Proteinuria in Pregnancy

   **Author(s):** Beers, Kelly; Patel, Niralee
   **Source:** Advances in chronic kidney disease; Nov 2020; vol. 27 (no. 6); p. 449-454
   **Publication Date:** Nov 2020
   **Publication Type(s):** Journal Article Review
   **PubMedID:** 33328060
   **Abstract:** A woman's body undergoes a myriad of changes throughout the course of a normal gestation. The kidneys play a central role in driving adjustments that guarantee maternal and fetal well-being, including a dramatic increase in glomerular filtration rate, alterations in tubular function, and changes in electrolyte and acid/base handling. Early in gestation, systemic vasodilation, driven by both a change in quantity of and response to various hormones, leads to increased renal blood flow and glomerular filtration rate. Vasodilation also results in activation of the renin-angiotensin-aldosterone axis, which combined with changing tubular handling causes alterations in total body stores of electrolytes and total body water, resulting in a lower serum sodium concentration. In addition, mild proteinuria, glucosuria, and a decrease in serum calcium and magnesium are common. The primary acid/base change seen in pregnancy is a mild respiratory alkalosis due to progesterone effects. This article provides an overview of the current understanding of the healthy response of the kidneys to pregnancy, an understanding of which is key to caring for the pregnant patient, and early identification of alterations that may indicate underlying kidney pathology in pregnancy.
   **Database:** Medline
2. Proteinuria during pregnancy: definition, pathophysiology, methodology, and clinical significance.

Author(s): Fishel Bartal, Michal; Lindheimer, Marshall D; Sibai, Baha M

Source: American journal of obstetrics and gynecology; Sep 2020

Publication Date: Sep 2020

Publication Type(s): Journal Article Review

PubMedID: 32882208

Abstract: Qualitative and quantitative measurement of urine protein excretion is one of the most common tests performed during pregnancy. For more than 100 years, proteinuria was necessary for the diagnosis of preeclampsia, but recent guidelines recommend that proteinuria is sufficient but not necessary for the diagnosis. Still, in clinical practice, most patients with gestational hypertension will be diagnosed as having preeclampsia based on the presence of proteinuria. Although the reference standard for measuring urinary protein excretion is a 24-hour urine collection, spot urine protein-to-creatinine ratio is a reasonable "rule-out" test for proteinuria. Urine dipstick screening for proteinuria does not provide any clinical benefit and should not be used to diagnose proteinuria. The classic cutoff cited to define proteinuria during pregnancy is a value of >300 mg/24 hours or a urine protein-to-creatinine ratio of at least 0.3. Using this cutoff, the rate of isolated proteinuria in pregnancy may reach 8%, whereas preeclampsia occurs among 3% to 8% of pregnancies. Although this threshold is widely accepted, its origin is not based on evidence on adverse pregnancy outcomes but rather on expert opinion and results of small studies. After reviewing the available data, the most important factor that influences maternal and neonatal outcome is the severity of blood pressures and presence of end organ damage, rather than the excess protein excretion. Because the management of gestational hypertension and preeclampsia without severe features is almost identical in frequency of surveillance and timing of delivery, the separation into 2 disorders is unnecessary. If the management of women with gestational hypertension with a positive assessment of proteinuria will not change, we believe that urine assessment for proteinuria is unnecessary in women who develop new-onset blood pressure at or after 20 weeks' gestation. Furthermore, we do not recommend repeated measurement of proteinuria for women with preeclampsia, the amount of proteinuria does not seem to be related to poor maternal and neonatal outcomes, and monitoring proteinuria may lead to unindicated preterm deliveries and related neonatal complications. Our current diagnosis of preeclampsia in women with chronic kidney disease may be based on a change in protein excretion, a baseline protein excretion evaluation is critical in certain conditions such as chronic hypertension, diabetes, and autoimmune or other renal disorders. The current definition of superimposed preeclampsia possesses a diagnostic dilemma, and it is unclear whether a change in the baseline proteinuria reflects another systemic disease such as preeclampsia or whether women with chronic disease such as chronic hypertension or diabetes will experience a different "normal" pattern of protein excretion during pregnancy. Finally, limited data are available regarding angiogenic and other biomarkers in women with chronic kidney disease as a potential aid in distinguishing the worsening of baseline chronic kidney disease and chronic hypertension from superimposed preeclampsia.

Database: Medline
3. The Effects of Isolated Proteinuria Detected After 20 Weeks of Pregnancy on Perinatal Outcomes

**Author(s):** Ozdemir O.; Arikan I.I.; Sel G.; Can M.; Harma M.; Harma M.I.

**Source:** SN Comprehensive Clinical Medicine; Sep 2020; vol. 2 (no. 9); p. 1661-1665

**Publication Date:** Sep 2020

**Publication Type(s):** Article

**Available at:** SN Comprehensive Clinical Medicine - from SpringerLink - Medicine

**Abstract:** Proteinuria is a component of preeclampsia, and the presence of proteinuria without an increase in blood pressure can precede preeclampsia. This study aims to investigate the perinatal effects of isolated proteinuria detected in a 24-h urine sample after the 20th week of pregnancy.

This is a prospective study of the perinatal outcomes of 60 pregnancies without proteinuria and matched 58 pregnancies with isolated proteinuria in patients consecutively admitted to the department of obstetrics at a university hospital in Turkey. The pregnant patients with proteinuria and without proteinuria were statistically similar with respect to age, gravidity, parity and the number of living children on enrolment. There were no significant differences in terms of gestational age at enrolment, gestational age at delivery, or intrauterine growth restriction (IUGR) between patients with isolated proteinuria and patients without proteinuria. However, preeclampsia developed significantly more frequently in patients with isolated proteinuria (20.6% vs 6.6%, p = 0.048). There were no significant differences in terms of newborn weight, Apgar scores, need for the neonatal intensive care unit (NICU), or umbilical artery blood pH in patients with proteinuria and without proteinuria. Isolated proteinuria after 20 weeks of pregnancy does not appear to impair maternal or foetal outcomes. Identifying pregnant women with risk factors for preeclampsia, ensuring they attend meticulous follow-up schedules and performing their delivery at tertiary health care centres would help to improve maternal and foetal morbidity and prevent perinatal mortality. Copyright © 2020, Springer Nature Switzerland AG.

**Database:** EMBASE

4. The Association Between GFR Evaluated by Serum Cystatin C and Proteinuria During Pregnancy.

**Author(s):** Kreepala, Chatchai; Srila-On, Atitaya; Kitporntheranunt, Maethaphan; Anakkamatee, Watcharapong; Lawtongkum, Pothum; Wattanavaekin, Krittanont

**Source:** Kidney international reports; Jun 2019; vol. 4 (no. 6); p. 854-863

**Publication Date:** Jun 2019

**Publication Type(s):** Journal Article

**PubMedID:** 31194092

**Available at:** Kidney international reports - from Unpaywall

**Abstract:** Introduction: Physiological changes in pregnancy result in increased cardiac output and renal blood flow, with a consequential increase in proteinuria. Data from studies of the relationship between proteinuria caused by isolated proteinuria and glomerular filtration rate (GFR) are still limited. The objective of this study was to investigate the effects of isolated proteinuria on the cystatin C-based GFR in the third trimester of pregnancy.

**Methods:** Data were collected from pregnant women in their third trimester whose serum creatinine levels were normal. The GFR of each participant was measured using serum cystatin C levels, and proteinuria was measured using urine protein-creatinine ratios. The participants were divided into 3 groups according to their level of proteinuria: normal (300 mg/d). Changes in GFR were recorded for each group.

**Results:** The study included 89 participants, of whom 66.3% had levels of proteinuria that did not differ from that of the
normal population (101.50 mg/d) was significantly associated with declined estimated glomerular filtration rate (eGFR) (r = -0.34, P = 0.01). The analysis found that proteinuria >491.27 mg/d led to a risk of GFR 101.5 mg/d, which could be an early biomarker for renal pathology rather than pregnancy physiology, suggesting that further workup and precaution is required.

Database: Medline

5. The impact of proteinuria on maternal and perinatal outcomes among women with pre-eclampsia.

Author(s): Guida, Jose P; Parpinelli, Mary A; Surita, Fernanda G; Costa, Maria L

Source: International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics; Oct 2018; vol. 143 (no. 1); p. 101-107

Publication Date: Oct 2018

Publication Type(s): Journal Article

PubMedID: 29572831

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library Science, Technology and Medicine Collection 2017

Available at International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics - from Wiley Online Library Science, Technology and Medicine Collection 2019

Abstract: OBJECTIVES To assess the impact of proteinuria on pregnancy outcomes among women with pre-eclampsia. METHODS The present retrospective cohort study included patients with pre-eclampsia who delivered at a referral maternity hospital in Brazil between January 1, 2009, and December 31, 2013. Patients were stratified into three groups based on 24-hour urinary protein excretion during pregnancy: mild (0.3-<2.0 g), severe (2.0-<5.0 g), and massive (≥5.0 g). RESULTS There were 293 patients included in the study; 88, 129, and 76 had mild, severe, and massive proteinuria, respectively. Chronic hypertension was the most frequent pre-existing condition among all women (86 [29.4%]). The mean pregnancy duration at the onset of maternal pre-eclampsia was longest in the mild group compared and decreased with increasing proteinuria severity (P<0.001). Preterm delivery was recorded among 205 of 293 (70.0%) neonates; there were 66 (22.5%) neonates that were preterm and in the massive proteinuria group. The incidence of severe pre-eclampsia was lowest in the mild proteinuria group (P=0.002) and tended to occur at 34 weeks. Cesarean delivery rates exceeded 80.0% in all groups. Most patients assessed at 40-60 days postpartum remained proteinuric (40/61[66%]). CONCLUSIONS Quantifying the severity of proteinuria could identify a subgroup of women with pre-eclampsia at increased risk of adverse outcomes.

