BULLETIN

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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

The International Academy of Human Reproduction
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OGASH

2019

OGASH WORLD BOARD

Preeclampsia/ EPHGestosis/ Rippmann Syndrome

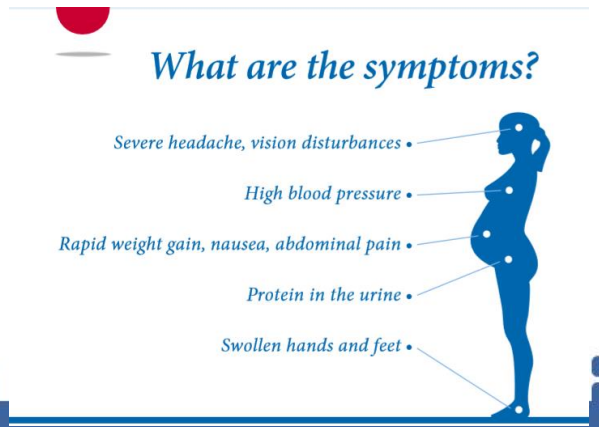
Millions of Dreams every year are broken by PE

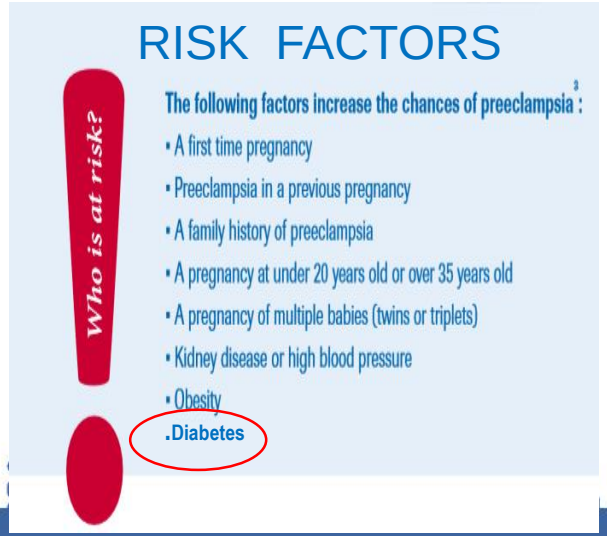
15%Preterm Birth

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

Pre-Pregnancy Diabetes

Tiype I

Type II

Gestational Diabetes

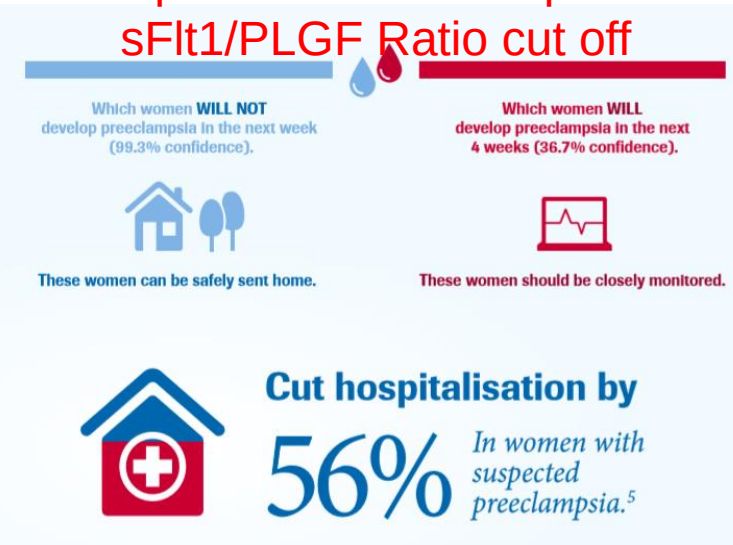
Manifest Diabetes

GDM

9,9 % complicated by Gestosis/PE

80% of women with suspected PE, will never develop it

A simple blood test can predict :
sFlt1/PLGF Ratio cut off



No financial relationships to disclose

BASICS OF EPH-GESTOSIS/RIPPMANN's SYNDROME 1.

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 that the mother. EPH-Gestosis is not a disease. It is a syndrome. The cardinal signs ands symptoms edema(E), proteinuria (P) and hypertension(H) may appear simultaneously, or singly. The causes of E, P and H are maynfold. 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 asses 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 osis by Edema (E) Proteinuria (P) and 1 lypertension(H) Classification:

Symptomatic: Pathogenetic

Mono EPH
Poly EP
EH
PH
EPH

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

El (Eclampsia imminent)
EC (Eclampsia convulsiva)

BASICS OF EPH-GESTOSIS/RIPPMANN's SYNDROME 2.

