

Identification of low PAPP-A MoM and allocation of pregnant women to high risk care and serial growth scans

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Key Amendments

Date	Amendments	Approved by

Summary and purpose

- A low level (< 5th centile) of the first trimester marker PAPP–A should be considered a major risk factor for delivery of a SGA neonate and a risk factor for other adverse pregnancy outcome.
- The 5th centile equates to 0.4 MoM and the 1st centile to 0.2 MoM.
- To provide information on potential adverse outcome associated with a low PAPP-A for clinicians and parents.
- To provide a pathway for appropriate notification of results, referral for Consultant led care and a pathway for implementation of appropriate surveillance to prompt early identification and management of potential adverse outcomes.
- To reduce maternal and fetal mortality and morbidity by increased surveillance and intervention where appropriate

Background

Pregnancy associated plasma protein A (PAPP-A) is a placental glycoprotein produced by syncytial trophoblast of the placenta, which cleaves insulin-like growth factor binding protein 4 (IGFBP4) and is a positive regulator of insulin-like growth factors (IGFs)¹, potentially influencing fetal growth and wellbeing.

Studies have tested the hypothesis that low maternal serum levels of PAPP-A in the first trimester are prognostic factors for adverse pregnancy outcomes associated with poor placental function²⁻⁶. International Guidelines on “The Investigation and Management of the Small for Gestational Fetus” have recommended that pregnant women with a serum PAPP-A <0.4MoM (5th centile) in the first trimester receive increased ultrasound surveillance for fetal growth disorders⁷.

In a large series of 49 801 women at 11+0 to 13+6 weeks, low PAPP–A (but not beta HCG) was inversely associated with risk of being small for gestational age (SGA). Using a 5th centile (0.415 MoM) cut off, ORs for a SGA infant (birthweight < 10th centile) and severe SGA (birthweight < 3rd centile) were 2.7 and 3.66 respectively¹).

<p>Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information and/or Key Document intranet page, which will provide approval and review information.</p>
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As a result of national recommendations for PAPP-A MoM to be included in the risk assessment for SGA in both the RCOG SGA guideline³ and the Savings Babies' lives stillbirth care bundle⁴, we will offer all women with a PAPP-A <5th centile serial growth scans.

At present in UK practice, PAPP-A is only used as part of combined screening for fetal chromosome anomaly (trisomies 21,18 and 13) and not as a biomarker for adverse outcome. Before any test (either individual or as a model) is introduced in this capacity into practice there must be an assessment of the interventions that may be introduced e.g. increased surveillance or pharmacological, to ensure that screening in a population is justified and these interventions must be effective in the group identified as high risk via the test or model. At present although aspirin has been suggested as a possible intervention in certain groups (e.g. those at high risk of pre-eclampsia based on previous history) there is no evidence for the effectiveness in a group selected by either PAPP-A as a stand-alone test or a model including PAPP-A.

This pathway details identifying low results and the process for ensuring all women receive appropriate antenatal care following a low PAPP-A level.

This pathway only applies to women with an isolated low PAPP-A i.e. whose combined test gives a low risk for trisomy 21, 18 and 13 and in whom the nuchal translucency was normal . If women are **high risk for chromosomal aberrations or had a NT > 3.5 mm** they should follow established pathways linking with fetal medicine. If further investigations / screening are normal with a low PAPP-A MoM they should have additional screening for SGA, this should be actioned by the screening team.

Pathway:

The antenatal screening midwives will identify any women with a low PAPP-A Mom using a 0.4 MoM cut off as the 5th centile and 0.2 MoM the 1st centile.

1. The screening midwives will obtain the hospital notes pertaining to these results.
2. Low PAPP-A MoM will be documented clearly in the hospital record.
3. Women will be sent a leaflet (Appendix 1) and the GP will be sent a letter (Appendix 2) explaining the result and a consultant clinic appointment with serial scans will be arranged.
4. Commencement on low dose aspirin will be recommended.

Antenatal clinic appointment plan schedule

20 weeks

- Seen in Consultant ANC, results explained (see patient information leaflet Appendix 1).
- Smoking cessation advice given if applicable.

Serial scans undertaken as per detection of IUGR (28/34/38 weeks)

- Induction of labour should be recommended at 40 weeks.

If PAPP-A less than 0.2 MoM for consideration of uterine artery Doppler and increased frequency of growth scans. These patients need a personalised plan of management and this may involve IOL earlier than 40 weeks.

Implementation and Audit

This process will be implemented from the 1st April 2018

A database will be kept by the screening midwives and an audit of the process will be conducted 6 months following the implementation of this pathway to assess compliance.

References

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- RCOG. The Investigation and Management of the Small-for-Gestational-Age Fetus. *Greentop Guideline NO 31: RCOG; 2014.*
- Saving Babies' Lives A Care Bundle for reducing stillbirth. NHS England Published 21/3/2016. <https://www.england.nhs.uk/wp-content/uploads/2016/03/saving-babies-lives-car-bundl.pdf>

Related guidance

- Saving Babies Lives Care bundle: Standard Operating Procedure
- IUGR Detection and Management of Small for Gestational Age Fetuses Guideline

Appendix 1 – Low PAPP-A Patient Information Leaflet



Low PAPP-A Leaflet



Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information and/or Key Document intranet page, which will provide approval and review information.

