

Macedonian Medical Master of Science (MSc) Theses Defended in 2012

Macedonian Journal of Medical Sciences*

Institute of Immunobiology and Human Genetics, Faculty of Medicine, Ss. Cyril and Methodius University of Skopje, Skopje, Republic of Macedonia

Abstract

Citation: Macedonian Journal of Medical Sciences. Macedonian Medical Master of Science (MSc) Theses Defended in 2012. *Maced J Med Sci.* 2013 June 15; 6(2):202-207. <http://dx.doi.org/10.3889/MJMS.1857-5773.2013.0295>.

Key words: Master of Science (MSc); Medical research; Republic of Macedonia.

***Correspondence:** Macedonian Journal of Medical Sciences. Institute of Immunobiology and Human Genetics, Faculty of Medicine, Ss. Cyril and Methodius University of Skopje, Republic of Macedonia. 50 Divizija No 16, PO Box 60, 1109 Skopje, Republic of Macedonia. Telephone: +389 2 3110556. Telefax: +389 2 3110558. EMail: mjms@ukim.edu.mk

Received: 12-Feb-2013; **Revised:** 20-Mar-2013; **Accepted:** 02-May-2013; **Online first:** 25-May-2013

Copyright: © 2013 Macedonian Journal of Medical Sciences. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Competing Interests: The authors have declared that no competing interests exist.

We present English abstracts of MSc theses defended in 2012 at the Faculty of Medicine, Ss. Cyril and Methodius University of Skopje, Republic of Macedonia. English summaries are published as they are translated by authors and included in the final version of defended MSc. Macedonian Medical Master of Science (MSc) theses are deposited in the Central Medical Library and National and University Library "St. Kliment Ohridski" in Skopje.

At the Faculty of Medicine in Skopje 10 MSc theses there were defended in 2012, three of them without English abstract (30.0%): one from the University Clinic of Anesthesiology, Resuscitation and Intensive Care, one from the University Clinic of Pediatric Diseases, and one from University Clinic of Neurosurgery.

Editorial Board does not take any responsibility either for the content, nor the quality of the abstracts. Primary responsibility for the quality of the MSc theses belongs to the mentors, to the institutions they are representing, and to the Vice-Dean of science.

Defended MSc can be cited as they are published in this and in the previous reports.

Meri Peshevska. Prognostic and predictive value of the Her2/neu protein in the patients with early breast cancer [MSc thesis]. Skopje, Republic of Macedonia: University Clinic of Oncology with Radiotherapy, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. *Maced J Med Sci.* 2013 June 15; 6(2):202-207.

Prognostic factors have a major role in modern oncology and represent the basis for planning the oncology therapy. Advances in molecular oncology and different researcher in oncogenesis in the BC allow detection of genes or proteins with different mechanisms of action, resulting in the appearance of

tumor and metastases. The most explored is Her2/neu gene with tyrosin kinase activity which participates in the cell cycle proliferation, progression, apoptosis and survival.

The aim of the study is to determine the expression of the Her 2/neu protein and its prognostic and predictive value in the patients with early breast cancer. The study has a combined retrospective- prospective approach and consists of 200 patients with EBC in the period from 01.01.2007-30.06.2008 year and the patients were operated and diagnosed with IHH expression of the Her 2/neu, Ki67, p53, and the status of ER and PR. According to the expression of

Her2/neu protein the patients were divided in two groups: Her2- and Her2+ and the results were compared between the groups. Her2+ group is randomized in the 3 subgroups:

1. 33 patients after completion of adjuvant HT are applied target therapy with Tr (AC+T→Tr)
2. 33 patients who take adjuvant HT with taxanes take a target therapy with Tr. (AC→T+Tr)
3. 34 patients who take adjuvant HT without target therapy with Tr.

The results of the study shown that in Her2 + groups patients who have received HT+Tr have for 0.13 greater probability of survival in comparison with the group without Tr. Survival time is 19.27-22.31 months (5-24 months)

COX regression analysis showed greatest significance in the therapy with Tr. (Wald = 6.25) independently from the type of giving concurrent or sequential.

This study showed that Her2 /neu protein is on independent prognostic factor in the patients with EBC, and indicates aggressive disease, rapid progression and poor prognosis.

Key words: *breast cancer; imunohistochemistry analysis; Her2 /neu protein; prognostic factor; predictive factor.*

Defended: January 4, 2012.

Mentor: Prof. Dr. Aneta Dimitrovska.