Definitions:

Edema Excessive(inadequate) increase of body-weight during Pregnancy, usually Due to fluid retension, 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

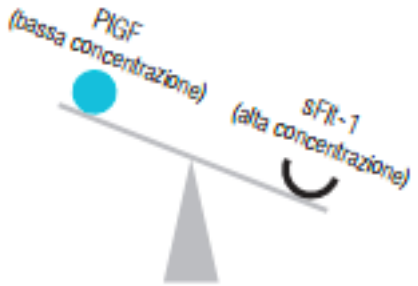
Proteinuria More than trace in one specimen. Preferably dipstick.

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 developping 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.



The Prognosis Study, 2016

sFlt-1/ PlGF Ratio reflects antiangiogenic imbalance in early or late PE

PROGNOSIS Study validated the CUT-OFF values of Elecsys sFlt-1/PlGF Ratio, predictive/diagnostic of preeclampsia

Early-onset preeclampsia – gestational week 20 – 33+6 days

sFlt-1/PlGF ≥ 85	Diagnosis	**99.5% specificity** the woman has preeclampsia Sensitivity: 88.0%
sFlt-1/PlGF < 85 ≥ 38	Prediction rule-in within next 4 weeks	**38.6% PPV** the woman is at high risk to develop preeclampsia within the next 4 weeks
sFlt-1/PlGF < 38	Prediction rule-out for the next 1 week	**99.1% NPV** the woman will not develop preeclampsia for the next 1 week

Late-onset preeclampsia – gestational week 34 to end of pregnancy

sFlt-1/PlGF ≥ 110	Diagnosis	**95.5% specificity** the woman has preeclampsia Sensitivity: 58.2%
sFlt-1/PlGF < 110 ≥ 38	Prediction rule-in within next 4 weeks	**38.6% PPV** the woman is at high risk to develop preeclampsia within the next 4 weeks
sFlt-1/PlGF < 38	Prediction rule-out for the next 1 week	**99.1% NPV** the woman will not develop preeclampsia for the next 1 week

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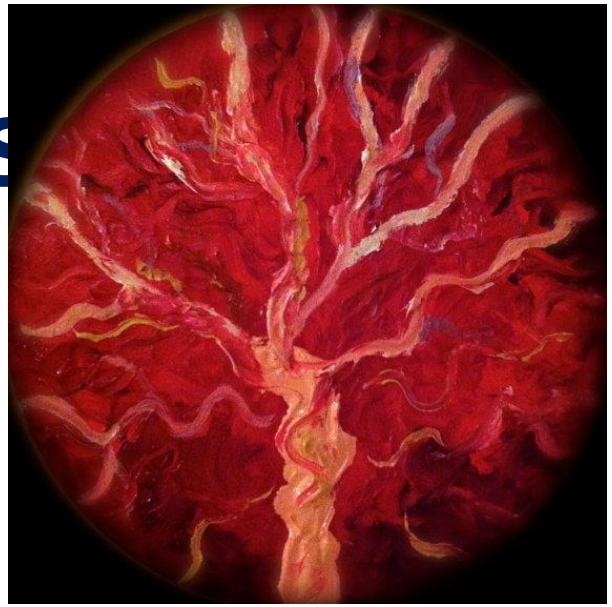
Placentomegalia and Diabetes



Hyperglycemia

+

Hyperinsulinism

→ Placentomegalia → Increased PlGF → Underestimative sFlt1/PlGF Ratio

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Our Study

Study Group → ***104 Diabetic Pregnancies***

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

Plasma Levels

- ✓ ***PlGF***
- ✓ ***sFLT-1***
- ✓ ***RATIO sFLT-1/PlGF***

«Gold Standard» for Gestosis/Preeclampsia Diagnosis:

Proteinuria ≥ 300 mg/24h Blood Pressure ≥ 140/90 mmHg

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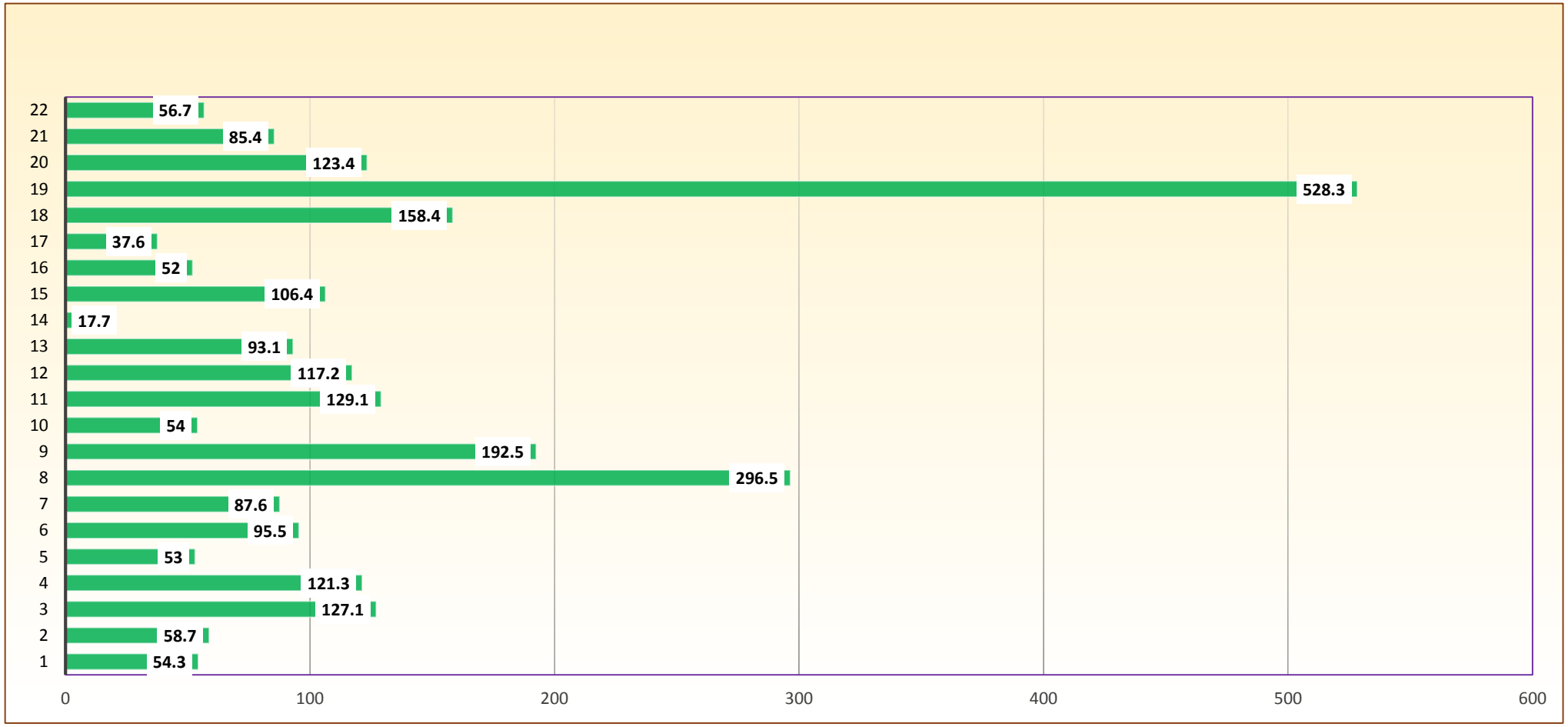
Study Targets

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

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

To Identify a best diagnostic sFlt-1/PlGF Ratio cut-off, if any, in Pregnancies associated with Diabetes

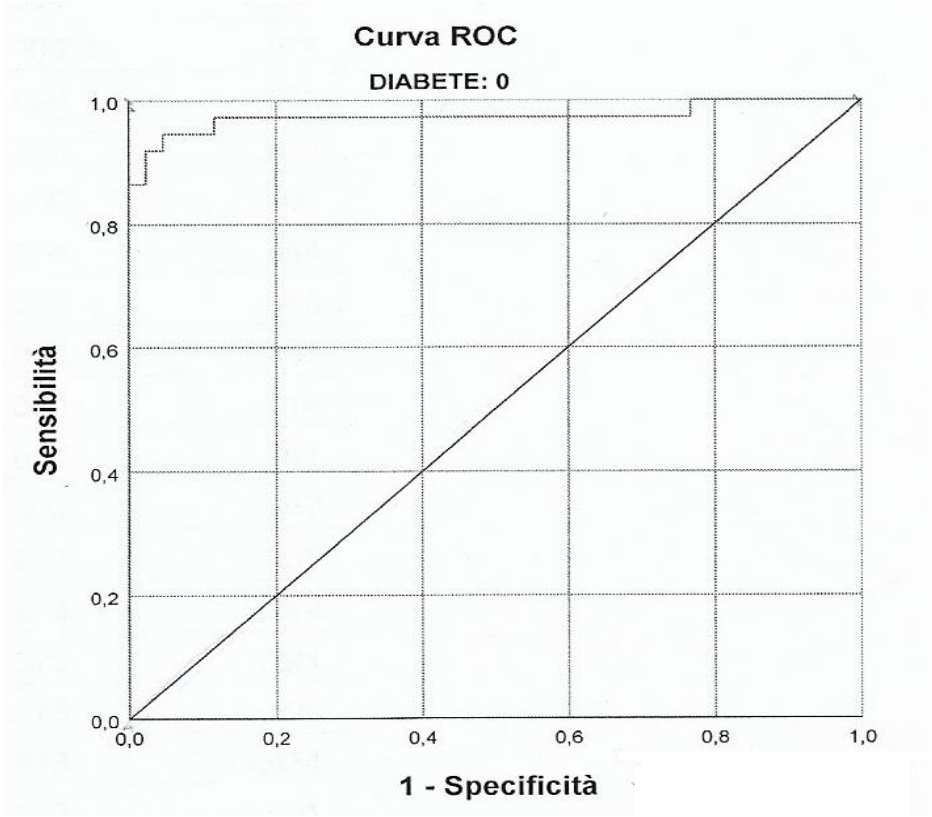
sFlt-1/PlGF Ratio in diabetic pregnancies complicated by Preeclampsia



