

Nephrinuria as a predictive tool for preeclampsia in women with a high-risk pregnancy

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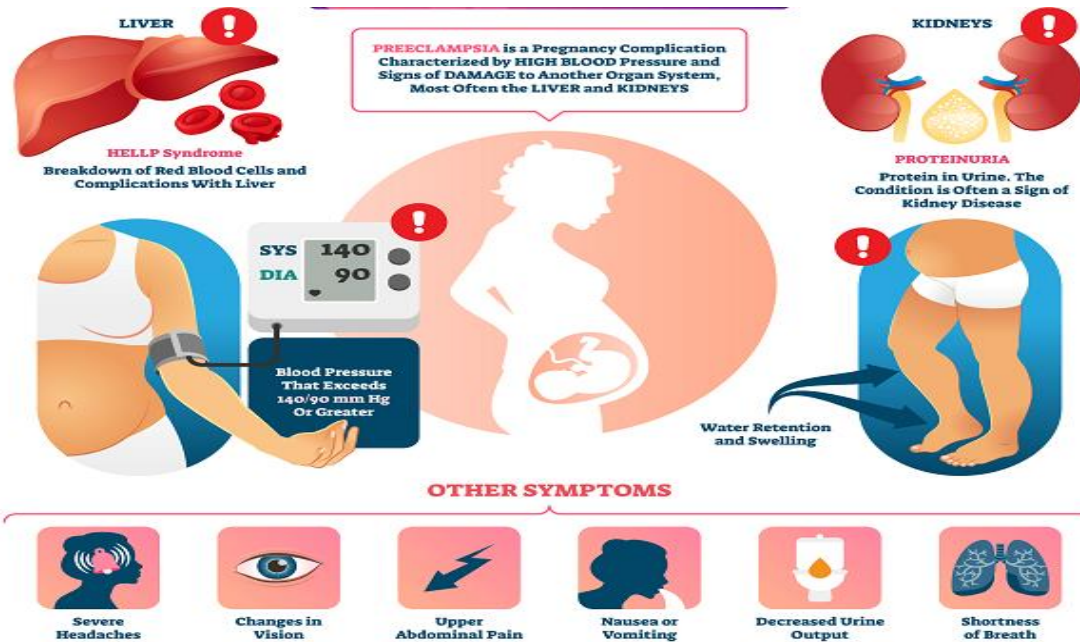
Conclusions



Background

What is preeclampsia?

The ACOG* defines preeclampsia as the presence of hypertension and proteinuria occurring after 20 weeks of gestation in a previously normotensive women¹



Preeclampsia (PE) is the leading global cause of maternal and perinatal morbidity and mortality worldwide, particularly in low- and middle-income countries²

Prediction of PE may prevent progression of disease and reduce maternal and fetal morbidity and mortality.

