Angiogenetic Factors Ratio in Diabetic Pregnancies at Preeclampsia/Gestosis Risk: Searching for a best diagnostic cut off

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http://gestosis.ge/eng/26_5.php
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Preeclampsia/ EPHGestosis/ Rippmann Syndrome

Millions of Dreams every year are broken by PE

- 15% Preterm Birth
- 8.5 millions women/year globally
- 42% of Maternal Death

Diagnosis: BP/uP/E standard of care affected by poor accuracy

Diabetes in Pregnancy

- 6-7% Pregnancies complicated by Diabetes

RISK FACTORS

Who is at risk?

- Severe headache, vision disturbances
- High blood pressure
- Rapid weight gain, nausea, abdominal pain
- Protein in the urine
- Swollen hands and feet
- Diabetes

A simple blood test can predict:

- sFlt1/PLGF Ratio cut off

No financial relationships to disclose
BASICS OF EPH-GESTOSIS/RIPPMANN’s SYNDROME

EPH-Gestosis/Rippmann’s Syndrome is the most important complication, killer No. 1 for babies and mothers, it is important to know that the baby is 100 times more in danger than the mother. EPH-Gestosis is not a disease. It is a syndrome. The cardinal signs and symptoms edema (E), proteinuria (P) and hypertension (H) may appear simultaneously, singly. The causes of E, P and H are manifold. Therefore it is illogical and even harmful to treat such a heterogeneous group in just one way. The causes of cardinal signs and symptoms vary greatly according to population group and its location. They should be discovered before a next pregnancy.

Over 100 names of this syndrome, more than 50 classifications and various techniques to assess the signs and symptoms make it possible to compare results worldwide. This confusion prevents the science from progress.

The OG, World OGASH Board and CSPP (http://gestosis.ge/eng/26_4.php) has suggested a sensible nomenclature, classifications and definitions, which could overcome this barrier.

Nomenclature EPH Gestosis (EPH-syndrome: EPH-Complex, Rippmann’s Syndrome) Pregnancy Gest ...

Complicated oxis by Edema (E) Proteinuria (P) and Hypertension (H) Classification:

Symptomatic: Pathogenetic

1. Super-imposed EPH-Gestosis
2. Transient/essential EPH-Gestosis
3. (no signs and symptoms after puerperium)
4. Concomitant Diseases
5. Unclassified EPH-Gestosis

Mono EPH
Poly EP
EH
PH
EPH

E1 (Eclampsia imminent)
EC (Eclampsia convulsive)
BASICS OF EPH-GESTOSIS/RIPPMANN’s SYNDROME

Definitions:
Edema Excessive (inadequate) increase of body-weight during Pregnancy, usually Due to fluid retention, i.e. more than 500g/week. 2000g/month 13 kg/entire pregnancy Demonstrable pretibial edema are of gestosis origine, if they are still present after night's bedrest.
Proteinuria More than trace in one specimen. Preferably dipstick.

Hypertension Last normal reading 135/85 First pathological reading 140/90

In Hypertension Increase of 30 mmHg systolic Increase of 15 mmHg diastolic Since EPH-Gestosis/Rippmann’s Syndrome is rampant in the developing countries with little or no facilities for prenatal care the methods to detect E, P and H have to be simple and for everybody to be understood and to be carried out.

EPH-gestosis means high risk pregnancy. It might just mean the pregnant patient has to be watched and monitored closely. Such EPH-Gestosis can be detected at a very early stage and treated adequately.

It is mandatory to examine each patient thoroughly two to three months after delivery to exclude all conditions which could lead to EPH-Gestosis again in a future pregnancy.
PROGNOSIS Study validated the CUT-OFF values of Elecsys sFlt-1/PIGF Ratio, predictive/diagnostic of preeclampsia.
Placentomegalia and Diabetes

Hyperglycemia

Hyperinsulinemia

Placentomegalia

Increased PlGF

Underestimation of sFlt1/PIGF Ratio

18th World Congress of the Academy of Human Reproduction
Dublin, 3-6 April 2019
Our Study

**Study Group** 104 Diabetic Pregnancies

**Control Group** 80 Not Diabetic Pregnancies at Risk for Other Gestosis /PE Risk Factors

**Plasma Levels**
- **✓** PIGF
- **✓** sFLT-1
- **✓** RATIO sFLT-1/PIGF

«Gold Standard» for Gestosis/Preeclampsia Diagnosis:
- Proteinuria ≥ 300 mg/24h
- Blood Pressure ≥ 140/90 mmHg
Study Targets

To Evaluate the real match between clinical diagnosis and diagnostic value of the sFlt-1/PIGF Ratio

To Verify Diagnostic Sensibility of the sFlt-1/PIGF Ratio in Diabetic Pregnancies

To Identify a best diagnostic sFlt-1/PIGF Ratio cut-off, if any, in Pregnancies associated with Diabetes
sFlt-1/PIGF Ratio in diabetic pregnancies complicated by Preeclampsia

The real concordance between clinical diagnosis and ratio 110 resulted MODERATE in Diabetics

K of Cohen=0.522
**ROC Curves**

**Not Diabetic Pregnant Women**

Ratio = 110  →  Sens 84% e Spec 100%
Ratio = 87  →  Sens 95% e Spec 95%

**Diabetic Pregnant Women**

Ratio = 110  →  Sens 40,9% e Spec 100%
Ratio = 52  →  Sens 72,7% e Spec 95,1%
New Best cut-off ?

**NOT Diabetics**
- Ratio = 105
  - Sensibility: 86.5%
  - Specificity: 100%

**Diabetics**
- Sensibility: 45.5%
- Specificity: 100%

Concordance between Clinical Diagnosis / Ratio

**OPTIMUM**
- $K$ di Cohen = 0.873

**MODERATE**
- $K$ di Cohen = 0.568
Conclusions

- It seems to emerge the need to use a different cut-off ratio, for early identification of Gestosis / PE Syndrome in the Diabetic Group Pregnancies.

- Best cut-off corresponds to a ratio value of 105 which, maintaining a specificity of 100%, could significantly increase by 5% the test diagnostic sensibility in comparison with standard cut-off, by shifting from 40.9% to 45.5%.

- The increased sensibility of the new cut off ratio, seems to correlate significantly to increased diagnostic precocity, adequate and effective treatment and decreased fetal-maternal complications.

Our Works are still in progress!