Database: Medline
6. Progression from isolated proteinuria to severe preeclampsia – Does severity of proteinuria matter?

**Author(s):** Tzur ; Rimon, Eli dr.; Geva, Gil dr.; Skornick-Rapaport, Avital dr.; Landsberg Asher, Isca dr.; Kupferminc, Michael J. prof.

**Source:** Pregnancy Hypertension; Oct 2018; vol. 13

**Publication Date:** Oct 2018

**Publication Type(s):** Academic Journal

**Database:** CINAHL

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7. Outcome of pregnancy with new onset proteinuria and progression to pre-eclampsia: A retrospective analysis.

**Author(s):** Chung, Wai Hang; To, William Wing Kee

**Source:** Pregnancy hypertension; Apr 2018; vol. 12 ; p. 174-177

**Publication Date:** Apr 2018

**Publication Type(s):** Journal Article

**PubMedID:** 29175169

**Abstract:**

**OBJECTIVE**

To examine maternal and neonatal outcomes of gestational proteinuria, and to identify maternal characteristics for progression to pre-eclampsia.

**STUDY DESIGN**

Retrospective cohort. Included all pregnant women who delivered between Jan 2014-Feb 2017 with new onset proteinuria in a single obstetric unit. Demographic, maternal and neonatal outcomes were compared.

**RESULT**

Eighteen (25%) out of 73 women with new onset gestational proteinuria developed pre-eclampsia. The incidence of gestational proteinuria was 0.54%. Compared with women that remained normotensive, those that developed hypertension had delivery at earlier gestation (p = .02), increased risk of fetal growth restriction (p = .01) and lower newborn birthweight (p = .002). Maximal proteinuria and fetal growth restriction were independent factors associated with development of pre-eclampsia. In particular, high proteinuria level ≥ 2 g/d constitute a major predictor for progression (p = .03).

**CONCLUSION**

Increased vigilance for antenatal surveillance is important in women with gestational proteinuria as a substantial portion progress to pre-eclampsia. Serial growth scan and proteinuria assay are suggested to predict possible pre-eclampsia development.

**Database:** Medline
8. Isolated proteinuria in Chinese pregnant women with pre-eclampsia: Results of retrospective observational study

Author(s): Cai J.; Wang T.; Li M.; Cheng X.; Zhang Y.

Source: Biomedical Research; 2017; vol. 28 (no. 11); p. 5162-5166

Publication Date: 2017

Publication Type(s): Article

Abstract: Objective: To evaluate obstetrical, maternal and neonatal outcomes of isolated proteinuria among Chinese pregnant women. Material(s) and Method(s): In this retrospective observational study, we have reviewed the medical records of Chinese pregnant women hospitalized in Department of Gynecology and Obstetrics, Renmin Hospital of Wuhan University, China between March 2013 to March 2016 who had new onset isolated proteinuria, and had urine albumin level of more than 300 mg in 24 h. Each Chinese pregnant woman was followed up from the time of admission to the time of discharge after delivery. Obstetrical, maternal and neonatal outcomes were assessed. Result(s): A total of 758 hospitalized women were screened for suspected hypertensive disorders at our hospital from March 2013 to March 2016 by collecting their 24 h urine protein. Out of 758 women, a total of 92 women were diagnosed with new onset isolated proteinuria, and were followed from the time of admission until delivery and discharge postpartum, and subjected in retrospective analysis. Of these, a total of 18 women developed Pre-Eclampsia (PE) during their pregnancy, and 11 women developed PE during postpartum period. Pregnant women who had progression to PE were due to greater values of proteinuria. We also noted that earlier PE onset was associated with early-onset proteinuria and multiple gestations. Irrespective of PE progression, maternal outcome was found favorable although high levels of proteinuria was associated with increased risk for intrauterine growth restriction and lower Apgar scores. Isolated proteinuria progressing to PE was associated with late PE onset, and did not affect maternal and neonatal outcomes among Chinese mothers. Conclusion(s): We suggest significant proportion of Chinese women with new onset isolated proteinuria will develop PE after delivery. Copyright © 2017, Scientific Publishers of India. All rights reserved.

Database: EMBASE
9. **Spot urine protein measurements in normotensive pregnancies, pregnancies with isolated proteinuria and preeclampsia.**

**Author(s):** Kattah, Andrea; Milic, Natasa; White, Wendy; Garovic, Vesna

**Source:** American journal of physiology. Regulatory, integrative and comparative physiology; Oct 2017; vol. 313 (no. 4); p. R418

**Publication Date:** Oct 2017

**Publication Type(s):** Journal Article

**PubMedID:** 28747409

Available at American journal of physiology. Regulatory, integrative and comparative physiology - from HighWire - Free Full Text

Available at American journal of physiology. Regulatory, integrative and comparative physiology - from Unpaywall

**Abstract:** We performed a prospective, longitudinal study of pregnant women presenting to their first obstetrics visits to characterize the changes in spot urine protein-to-creatinine (UPCR) and albumin-to-creatinine ratios (UACR) in normotensive pregnancies, as well as identify clinical characteristics associated with isolated proteinuria and preeclampsia. We measured spot urinary albumin, protein, and creatinine at the first prenatal visit, end of the second trimester, and at delivery. In the normotensive pregnancies (n = 142), we found that from the beginning of pregnancy to delivery, UACR increased by a median [interquartile range (IQR)] of 14.7 mg/g Cr (3.74-51.8) and UPCR by 60 mg/g Cr (30-130) (P 300 mg/g Cr in the absence of hypertension) was identified in 19/142 (13.4%) normotensive pregnancies. Increases in systolic and diastolic blood pressure from early pregnancy to delivery and increases in UACR from early to midpregnancy were associated with isolated proteinuria at delivery. Twelve women developed preeclampsia. Nulliparity, early, and midpregnancy diastolic blood pressures were strongly associated with the development of preeclampsia, but early changes in UACR were not. In conclusion, women who develop isolated proteinuria at delivery have a larger increase in blood pressure than women without proteinuria and have a "microalbuminuric" phase earlier in gestation, unlike women who develop preeclampsia. These findings suggest a different mechanism of urine protein excretion in women with isolated proteinuria as compared with women with preeclampsia, where proteinuria has a more abrupt onset.

**Database:** Medline
10. Examination of Prepregnancy and Pregnancy Urinary Protein Levels in Healthy Nulliparous Women.

**Author(s):** Phillips, Julie K; McBride, Carole A; Hale, Sarah A; Solomon, Richard J; Badger, Gary J; Bernstein, Ira M

**Source:** Reproductive sciences (Thousand Oaks, Calif.); Mar 2017; vol. 24 (no. 3); p. 407-412

**Publication Date:** Mar 2017

**Publication Type(s):** Research Support, N.i.h., Extramural Journal Article

**PubMedID:** 27460407

Available at [Reproductive sciences (Thousand Oaks, Calif.)](https://www.unpaywall.org/open-access/10.1177/1938037316688969) - from Unpaywall

**Abstract:** During pregnancy, abnormal proteinuria is defined as urine protein excretion greater than 300 mg/24 h. Although widely accepted, this definition is not based on clinical outcomes. Our study aimed to longitudinally examine proteinuria in healthy women prior to, and in late pregnancy and to compare inpatient and outpatient 24-hour urine collections. Nulliparous women planning to conceive were recruited and completed a 24-hour urinary collection. Those who subsequently conceived completed a second 24-hour urinary collection in late pregnancy. In the first 5 years of the study, urinary collections were completed during an inpatient admission; all collections during the latter part of the study were performed as outpatients. Urine protein was measured using the VITROS UPRO Slide kit. Wilcoxon signed rank tests were used for paired comparisons of prepregnancy and late pregnancy proteinuria and Wilcoxon rank sum tests were used to compare inpatient and outpatient collections. Among 134 women completing a prepregnancy collection, median urinary protein excretion was 188 mg/24 h (IQR 103-280). Sixty-five women subsequently conceived and completed a late pregnancy collection. In healthy women, urinary protein increased to 254 mg/24 h during pregnancy (IQR 166-396). Forty-five percent of women exceeded the defined normal threshold of proteinuria in 24 hours in the absence of disease. Inpatient collections resulted in higher levels of urinary protein than outpatient at both time points. Our data suggest that significant proteinuria is present in healthy nonpregnant women. Even in the absence of disease, proteinuria increases during pregnancy. Outpatient collections may underestimate proteinuria, especially in late pregnancy.

