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# RISK FACTORS FOR PROTEINURIA IN PREGNANCY

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***Abstract* - The high level of proteinuria in pregnant women causes consequences for the mother and fetus. This study focused on proteinuria and the risk factors related to it. 470 pregnant women were included in this study. The data regarding socio-demographic details, gestation age, parity and obstetrics history were collected. Proteinuria, blood pressure and glycemia were measured. Proteinuria was detected among 25.7% of the participants. Hypertension, diabetes, the second and third trimesters, higher maternal pre-pregnancy body mass index (BMI), younger and older age, nulliparity, low educational and rural women were independently associated with increased odds of proteinuria in pregnancy. Diabetes mellitus, the third trimester and obesity were superior to the others factors in predicting the development of proteinuria.**

***Index Terms*: proteinuria in pregnancy, trimesters, pre-pregnancy BMI.**

## I. INTRODUCTION

In pregnancy the renal hemodynamic changes mean that greater quantities of colloids and solute pass by the glomerular barrier per unit time. In addition there are changes in glomerular permeability and altered tubular reabsorption of filtered proteins that may result in increased excretion of protein. It is normal in pregnancy after 20 weeks gestation for total protein excretion to reach 0.3g over 24 hours and for urinary albumin excretion to reach 0.2g over 24 hours [1]. It has been suggested that the threshold for normal total protein excretion be lowered to 0.2 g over 24 hours [2].

It has been suggested that proteinuria is a consequence of two mechanisms [3]. It can be due to the abnormal transglomerular passage of proteins due to increased permeability of the glomerular capillary wall and the impaired reabsorption by the epithelial cells of the proximal tubuli.

The presence of proteinuria is seen as a possible indication of many complications in pregnancy, from urinary tract infection to chronic renal disease and it remains central to the diagnosis of pre-eclampsia in a hypertensive pregnancy.

The incidence of proteinuria (and/or hypertension) arising in pregnancy varies according to the definition and to parity, age and underlying medical disease [4,5]. Proteinuria can be caused by the pregnancy itself, or may exist from before conception (being unrelated to the pregnancy). However as pregnancy may be the first point of medical contact for many women, pre-existing proteinuria may be first diagnosed at this time. Hypertension with proteinuria is clearly associated with increased fetal and maternal morbidity, especially if occurring remote from term [6-8]. Quantification of proteinuria in the pregnancy is important not only for making diagnosis, but also for predicting maternal and fetal outcome.

Considering the importance of proteinuria in the outcome pregnancy we realized this study to identify the potential risk factors related to the urinary excretion of protein in pregnant woman.

## II. MATERIAL AND METHODS

In the study were enrolled 470 pregnant women of age ranging between 17-42 years presented for the routine control and those admitted in the obstetric department of the regional hospital of Shkodra city in North Albania.

A validated questionnaire was administered to all participants who presented for health checkup. The

questionnaire collected information about their age, education, residence, parity, health status (diabetes, hypertension, medication) and anthropometric parameters – pre-pregnancy weight and height to calculate body mass index. Most of these data are also related with health, social and environmental questions.

A fresh urine and blood sample were also collected from all subjects. For the determination of the proteinuria in the urine samples have been used the following methods based on Henry [9]: the qualitative method with sulphosalicylic acid, the semi-quantitative method using dipstick urine, and the Heller method.

Gestational age, or the age of the baby, is calculated from the first day of the mother's last menstrual period. Hypertension was defined by an average of systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg and/or concomitant use of antihypertensive medications by self-report (known hypertensive) [10]. Pre-pregnancy of the body mass index (BMI) was calculated from weight and height measures as weight ( kg) divided by the square of height ( $m^2$ ) and was categorized as underweight (<18.5 $kg/m^2$), normal (18.5-24.9 $kg/m^2$), overweight (25–29.9) or obese (≥30) according to the 2000 WHO criteria [11]. Diabetes was ascertained either by self-reported physical diagnosis or by a measure of fasting blood sugar ≥ 126 mg/dl. Serum glucose level in the study subjects was measured through the methods described by Trinder [12].