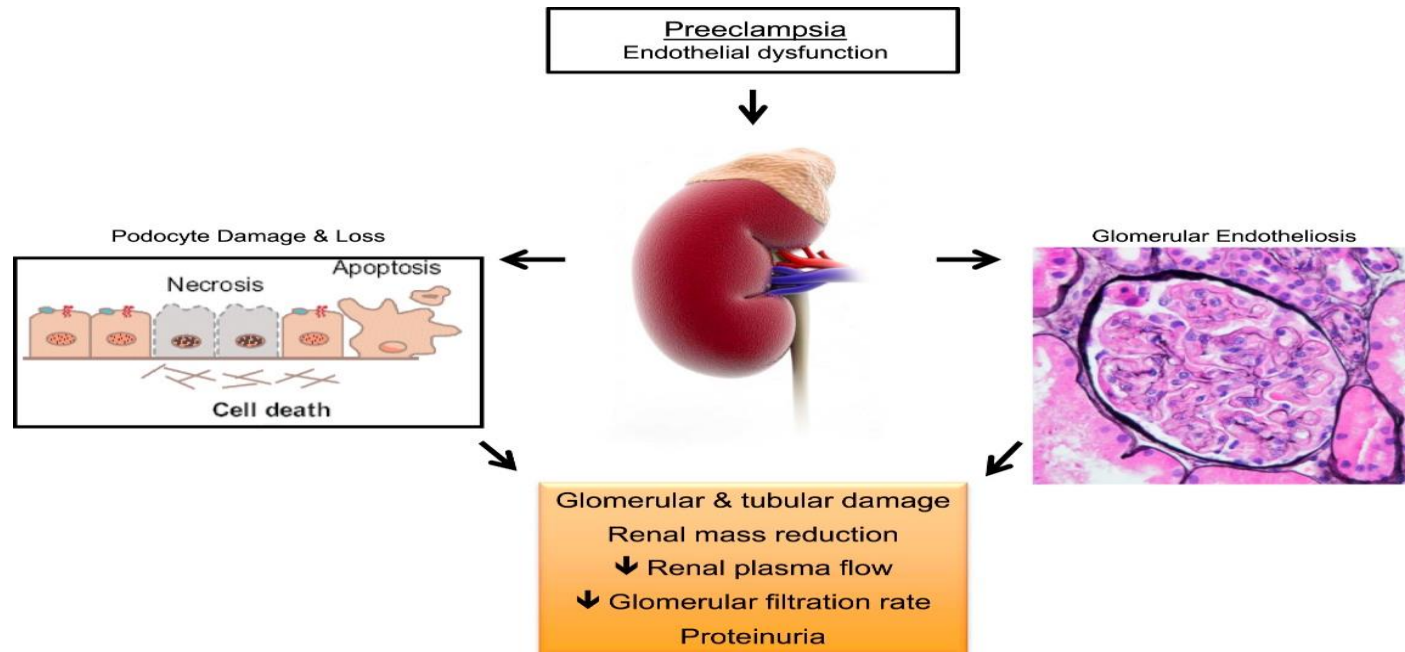
*American College of Obstetrics and Gynecology

Pathogenesis of preeclampsia

Major role in pathogenesis of PE - endothelial dysfunction and multi organ involvement including kidneys³

Podocyte damage has an important role in pathogenesis of PE, including necrosis, apoptosis and detachment from the glomerular basement membrane (GBM) and their shedding through urine – podocyuria⁴

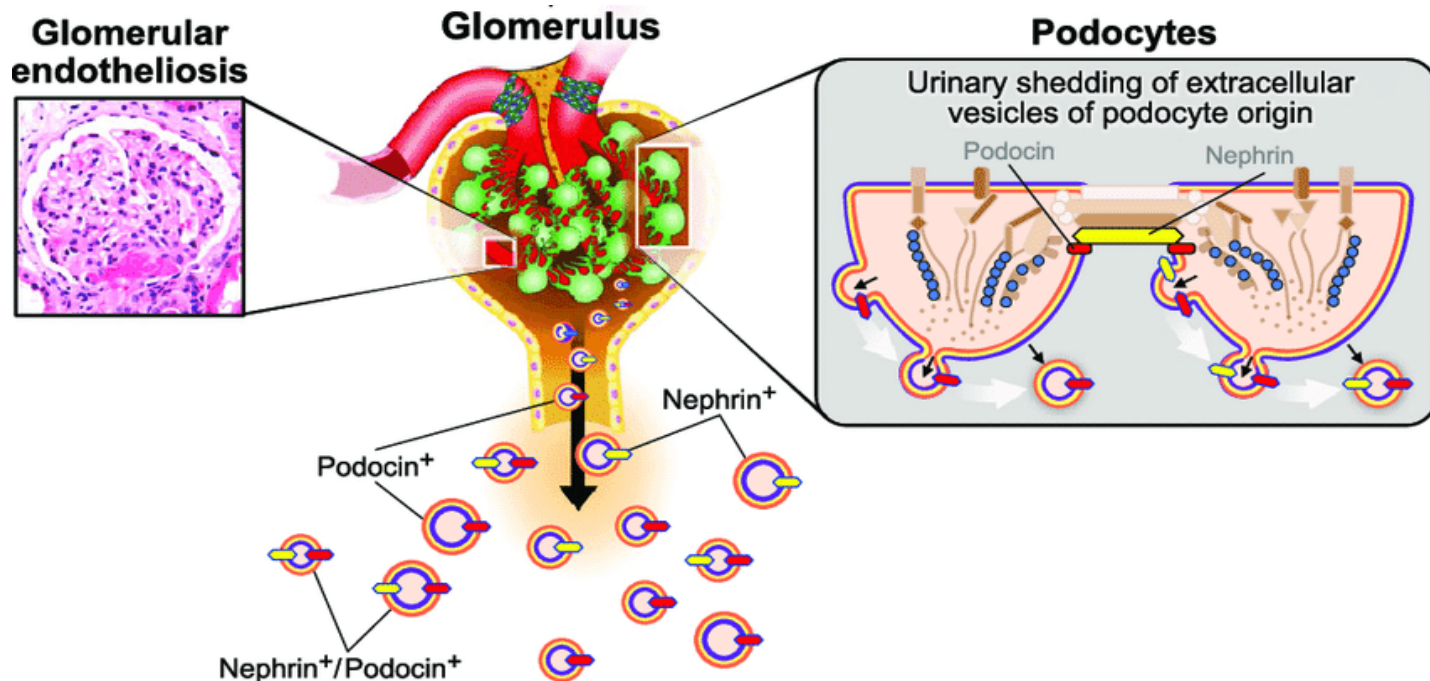
Podocyuria has sensitivity and specificity of 100% in diagnosis of PE⁵