**Database:** Medline

**Author(s):** Mateus, Julio; Newman, Roger; Sibai, Baha M; Li, Qing; Barton, John R; Combs, C Andrew; Guzman, Edwin; Boggess, Kim A; Gyamfi, Cynthia; von Dadelszen, Peter; Woelkers, Doug

**Source:** AJP reports; Jan 2017; vol. 7 (no. 1); p. e49

**Publication Date:** Jan 2017

**Publication Type(s):** Case Reports

**PubMedID:** 28348923

Available at AJP reports - from Europe PubMed Central - Open Access

Available at AJP reports - from Unpaywall

**Abstract:**

**Objective**  The objective of this study was to compare clinical outcomes of preeclamptic pregnancies according to the proteinuria level. Study Design  Secondary analysis of a multicenter prospective cohort study of women with preeclampsia (PE) symptomatology. Nonproteinuria, mild-proteinuria, and massive-proteinuria PEs were defined as: < 165 mg in 12 hours or < 300 mg in 24 hours, 165 mg to 2.69 g in 12 hours or 300 mg to 4.99 g in 24 hours, and ≥ 2.7 g in 12 hours or ≥ 5.0 g in 24 hours, respectively. Individual and composite maternal, fetal, and neonatal outcomes were compared among the PE groups. Results  Of the 406 analyzed pregnancies, 36 (8.8%) had massive-proteinuria PE, 268 (66.0%) mild-proteinuria PE, and 102 (25.1%) nonproteinuria PE. Compared with the other groups, massive-proteinuria PE women had significantly higher blood pressures (p < 0.001), epigastric pain (p = 0.007), and uric acid serum levels (p < 0.001) prior to delivery. Composite maternal morbidity was similar across the groups. Delivery < 340/7 weeks occurred in 80.6, 49.3, and 22.5% of massive-proteinuria, mild-proteinuria, and nonproteinuria PE groups, respectively (p < 0.0001). Composite adverse neonatal outcomes were significantly higher in the massive-proteinuria PE compared with the other groups (p = 0.001). Conclusion  While potentially not important diagnostically, massive proteinuria is associated with more severe clinical manifestations of PE prompting earlier delivery.

**Database:** Medline

12. The outcome of pregnancy with new onset proteinuria without hypertension: retrospective observational study.

**Author(s):** Ekiz, Ali; Kaya, Basak; Polat, Ibrahim; Avci, Muhittin Eftal; Ozkose, Burak; Kicik Caliskan, Razive; Yildirim, Gokhan

**Source:** The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians; 2016; vol. 29 (no. 11); p. 1765-1769

**Publication Date:** 2016

**Publication Type(s):** Journal Article Observational Study

**PubMedID:** 26135772

**Abstract:**

**OBJECTIVE**  The aim of this study was to evaluate preeclampsia progression of isolated proteinuria and associations with pregnancy outcome.  **METHOD**  We performed a retrospective analysis in patients who were hospitalized for evaluation of new onset proteinuria without hypertension after 20 weeks of gestation between January 2012 and January 2014. One hundred fifty-seven patients who met the inclusion criteria were enrolled in the study.  **RESULTS**  After detection of new onset proteinuria, 53 of 157 (33.7%) patients developed preeclampsia and the incidence of gestational proteinuria was found to be 0.33%. Twenty-four hours urine proteinuria testing results were significantly higher in preeclampsia (PE) group compared with the gestational proteinuria (GP) group (p < 0.01). Patients who developed preeclampsia delivered significantly earlier than the GP
group (p < 0.01). The weights of the infants born to mothers in the PE group were significantly lower than the other group (p < 0.01).

**CONCLUSION**

The incidence of gestational proteinuria was lower than the previous studies. Preeclampsia developed in 33% of patients with new onset proteinuria in pregnancy. In patients who developed PE had significantly higher proteinuria, lower delivery time and birth weight in their infants. Therefore, patients with new onset proteinuria should be followed-up for preeclampsia development and associated morbidities.

**Database:** Medline

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**13. Isolated gestational proteinuria preceding the diagnosis of preeclampsia - an observational study.**

**Author(s):** Yamada, Takahiro; Obata-Yasuoka, Mana; Hamada, Hiromi; Baba, Yosuke; Ohkuchi, Akihide; Yasuda, Shun; Kawabata, Kosuke; Minakawa, Shiori; Hirai, Chihiro; Kusaka, Hideto; Murabayashi, Nao; Inde, Yusuke; Nagura, Michikazu; Umezume, Takeshi; Itakura, Atsuo; Maeda, Makoto; Sagawa, Norimasa; Ohno, Yasumasa; Kataoka, Soromon; Fujimori, Keiya; Kudo, Yoshiki; Ikeda, Tomoaki; Nakai, Akihito; Minakami, Hisanori

**Source:** Acta obstetricia et gynecologica Scandinavica; Sep 2016; vol. 95 (no. 9); p. 1048-1054

**Publication Date:** Sep 2016

**Publication Type(s):** Multicenter Study Journal Article Observational Study

**PubMedID:** 27109750


**Abstract:** INTRODUCTION Some pregnant women develop significant proteinuria in the absence of hypertension. However, clinical significance of isolated gestational proteinuria (IGP) is not well understood. This study aimed to determine the prevalence of IGP in singleton pregnancies and the proportion of women with IGP who subsequently developed preeclampsia (IGP-PE) among all PE cases.

MATERIAL AND METHODSThis was an observational study of 6819 women with singleton pregnancies at 12 centers, including 938 women with at least once determination of protein-to-creatinine ratio (P/Cr). Significant proteinuria in pregnancy (SPIP) was defined as P/Cr (mg/mg) level >0.27. IGP was defined as SPIP in the absence of hypertension. Gestational hypertension (GH) preceding preeclampsia (GH-PE) was defined as preeclampsia (PE) in which GH preceded SPIP. Simultaneous PE (S-PE) was defined as PE in which both SPIP and hypertension occurred simultaneously.

RESULTS IGP and PE were diagnosed in 130 (1.9%) and 158 (2.3%) of 6819 women, respectively. Of 130 women with IGP, 32 (25%) progressed to PE and accounted for 20% of all women with PE. Hence, women with IGP had a relative risk of 13.1 (95% CI; 9.2-18.5) for developing PE compared with those without IGP [25% (32/130) vs. 1.9% (126/6689)]. At diagnosis of SPIP, P/Cr levels already exceeded 1.0 more often in women with S-PE than in those with IGP-PE [67% (33/49) vs. 44% (14/32), respectively, p = 0.031].

**CONCLUSION** IGP is a risk factor for PE, and IGP-PE accounts for a considerable proportion (20%) of all PE.

**Database:** Medline
14. Maternal and perinatal outcomes in preeclampsia according to the magnitude of proteinuria: Results from a high risk referral center in Brazil

**Author(s):** Guida J.P.S.; Surita F.G.; Parpinelli M.A.; Moraes L.D.; Souza E.C.A.; Pinheiro A.; Teixeira Souza R.; Laura M.; Costa L.

**Source:** Pregnancy Hypertension; Jul 2016; vol. 6 (no. 3); p. 223

**Publication Date:** Jul 2016

**Publication Type(s):** Conference Abstract

**Abstract:** Introduction: Preeclampsia (PE) is one of the leading causes of maternal and neonatal morbidity and mortality worldwide. It is defined as new onset hypertension developing P20 weeks and proteinuria or evidence of maternal organ dysfunction. The magnitude of proteinuria was a marker for severity and when higher than 2 g/24 h indicated aggressive treatment. This was recently revised and no longer defines severity, but there are still gaps in understanding how different levels of increased proteinuria impact on maternal and perinatal outcomes and its long term consequences. Objective(s): To review all cases of PE with proteinuria >=2 g/24 h followed at the State University of Campinas (UNICAMP) in a 5 year period, and compare maternal and perinatal outcomes according to the magnitude of proteinuria. Method(s): Retrospective cohort of all pregnant women with proteinuria >=2 g/24 h followed at UNICAMP from January 2009 to December 2013. Women with previous nephropathy, without diagnosis of PE or delivery elsewhere were excluded from the analysis. Data on demographic characteristics, onset of symptoms, laboratory findings, maternal and fetal/neonatal outcomes were recorded. Data were stored and analyzed using the Epi-Info 7; continuous variables were compared using ANOVA and categorical variables analyzed by x2 or Fisher exact tests. Result(s): 269 women were screened for review, 19 were excluded for delivering elsewhere, 41 were excluded due to previous nephropathy, 8 due to absence of PE and 5 for postpartum PE (with normal proteinuria during gestation). The current analysis included 196 women. The median age was 28 (+/-7.1), majority white (69%) and nearly half primigravida. The average overall magnitude of proteinuria was 5.1 g/24 h (+/-3.7). Cesarean delivery was the most frequent route of delivery (84%) and the mean gestational age at delivery 33 weeks (+/-3.8). The majority of cases presented severe PE (80%). Less then half of the women attended postpartum care and among those, most remained with abnormal proteinuria in early (80%) and late (76%) puerperium (followed up to 3 months postpartum). We considered 3 groups of cases according to the magnitude of proteinuria: >=2 and <5 g/24 h (n = 124), >=5 and <10 g/24 h (n = 43) and >=10 g/24 h (n = 18). A summarized comparison among these groups is in Table 1.