Data analyses and calculation were performing by using the Statistical Package for the Social Sciences (SSPS for windows, version 21). Chi-squared test was used to determine the association between categorical variables. The relationship between the risk factors and proteinuria was analyzed by using binary logistic regressions. Odds rations (OR) and their 95% confidence intervals (95% Cl) are presented. The p-value of less than or equal to 0.05 was considered significant.

## III. RESULTS AND DISCUSIONS

The study population consisted of 470 pregnant women from Shkodra Region. Proteinuria was detected among 25.7% of the participants. While the prevalence of hypertension and diabetes resulted 11.9% and 1.1% respectively. In the table 1 are showed the data of the study population. Prevalence of proteinuria was higher in age groups <24 and >35 years old than in the other two groups. We observed a statistically significant difference between prevalence of proteinuria and trimesters. So proteinuria was higher in the third and second trimesters (33.5% and 23.8% respectively) comparing with the first trimesters (4.9%) Regarding parity, proteinuria was more prevalent among nulliparous (31.2%) than multiparous women (19.7%). Analysis of the educational status of the subjects showed significant differences at various educational levels between proteinuric and non proteinuric pregnant woman. So, proteinuria was higher among women with low education (34.5%). The presence of urinary protein was more prevalent among rural than urban residence (32.1% vs 20.2%). The prevalence of proteinuria gets higher with increase of weight, being more frequent among obese and overweight women (54.2% and 43.8% respectively) compared with normal and underweight women (20.8% and 23.85 respectively). Also, proteinuria was more common among hypertensive and diabetic pregnant women (53.6% and 80% respectively) compared with non hypertensive and non diabetic pregnant women (22% and 25.2% respectively).

We also analyze the relationship between proteinuria and risk factors. The unadjusted and adjusted odds ratios (OR) of factors associated with proteinuria among all participants is presented in Table 2. Factors associated with the development of proteinuria in univariate analysis were: the age - age groups <24 and >35 years old increase likelihood of proteinuria 2.1 and 3.3 respectively (OR 2.1 and OR 3.3 $p<0.05$) compared with women age groups 25-29 years; trimesters – women in the third and second trimester have more likely to develop proteinuria (OR 10.1 and OR 6.3 $p<0.05$) than the women in the first trimester; parity-nulliparous increase likelihood of proteinuria 1.8 times (OR 1.8 $p<0.05$) compared with multiparous women; education- women of elementary and middle education was observed to be associated with greater likelihood of proteinuria (OR 2.3 and OR 1.8 $p<0.05$) compared with women of high education; residence - living in rural area increase likelihood of proteinuria 1.7 times compared with women who live in urban area; BMI- obesity increase the likelihood of proteinuria 4.5 times (OR 4.5 $p<0.05$) and overweight 3 times (OR 3 $P<0.05$) compared to women with normal BMI; hypertension – women subjects with hypertension were significantly more likely to exhibit proteinuria, with an OR of 4.1 ($p<0.05$) compared with non hypertensive women; diabetes - women with diabetes have 11.9 times more likely to develop proteinuria (OR 11.9 $p<0.05$) than non diabetic women.

Also after adjusted for hypertension, diabetes and trimesters in multivariate analysis resulted that the risk factors which influence in the development of proteinuria are almost the same with those in univariate analysis. The only difference was the relation of proteinuria and the middle education. In multivariate analysis the middle education was not statistically significant (p>0.05).