Katerina A. Andreeska. Impact of Metabolic syndrome on the occurrence of cardiovascular diseases in postmenopausal women [MSc thesis]. *Skopje, Republic of Macedonia: Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.*

Aim: The aim of this survey shall be defined the impact of metabolic syndrome on the occurrence of CVD in postmenopausal women and through the evaluation of the results to make correlation between the occurrence of CVD in postmenopausal women without metabolic syndrome and postmenopausal women with metabolic syndrome. Material and methods: in cross-sectional study were included 120 women divided in 2 groups/ premenopausal/ 30 and postmenopausal/ 90 postmenopausal were divided in those with (66.67%) and without metabolic syndrome (33.33%). In each patient was taken detailed history into the possible existence of cardiovascular disease. Metabolic syndrome was defined in accordance with the criteria of the APT III. We were taking the following parameters: physical weight, height, WC, systolic, diastolic blood pressure, BMI, CRP, urea, creatinine, uric acid, HDL, LDL, FSH

and TGL Mean (standard deviation) age was 41 ± 6.08 in premenopausal women and 59.69 ± 7.74 in postmenopausal women. We determined that in postmenopausal women metabolic syndrome and its components are markedly increased. For $p < 0.001$, postmenopausal women have increased BMI, WC, CRP, and physical weight. For $Z = -2.51$, $p < 0.05$ ($p = 0.01$) postmenopausal women shall have value for the TGL, HDL, LDL. In premenopausal women 0.19 (OR = $0.19 \pm 95\%$, CI: 0.04, < OR < 0.84) risk for the presence of coronary heart disease is less and that is significant. In postmenopausal women with metabolic syndrome (66.67%) worsening of the metabolic profile is increased. For $p < 0.001$ these women shall have high HDL, LDL, CRP, TGL, cholesterol, glucose and WC. In postmenopausal women with metabolic syndrome (OR = $5.21 \pm 95\%$, CI: 1.42 < OR < 19.18) risk for the presence of coronary disease is higher, than in postmenopausal women, without metabolic syndrome (33.33%), and that is significant.

Conclusion: In postmenopause we have worsening of the metabolic profile and increased CVD.

Key words: *menopause; metabolic syndrome; cardiovascular diseases.*

Defended: January 19, 2012.

Mentor: Dr. Sci. Silvana Jovanova.

Ristevska Gordana. Brain-derived neurotrophic factors as biological marker in depressive disorder [MSc thesis]. *Skopje, Republic of Macedonia: University Clinic of Psychiatry, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.*

Aim: Recent studies suggested a role of brain-derived neurotrophic factor (BDNF) in depression. While BDNF levels are lower in depressed patients, antidepressant treatment increases serum BDNF levels of depressed patients. This study aims to test the serum BDNF levels in depressed subjects who have exacerbated depressive symptomatology and to compare them with the serum BDNF levels of healthy control subjects; to test the effect of antidepressant treatment on serum BDNF levels in patients with depressive disorder and to explore the possibility of using serum BDNF levels as a biological marker for depressive disorder.

Methods: Thirty patients (14 women, 16 men) diagnosed with depressive episode according ICD-10 were included in the study. 23 patients had their first episode and were drug - naive; the other 7 patients were drug - free for at least 4 weeks. The severity of depression was assessed with Hamilton Depression Rating Scale (HDRS). The control group consisted of 30 age- and sex- matched subject without any psychiatric disorder. Blood samples were collected at

the baseline and after achieved remission (HDRS decrease of minimum 50%).

Results: Before antidepressant treatment the mean serum BDNF level was 12.51 ± 6.17 ng/ml and the mean HDRS score was 28.4 ± 3.65 . Serum BDNF levels of the depressed patients were significantly lower than in the control group (26.89 ± 9.67 ng/ml). At the end of the study, the mean serum BDNF level was 23.51 ± 10.76 ng/ml whereas the mean HDRS score was 7.47 ± 3.18 . From the baseline to the remission after 8.07 weeks of treatment, the increase in serum BDNF level and the decrease in HDRS score were statistically significant, respectively. When we compared the serum BDNF levels of depressed patients at remission with levels of the controls, there was no statistically significant difference.

Conclusion: Our study suggests that low BDNF levels may play a pivotal role in the pathophysiology of depressive disorder and the antidepressants may increase BDNF in depressed patients, which may be considered as a nonspecific peripheral marker of depression.

Key words: *Depressive disorder; BDNF; Brain-derived neurotrophic factor.*

Defended: January 20, 2012.