Podocyturia and nephrinuria in PE

Nephrinuria is a hallmark of podocytopathies. Nephrin appears in urine in early course of renal dysfunction in PE, may precede microalbuminuria, rendering it as a possible predictive marker of PE⁶

Several recent studies have described the potential role of urinary nephrin as a predictive biomarker of PE^{7, 8, 9}



⁶Kandasamy Y, et al. Biomark Res. 2014;2:21. ⁷Wang Y, et al. Am J Physiol Renal Physiol 2012; 302(9): F1084–9. ⁸Son GH, et al. Eur J Obstet Gynecol Reprod Biol 2013; 166(2): 139–144. ⁹Jung YJ, et al. Yonsei Med J 2017; 58(2): 401-406.

What is the role of laboratory scientist in prediction of PE?

To investigate the novel predictive biomarkers of PE which can be measured in blood or urine

A predictive laboratory test of PE must have high sensitivity and specificity and must provide an adequate positive predictive value¹⁰

Potential biomarkers in blood and urine, that may accomplish above mentioned criteria are: soluble fms-like tyrosine kinase 1 (sFlt-1), placental growth factor (PlGF), alpha-fetoprotein (AFP), placental protein 13 (PP13), urinary glycosaminoglycans/proteoglycans (GAGs and PGs), pregnancy-associated plasma protein-A (PAPP-A), endoglin, cystatin C, free fetal hemoglobin (HbF), vascular endothelial growth factor (VEGF), P-selectin, A disintegrin, metalloprotease 12 (ADAM12), Pentraxin 3 (PTX3) and kidney markers, particularly podocyte specific proteins such as **nephrin**^{11, 12}

Objective

To evaluate the potential role of urinary nephrin in prediction of PE in women with a high-risk pregnancy.