TABLE 1. CHARACTERISTICS OF THE STUDY POPULATION

| | Total | Proteinuria n (%) | | |
|---|---|---|---|---|
| | n (%) | Negative (349) | Positive (121) | p |
| Age group (years) | | | | |
| <24 | 145(30.9) | 99 (68.3) | 46 (31.7) | |
| 25-29 | 183(38.9) | 150 (82) | 33 (18) | 0.005 |
| 30-34 | 111(23.6) | 82 (73.9) | 29 (26.1) | |
| ≥35 | 31(6.6) | 18(58.1) | 13 (41.9) | |
| Trimesters | | | | |
| I | 63(13.4) | 60(95.2) | 3(4.8) | |
| II | 189 (40.2) | 144(76.2) | 45(23.8) | 0.000 |
| III | 218 (46.4) | 145(66.5) | 73(33.5) | |
| Parity | | | | |
| Nulliparous | 247(52.6) | 170(68.8) | 77(31.2) | |
| Multiparous | 223(47.4) | 179(80.3) | 44(19.7) | 0.005 |
| Education level | | | | |
| Elementary | 110 (23.4) | 72 (65.5) | 38 (34.5) | |
| Middle | 156 (33.2) | 111 (71.2) | 45 (28.8) | 0.005 |
| High | 204 (43.4) | 161 (81.4) | 38 (18.6) | |
| Residence | | | | |
| Rural | 218 (46.4) | 148 (67.9) | 70 (32.1) | |
| Urban | 252 (53.6) | 201 (79.8) | 51 (20.2) | 0.003 |
| Pre-pregnancy BMI ($kg/m^2$) | | | | |
| Underweight | 21(4.5) | 16(76.2) | 5(23.8) | |
| Normal | 361(76.8) | 286(79.2) | 75(20.8) | 0.000 |
| Overweight | 64(13.6) | 36(56.3) | 28(43.8) | |
| Obese | 24 (5.1) | 11(45.8) | 13(54.2) | |
| Hypertension | | | | |
| Yes | 56 (11.9) | 26(46.4) | 30(53.6) | |
| No | 414 (88.1) | 323(77) | 91(22) | 0.000 |
| Diabetes | | | | |
| Yes | 5(1.1) | 1(20) | 4(80) | 0.005 |
| No | 465(98.9) | 348(74.8) | 117(25.2) | |

TABLE 2. UNIVARIATE AND MULTIVARIATE ANALYSIS

| Variabel | Univariate analysis | | | Multivariate analysis | | |
|---|---|---|---|---|---|---|
| | OR | 95% Cl | p | OR | 95% Cl | p |
| Age group (years) | | | | | | |
| <24 | 2.1 | 1.3-3.5 | 0.004 | 1.9 | 1.1-3.4 | 0.018 |
| 25-29 | 1 | - | - | 1 | - | - |
| 30-34 | 1.6 | 0.9-2.8 | 0.101 | 1.6 | 0.9-2.9 | 0.143 |
| ≥35 | 3.3 | 1.5-7.4 | 0.004 | 3 | 1.2-7.2 | 0.016 |
| Trimester | | | | | | |
| I | 1 | - | - | 1 | - | - |
| II | 6.3 | 1.9-21 | 0.003 | 6.7 | 2-23 | 0.002 |
| III | 10.1 | 3.1-33 | 0.000 | 10.3 | 3.1-34.7 | 0.000 |
| Parity | | | | | | |
| Nulliparous | 1.8 | 1.2-2.8 | 0.000 | 1.8 | 1.2.9 | 0.009 |
| Multiparous | 1 | - | - | 1 | - | - |
| Education level | | | | | | |
| Elementary | 2.3 | 1.4-3.9 | 0.002 | 2 | 1.1-3.6 | 0.015 |
| Middle | 1.8 | 1.1-2.9 | 0.023 | 1.6 | 0.9-2.7 | 0.090 |
| High | 1 | - | - | 1 | - | - |
| Residence | | | | | | |
| Rural | 1.7 | 1.2-1.8 | 0.004 | 1.6 | 1-2.5 | 0.045 |
| Urban | 1 | - | - | 1 | - | - |
| Pre-pregnancy BMI ($kg/m^2$) | | | | | | |
| Underweight | 1.2 | 0.4-3.4 | 0.74 | 1.3 | 0.5-3.8 | 0.615 |
| Normal | 1 | - | - | 1 | - | - |
| Overweight | 3 | 1.7-5.2 | 0.000 | 2 | 1.1-3.7 | 0.030 |
| Obese | 4.5 | 1.9-10.5 | 0.000 | 2.8 | 1.1-6.9 | 0.029 |
| Hypertension | | | | | | |
| Yes | 4.1 | 2.3-7.3 | 0.000 | 4.3 | 2.3-7.6 | 0.000 |
| No | 1 | - | - | 1 | | |
| Diabetes | | | | | | |
| Yes | 11.9 | 1.3-107.5 | 0.027 | 10.4 | 1.1-99 | 0.044 |
| No | 1 | - | - | 1 | - | - |