Mentor: Prof. Dr. Vesna Pejaska Gerazova.

Aleksandra Babulovska. Comparative clinical-epidemiological study of the therapeutic approach with buprenorphin and methadone in heroine addiction [MSc thesis]. Skopje, Republic of Macedonia: Institute of Epidemiology and Biostatistics with Medical Informatics, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.

Subject: Drug addiction is considered as one of the biggest problems of our time. Production, transport and drug abuse, mostly heroine is at constant increase in Republic of Macedonia as in the world. Practice of the treatment of heroine addicts with buprenorphin is increasingly advisable in the world proportions compared to the treatment with methadone. The aim of the research conducted within the frame of this master thesis is to compare the experiences from the therapeutic approach with buprenorphin and methadone in heroine addiction.

Materials and methods: The research represents descriptive and analytical (case control) study conducted in the period of 2011 on the University Clinic for toxicology and Center for Addictions Kisela Voda in Skopje. The study covered total number of 140 heroine addicts divided in two groups of 70 examinees who minimum 3 months before the start of the research have been voluntarily enrolled in the maintenance treatment with buprenorphin (research/inquiry group) and methadone (controlled

group). Both groups were followed for: (1) maintenance dose: (2) the effect of duration of the heroine addiction on the amount of the maintenance dose: (3) the effect of the average daily dose of abused heroine over the amount of the maintenance dose: (4) advantages and disadvantages of the therapeutic treatment with buprenorphin and methadone in heroine addiction. Sample of examinees is random. In both groups the examinees were selected in accordance with previously determined inclusive and exclusive criteria and were paired upon all characteristic that can affect the aims of the research.

Results: In regards to the average time of heroine abuse, there is a significant difference of two years (t -test < 0.05) between research/inquiry group (5.9 ± 2.3) and controlled group (7.8 ± 2.4). The daily dose of abused heroine at the largest part of examinees of both groups, 47.1% vs 50%, is 0.5 gr. Fifty percent of the addicts of the subjected to the buprenorphin treatment and methadone and of methadone 43.3 ± 16.9 mg. After seven days, buprenorphin maintenance dose in the research/inquiry group is 10.8 ± 4.8 mg, and methadone maintenance dose in the controlled group is 75.3 ± 23.8 mg. Half of the examinees of both, the research/inquiry group and the controlled group, received maximum dose of buprenorphin > 12 mg i.e. maximum dose of dose of methadone > 107.5 mg.

The results have shown that there is a positive and direct correlation between the daily dose of abused heroine and the maintenance buprenorphin dose ($R = 0.74$, $p < 0.05$) i.e. methadone dose ($R = 0.65$, $p < 0.05$). The most often psychiatric disorder in the both groups is personality disorder, in 25.7% vs 34.3% and the rarest is affective disorder, in 1.43% of the examinees of the controlled group. There is no significant difference in the cases of occurrence of depressive disorder between the examinees of the both groups (Yates corrected = 0.39, $df = 1$, $p = 0.53$).

Heroine abuse has been registered at 28.6% of the examinees subjected to buprenorphin treatment and at 47.1% of those subjected to methadone treatment. Consequently the examinees on buprenorphin and methadone treatment most often abused cannabis (48.6%) and benzodiazepines (87.1%). Heroine addicts subjected to buprenorphin therapy significantly less abuse cocaine compared to addicts subjected to methadone treatment (Yates chi-square = 8.77, $df = 1$, $p = 0.003$).

At the beginning of the treatment the withdrawal symptoms are more frequent during the therapy with buprenorphin in comparison to methadone. However, the difference is insignificant in all analyzed abstinence syndromes (yawning, nose running, piloerection, eyes tearing, tremor, mydriasis, feeling hot and cold waves, muscle cramps, discomfort, nausea and vomiting, stomach spasm, anxiety and sweating).

Conclusion: It is necessary that the analysis of the advantages and disadvantages of the therapeutic

approach with buprenofin and methadone at heroine addicts stays in the focus of the research interest of national researches.

Key words: Heroine addiction; methadone treatment; buprenofin treatment; comparison.

Defended: April 11, 2012.

Mentor: Prof. Dr. Vesna Velik Stefanovska.

Valentina Andova. Echocardiographic evaluation of right ventricular myocardial infarction and right ventricular systolic dysfunction in patient with acute left ventricular myocardial infarction [MSc thesis]. Skopje, Republic of Macedonia: Institute of Heart Diseases, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.