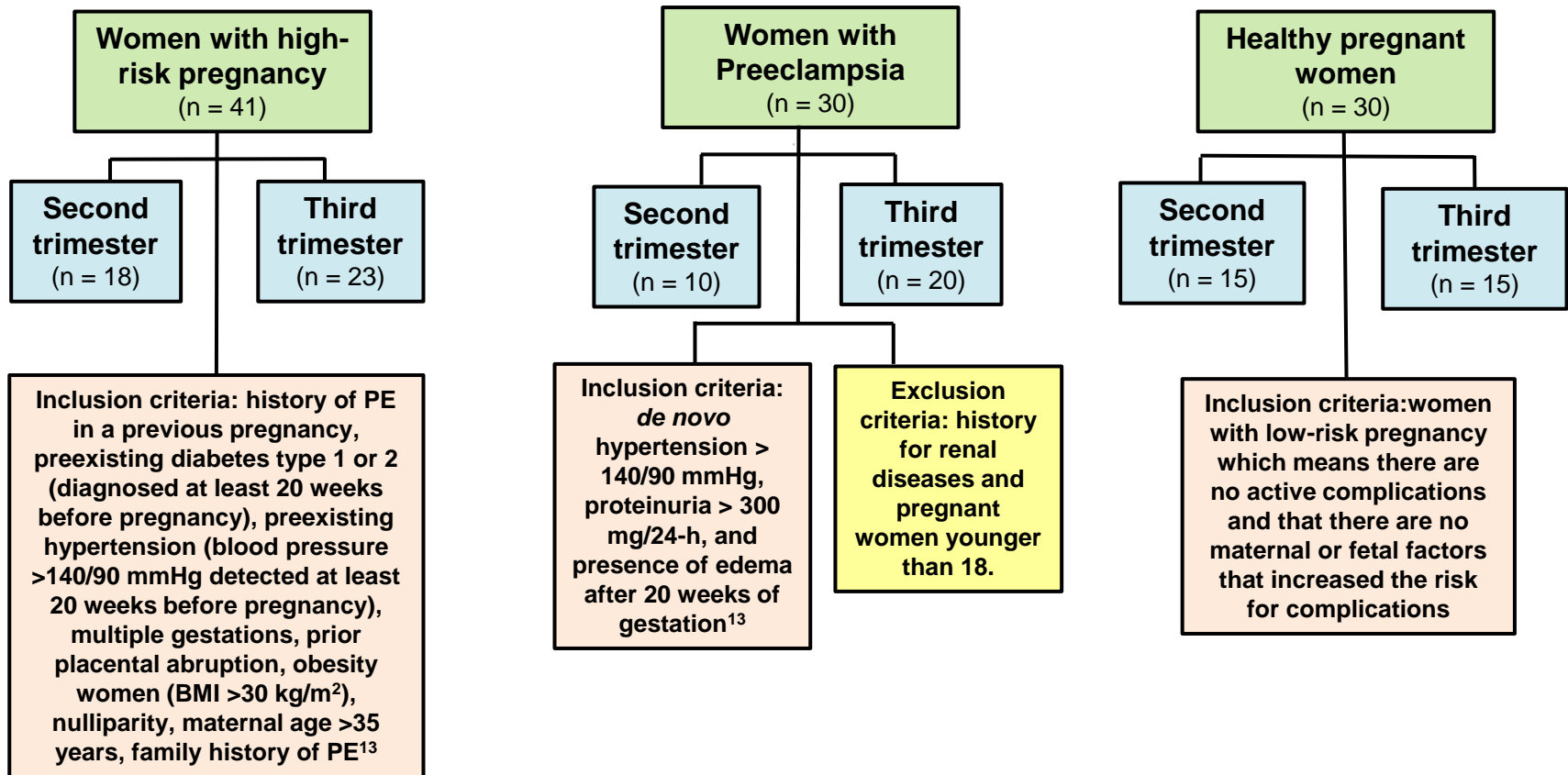




Methods

Study design and population

- Study design: cross sectional
- Study population:



Material

- **Urine - nephrin, creatinine, microalbumin, chemical analyses**
- **Urinary microalbumin to creatinine ratio (UM/CR) - determined as the urinary microalbumin concentration divided by the urinary creatinine concentration (mg/g).**
- **Venous blood – urea, creatinine, total protein, albumin, glucose**
- **Questionnaire form – data on interest (age, gestational week, weight, height, glycaemic control, blood pressure, etc.)**



Methods-measurements

- ELISA - (indirect competitive) - nephrin
- Immunoturbidimetric method - microalbumin
- Photometric method - biochemical parameters
- Cockroft & Gault formula - eGFR