Adjusted variables are diabetes, hypertension, and trimesters

Young and older age are considered to be a risk factor for a number of pathologies in pregnancy. In present study, proteinuria was observed in young and older mothers. This observation is in accordance to study conducted by Suvi Leppälahti et al. [13] and Chadban SJ et al. [14]. Increased risk of proteinuria is directly associated with pre-BMI of the pregnant women. The finding is consistent with previous study which proved a statistically significant effect of pre-BMI on the incidence of proteinuria [15]. In the study conducted by Djrolo, F. et al. [16] medical complications of pregnancy were more frequent in obese women than in women with normal weight since obese women showed higher frequency of proteinuria (24,1% versus 10,5%, $p<0.05$) and high blood pressure (25.9% versus 4.5%, $p<0.001$). Our data show that urinary protein excretion increased through the trimesters; this is attributable to the physiologic al increase in renal plasma flow and glomerular filtration rate; these changes resolve after pregnancy [17]. In study conducted by Li, J. et al. [18] urinary excretion of albumin was significantly elevated in women with pregnancy induced hypertension compared to normal pregnant women at different gestational ages ($P < 0.05$-$0.01$).

The proteinuria of late pregnancy is exaggerated in women with diabetes, which also increases the risk of preeclampsia. This fact is further supported by the results of the study conducted by Mardi, T.G. and Lutfi, M.F. [19] which demonstrated that pregnant women with proteinuria had poor glycemic control and higher systolic blood pressure compared with those with no proteinuria. As can be seen from the table 2 proteinuria was higher if the woman was nulliparous. Similar results are also presented in the publication of Macdonald-Wallis, C. et al. [20] where

is mentioned that higher maternal pre-pregnancy body mass index (BMI), younger age, nulliparity and twin pregnancy were independently associated with increased odds of any proteinuria in pregnancy.

## IV. CONCLUSION

Our study presents an overview of the potential risk factors related to proteinuria. Identification of these factors helps us to determine women population groups that are more in risk by this pathology. These population groups are strictly recommended to do continue and detailed medical controls in medical centers. It is important that different stakeholders should realize awareness campaigns for the effects of proteinuria. Early diagnosis and treatment through regular antenatal checkup is a key factor to prevent proteinuria and its complications.

State health policies should concentrate not only in pregnant women health control but also in those not pregnant which can be a potential group in risk for development of proteinuria.

## V. REFERENCES

[1] K. Higby, C. R. Suiter, J. Y. Phelps, T. Siler-Khodr and O. Langer. Normal values of urinary albumin and total protein excretion during pregnancy. Am. J Obstet. Gynaecol. 1994. 171: 984–989.

[2] V. S. Kuo, G. Koumanantakis, and E. D. M. Gallery. Proteinuria and its assessment in normal and hypertensive pregnancy. Am. J Obstet Gynecol. 1992. 167: 723–728.

[3] G. D'Amico and C. Bazzi. Pathophysiology of proteinuria. Kidney International; 2003; 63: 809–825.

[4] P. R. Garner, M. E. D'Alton, D. K. Dudley, P. Huard and M. Hardie. Preeclampsia in diabetic pregnancies. Am. J. Obstet. Gynecol. 1990. 163: 505–508.

