negative effect of corticosteroids on infant body length and head circumference at birth was also noted by *Thorp et al*. in their retrospective study, in which they analyzed the impact of antenatal corticosteroid administration on infants treated in 100 different neonatal intensive care units in the USA [10]. Also, there is evidence indicating the teratogenic potential of corticosteroids and the association between the systemic use of

corticosteroids during the period of organogenesis and the occurrence of cleft lip and palate in the fetus [7].

Hypertensive disorders are common in pregnancy and require urgent and adequate treatment [11,12]. According to the official guidelines of gynecological associations, methyldopa is the antihypertensive drug of first choice in pregnancy because it has no proven teratogenic potential [13]. However, it seems that the use of methyldopa during pregnancy is not entirely without risk to the fetus. Thus, *Hoeltzenbein et al.* showed that newborns of methyldopa-treated mothers had a higher rate of reduced birth weight after adjustment for sex and gestational age at birth and a smaller head circumference in male newborns [14]. Similarly, *Orbach et al.* noticed a negative influence of methyldopa on the body weight of newborns of both genders [15], which is in accordance with our results.

Inadequately treated urinary infections in pregnancy pose a great risk to the fetus, as they are associated with an increased risk of spontaneous abortions, premature births, and low birth weight newborns [16,17]. The results of epidemiological studies that examined the potential impact of maternal antibiotic therapy on fetal growth and development parameters are quite controversial. Thus, the results of some studies showed that the use of antibiotics during pregnancy was accompanied by an increase in the body weight of newborns at birth [18,19], while other authors came to the opposite conclusion, indicating that newborns whose mothers used antibiotics during pregnancy had a lower body weight at birth [20,21].

In conclusion, clinicians should pay special attention to pregnant women who use corticosteroids, methyldopa, and antibiotics during pregnancy in order to prevent smaller values of newborn birth size parameters.

Keywords: Newborn birth size; birth weight; birth lenght; birth head circumference; drugs

REFERENCES

[1] Kheirouri S, Alizadeh M. Impact of prenatal maternal factors and birth order on the anthropometric status of newborns in Iran. J Biosoc Sci. 2017; 49(2): 251-264. [CrossRef]

[2] Zeljkovic A, Vekic J, Spasic S, Jelic-Ivanovic Z, Spasojevic-Kalimanovska V, Gojkovic T, Ardalic D, Mandic-Markovic V, Cerovic N, Mikovic Z. Changes in LDL and HDL subclasses in normal pregnancy and associations with birth weight, birth length and head circumference. Matern Child Health J. 2013; 17(3): 556-565. [CrossRef]

[3] Lunde A, Melve KK, Gjessing HK, Skjaerven R, Irgens LM. Genetic and environmental influences on birth weight, birth length, head circumference, and gestational age by use of population-based parent-offspring data. Am J Epidemiol. 2007; 165(7): 734-741. [CrossRef]

[4] Parazzini F, Benedetto C, Bortolus R. Nifedipine versus expectant management in mild to moderate hypertension in pregnancy. Br J Obstet Gynaecol. 1998; 105(7): 718–722. [CrossRef]

[5] Karahanoglu E, Altinboga O, Akpinar F, Demirdag E, Ozdemirci S, Akyol A, Yalvac S. Nifedipine increases fetoplacental perfusion. J Perinat Med. 2017; 45(1): 51-55. [CrossRef]

[6] Milosavljević J, Pejčić A, Arsenijević P, Dimitrijević A, Milosavljević M, Mihajlović D, Janković S. Testing of new instrument for measuring quality and diversity of nutrition in pregnancy. Ginekol Pol. 2023; 94(1): 73-78. [CrossRef]

[7] Kemp MW, Newnham JP, Challis JG, Jobe AH, Stock SJ. The clinical use of corticosteroids in pregnancy. Hum Reprod Update. 2016; 22(2): 240-259. [CrossRef]

[8] Crowther CA, McKinlay CJ, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database Syst Rev. 2015; 2015(7): CD003935. [CrossRef]

[9] Rodriguez A, Wang Y, Ali Khan A, Cartwright R, Gissler M, Järvelin MR. Antenatal corticosteroid therapy (ACT) and size at birth: A population-based analysis using the Finnish Medical Birth Register. PLoS Med. 2019; 16(2): e1002746. [CrossRef]

[10] Thorp JA, Jones PG, Knox E, Clark RH. Does antenatal corticosteroid therapy affect birth weight and head circumference? Obstet Gynecol. 2002; 99(1): 101-108. [CrossRef]

[11] Brown CM, Garovic VD. Drug treatment of hypertension in pregnancy. Drugs. 2014; 74(3): 283-296. [CrossRef]

[12] Mammaro A, Carrara S, Cavaliere A, Ermito S, Dinatale A, Pappalardo EM, Militello M, Pedata R. Hypertensive disorders of pregnancy. J Prenat Med. 2009; 3(1): 1-5.

[13] Butalia S, Audibert F, Côté AM, Firoz T, Logan AG, Magee LA, Mundle W, Rey E, Rabi DM, Daskalopoulou SS, Nerenberg KA; Hypertension Canada. Hypertension

Canada's 2018 Guidelines for the Management of Hypertension in Pregnancy. Can J Cardiol. 2018; 34(5): 526-531. [CrossRef]

[14] Hoeltzenbein M, Beck E, Fietz AK, Wernicke J, Zinke S, Kayser A, Padberg S, Weber-Schoendorfer C, Meister R, Schaefer C. Pregnancy outcome after first trimester use of methyldopa: A prospective cohort study. Hypertension. 2017; 70(1): 201-208. [CrossRef]

[15] Orbach H, Matok I, Gorodischer R, Sheiner E, Daniel S, Wiznitzer A, Koren G, Levy A. Hypertension and antihypertensive drugs in pregnancy and perinatal outcomes. Am J Obstet Gynecol. 2013; 208(4): 301.e1-6. [CrossRef]

[16] Harbison AF, Polly DM, Musselman ME. Antiinfective therapy for pregnant or lactating patients in the emergency department. Am J Health Syst Pharm. 2015; 72(3): 189-197. [CrossRef]

[17] Lamont HF, Blogg HJ, Lamont RF. Safety of antimicrobial treatment during pregnancy: A current review of resistance, immunomodulation and teratogenicity. Expert Opin Drug Saf. 2014; 13(12): 1569-1581. [CrossRef]

[18] Jepsen P, Skriver MV, Floyd A, Lipworth L, Schønheyder HC, Sørensen HT. A population-based study of maternal use of amoxicillin and pregnancy outcome in Denmark. Br J Clin Pharmacol. 2003; 55(2): 216-221. [CrossRef]

[19] Czeizel AE, Rockenbauer M, Olsen J. Use of antibiotics during pregnancy. Eur J Obstet Gynecol Reprod Biol. 1998; 81(1): 1-8. [CrossRef]

[20] Vidal AC, Murphy SK, Murtha AP, Schildkraut JM, Soubry A, Huang Z, Neelon SE, Fuemmeler B, Iversen E, Wang F, Kurtzberg J, Jirtle RL, Hoyo C. Associations between antibiotic exposure during pregnancy, birth weight and aberrant methylation at imprinted genes among offspring. Int J Obes (Lond). 2013; 37(7): 907-913. [CrossRef]

[21] Mueller NT, Rifas-Shiman SL, Blaser MJ, Gillman MW, Hivert MF. Association of prenatal antibiotics with foetal size and cord blood leptin and adiponectin. Pediatr Obes. 2017; 12(2): 129-136. [CrossRef]