**Conclusion(s):** Quantification of proteinuria remains an important tool in the diagnosis of PE but its magnitude alone, should not guide management. Massive proteinuria presented significantly more in primigravida and proteinuria P5 g/24 h presented decreased gestational age at resolution. Future studies must address systematic follow-up of these women during pregnancy, latency from diagnosis to resolution, and the women's perspective upon diagnosis of massive proteinuria. A postpartum follow-up is critical, to assess long term consequences of massive proteinuria during pregnancy.

(Table Presented).

**Database:** EMBASE
15. Isolated proteinuria is a risk factor for pre-eclampsia: A retrospective analysis of the maternal and neonatal outcomes in women presenting with isolated gestational proteinuria

Author(s): Shinar S.; Asher-Landsberg J.; Schwartz A.; Ram-Weiner M.; Kupferminc M.J.; Many A.

Source: Journal of Perinatology; Jan 2016; vol. 36 (no. 1); p. 25-29

Publication Date: Jan 2016
Publication Type(s): Article
PubMedID: 26513453

Abstract:Objective: To examine maternal and neonatal outcomes of isolated proteinuria and define maternal characteristics for progression to pre-eclampsia. Study Design: Retrospective cohort study. Data from all hospitalized pregnant women between 2009 and 2014 with new onset isolated proteinuria of over 300 mg/24 h at admission were obtained. Follow-up was performed from the time of admission to the hospital to the time of discharge postpartum. Obstetrical, maternal and neonatal outcomes were obtained. Result(s): Ninety-five pregnant women diagnosed with new onset isolated proteinuria were followed to term. Thirteen women developed pre-eclampsia during pregnancy and eight developed pre-eclampsia postpartum. Maternal characteristics for progression to pre-eclampsia were greater maximal values of proteinuria. Earlier pre-eclampsia onset was associated with early-onset proteinuria and multiple gestation. Although greater values of proteinuria were associated with increased risk for intrauterine growth restriction and lower Apgar scores, maternal outcome was favorable, regardless of pre-eclampsia progression. Isolated proteinuria progressing to pre-eclampsia was associated with late pre-eclampsia onset and favorable maternal and neonatal outcomes. Conclusion(s): A significant proportion of women with new onset isolated proteinuria will develop pre-eclampsia. In these women, close follow-up is recommended until after delivery. Copyright © 2016 Nature America, Inc.

Database: EMBASE

**Author(s):** Erkenekli, Kudret; Iskender, Cantekin; Oztas, Efser; Özgü-Erdinç, Ayse Seval; Yucel, Aykan; Uygur, Dilek

**Source:** Hypertension in pregnancy; Nov 2015; vol. 34 (no. 4); p. 495-505

**Publication Date:** Nov 2015

**Publication Type(s):** Journal Article

**PubMedID:** 26650758

**Abstract:** OBJECTIVE The present study aimed to investigate perinatal outcomes and to describe antenatal factors for development of preeclampsia (PE) in patients with isolated proteinuria in pregnancy. METHODSThis retrospective case control study consisted of patients with isolated proteinuria between 2009 and 2014. The patients were considered as gestational proteinuria (GP) (group 1, n: 35) if they remain normotensive. Patients who develop PE after onset of proteinuria were allocated into group 2 (n: 19). Perinatal outcomes of patients in each group were compared. Logistic regression analysis was performed to detect antenatal risk factors for PE. RESULTSThe rate of small for gestational age (SGA) fetuses was higher in patients with isolated proteinuria than control group. In the logistic regression model, maternal age and completed gestational weeks at onset of proteinuria decreased the risk of PE in multivariate analysis (OR: 0.849 (95% CI: 0.731-0.986), OR: 0.732 (95% CI: 0.594-0.902) respectively). Systolic BP at onset of proteinuria, however, was associated with an independently increased risk of PE (OR: 1.181 (95% CI: 1.046-1.333)). CONCLUSION Maternal clinical characteristics, but not laboratory features may help to predict development of PE.

**Database:** Medline

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17. Isolated proteinuria-A heralding sign for preeclampsia? A retrospective analysis of the obstetrical and neonatal outcomes in women presenting with proteinuria during pregnancy

**Author(s):** Shinar S.; Schwartz A.; Ram-Weiner M.; Kupferminc M.; Many A.

**Source:** Pregnancy Hypertension; Jan 2015; vol. 5 (no. 1); p. 39

**Publication Date:** Jan 2015

**Publication Type(s):** Conference Abstract

**Abstract:** Objectives: In 2013 the American Task force on Hypertensive diseases defined new criteria for preeclampsia (pet) without proteinuria and excluded the severity of proteinuria from criteria defining pet with severe signs. Still, the majority of women presenting with pet also exhibit proteinuria. It remains disputed whether isolated proteinuria is part of the pet continuum or whether it is a physiological alternation in kidney function in pregnancy. Our aim was to examine maternal and neonatal outcomes of isolated proteinuria and define risk factors for progression to pet. Method(s): Retrospective cohort study. Data from all hospitalized pregnant women with isolated proteinuria of over 300 mg/24 h at admission between 2009 and 2014, was obtained. We followed this study group from the time of admission to the hospital to the time of discharge postpartum, obtaining maternal and neonatal outcomes. Result(s): During the 5 year period 99 women were diagnosed with isolated proteinuria. 13 women developed pet during pregnancy, and an additional 8 developed pet postpartum (21%). No risk factors for proteinuria were found, however the earlier the diagnosis of proteinuria the higher were the maximal values of proteinuria reached. Risk factors for progression of pet were primiparity (p = 0.01) and greater values of proteinuria (p = 0.005). Among women who developed pet, an earlier diagnosis was made for those with early onset proteinuria (p = 0.002), well established risk factors for pet (p = 0.01) and multiple gestations (p = 0.002). Neonatal outcome was equivocal regardless of progression to pet and levels
of proteinuria. Conclusion(s): To date this is the largest series of women with isolated proteinuria followed to term. We conclude that isolated proteinuria is a risk factor for preeclampsia, with greater chances of developing preeclampsia among primiparous women with higher values of proteinuria. While proteinuria itself is negligible, chances of preeclampsia are high and close follow-up is recommended until after delivery.

**Database:** EMBASE

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**18. Clinical features of isolated gestational proteinuria progressing to pre-eclampsia: retrospective observational study.**

**Author(s):** Akaishi, Rina; Yamada, Takahiro; Morikawa, Mamoru; Nishida, Ryutaro; Minakami, Hisanori

**Source:** BMJ open; Apr 2014; vol. 4 (no. 4); p. e004870

**Publication Date:** Apr 2014

**Publication Type(s):** Journal Article Observational Study

**PubMedID:** 24747797

Available at BMJ open - from HighWire - Free Full Text

Available at BMJ open - from Europe PubMed Central - Open Access

Available at BMJ open - from ProQuest (Health Research Premium) - NHS Version

Available at BMJ open - from Unpaywall

**Abstract:** OBJECTIVES Some women with isolated gestational proteinuria (IGP) later develop hypertension and are diagnosed with pre-eclampsia (PE). This study was performed to determine whether clinical features of such proteinuria preceding PE (P-PE) differ from those of other PE (O-PE). DESIGN Retrospective observational study after approval of the institutional review board of ethics. SETTING A single university hospital. Proteinuria was defined as a protein-to-creatinine ratio (mg/mg; P/Cr) of ≥0.27 in the spot urine specimen. IGP was defined as proteinuria in the absence of hypertension. P-PE was defined as PE in which proteinuria preceded hypertension by more than 2 days. PARTICIPANTS All of 10 and 18 consecutive women with P-PE and O-PE, respectively, who gave birth between January 2008 and August 2013. RESULTS Proteinuria appeared earlier (at 30.2±3.0 vs 35.3±4.3 weeks, p=0.001), the P/Cr level was greater at birth (7.28±2.14 vs 3.19±2.49, p<0.001), net maternal weight gain during the last antenatal 1 week was greater (3.1±1.8 vs 1.3±1.7 kg, p=0.023) and length of pregnancy was shorter (32.5±1.9 vs 36.1±3.6 weeks, p=0.001) in women with P-PE than in O-PE. The duration of IGP was 10.0±5.9 days (range 3-20), and the time interval until delivery after diagnosis of PE was 6.1±8.2 days (range 0-23) in 10 women with P-PE. The P/Cr levels at birth were significantly inversely correlated with the antenatal lowest antithrombin activity and fibrinogen levels among the 28 women with PE. CONCLUSION Women with P-PE were likely to exhibit greater proteinuria in the urine, greater water retention in the interstitial space and more enhanced coagulation-fibrinolysis, thus suggesting that they may constitute a more severe form of PE than women with O-PE do.

**Database:** Medline
19. Excessive urinary tract dilatation and proteinuria in pregnancy: A common and overlooked association?