[5] G. A. Dekker, J. I. De Vries, P. M. Doelitzsch, P. C. Huijgens, B. M. Von Blomberg, C. Jakobs and H. P. Van Geijn. Underlying disorders associated with severe early-onset preeclampsia. Am J Obstet Gynecol; 1995. 173: 1042– 1048.

[6] E. W. Page and R. Christianson. Influence of blood pressure changes with and without proteinuria upon outcome of pregnancy. Am J Obstet Gynaecol; 1976. 126: 821–29.

[7] L. C. Chesley. Superimposed pre-eclampsia or eclampsia. Hypertensive disorders in Pregnancy. New York: Appleton-Century-Crofts. 1978.

[8] B. M. Sibae, T. N. Abdella and G. D. Anderson. Pregnancy outcome in 211 patients with mild chronic hypertension. Obstet Gynaecol; 1983; 61: 571–76.

[9] J. B. Henry. Clinical Diagnosis and Management by Laboratory Methods. 19th ed. Philadelphia: W.B. Saunders. 1996.

[10] A. V. Chobanian, G. L. Bakris, H. R. Black, W. C. Cushman, L. A. Green, J. L. Izzo JR, D. V. Jones, B. J. Materson, S. Oparil, J. T. Wright JR and E. J. Rosella. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA; 2003; 289: 2560–2572.

[11] WHO. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser; 894: i–xii, 1–253. 2000.

[12] P. TRINDER: Determination of Glucose in Blood Using Glucose Oxidase with an Alternative Oxygen Acceptor. Ann Clinic Biochem, 6, 24. 1969.

[13] S. Leppälahti, M. Gissler, M. Mentula and O. Heikinheimo. Is teenage pregnancy an obstetric risk in a welfare society? A population-based study in Finland, from 2006 to 2011. Obstetrics and gynaecology. BMJ Open 2013; 3:e003225 doi:10.1136/bmjopen-2013-003225.

[14] S. J. Chadban, E. M. Briganti, P. G. Kerr, D. W. Dunstan, T. A. Welborn, P. Z. Zimmet and R. C. Atkins. Prevalence of kidney damage in Australian adults: The AusDiab Kidney Study. J Am Soc Nephrol.; 14: S131–S138. 2003.

[15] O. Hrazdilová, V. Unzeitig, V. Znojil, L. Izakovicová-Hollá, P. Janků and A. Vasku. Relationship of age and the body mass index to selected hypertensive complications in pregnancy. Int J Gynecol Obstet. 75 (2): 165-9. 2001.

[16] F. Djrolo, A. Megnigbeto Obey, J. De Souza, I. Takpara, P. Santos and E. Alihonou. Influence of maternal weight on pregnancy outcome in Cotonou (Benin). J Gynecol Obstet Biol Reprod (Paris). 31 (3): 243-7. 2000.

[17] K. Conrad and M. D. Lindheimer. In: Lindheimer MD, Roberts JM, Cunningham FG, Eds. Renal and Cardiovascular Alterations. Chesley's Hypertensive Disorders in Pregnancy, 2nd ed. Stamford, Conn.: Appleton and Lange. 1999.

[18] J. Li, Y. Chu and J. Zhou. Urinary proteins during pregnancy in women with and without pregnancy induced hypertension. Zhonghua Fu Chan Ke Za Zhi. 30 (7): 395-7. 1995.

[19] T. G. Mardi and M. F. Lutfi. Risk factors for gestational diabetes mellitus in Sudanese pregnant women. Int. J. Med. Biomed. Res. 1 (1): 79-84. 2012

[20] C. Macdonald-Wallis, D. A. Lawlor, J. Heron, A. Fraser, S. M. Nelson, and K. Tilling. Relationships of risk factors for pre-eclampsia with patterns of occurrence of isolated gestational proteinuria during normal term pregnancy.6(7):e22115.doi: 10.1371/journal.pone.0022115. Epub 2011 Jul 18. 2011.