Chickenpox in Pregnancy - Full Clinical Guideline

Reference no.: UHDB/07:23/C3

Contents

1. Introduction

Varicella, the primary infection with herpes varicella zoster virus, in pregnancy may cause maternal mortality or serious morbidity. It may also cause fetal varicella syndrome and varicella infection of the newborn, previously known as neonatal/congenital varicella.

2. Purpose and outcomes

- The guideline aims to ensure that staff are aware of the management of pregnant women who either develop chickenpox or are at a high risk of developing it
- To maintain a multidisciplinary approach to care
- To reduce the incidence of perinatal and maternal morbidity and mortality associated with chickenpox in pregnancy

3. Abbreviations

FVS - Fetal varicella syndrome

HZ - Herpes Zoster
Ig G - Immunoglobulin G
Ig A - Immunoglobulin A
VZ - Varicella zoster
VZIG - Varicella Zoster Immune Globulin
VZV - Varicella zoster virus

4. Definitions used

- **Varicella zoster** (varicella): The primary infection with herpes varicella zoster virus (VZV)
- **VZV**: DNA virus of the herpes family
- **Herpes zoster** (HZ) **/ zoster / shingles**: Reactivation of the primary varicella infection to cause a vesicular erythematous skin rash in a dermatomal distribution.
- **VZIG**: Human immunoglobulin product manufactured from the plasma of non-UK donors with high VZV antibody titres
- **Fetal varicella syndrome** (FVS): If the pregnant woman develops varicella or shows serological conversion in the first 28 weeks of pregnancy, she has a small risk of fetal varicella syndrome which is characterised by one or more of the following:
    - Skin scarring in a dermatomal distribution
    - Eye defects (microphthalmia, chorioretinitis, cataracts)
    - Hypoplasia of the limbs
    - Neurological abnormalities (microcephaly, cortical atrophy, mental retardation and dysfunction of bowel and bladder sphincters).
- **Varicella infection of the newborn**: VZV infection in early neonatal life resulting from maternal infection near the time of delivery or immediately postpartum or from contact with a person other than the mother with chickenpox or shingles during this time
- **Significant contact**: Contact with an infected person in the same room for 15 minutes or more, face to face contact and contact in setting of a large open ward.

5. Key Responsibilities/Duties

- Medical staff to be aware of the indications for VZIG in susceptible pregnant women
- Doctor to be aware of indications, dose and duration of aciclovir for treatment of pregnant women with chickenpox
- Doctor to consider admitting pregnant women with chickenpox who are at high risk of complications
- Medical staff to liaise with Consultant Virologist if any doubt or advice uncertain

6. Background

6.1 Mode of infection and clinical features

- VZV is highly contagious and transmitted by respiratory droplets and by direct personal contact with vesicle fluid or indirectly via fomites.
- The incubation period is 1-3 weeks and the disease is infectious 48 hours before the rash appears and continues to be infectious until the vesicles crust over (usually about 5 days).
- The primary infection is characterised by fever, malaise and a pruritic rash that develops into crops of maculopapules which become vesicular and crust over before healing.

6.2 Complications of chickenpox in pregnancy

Primary varicella zoster (VZ) infection in pregnancy can be associated with an adverse outcome in three possible ways:

- **Maternal VZ infection**:

Primary VZ infection is much less common in adults but it is associated with greater morbidity,namely pneumonia, hepatitis andencephalitis.
Pneumonia occurs in approximately 10% of pregnant women with chickenpox and severity increases with advancing gestation. Mechanical ventilation may be required and mortality rates between 3-14% have beenreported

- **Fetal Varicella Syndrome**
  The risk is estimated to be approximately 1-2% upto 20 weeks. The risk isless than 1% if maternal infection occurs in first trimester and is not associated with an increased risk of spontaneous miscarriage at this time. FVS is extremely rare if maternal infection occurs between20 and 28 weeks. No case of FVS has been reported when maternalinfection has occurred after 28 weeks. FVS does not occur at the time of the initial fetal infection but results from a subsequent herpes zoster reactivation in utero and only occurs in a minority of infected fetuses. The prenatal diagnosis of FVS is essentially by ultrasound. Cordocentesis and amniocentesis for VZ antibodies are of limited value.

- **Varicella Infection of the Newborn**
  Transplacental passage of the virus appears to increase as gestationadvances. Risk of severe neonatal infection is greatest when the onset of the rash is5 days before and up to 2 days after delivery. Babies with no clinical evidence of varicella infection at birth can develop HZ in infancy, consistent with reactivationof the virus after a primary infectionin-utero.