Author(s): Piccoli G.B.; Vigotti F.N.; Daidola G.; Deagostini M.C.; Ferraresi M.; Attini R.; Parisi S.; Todros T.; De Pascale A.; Veltri A.; Porpiglia F.

Source: BMC Nephrology; 2013; vol. 14 (no. 1)

Publication Date: 2013

Publication Type(s): Article

PubMedID: 23446427

Available at BMC nephrology - from BioMed Central
Available at BMC nephrology - from SpringerLink - Medicine
Available at BMC nephrology - from Europe PubMed Central - Open Access
Available at BMC nephrology - from ProQuest (Health Research Premium) - NHS Version
Available at BMC nephrology - from Unpaywall

Abstract: Background: Proteinuria and dilatation of the urinary tract are both relatively common in pregnancy, the latter with a spectrum of symptoms, from none to severe pain and infection. Proteinuria is a rare occurrence in acute obstructive nephropathy; it has been reported in pregnancy, where it may pose a challenging differential diagnosis with pre-eclampsia. The aim of the present study is to report on the incidence of proteinuria (0.3; 0.5g/day) in association with symptomatic-severe urinary tract dilatation in pregnancy. Methods. Case series. Setting(s): Nephrological-Obstetric Unit dedicated to pregnancy and kidney diseases (January 2000-April 2011). Source: database prospectively updated since the start of the Unit. Retrospective review of clinical charts identified as relevant on the database, by a nephrologist and an obstetrician. Result(s): From January 2000 to April 2011, 262 pregnancies were referred. Urinary tract dilatation with or without infection was the main cause of referral in 26 cases (predominantly monolateral in 19 cases): 23 singletons, 1 lost to follow-up, 1 twin and 1 triplet. Patients were referred for urinary tract infection (15 cases) and/or renal pain (10 cases); 6 patients were treated by urologic interventions (JJ stenting). Among them, 11 singletons and 1 triple pregnancy developed proteinuria 0.3g/day (46.1%). Proteinuria was 0.5g/day in 6 singletons (23.1%). Proteinuria resolved after delivery in all cases. No patient developed hypertension; in none was an alternative cause of proteinuria evident. No significant demographic difference was observed in patients with renal dilatation who developed proteinuria versus those who did not. An association with the presence of JJ stenting was present (5/6 cases with proteinuria 0.5g/day), which may reflect both severer obstruction and a role for vesico-ureteral reflux, induced by the stent. Conclusion(s): Symptomatic urinary tract dilatation may be associated with proteinuria in pregnancy. This association should be kept in mind in the differential diagnosis with other causes of proteinuria in pregnancy, including pre-eclampsia. © 2013 Piccoli et al; licensee BioMed Central Ltd.

Database: EMBASE
20. Pre-eclampsia or chronic kidney disease? The flow hypothesis.

**Author(s):** Piccoli, Giorgina B; Gaglioti, Pietro; Attini, Rossella; Parisi, Silvia; Bossotti, Carlotta; Olearo, Elena; Oberto, Manuela; Ferraresi, Martina; Rolfo, Alessandro; Versino, Elisabetta; Biolcati, Marilisa; Todros, Tullia

**Source:** Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association; May 2013; vol. 28 (no. 5); p. 1199-1206

**Publication Date:** May 2013

**Publication Type(s):** Journal Article

**PubMedID:** 23314318

**Abstract:**

**BACKGROUND** Chronic kidney disease (CKD) and pre-eclampsia (PE) occur in 3-5% of pregnancies. They often share hypertension and proteinuria and a differential diagnosis may be impossible. However, in PE, the pathogenesis is related to abnormal placentation, which can be detected by abnormal uterine and umbilical Doppler flow velocities, while in CKD, an intrinsic kidney disease is present. We hypothesize that Doppler studies can help to differentiate PE from CKD, as the flow velocities are altered in PE and normal in CKD.

**METHODS** We retrospectively selected patients who were followed in our Materno-Fetal Unit (2005-10) and had at least one flow measurement in our setting. CKD patients were included in the presence of proteinuria (≥ 300 mg/day) and hypertension, mimicking PE. The clinical charts were reviewed by the same operators; the clinical diagnoses were taken as reference. Three flow patterns were considered: alteration of both flow velocity waveforms (FVWs) (uterine and umbilical arteries), hypothesized as predictive of PE; normal FVWs at both levels, hypothesized as predictive of CKD; altered FVWs in either artery, considered 'mixed'. Uterine FVWs were considered pathological according to the classical cut-point (RI > 0.58). Umbilical flows were evaluated according to standards adjusted for gestational age. Statistical analysis was performed in SPSS.

**RESULTS** The analysis included 61 cases. The presence of normal FVWs was significantly associated with the diagnosis of CKD (P = 0.0018). Conversely, the presence of both altered flows was significantly associated with PE (P = 0.0233).

**CONCLUSIONS** In the presence of proteinuria and hypertension, normal flows suggest CKD altered flows PE. Prospective studies are needed to refine this hypothesis based on the first Doppler criteria supporting the differential diagnosis between CKD and PE.

**Database:** Medline
21. Relationships of risk factors for pre-eclampsia with patterns of occurrence of isolated gestational proteinuria during normal term pregnancy.

Author(s): Macdonald-Wallis, Corrie; Lawlor, Debbie A; Heron, Jon; Fraser, Abigail; Nelson, Scott M; Tilling, Kate

Source: PloS one; 2011; vol. 6 (no. 7); p. e22115

Publication Date: 2011

Publication Type(s): Research Support, Non-u.s. Gov't Research Support, N.i.h., Extramural Journal Article

PubMedID: 21789220

Available at PloS one - from Public Library of Science (PLoS)
Available at PloS one - from Europe PubMed Central - Open Access
Available at PloS one - from ProQuest (Health Research Premium) - NHS Version
Available at PloS one - from Unpaywall

Abstract: BACKGROUND Isolated gestational proteinuria may be part of the pre-eclampsia disease spectrum. Confirmation of its association with established pre-eclampsia risk factors and higher blood pressure in uncomplicated pregnancies would support this concept. METHODS Data from 11,651 women from the Avon Longitudinal Study of Parents and Children who had a term live birth but did not have pre-existing hypertension or diabetes or develop gestational diabetes or preeclampsia were used. Proteinuria was assessed repeatedly (median 12 measurements per woman) by dipstick and latent class analysis was used to identify subgroups of the population with different patterns of proteinuria in pregnancy. RESULTS 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. Women who experienced proteinuria showed five patterns: proteinuria in early pregnancy only (≤ 20 weeks gestation), and onset at 21-28 weeks, 29-32 weeks, 33-36 weeks and ≥ 37 weeks gestation. There were higher odds of proteinuria onset after 33 weeks in obese women and after 37 weeks in nulliparous women compared with normal weight and multiparturient women respectively. Smoking in pregnancy was weakly negatively associated with odds of proteinuria onset after 37 weeks. Twin pregnancies had higher odds of proteinuria onset from 29 weeks. In women with proteinuria onset after 33 weeks blood pressure was higher in early pregnancy and at the end of pregnancy. CONCLUSION Established preeclampsia risk factors were related to proteinuria occurrence in late gestation in healthy term pregnancies, supporting the hypothesis that isolated gestational proteinuria may represent an early manifestation of pre-eclampsia.

Database: Medline
22. Does the degree of proteinuria in early pregnancy correlate with risk of preeclampsia in pregestational diabetes?

**Author(s):** Durnwald C.; Lynch C.; Landon M.

**Source:** American Journal of Obstetrics and Gynecology; Jan 2011; vol. 204 (no. 1)

**Publication Date:** Jan 2011

**Publication Type(s):** Conference Abstract

**Abstract:**

**OBJECTIVE:** To determine if mild proteinuria (150-300 mg/24 hour collection)<20 weeks gestation increases the risk of developing preeclampsia in women with pregestational diabetes.

**STUDY DESIGN:** Retrospective study of women with preexisting (Type 1 and 2) diabetes enrolled in a diabetes in pregnancy program from 2004-2008. On enrollment, women completed a 24 hour urine collection to evaluate baseline renal function. Protein excretion in 24 hour urine (24 HP) was measured via pyrogallol red method. Women were divided into 3 categories as follows: Normal <150 mg/dL, Elevated 150-300 mg/dL and Nephropathy > 300mg/dL. The association between level of proteinuria and development of preeclampsia was analyzed.

**RESULT(S):** Of those studied (n=90), 52 had Normal 24HP, 24 had Elevated 24HP, and 14 had Nephropathy. Preeclampsia was diagnosed in 21 (23.3%) of pregnancies. Mean gestational age at diagnosis was 35.2 weeks (range 28.4-38.4 wks). There was no difference in rates of preeclampsia in those women with Elevated 24HP (17.9%) compared with Normal (16.6%), p=0.89. In contrast, women with Nephropathy had significantly higher rates of preeclampsia (47.4%) compared with Normal (47.4 vs. 16.6%, p=0.005). Baseline hemoglobin A1c of women developing preeclampsia was similar to those who remained normotensive (7.9% vs. 8.1%, p=0.64). After controlling for race, maternal age, prior history of preeclampsia, chronic hypertension and hemoglobin A1c, only Nephropathy levels of early proteinuria were associated with an increased risk of developing preeclampsia.