The real concordance between clinical diagnosis and ratio 110 resulted MODERATE in Diabet
K of Cohen=0,522

ROC Curves

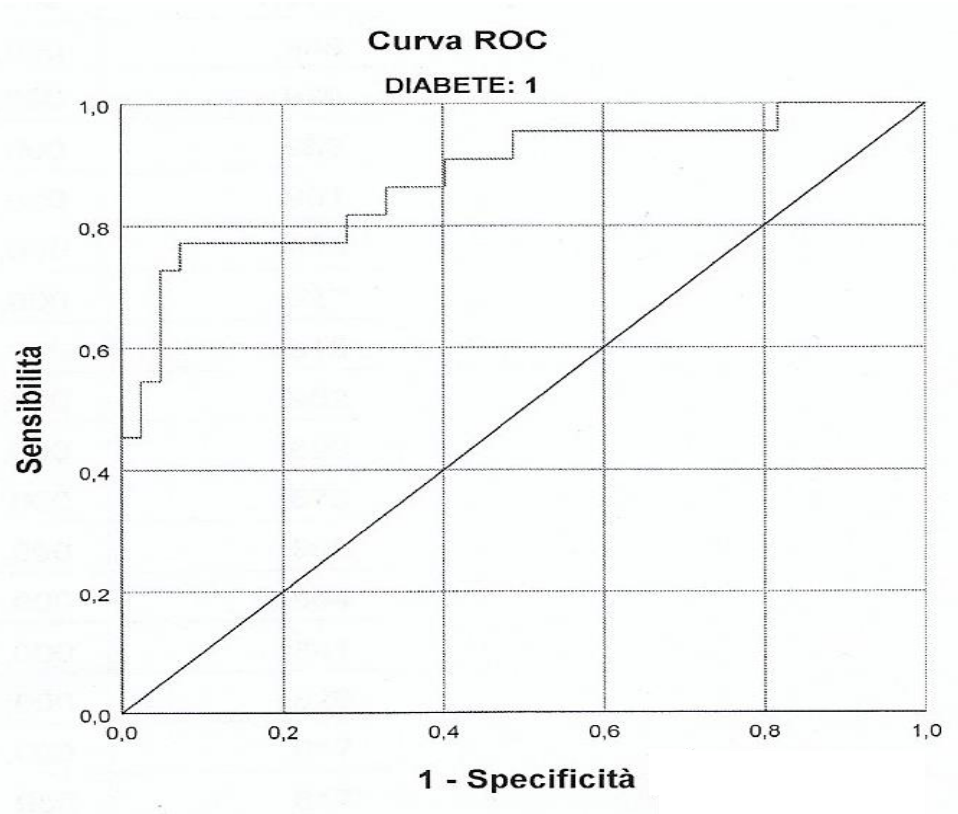
Not Diabetic Pregnant Women



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 ?

Ratio=105

NOT Diabetics
Pgs
Sensibility 86,5%
Specificity 100%

Diabetics
Pgs
Sensibility 45,5%
Specificity 100%

Concordance between Clinical Diagnosis /Ratio

OPTIMUM
K di Cohen=0,873

MODERATE
K di Cohen=0,568

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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, mainteining a specificity of 100%, could significantly increase of 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

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Thank You for Your Attention !