7. <u>Recommendations</u>

7.1 Pre-conceptual management of a woman found to be seronegative for varicella-zoster virus Immunoglobulin G (VZV IgG):

- Consider varicella vaccination which consists of two injections 4-8 weeks apart. Pregnancy should be avoided for at least 4 weeks following the second vaccination because the vaccine contains a live attenuated virus.

7.2 Management of a pregnant woman with no/doubtful past medical history of chickenpox or known to be seronegative for VZV IgG

- Varicella vaccination should not be given during pregnancy because it contains a live attenuated virus
- Advise to avoid contact with chickenpox and shingles during pregnancy and to inform healthcare professionals of any potential exposure without delay

7.3 Management of a pregnant woman following significant contact with chickenpox or shingles

- Any pregnant woman who comes into contact with chickenpox or shingles must havea careful childhood and recent contact history taken.
- It is very important to elucidate the contact history with particular respect to the certainty of the infection, the infectiousness (vesicular rash or development of rash within 48 hours of contact) and the degree of exposure. It is important to know exactly when contact with the infected individual occurred.
- If the pregnant woman has a previous history of chickenpox or shingles, she is immune to primary VZ infection and no further action need be takenbut she should be asked to notify her doctor or midwife early if a rash develops.
- If the pregnant woman has no/doubtful previous history of varicella, then check serum for VZV IgG. At least 80-90% of women will be positive and can be reassured. The virology laboratory maybe able to use serum stored from booking antenatal bloods thus saving time. Contact either the virology lab, or Consultant Virologist. If a new sample is required, send 10mls of clotted blood (red top bottle) to Microbiology.

History	Testing	Treatment
A history of chickenpox or shingles or 2 recorded doses of varicella vaccine	Do not test.	Assume immune. No need for PEP.
Uncertain or no history of chickenpox or shingles and Unknown or negative varicella vaccine history	Test antenatal booking bloods* (if available) for VZV IgG.	If VZV IgG positive – reassure, patient is immune, do not issue PEP. If VZV IgG negative or equivocal on a qualitative assay, retest with a confirmatory quantitative assay. If quantitative assay is ≥100 mIU/ml – reassure, PEP is not indicated. If the result from quantitative testing will not be available within 10 days of exposure, AND the individual is VZV IgG negative (qualitative testing) then treat with antivirals. If the result from quantitative testing will not be available within 10 days of exposure, AND the individual is VZV IgG equivocal (qualitative testing) then PEP is not recommended.

* For women with an uncertain or negative history of chickenpox, antenatal booking bloods should be tested unless there is a recorded chickenpox exposure in this pregnancy, in which case a fresh sample should be taken for testing if the booking sample is negative.

Table from the UKHSA Guidelines on Chicken pox in pregnancy Guidelines on post exposure prophylaxis for varicella or shingles (publishing.service.gov.uk)

Pregnant women are at high risk of severe chickenpox following an exposure to chickenpox or herpes zoster and Varicella-Zoster Virus (VZV) prophylaxis is recommended if they fulfil both the following criteria:

1. Significant exposure* to chickenpox or herpes zoster during the infectious period (which is classed as face:face exposure, or in the same room for 15 minutes or longer)
2. No antibodies to VZV. Urgent VZV IgG antibody testing can be performed on discussion with the laboratory. This needs performing within 24 hours

*See the UKHSA guidance and The Green Book listed in the references below for definitions of significant exposure and immunosuppression

Types of prophylaxis

- Oral antivirals (e.g. aciclovir and valaciclovir) are now the first choice of PEP for susceptible immunosuppressed individuals, all susceptible pregnant women at any stage of pregnancy and infants at high risk.
- Varicella Zoster Immunoglobulin (VZIG) temporarily increases an individual's antibody levels, for up to 3 weeks, thereby preventing or attenuating infection. Up to 50% of patients may still develop chicken pox despite having received VZIG and subclinical seroconversion can occur. VZIG is only indicated for neonates within 7 days of exposure.