**CONCLUSION(S):** Mild proteinuria above 150 mg/24 hours in early pregnancy is not associated with an increased risk of preeclampsia in women with pregestational diabetes, whereas nephropathic levels do increase the risk.

**Database:** EMBASE

23. The kidney in normal pregnancy and preeclampsia.

**Author(s):** Cornelis, Tom; Odutayo, Ayodele; Keunen, Johannes; Hladunewich, Michelle

**Source:** Seminars in nephrology; Jan 2011; vol. 31 (no. 1); p. 4-14

**Publication Date:** Jan 2011

**Publication Type(s):** Journal Article Review

**PubMedID:** 21266261

**Abstract:** Complicating up to 8% of pregnancies, preeclampsia is, in fact, the most common glomerular disease worldwide. In this article, we review the effect of normal pregnancy on the kidney as well as the role of the kidney in preeclampsia. We discuss blood pressure in pregnancy and preeclampsia, followed by the physiology of hyperfiltration in normal pregnancy as well as the pathophysiology of hypofiltration and proteinuria in preeclampsia. Recent studies have suggested that the clinical syndrome of preeclampsia, which recovers rapidly after delivery of the placenta, is caused by impaired vascular endothelial growth factor signaling that disturbs the status of vascular dilatation as well as the symbiosis between the glomerular endothelium and the podocytes. Finally, we discuss the intriguing association between chronic kidney disease (CKD) and preeclampsia. We hypothesize that the imbalance between angiogenic and anti-angiogenic factors, which may be common to both preeclampsia and CKD, might explain why CKD predisposes pregnant women to develop preeclampsia.

**Author(s):** Morikawa, Mamoru; Yamada, Takashi; Minakami, Hisanori

**Source:** Current opinion in obstetrics & gynecology; Dec 2009; vol. 21 (no. 6); p. 491-495

**Publication Date:** Dec 2009

**Publication Type(s):** Journal Article Review

**PubMedID:** 19633554

Available at Current opinion in obstetrics & gynecology - from Ovid (LWW Total Access Collection 2019 - with Neurology)

Available at Current opinion in obstetrics & gynecology - from Ovid (Journals @ Ovid)

Available at Current opinion in obstetrics & gynecology - from Ovid (Journals @ Ovid) - London Health Libraries

**Abstract:** PURPOSE OF REVIEWThe outcome of pregnancy in patients with isolated proteinuria is believed to be favorable. However, whether women with isolated proteinuria are at risk for progressing to preeclampsia has not been extensively studied. RECENT FINDINGS The amount of proteinuria is thought to increase in the early third trimester, irrespective of whether preeclampsia has been diagnosed. A dipstick urinalysis has a poor sensitivity (ranging from 22 to 86%) for the detection of significant proteinuria (> or = 0.3 g/day). Measurements of the levels of circulating angiogenic factors such as soluble fms-like tyrosine kinase 1, soluble endoglin, vascular endothelial growth factor, and placental growth factor suggest that gestational proteinuria is a mild variant of preeclampsia. In one study, women with isolated proteinuria (> or = 0.3 g/day) were found to be more likely to progress to preeclampsia than women with isolated hypertension. A considerable number of women with eclampsia exhibited proteinuria alone during their last antenatal visit performed within a week prior to their first convulsion. SUMMARY The outcome of women with a retrospective diagnosis of gestational proteinuria is generally favorable. However, a considerable number of women with isolated proteinuria develop hypertension and progress to preeclampsia. Therefore, the statement that the 'outcome of pregnancy in patients with isolated proteinuria is favorable' is misleading. Physicians should be aware of this type of preeclampsia when counseling patients. One possible explanation for the difficulty in diagnosing this form of preeclampsia might be the low sensitivity of the dipstick urinalysis technique for the detection of significant proteinuria.

**Database:** Medline
25. Proteinuria in the uncomplicated twin pregnancy

Author(s): Smith N.; Lyons J.; McElrath T.
Source: American Journal of Obstetrics and Gynecology; Dec 2009; vol. 201 (no. 6)
Publication Date: Dec 2009
Publication Type(s): Conference Abstract

Abstract: OBJECTIVE: We have observed that women with twin pregnancies appear to have higher rates of proteinuria without accompanying hypertension than do those with singletons. Protein to creatinine ratios (p:c ratio) in excess of 0.19 predict proteinuria greater than 300mg in a 24 hour collection. We compare rates of high p:c ratios in non-preeclamptic singleton and twin pregnancies in order to better understand normal protein excretion in twins. STUDY DESIGN: A sequential sample of 102 (51 twins, 51 singletons) healthy patients without preeclampsia, gestational diabetes, intrauterine growth restriction, history of premature delivery or other medical comorbidities were selected from the Predictors of Preeclampsia Study to compare protein-to-creatinine ratio by fetal number. Samples were collected between 34 and 38 weeks gestation, and a clinically significant high p:c ratio was defined as greater than 0.19. Non-parametric statistical comparisons and logistic regression were used for analysis. RESULT(S): Women with twin pregnancies were significantly more likely to have protein to creatinine ratios greater than 0.19 (p=0.003), and median p:c ratio was significantly higher in twins (p=0.003). Median p:c ratio for singletons was 0.15, and for twins 0.2. Groups differed in maternal age (mean 31.3 vs 35.3 years, p=0.0003) and gestational age at sample collection (35.6 vs 34.8 weeks, p=0.001), and were similar in weight, BMI, race, and smoking status. Using multiple logistic regression to control for the confounders of maternal age and gestational age yielded an adjusted OR for p:c ratio greater than 0.19 of 4.23 (1.61, 11.06). CONCLUSION(S): Women with uncomplicated twin pregnancies have higher rates of elevated protein to creatinine ratios than do women with singletons, suggesting that normal protein excretion in this group is greater than that in singleton gestations.

Database: EMBASE
26. Pregnancies complicated by mild pre-eclampsia: How high risk are they?

**Author(s):** Varughese A.; Walsh J.; Robson M.; O’Herlihy C.

**Source:** International Journal of Gynecology and Obstetrics; Oct 2009; vol. 107

**Publication Date:** Oct 2009

**Publication Type(s):** Conference Abstract


**Abstract:** Background: The management of patients with mild pre-eclampsia varies considerably between centres and clinicians. Some have a policy that all patients with pre-eclampsia regardless of severity should be managed in hospital due to the unpredictable nature of the disease, while many centres, including our own, manage mild disease on an outpatient basis. The degree of proteinuria is often used as a marker of severity in deciding how intensive monitoring should be. On this basis we have audited the outcome of pregnancies complicated by pre-eclampsia with mild proteinuria, between 0.3 grammes and 0.5 grammes in a 24 hour period, who were delivered in the National Maternity Hospital, Dublin, Ireland in the year 2008. Method(s): We performed a retrospective chart review of all patients in the National Maternity Hospital over a 12 month period with pre-eclampsia and mild proteinuria. Result(s): There were 54 patients with mild proteinuria between 0.3 g and 0.5 g. Of these there were 8 preterm deliveries and 1 stillbirth. Overall the risk of preterm delivery, caesarean delivery and intrauterine growth restriction were all significantly increased. Conclusion(s): The incidence of adverse obstetric outcome was significantly increased in women with preeclampsia associated with mild proteinuria. These pregnancies are certainly high risk and should be managed as such.

**Database:** EMBASE

27. Circulating angiogenic factors in gestational proteinuria without hypertension

**Author(s):** Holston A.M.; Qian C.; Yu K.F.; Levine R.J.; Epstein F.H.; Karumanchi S.A.

**Source:** American Journal of Obstetrics and Gynecology; Apr 2009; vol. 200 (no. 4); p. 392

**Publication Date:** Apr 2009

**Publication Type(s):** Article

**PubMedID:** 19168169

Available at [American journal of obstetrics and gynecology](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2675947/) - from Unpaywall

**Abstract:** Objective: Our goal was to determine whether obstetric outcomes and serum angiogenic factors are altered in women with gestational proteinuria without hypertension. Study Design: We performed a nested case-control study of 108 women with gestational proteinuria and compared them with 1564 randomly selected women with normotension without proteinuria during pregnancy (control subjects) and with 319 women who experienced preeclampsia. Result(s): Women with gestational proteinuria had greater body-mass index and higher blood pressure at study enrollment. Adverse obstetric outcomes were infrequent. Levels of free placental growth factor were lower than control levels beginning early in gestation. Compared with gestational-age matched control subjects, free placental growth factor was reduced beginning 6-8 weeks before proteinuria. Although soluble fms-like tyrosine kinase 1 and soluble endoglin concentrations were elevated 1-2 weeks before proteinuria, these elevations were modest and transient. After the onset of proteinuria, angiogenic factor levels generally did not differ significantly from control levels. Conclusion(s): Gestational proteinuria in healthy nulliparous women appears to be a mild variant of preeclampsia. © 2009 Mosby, Inc. All rights reserved.

**Database:** EMBASE
28. Pregnancy outcome of women who developed proteinuria in the absence of hypertension after mid-gestation.