This master study was performed on 122 pts split in 2 groups. First group (n = 58) were pts with EDG and/or echocardiographic signs of right ventricular myocardial infarction (RVMI) and RV dysfunction. Second group (n = 64) were pts without these signs. We used ECG, ECHO and coronary angiography as standard methods for optimal diagnosis. Prognostic values of RVMI and RV systolic dysfunction were determined with monitoring of the occurrence of intrahospital events.

The results showed that the highest risk of the occurrence of RVMI was within the pts with acute myocardial infarction on inferior wall. There was no important correlation between occurrence of RVMI and demographic data, anthropometric measurements, risk factors and blood pressure values. Patients with RVMI showed significantly higher frequency of RV failure than pts without RVMI. On the other hand pts with RVMI had significantly lower values of echocardiographic parameters of global and regional RV dysfunction. Presence of tricuspid regurgitation was much more frequent within the pts with RVMI. Echocardiographic measurements of pulmonary pressure showed much higher values within the pts with RVMI. Coronary angiography showed significantly higher presence of pathological changes (stenosis \geq 50-99% or occlusion 100%) on right coronary artery within the pts with RVMI. Stenosis or occlusion of artery is main factor for RVMI. Intrahospital complications occurred in 23% of pts (out of 122 total numbers of pts). 32.8% out of these 23% of total pts had ECG signs of RVMI which was significantly higher presence than with the pts without RVMI. Regarding the intrahospital events the only differences between pts with and without RVMI were in occurrences of atrio-ventricular block significantly increases the risk of RVMI. Patients with RVMI had worse prognosis including shorter cumulative period of time without intrahospital events occurrence. As most predictive factors for poor intrahospital prognosis are age (older more than younger), presence of clinical signs and symptoms of

RV failure, presence of ECG signs of RVMI, lower value of TAPSE, higher values of right atrial pressure and lack of coronary angiography.

Conclusion: Electrocardiography and echocardiography are the most important methods with high accuracy, sensitivity, specificity for determination of presence of RVMI and RV dysfunction as well as in determination of intrahospital prognosis in patients with RVMI. Treatment of these patients with percutaneous coronary intervention guarantees much better prognosis.

Key words: right ventricular myocardial infarction; left ventricular myocardial infarction; electrocardiography; echocardiography; percutaneous coronary intervention.

Defended: June 12, 2012.

Mentor: Prof. Dr. Ljubica Georgievska - Ismail.

Aleksandra Panovska-Petrusheva. Comparative evaluation on the turnover of sodium in neurosurgical patients [MSc thesis]. Skopje, Republic of Macedonia: University Clinic of Anesthesiology, Resuscitation and Intensive Care, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.

Abstract not available.

Key words: Not available.

Defended: June 14, 2012.

Mentor: Prof. Dr. Marija Sholjakova.

Evica Bojadjeva. Prognostic factors in acute lymphoblastic leukemia and lymphoblast lymphoma in childhood [MSc thesis]. Skopje, Republic of Macedonia: University Clinic of Pediatric Diseases, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.

Abstract not available.

Key words: Not available.

Defended: June 14, 2012.

Mentor: Higher Sci. Coll. Dr. Kata Martinova.

Melisa Stefanova. Predictive value of ^{99m}Tc - MIBI scintigraphy in evaluation of the malignant lesions of the locomotor system. [MSc thesis]. Skopje, Republic of Macedonia: Institute of Pathophysiology and Nuclear Medicine, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.

Purpose: To assess the value of ^{99m}Tc -hexakis-2-methoxyisobutylisonitrile (MIBI) scintigraphy compare with classical ^{99m}Tc -methylene diphosphonate (MDP) bone scintigraphy in patients with clinical and radiologic features of benign and malignant lesions of the locomotor system.

Material and methods: The study included 30 patients (18 with benign and 12 malignant lesion). Each patient underwent three-phase bone scanning with ^{99m}Tc -MDP. After 3-7 days was performed ^{99m}Tc -MIBI scintigraphy (early phase 10 minutes after application and late phase 1 hour after application of the radiotracer). The MDP and MIBI scans were evaluated by visual and semiquantitative analysis. The ratio of the control of the lesion to the of the contralateral normal area (T/N) was calculated from the region of interest drawn on the MIBI and MDP scans.

