Low PAPP-A

This guidance does not override the individual responsibility of health professionals to make appropriate decision according to the circumstances of the individual patient in consultation with the patient and /or carer. Health care professionals must be prepared to justify any deviation from this guidance.

Introduction

Guideline for management of Low PAPP-A.
For Patient Information, signpost to Low PAPP-A - Worcestershire Acute Hospitals NHS Trust (Translatable through the browser, also available in Badgernet)

This guideline is for use by the following staff groups:

Midwives
Doctors

Lead Clinician(s)

Dr Anna Fabre Gray	Consultant Obstetrician
Dr Manisha Rasheed	Clinical Fellow – Obstetrics
Dr Reham Marie	Consultant Obstetrician

Approved by *Maternity Governance Meeting* on:	24th October 2025
Approved by Medicines Safety Committee on:	N/A
Review Date: This is the most current document and should be used until a revised version is in place	24th October 2028

Key amendments to this guideline

Date	Amendment	Approved by:
Nov 2019	Updated guidance	MGM
Oct 2025	Updates to management of Low PAPP-A with Normal growth scans (can return to normal pathway)	MGM

Inclusion statement

We recognise that although our policy uses words such as women/woman, not all birthing people or post-natal parents will identify as such. We encourage all staff to be welcoming of the diversity of our local population, be respectful of preferred language, pronouns, and adapt their communication appropriately. All staff should accommodate mothers and parents with individual needs or disabilities, whether they be physical or not visible, and adapt their care to support them with their pregnancy.

Contents

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), releasing IGF from its inhibitor 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 function [2-6]. 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 disorders[7].

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 respectively[1]).

As a result of national recommendations for PAPP-A MoM to be included in the risk assessment for SGA in both the RCOG SGA guideline[3] and the Savings Babies' lives stillbirth care bundle[4], 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 PAPP-A result below 0.4 MoM

1. The results are generated from the woman's first trimester combined screening and is a bi-product result. From this result Low Papp-A will be actioned.
2. Low PAPP-A MoM will be documented clearly in the Badgernet record.
3. Women will be sent a leaflet, and the GP will be sent a letter (Appendix 1) explaining the result and a consultant clinic appointment with serial scans will be arranged.
4. Commencement on low dose aspirin will be recommended as per Aspirin SOP.
5. Screening team will request uterine artery dopplers for by 24wks.

Antenatal clinic appointment plan schedule

20 weeks

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

Serial scans undertaken as per detection of IUGR (32/36/39 weeks).

If PAPP-A less than 0.4 MoM for consideration of uterine artery Doppler and growth scans from 28/40 if abnormal uterine artery doppler.

Where normal growth and no other risk factors, discharge to MLC/routine care pathway.

References

- Lawrence JB, Oxvig C, Overgaard MT, Sottrup-Jensen L, Gleich GJ, Hays LG, et al. The insulin-like growth factor (IGF)-dependent IGF binding protein-4 protease secreted by human fibroblasts is pregnancy-associated plasma protein-A. Proceedings of the National Academy of Sciences of the United States of America. 1999 Mar 16;96(6):3149-53.

- Dugoff L, Hobbins JC, Malone FD, Porter TF, Luthy D, Comstock CH, et al. First-trimester maternal serum PAPP-A and free-beta subunit human chorionic gonadotropin concentrations and nuchal translucency are associated with obstetric complications: a population-based screening study (the FASTER Trial). Am J Obstet Gynecol. 2004 Oct;191(4):1446-51.

- Krantz D, Goetzl L, Simpson JL, Thom E, Zachary J, Hallahan TW, et al. Association of extreme first-trimester free human chorionic gonadotropin-beta, pregnancy-associated plasma protein A, and nuchal translucency with intrauterine growth restriction and other adverse pregnancy outcomes. Am J Obstet Gynecol. 2004 Oct;191(4):1452-8.

- Smith GC, Shah I, Crossley JA, Aitken DA, Pell JP, Nelson SM, et al. Pregnancy-associated plasma protein A and alpha-fetoprotein and prediction of adverse perinatal outcome. Obstet Gynecol. 2006 Jan;107(1):161-6.

- Barrett SL, Bower C, Hadlow NC. Use of the combined first-trimester screen result and low PAPP-A to predict risk of adverse fetal outcomes. Prenat Diagn. 2008 Jan;28(1):28-35.

- Spencer CA, Allen VM, Flowerdew G, Dooley K, Dodds L. Low levels of maternal serum PAPP-A in early pregnancy and the risk of adverse outcomes. Prenat Diagn. 2008 Nov;28(11):1029-36.

- Bilagi A, Burke DL, Riley RD, Mills I, Kilby MD, Morris RK. Association of maternal serum PAPP-A levels, nuchal translucency and crown rump length in first trimester with adverse pregnancy outcomes: Retrospective cohort study. Submitted to BJOG August 2016.

- 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

Fetal Growth Restriction (FGR)

Appendix 1: GP Letter

Worcestershire Acute Hospitals NHS Trust

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 150mgs 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 from 20 weeks gestation. 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

Monitoring

Page/ Section of Key Document	Key control:	Checks to be carried out to confirm compliance with the Policy:	How often the check will be carried out:	Responsible for carrying out the check:	Results of check reported to: *(Responsible for also ensuring actions are developed to address any areas of non-compliance)*	Frequency of reporting:
	WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
	New Process of Low Papp-A management	Local Audit	6 monthly	Junior Doctors	Maternity Audit Meeting	6 Months

Contribution List

This key document has been circulated to the following individuals for consultation;

Designation
Maternity Governance Meeting
Maternity Guidelines Committee

This key document has been circulated to the chair(s) of the following committee's / groups for comments;

Committee
Maternity Quality Governance Meeting