**Author(s):** Morikawa, Mamoru; Yamada, Takashi; Yamada, Takahiro; Cho, Kazutoshi; Yamada, Hideto; Sakuragi, Noriaki; Minakami, Hisanori

**Source:** Journal of perinatal medicine; 2008; vol. 36 (no. 5); p. 419-424

**Publication Date:** 2008

**Publication Type(s):** Journal Article

**PubMedID:** 18605971

**Abstract:**

OBJECTIVE: To characterize the clinical features of women with singleton pregnancies who develop proteinuria in the absence of hypertension after mid-gestation.

METHODS: Seventy-nine women who developed proteinuria and/or hypertension at and after 20 weeks of gestation were reviewed, focusing on the gestational week at which significant proteinuria (>0.3 g/day) and/or hypertension developed.

RESULTS: Thirty-seven (47%) women exhibited new-onset proteinuria (>0.3 g/day) in the absence of hypertension, 33 (42%) exhibited new-onset hypertension in the absence of proteinuria, and 9 (11%) exhibited both proteinuria and hypertension. Nineteen (51%) of 37 women who exhibited new proteinuria in the absence of hypertension and 5 (15%) of 33 women who exhibited new hypertension in the absence of proteinuria progressed to preeclampsia (P=0.002). Among women who exhibited new proteinuria, 10 (77%) out of 13 women and 9 (38%) out of 24 women who developed proteinuria at or=32 weeks, respectively, progressed to preeclampsia (P=0.022). CONCLUSION: Women with new-onset proteinuria in the absence of hypertension may be more likely to progress to preeclampsia than women with a presumptive diagnosis of gestational hypertension, and the likelihood of progression may be significantly greater among women with earlier presentation.

**Database:** Medline

29. Measuring protein excretion in pregnancy

**Author(s):** Holt J.L.; Mangos G.J.; Brown M.A.

**Source:** Nephrology; Oct 2007; vol. 12 (no. 5); p. 425-430

**Publication Date:** Oct 2007

**Publication Type(s):** Review

**PubMedID:** 17803463

**Available at:** Nephrology (Carlton, Vic.) - from Wiley Online Library Science, Technology and Medicine Collection 2019

**Available at:** Nephrology (Carlton, Vic.) - from Unpaywall

**Abstract:**

The recognition and detection of proteinuria has been acknowledged as an important clinical marker of renal disease since 1827 when Richard Bright published his landmark medical case reports. In more recent times, the broader community of clinicians has come to share the enthusiasm of nephrologists in recognizing the importance of protein excretion, not only as a marker of current renal disease but also as a predictor of long-term renal and cardiovascular morbidity and mortality. It is important that methods for detecting and measuring proteinuria are accurate, and this is particularly relevant to diseases that are defined by the detection of proteinuria, such as preeclampsia. This review will first discuss current knowledge of protein handling by the normal kidney, then the changes in normal and hypertensive pregnancy, and finally, how recent advances in our
understanding of proteinuria may affect our future management of hypertensive pregnancies. © 2007 The Authors.

**Database:** EMBASE

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**30. Clinical significance of proteinuria in pregnancy**

**Author(s):** Airoldi J.; Weinstein L.

**Source:** Obstetrical and Gynecological Survey; Feb 2007; vol. 62 (no. 2); p. 117-124

**Publication Date:** Feb 2007

**Publication Type(s):** Review

**PubMedID:** 17229328

Available at Obstetrical & gynecological survey - from Ovid (LWW Total Access Collection 2019 - with Neurology)

**Abstract:** Urinary protein excretion is considered abnormal in pregnant women when it exceeds 300 mg/24 hours at anytime during gestation, a level that usually correlates with 1+ on urine dipstick. Proteinuria documented before pregnancy or before 20 weeks' gestation suggests preexisting renal disease. The National High Blood Pressure Education Program Working Group recommended that the diagnosis of proteinuria be based on the 24-hour urine collection. Preeclampsia is the leading diagnosis that must be excluded in all women with proteinuria first identified after 20 weeks of gestation. Given the vasospastic nature of this condition, when it is present, the degree of proteinuria may fluctuate widely from hour-to-hour. Hypertension or proteinuria may be absent in 10-15% of patients with HELLP syndrome and in 38% of patients with eclampsia. The acute onset of proteinuria and worsening hypertension in women with chronic hypertension is suggestive of superimposed preeclampsia, which increases adverse outcomes. However, because proteinuria is not independently predictive of adverse outcome, an exclusive proteinuric criterion as an indication for preterm delivery in preeclampsia should be discouraged. TARGET AUDIENCE: Obstetricians & Gynecologists, Family Physicians

**LEARNING OBJECTIVES:** After completion of this article, the reader should be able to state that measurement of urinary protein levels by simple techniques are not sensitive or specific, recall that both hypertension and proteinuria may be absent in patients with preeclampsia, and explain that proteinuria is not predictive of adverse outcomes and that delivery should not be based on protein excretion alone. © 2007 Lippincott Williams & Wilkins, Inc.

**Database:** EMBASE
31. Is early-pregnancy proteinuria associated with an increased rate of preeclampsia in women with pregestational diabetes mellitus?

**Author(s):** How H.Y.; Sibai B.; Lindheimer M.; Caritis S.; Hauth J.; Klebanoff M.; MacPherson C.; Van Dorsten P.; Miodovnik M.; Landon M.; Paul R.; Meis P.; Thurnau G.; Dombrowski M.; Roberts J.

**Source:** American Journal of Obstetrics and Gynecology; Mar 2004; vol. 190 (no. 3); p. 775-778

**Publication Date:** Mar 2004

**Publication Type(s):** Article

**PubMedID:** 15042013

**Abstract:** Objective: The purpose of this study was to determine whether the rate of preeclampsia in pregnant diabetic women is increased in those women with early-pregnancy proteinuria of 190 to 499 mg/24 hours compared with women with proteinuria of < 190 mg/24 hours. Study design: Secondary analysis was performed with relevant data from 194 pregnant women with type 1 and type 2 diabetes mellitus whose condition required insulin and who were enrolled previously in a multicenter trial of low-dose aspirin for the prevention of preeclampsia. The women were assigned to 1 of 3 groups, based on the level of proteinuria at enrollment (13-26 weeks of gestation). Group 1 comprised women with < 190 mg protein/24 hours (n = 94); group 2 comprised women with 190 to 499 mg protein/24 hours (n = 35); and group 3 comprised women with >= 500 mg protein/24 hours (n = 65). The rate of preeclampsia, according to strict predefined criteria, was then determined. Result(s): The rate of preeclampsia was not increased statistically significantly in patients with early-pregnancy proteinuria of 190 to 499 mg/24 hours (7/35 women; 20%) when compared with women with proteinuria of < 190 mg/24 hours (16/94 women; 17%). Conclusion(s): We did not find an increased rate of preeclampsia in women with pregestational diabetes mellitus with early-pregnancy proteinuria of 190 to 499 mg/24 hours when compared with women with pregestational diabetes mellitus with proteinuria of < 190 mg/24 hours. © 2004 Elsevier Inc. All rights reserved.

**Database:** EMBASE
32. The significance of serum uric acid, creatinine and urinary microprotein levels in predicting pre-eclampsia

Author(s): Weerasekera D.S.; Peiris H.

Source: Journal of Obstetrics and Gynaecology; Jan 2003; vol. 23 (no. 1); p. 17-19

Publication Date: Jan 2003

Publication Type(s): Article

PubMedID: 12623475

Abstract: The object of this study was to determine whether serum uric acid, serum creatinine and urinary microprotein levels could be used to identify women who might subsequently develop pre-eclampsia during pregnancy. This is a cross-sectional descriptive study performed on women attending the University antenatal clinic in Colombo South Teaching Hospital, Sri Lanka. Serum uric acid, creatinine and microproteinuria levels were determined in 256 women attending the antenatal clinic at 28 weeks of pregnancy. Subsequently they were followed-up at 2-weekly intervals until 36 weeks and weekly thereafter until delivery. At each visit blood pressure was recorded and serum uric acid, creatinine and microprotein levels were determined. Fifty-nine women developed blood pressures of 140/90 mmHg or more during the study period. Serum uric acid and serum creatinine levels did not show any significant difference before the elevated blood pressures were recorded. Microproteinuria levels of more than 375 mg/l were recorded in 43 women before elevation of their blood pressure. Sixty-five women of 197 who remained normotensive had microproteinuria levels of more than 375 mg/l. The sensitivity and specificity of microproteinuria levels of more than 375 mg/l as a screening test for prediction of pre-eclampsia was 73% and 67%, respectively. Therefore, microproteinuria of more than 375 mg/l may be used as a cut-off value and as a screening test for the early detection of women at risk of developing pre-eclampsia. Serum uric acid and creatinine had no predictive value as a screening test for pre-eclampsia.

Database: EMBASE

33. Albumin excretory rate in normal and hypertensive pregnancy

Author(s): Brown M.A.; Wang M.-X.; Buddle M.L.; Carlton M.A.; Cario G.M.; Zammit V.C.; Whitworth J.A.

