The present disclosure, in a second aspect, relates to a method for diagnosing whether a pregnant subject is not at risk for preeclampsia within a short window of time comprising:

a) determining the amounts of the biomarkers (i) sFlt-1 and P1GF or (ii) Endoglin and PlGF in a sample of said subject;

b) calculating a ratio from said amounts of (i) sFlt-1 and P1GF or (ii) Endoglin and PlGF determined in the sample in step a); and

c) comparing the value of the ratio with a reference value, whereby a subject being not at risk for developing preeclampsia within a short period of time is diagnosed if the value of the ratio is identical or decreased compared to the reference value, wherein said reference allows for making the diagnosis with a negative predictive value of at least about 98%.

The present disclosure, in a ~~second~~ third aspect, relates to use of at least one of the biomarkers sFlt-1, Endoglin and PlGF or at least one detection agent therefor which specifically bind thereto in a sample obtained from ~~of~~ a pregnant subject for diagnosing whether said subject is not at risk for developing preeclampsia within a short period of time.

The present disclosure, in a ~~third~~ fourth aspect, relates to a device adapted for diagnosing whether a pregnant subject is not at risk for developing preeclampsia within a short period of time by carrying out the method as defined herein comprising:

a) an analyzing unit comprising at least one detection agent which specifically binds to at least one angiogenesis biomarker selected from the group consisting of: sFlt-1, Endoglin and PlGF, said unit being adapted for determining the amount of sFlt-1, Endoglin and/or PlGF in a sample of a pregnant subject; and

b) an evaluation unit comprising a data processor having implemented an algorithm for comparing the amount with a reference, whereby a subject being not at risk for developing preeclampsia within a short period of time is diagnosed if the amount is identical or decreased compared to the reference in the cases of sFlt-1 and Endoglin and identical or increased in the case of PlGF, wherein said reference allows for making the diagnosis with a negative predictive value of at least about 98%.

The present disclosure, in a ~~fourth~~ fifth aspect, relates to a kit adapted for carrying out the method as defined herein comprising at least one detection agent for determining the amount of an angiogenesis biomarker selected from the group consisting of: sFlt-1, Endoglin and PlGF, as well as instructions for carrying out the said method.

The term "preeclampsia" as used herein refers to a medical condition which is characterized by hypertension and proteinuria. Preeclampsia occurs in pregnant female

Claims

1. A method for diagnosing whether a pregnant subject is not at risk for preeclampsia within a short window of time comprising:

a) determining the amount of at least one angiogenesis biomarker selected from the group consisting of sFlt-1, Endoglin and PlGF in a sample of said subject; and

b) comparing the amount with a reference, whereby a subject being not at risk for developing preeclampsia within a short period of time is diagnosed if the amount is identical or decreased compared to the reference in the cases of sFlt-1 and Endoglin and identical or increased in the case of PlGF, wherein said reference allows for making the diagnosis with a negative predictive value of at least about 98%.

2. ~~The~~ A method ~~of claim 1, wherein said method comprises in step~~ for diagnosing whether a pregnant subject is not at risk for preeclampsia within a short window of time comprising:

a) ____determining the amounts of the biomarkers (i) sFlt-1 and P1GF or (ii) Endoglin and PlGF in ~~the~~ a sample of said subject;

b) ____calculating a ratio from said amounts of (i) sFlt-1 and P1GF or (ii) Endoglin and PlGF determined in the sample in step a); and ~~in step~~

c) ____comparing the value of the ratio with a reference value, whereby a subject being not at risk for developing preeclampsia within a short period of time is diagnosed if the value of the ratio is identical or decreased compared to the reference value, wherein said reference allows for making the diagnosis with a negative predictive value of at least about 98%.