You have been given this leaflet because your recent combined screening blood test has shown that you have low PAPP-A levels. Please read this information carefully and if you have any further questions you should contact the Antenatal screening team (telephone number opposite).

What is PAPP-A?

PAPP-A is a protein produced by the placenta (afterbirth). It is one of the hormones that are measured during the 12 week combined screening test.

Low PAPP-A can be associated with Down's syndrome. You are low risk for this but the test has given us more information about your pregnancy in other ways.

Research tells us that in **some** women with low PAPP-A the placenta may not work as well as it should so they **may** be affected by:

- Low birth weight babies
- Raised blood pressure and protein in the urine, known as pre-eclampsia.

The risk of these complications is still small but we would like to offer you extra care during your pregnancy to monitor you more closely.

What will this mean for my pregnancy?

You will now be placed under the care of a Consultant Obstetrician and you will be sent an appointment to see them after your detailed scan, usually between 22-24 weeks. This will give you the opportunity to ask questions and discuss the plan of care for the rest of your pregnancy. In the meantime we will write to your GP to inform them and also ask them to prescribe you 75mg of Aspirin to take once a day until delivery. This is because Aspirin can help the way the placenta works and reduce the risk of complications.

In addition you will be offered a series of growth scans to monitor the growth of your baby and the liquor volume (water around baby).

During your pregnancy we will continue to check your blood pressure and urine at your routine antenatal appointments. This is so any changes can be identified at an early stage.

Who can I speak to for further information?

We understand that receiving the news that you have low PAPP-A levels may be worrying but please be reassured by the close surveillance that you are going to receive and that the majority of babies will have normal growth.

However, if you would like to speak a member of the Antenatal Screening team further please call **01905 768945**.

Patient Experience

Being admitted to hospital can be a worrying and unsettling time. If you have any concerns or questions you should speak to a member of staff in the ward or department who will do their best to reassure you. If you are not happy with their response, you can ask to speak to someone in charge.

Patient Advice and Liaison Service (PALS)

Our PALS staff will provide advice and can liaise with staff on your behalf if you feel you are unable to do so. They will also advise you what to do if your concerns have not been addressed. If you wish to discuss making a formal complaint PALS can provide information on how to do this. Telephone: 0300 123 1732. Monday to Thursday 8.30am to 4.30pm. Friday 8.30am to 4pm.

An answerphone operates outside office hours. Or email us at: wah-tr.PET@nhs.net

Feedback

Feedback helps us highlight good practice and where we need to improve. There are lots of ways you can give feedback including completing a Friends and Family Test card or undertaking a survey. For further information please speak to a member of staff, see our Patient Experience leaflet or visit www.worcsacute.nhs.uk/contact-us

If you would like this leaflet in an alternative language or format, such as audio or braille, please ask a member of staff.

Polish

Jeżeli są Państwo zainteresowani otrzymaniem niniejszej ulotki w innej wersji językowej lub formacie, prosimy zwrócić się w tej sprawie do członka naszego personelu.

Bengali

আপনি যদি এই লিফলেটটি অন্য ভাষায় বা ফর্ম্যাটে পেতে চান যেমন, অডিও বা ব্রেইল তাহলে অনুগ্রহ করে সদস্য বা কর্মীদেরকে তা জানান।

Urdu

اگر اس کتابچہ کو آپ کسی متبادل زبان یا ہیئت جیسے آڈیو یا بریل میں چاہتے ہیں، تو برائے کرم اسٹاف رکن سے مانگیں۔

Romanian

Pentru a obține această broșură în altă limbă sau în alt format fie audio sau limbajul Braille, vă rugăm să apelați la un membru al personalului.

Portuguese

Caso deseje este folheto numa língua ou formato alternativos, tal como ficheiro áudio ou em Braille, por favor dirija-se a um dos nossos funcionários.

Chinese(Mandarin)

如果您想要本手册的替代语言或格式的版本，如音频或盲文，请向工作人员咨询

WAHT- Version Review Date
<http://www.worcsacute.nhs.uk>

Appendix 2 – Low PAPP-A GP letter



Worcestershire Royal Hospital
Charles Hastings Way
Worcester
WR5 1DD

Date

Dear

We are writing to inform you that your pregnant patient
DOB.....has been identified as having Low PAPP-A. We have already contacted her to inform her of this and provided her with an information leaflet.

As a result of this she will need to be commenced on low dose Aspirin 75mgs OD. This is because low PAPP-A can be a marker of poor placental function and therefore the Aspirin can reduce the risk of both growth restriction and pre-eclampsia. We would be most grateful if you could arrange this prescription.

A Consultant Obstetrician will see her between 22-24wks. This appointment will automatically be sent out. There is no need to do a referral.

Kind Regards

Antenatal Screening Midwives
Worcestershire Acute Hospitals NHS Trust
01905 768945