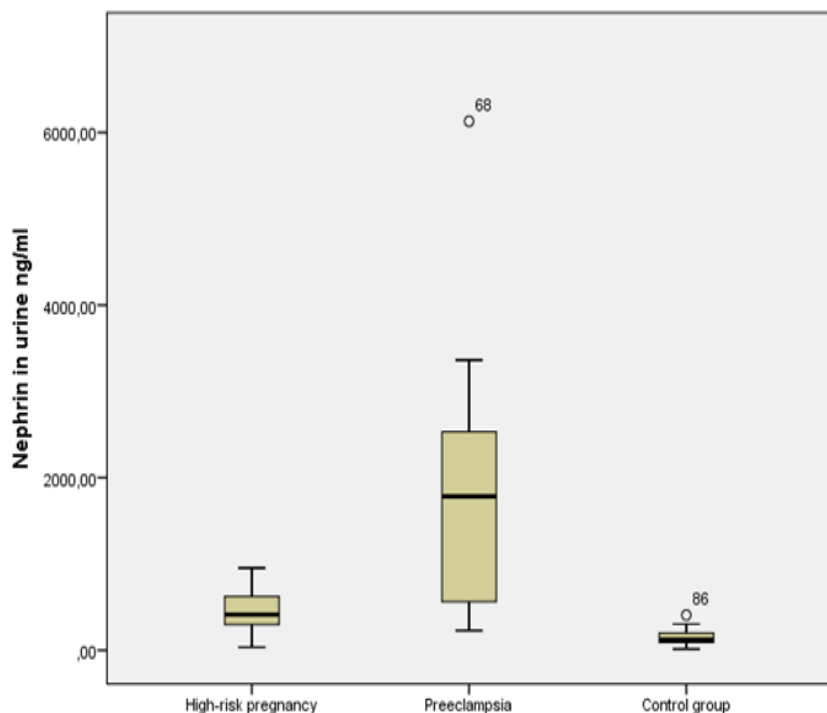


- **Statistical packages and methods – SPSS 17 and MedCalc Software, Kruskal-Wallis test (one-way ANOVA), Mann-Whitney U test, ROC analysis**



Results and Discussion

Levels of urinary nephrin in studied groups and subgroups of pregnant women



Urinary nephrin	n	\bar{x}	SD	Media n	p value
Second trimester PE	10	1850	1659	1711	<0.05
Second trimester high-risk pregnancy	21	414	192	409	

Urinary nephrin	n	\bar{x}	SD	Media n	p value
Third trimester PE	20	1845	980	2027	<0.05
Third trimester high-risk pregnancy	20	500	267	546	

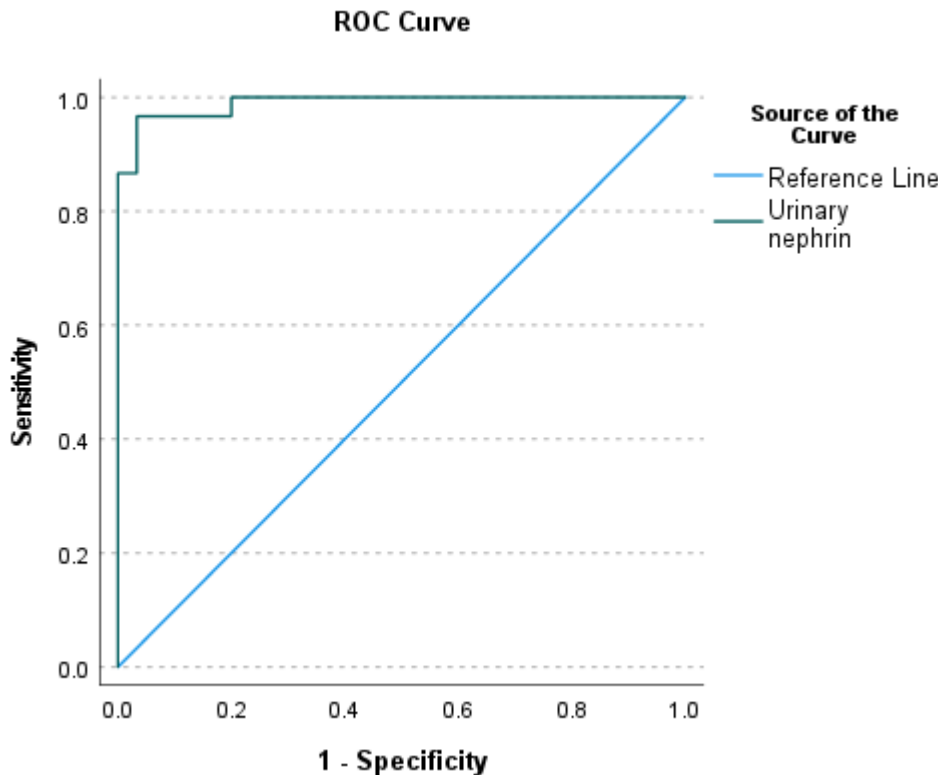
- ✓ Statistically significant difference in urinary nephrin levels, among studied groups and subgroups of pregnant women