~~3. The method of claim 2, wherein said method comprises prior to step b) the further step of calculating a ratio from said amounts of sFlt-1 or Endoglin and PlGF determined in the sample in step a).~~

43. The method of claim 2 ~~or 3~~, wherein said reference value is about 46 or less, preferably, is about 33.

~~5~~4. The method of ~~any one of~~ claims 2 ~~to~~or 43, wherein said reference value is about 38 or less, preferably is about 38.

~~6~~5. The method of any one of claims 1 to ~~5~~4, wherein said short period of time is a time period from about 1 to about 2 weeks.

~~7~~6. The method of any one of claims 1 to ~~6~~5, wherein said pregnant subject is between about week 20 and about week 40 of gestation.

~~8~~7. The method of any one of claims 1 to ~~7~~6, wherein said sample is a blood, plasma, serum or urine sample.

~~9~~8. The method of any one of claims 1 to ~~8~~7, wherein said method further comprises recommending a patient management measure based on the diagnosis.

~~10~~9. The method of claim ~~9~~8, wherein said patient management measure (i) is selected from the group of the following measures if the subject is not diagnosed as being not at risk for developing preeclampsia: close monitoring, hospitalization, administration of blood pressure reducing agents and life style recommendations, and (ii) is ambulant monitoring if the subject is diagnosed as being not at risk for developing preeclampsia.

~~11~~10. Use of at least one of the biomarkers sFlt-1, Endoglin and PlGF or at least one detection agent therefor which specifically bind thereto in a sample ~~of~~ obtained from a pregnant subject for diagnosing whether said subject is not at risk for developing preeclampsia within a short period of time.

~~12~~11. The method of any one of claims 1 to ~~10~~9 or the use of claim ~~11~~10, wherein said subject has been identified to be at risk for developing preeclampsia, eclampsia and/or HELLP syndrome based on abnormal Doppler ultrasonography results.

~~13~~12. A device adapted for diagnosing whether a pregnant subject is not at risk for developing preeclampsia within a short period of time by carrying out the method of any one of claims 1 to ~~10~~9 or ~~12~~11 comprising:

a) an analyzing unit comprising at least one detection agent which specifically binds to at least one angiogenesis biomarker selected from the group consisting of: sFlt-1, Endoglin and PlGF, said unit being adapted for determining the amount of sFlt-1, Endoglin and/or PlGF in a sample of a pregnant subject; and

b) an evaluation unit comprising a data processor having implemented an algorithm for comparing the amount with a reference, whereby a subject being not at risk for developing preeclampsia within a short period of time is diagnosed if the amount is identical or decreased compared to the reference

in the cases of sFlt-1 and Endoglin and identical or increased in the case of PlGF, wherein said reference allows for making the diagnosis with a negative predictive value of at least about 98%.

~~14~~13. The device of claim ~~13~~12, wherein said analysing unit comprises detection agents for determining the amounts of the biomarkers(i) sFlt-1 and P1GF or (ii) Endoglin and PlGF in the sample of said subject and wherein said algorithm implemented in the evaluation unit compares the value of ratio of the amount of (i) sFlt1 and P1GF or (ii) Endoglin and PlGF with a reference value, whereby a subject being not at risk for developing preeclampsia within a short period of time is diagnosed if the value of the ratio is identical or decreased compared to the reference value.

~~15~~14. The device of claim ~~13~~12 or ~~14~~13, wherein said algorithm implemented in the evaluation unit further calculates a ratio of the amount of (i) sFlt1 and P1GF or (ii) Endoglin and PlGF.

~~16~~15. A kit adapted for carrying out the method of any one of claims 1 to ~~10~~9 or ~~12~~11 comprising at least one detection agent for determining the amount of an angiogenesis biomarker selected from the group consisting of: sFlt-1, Endoglin and PlGF, as well as instructions for carrying out the said method.

~~17~~16. The kit of claim ~~16~~15, wherein said kit comprises a detection agent for determining the amount of sFlt1 and/or Endoglin and a detection agent for determining the amount of PlGF in a sample of a pregnant subject.