Source: Clinical Science; 1994; vol. 86 (no. 3); p. 251-255

Publication Date: 1994

Publication Type(s): Article

PubMedID: 8156734

Abstract: The purpose of this study was to determine whether the 24 h urinary albumin excretory rate was increased in the third trimester of normal pregnancy or in pregnant women with hypertension who had 24 h urinary total protein excretion within the normal range. Twenty-four hour urinary creatinine and albumin excretions were determined prospectively in 26 nonpregnant and 115 pregnant women in their third trimester (40 in normal pregnancy, 38 with mild preeclampsia, 20 with severe pre-eclampsia, 17 with essential hypertension) in whom urinary total protein excretion was normal. Both the urinary albumin excretion rate and the urinary albumin/creatinine ratio were compared among the groups. The clearance of albumin relative to that of creatinine was also calculated in the hypertensive women and in 14 of the non-pregnant women and nine of the normal pregnant women. The twenty-four hour urinary albumin excretion rate was similar in non-pregnant [8(5-10) mg/day; median (interquartile range)] and normal pregnant [7(6-10) mg/day] women. Women with essential hypertension [6(4-16)mg/day] and mild preeclampsia [7(4-10) mg/day] had a urinary albumin excretion rate similar to that of normal
pregnant women. Women with severe pre-eclampsia had an urinary albumin excretion rate increased [13(7-32) mg/day] compared with other groups (P < 0.05). The clearance of albumin relative to that of creatinine was elevated significantly only in women with severe pre-eclampsia compared with normal pregnant women (0.00054 versus 0.00012; P < 0.05). Blood pressures were similar among all hypertensive groups. The upper limit of the urinary albumin excretion rate was 20 mg/day in normal pregnant women, similar to that in non-pregnant women. Urinary albumin excretion is unchanged in the third trimester of normal pregnancy, but is increased in women with features of severe pre-eclampsia who have normal total urinary protein excretion. This is not fully explained by a reduction in glomerular filtration rate nor by different systemic blood pressures, and probably reflects enhanced glomerular capillary permeability, possibly with altered maximum renal tubular reabsorption capacity for albumin.

**Database:** EMBASE

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34. **Proteinuria and its assessment in normal and hypertensive pregnancy**

**Author(s):** Kuo V.S.; Koumantakis G.; Gallery E.D.M.

**Source:** American Journal of Obstetrics and Gynecology; 1992; vol. 167 (no. 3); p. 723-728

**Publication Date:** 1992

**Publication Type(s):** Article

**PubMedID:** 1530030

**Abstract:** Objectives: The purposes of this study were (1) to determine 24-hour urinary protein excretion rates in normal human pregnancy and (2) to assess the reliability of assessment of proteinuria by dipstick measurement. Study design: At 17 to 20 and 33 to 36 weeks of pregnancy, 174 normal volunteers collected a 24-hour urine sample; the volume and the protein and creatinine concentrations were measured. The result for protein was compared with dipstick analysis of an early morning midstream urine sample collected at the conclusion of the 24-hour period. Sixty-eight consecutive inpatients admitted to the antenatal ward with hypertension and positive urine dipstick tests for protein underwent the same procedure. The interobserver variability in assessment of proteinuria by dipstick was assessed with the aid of 66 volunteers from the hospital staff. Result(s): The upper 95% confidence limit of the normal population was <200 mg per 24 hours, at both stages of pregnancy investigated. In these women and in the hypertensive inpatients a high proportion of false-positive and false-negative results was found with dipstick analyses. Interobserver variation in assessment of proteinuria by dipstick was high, with an 18% false-positive rate and a false-negative rate approaching 40% for samples with 30 mg/dl. Even in the presence of 100 mg/dl the false-negative rate was 7%, whereas the concentration of protein was significantly underestimated in 20% of samples with 500 mg/dl. Conclusion(s): Dipstick urinalysis cannot be relied on either to detect or to exclude the presence of proteinuria in pregnant women.

**Database:** EMBASE
35. Natural history of chronic proteinuria complicating pregnancy.

**Author(s):** Stettler, R W; Cunningham, F G

**Source:** American journal of obstetrics and gynecology; Nov 1992; vol. 167 (no. 5); p. 1219-1224

**Publication Date:** Nov 1992

**Publication Type(s):** Journal Article

**PubMedID:** 1442970

**Abstract:** OBJECTIVE Although the significance of proteinuria is well-documented for pregnancy complicated by preeclampsia or diabetes, protein excretion of up to 300 mg per day is considered normal for uncomplicated pregnancy. Our purpose was to determine the significance of otherwise "asymptomatic" proteinuria identified during pregnancy. STUDY DESIGN We reviewed the perinatal outcome of 65 pregnancies in 53 women with the following criteria: (1) proteinuria exceeding 500 mg per day, (2) no previously known renal disease, (3) no reversible renal dysfunction, and (4) no evidence for preeclampsia at discovery. RESULTS Renal insufficiency coexisted in 62% of women, and 40% had chronic hypertension. Excluding 8 abortions, 53 (93%) of 57 pregnancies resulted in live infants; 45% of infants were delivered preterm and 23% had growth retardation. Of these 57 women, 62% demonstrated clinical evidence compatible with superimposed preeclampsia, and although the incidence of preeclampsia was increased with isolated proteinuria (29%), it was increased even more when there was associated chronic hypertension (incidence 100%) or renal insufficiency (incidence 58%). All 21 women who eventually underwent renal biopsy had histologic evidence of renal disease. To date, with only a limited follow-up of these 53 women, 11 (20%) have progressed to end-stage renal disease. CONCLUSION "Asymptomatic" proteinuria is associated with a number of adverse pregnancy outcomes and serious long-term maternal morbidity.

**Database:** Medline

36. Urinary albumin excretion in normal pregnancy and pregnancy-induced hypertension

**Author(s):** Misiani R.; Marchesi D.; Tiraboschi G.; Gualandris L.; Pagni R.; Goglio A.; Amuso G.; Muratore D.; Bertuletti P.; Massazza M.

**Source:** Nephron; 1991; vol. 59 (no. 3); p. 416-422

**Publication Date:** 1991

**Publication Type(s):** Article

**PubMedID:** 1758531

**Abstract:** We measured the urinary excretion of albumin in 67 healthy primigravidae, at monthly intervals, from 16 to 36 weeks of gestation and 12 weeks postpartum. Of the 67 primigravidae, 55 completed a normal pregnancy and 12 developed pregnancy-induced hypertension. In the latter group, an additional measurement of urinary albumin excretion was performed at 24 weeks postpartum. The aims of the study were: to look for changes of urinary albumin excretion during the progression of normal pregnancy; to assess if microalbuminuria could be an early feature of pregnancy-induced hypertension; to evaluate the effects of physical activity on the excretion of albumin in normal pregnancy and pregnancy-induced hypertension. In contrast with glomerular hyperfiltration and increased urinary total protein, two recognized characteristics of the pregnant state, we found that normal primigravidae, during the day, excrete significantly less albumin (p between <0.01 and <0.001) in comparison with the postpartum period and nonpregnant women. Normal primigravidae, as a group, showed parallel changes of urinary albumin excretion and diastolic blood pressure throughout pregnancy and postpartum, suggesting an important physiologic role of hemodynamic factors in regulating glomerular permeability to albumin. The daytime urinary albumin excretion in patients developing pregnancy-induced hypertension was significantly higher (p
between <0.005 and <0.001) than in normal pregnancy from the 28th gestational week onwards. The increased urinary albumin excretion preceded the onset of hypertension and tended to persist long after blood pressure had returned to normal levels. We conclude that the pregnant state changes the pattern of urinary protein excretion in normal primigravidae, and that the overt clinical manifestations of pregnancy-induced hypertension are preceded and followed by long-lasting phases of increased urinary albumin loss.

**Database:** EMBASE

37. Pregnancy-induced hypertension without proteinuria: Is it true preeclampsia?

**Author(s):** Morgan M.A.; Thurnau G.R.

**Source:** Southern Medical Journal; 1988; vol. 81 (no. 2); p. 210-213

**Publication Date:** 1988

**Publication Type(s):** Article

**PubMedID:** 3340875

**Abstract:** A profile scoring system has recently been developed as a standardized method of early identification and severity assessment of pregnancy-induced hypertension (PIH). The purpose of this study is twofold: (1) to compare the PIH profile scores of patients demonstrating mild PIH without proteinuria with those of patients demonstrating mild PIH with proteinuria, and (2) to introduce the PIH profile graph as a standardized clinical assessment tool. Serial PIH profile data after 24 weeks' gestation from 46 term primigravid patients with mild PIH (group 1 = 19 patients without proteinuria; group 2 = 27 patients with proteinuria) were plotted on PIH profile graphs and compared. Profile scores from ten normotensive primigravidas at term served as controls. Serial profile scores for groups 1 and 2 showed similar patterns on the profile graph. Based on these data, we believe that PIH without proteinuria is clinically and biochemically a manifestation of true preeclampsia before the onset of proteinuria. Furthermore, the PIH profile graph allows one to identify subtle changes in the disorder and to anticipate the development of severe preeclampsia.

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