Comparison of laboratory and clinical parameters

Laboratory and clinical parameters	Pregnant women with PE n=30	Women with a high-risk pregnancy n=41	Healthy pregnant women n=30	Kruskal - Wallis p value
Age (years)	27.7±4.7	29.1±5.6	29.4±6.0	0.376
BMI (kg/m ²)	29.3±4.6	29.9±3.6	25.7±3.3	<0.001
Blood glucose (mmol/L)	5.2±0.5	5.9±1.2	4.6±0.5	<0.001
UM/CR (mg/g)	214.3±160.3	169.0±271.7	15.8±11.0	<0.001
SBP (mm/Hg)	151.8±13.8	145.6±26.6	119±5.4	<0.001
DBP (mm/Hg)	95.1±7.4	90.1±13	77.3±6.0	<0.001
Total proteins (g/L)	67.6±7.2	69±6.2	68.3±5.5	0.562
Albumin (g/L)	34.2±5.1	35.4±4.7	39.1±4.1	0.001
Blood urea (mmol/L)	5.5±1.2	6.3±2.3	5.0±1.9	0.045
Blood creatinine (μmol/L)	70.7±9.2	69.4±11.9	56.8±4.6	<0.001
eGFR (mL/min/1.73m ²)	91.3±15.1	97.5±26.9	95.5±9.6	0.372
u-nephrin (ng/ml)	1846.7±1248.2	455.9±235.4	151.6±90.1	<0.001

Results are shown as mean ± SD. BMI - body mass index, UM/CR - urinary microalbumin to creatinine ratio, SBP - systolic blood pressure, DBP - diastolic blood pressure, eGFR - (estimated Glomerular Filtration Rate), u-nephrin - urinary nephrin

Non-parametric ROC analysis



ROC parameter	
AUC	0.990
95% CI	0.922-1
Significance level p (Area=0.5)	<0.0001
Youden index J	0.9333
Cut-off value	>304.6
Sensitivity (%)	96.7
Specificity (%)	96.7
NPV (%)	96.7
PPV (%)	96.7
Diagnostic effectiveness (accuracy) (%)	96.7

AUC- the area under the ROC curve, CI - confidence interval, NPV- negative predictive value, PPV- positive predictive value, u-nephrin - urinary nephrin

✓ High sensitivity and specificity of urinary nephrin in prediction of PE

Limitations and recommendations

Limitations of the study:

- small sample size,
- cross-sectional nature of study

Recommendations for future research:

- We recommend large, prospective studies in order to further assess the value of urinary nephrin in prediction of PE. If further studies confirm our preliminary results, urinary nephrin could be implemented in clinical and laboratory practice as a routinely biomarker for prediction of PE

Conclusions

With the preliminary results from this study:

- ✓ High percent of women with PE and women with a high-risk pregnancy had elevated levels of urinary nephrin,
- ✓ Higher urinary nephrin levels in women with PE compared to women with a high-risk pregnancy, and healthy pregnancies,
- ✓ Higher urinary nephrin levels in women with PE compared to women with a high-risk pregnancy in second and third trimester of pregnancy,
- ✓ Urinary nephrin had high sensitivity and specificity in prediction of PE

Nephrinuria could be important predictive tool for PE in a women with a high-risk pregnancy!

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Thank you for your attention!