Results: Visual analysis showed that between malignant and benign lesions have a statistically significant difference in MIBI scans ($p < 0.05$), compare to the MDP scintigraphy ($p = 0.3408$). There are no statistically significant differences ($p = 0.0754$) between mean values of T/N (4.91 ± 2.84 for malignant and 3.67 ± 3.34 for benign lesions) on MDP bone scans. The MIBI-uptake ratio in malignant lesions (2.71 ± 1.41 and 2.25 ± 1.02) was significantly higher ($p = 0.0004$) than that in benign lesions (1.34 ± 0.46 and 1.22 ± 0.28) for early and late stages respectively. The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of the MIBI-uptake ratio for malignant lesions were 91.7%, 72.2%, 80%, 68.6% and 92.9%, respectively, compare to the value of the ^{99m}Tc -MDP scintigraphy (100%, 33%, 60%, 50%, 100%, respectively).

Conclusion: ^{99m}Tc -MIBI scintigraphy can be a useful additional diagnostic method in distinguishing between malignant and benign lesions of the locomotor system by applying visual and semiquantitative analysis. Although it cannot replace tissue biopsy as a definitive diagnostic modality, her role is justified in the preoperative evaluation of patients with benign and malignant lesions of the locomotor system.

Key words: ^{99m}Tc -MIBI scintigraphy; tumors of the locomotor system; conventional ^{99m}Tc -MDP bone scintigraphy.

Defended: June 20, 2012.

Mentor: Prof. Dr. Daniela Miladinova.

Robert Shumkovski. Evaluation of the mitotic index as prognostic factor for the outcome of the treatment for meningiomas [MSc thesis]. Skopje, Republic of Macedonia: University Clinic of Neurosurgery, Faculty of Medicine, Ss Cyril and

Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.

Abstract not available.

Key words: Not available.

Defended: September 24, 2012.

Mentor: Prof. Dr. Ilija Pangovski.

Kornelija Trajkova. The role of the vaginal pH value in the prediction of preterm delivery [MSc thesis]. Skopje, Republic of Macedonia: University Clinic of Gynecology and Obstetrics, Faculty of Medicine, Ss Cyril and Methodius University of Skopje; 2012. Maced J Med Sci. 2013 June 15; 6(2): 202-207.

Summary: Genital infections in pregnancy are one of the main reason for increasing rate of preterm delivery. Bacterial vaginosis or anaerobe dysbiosis has a significant prevalence of 20% and relative risk for abortion and preterm delivery from 1.4 to 6.9%. Adequate treatment especially in the early stadium of pregnancy leads to evident reduction of prematurity. Vaginal pH measurement during pregnancy is one of the recommendations of the WAPM for the prevention of preterm delivery. It has been implemented in more than twenty countries and it seems to be a unique sign in the diagnostic process for the prompt detection of precursors versus detection of infection. Regular measurements provide a significant reduction of prematurity.

Purpose: To determine if the abnormal vaginal pH increases the risk of preterm delivery; to determine the correlation between preterm delivery and the microbiological smears and if there is a difference in the duration of pregnancy in women with increased vaginal pH treated in early pregnancy versus those in not treated women.

Material and methods: Prospective study that included 200 outpatients and hospitalized pregnant women from the University Clinic of Obstetrics and Gynecology, before 37 week of gestation, with or without signs of preterm labor, divided in two groups: women with signs of preterm labor and women enrolled in the study from the first trimester with regular vaginal pH measurement, using indicator strips, with a cut-off value of 4.5. We made a microbiological analysis of the four standard smears. After the investigation, each group was divided into three subgroups according to the vaginal pH value: women with normal pH value, women with increased pH value, women with increased pH value treated with therapy for normalization and women with increased pH value without therapy.

Results: The results showed significant incidence of the preterm delivery among women with signs of preterm labor comparing to those from the regular controlled group and treated if needed (86% vs. 11%).

85% of women with signs of preterm delivery had abnormal pH value, which confirms the correlation of the increased vaginal pH with the process of preterm delivery. We also registered positive statistically relationship between vaginal pH value and the results of the microbiological analysis and concerning the microbes isolated, the results showed correlation of the presence of *Gardnerella*, as well as for *Ureaplasma urealyticum* with increased vaginal pH value. The study confirmed the efficacy of the local therapy for normalization and maintenance of the vaginal pH value.

Conclusion: Increased vaginal pH value increases the risk of preterm delivery. The results confirmed the correlation between increased vaginal pH value and preterm delivery, especially in the group with signs of preterm labor. The vaginal pH measurement is a method to determine and follow the condition the vaginal milieu.

Key words: *Vaginal pH; preterm delivery.*

Defended: November 7, 2012.

Mentor: Prof. Dr.Gordana Adamova.