Choice of prophylaxis

Pregnant women exposed, who are VZV antibody negative	Oral antiviral (see below for dosing) unless there are contraindications
Neonates	Group 1 Neonates whose mothers develop chickenpox (but not shingles) in the period 7 days before to 7 days after delivery: VZIG can be given without VZV IgG antibody testing of the neonate or mother; in addition,

	prophylactic intravenous aciclovir (10 mg/kg every 8 hours for 10 days) should also be considered in addition to the VZIG for infants whose mothers develop chickenpox 4 days before to 2 days after delivery as they are at the highest risk of fatal outcome despite VZIG prophylaxis**.** As this will be an intrauterine exposure, treatment should be started as soon as possible and there is no need to wait for 7 days. Group 2: VZV antibody-negative infants under one year who have remained in hospital since birth who are born before 28 weeks gestation or weighed less than 1,000g at birth or VZV antibody-negative infants who have a severe congenital or other underlying condition that requires prolonged intensive or special care during the first year of life
Immunosuppressed patients	Oral antiviral (see below for dosing) unless there are concerns about malabsorption or renal toxicity

Antiviral Prophylaxis

Antivirals should be given from day 7 to day 14 after exposure. If the patient presents after day 7 of exposure, a 7 day course of antivirals can be started up to day 14 after exposure, if necessary. Antiviral of choice is Aciclovir 800mg four times a day

Dosage and Administration of VZIG

VZIG will be issued from the Colindale Rabies and Immunoglobulin Service (RIgS) following discussion with a clinical virologist and completion of the requisition form. Post exposure prophylaxis for chickenpox and shingles - GOV.UK (www.gov.uk)

This form will be emailed to RIGS and pharmacy. The VZIG will then be delivered directly to the pharmacy department for collection and administration. (Pharmacy – please see guidance on Q Pulse for further detail on supply).

VZIG is given by slow intramuscular injection in the upper outer quadrant of the buttock or the anterolateral thigh.

7.4 Management of a pregnant woman with chickenpox

- The pregnant woman with varicella should be isolated from all other pregnant women and neonates until the lesions have crusted over (usually about 5 days from onset of the rash)
- Contact a Consultant Virologist .
- Offer symptomatic treatment and hygiene measures to prevent secondary bacterial infection of the lesions
- **All women with chickenpox who are more than 20 weeks pregnant should be prescribed oral aciclovir if they present within 24 hours of the onset of rash**. Oral aciclovir (800mg five times a day for 7 days) reduces the severity and duration of the illness. **Aciclovir should be used cautiously before 20 weeks of gestation**. Women should be informed of the potential risk and benefits of treatment with aciclovir (no increase in the risk of fetal malformation although theoretical risk of teratogenesis in the first trimester)

VZIG has no therapeutic benefit once chickenpox has developed

- Refer to FM specialist at 16- 20 weeks' gestation or 5 weeks after infection for discussion and detailed USS
- Hospitalise and consult a senior physician in following conditions:
    - if any respiratory symptoms occur
    - if any neurological symtpoms occur i.e. photophobia, seizures, drowsiness
    - if the lesions are dense and haemorrhagic
    - if new lesions continue to develop 6 days after the onset
- Consider a hospital assessment even in absence of complications in women who are at greater risk of pneumonitis. They are:
    - those who smoke cigarettes
    - those with chronic obstructive lung disease
    - those who are taking corticosteroids
    - those who have a more extensive or haemorrhagic rash
    - those who are in the latter half of pregnancy
    - greater than 100 skin lesions and presence of pharyneal lesions
- Varicella pneumonia is an indication for treatment with intravenous Acyclovir. In certain circumstances it may be necessary to consider mechanical ventilation. In the third trimester of pregnancy this may be facilitated by delivery, but elective delivery at this time will be associated with a high risk of neonatal varicella.
- **If the maternal infection occurs in the last four weeks of pregnancy, there is a significant risk of varicella infection of the newborn. Elective delivery should i d e a l l y be avoided until 7 days after the onset of maternal** rash to allow for passive transfer of antibodies from the mother to the baby unless continuing with the pregnancy poses additional risks to the mother and/or baby.
- Inform all the intrapartum care givers about maternal infection with chickenpox. Non-immune staff should avoid contact with woman if possible.
- Inform neonatal unit.
  Neonatal ophthalmic examination should be organised at birth.
  If birth occurs within 7 days after the onset of maternal rash, or if the mother develops chickenpox within 7 days of giving birth, then the neonate should be given prophylactic VZIG +/- acyclovir as soon as possible (see prophylaxis table)

7.5 Management of a postnatal woman found to be sero-negative for VZV IgG

- Consider varicella vaccination. The woman can be reassured it is safe to breastfeed following vaccination. NB; pregnancy should be avoided for at least 4 weeks following second dose.

8. <u>Anaesthetic recommendations and considerations</u>

Maternal varicella has implications for the anaesthetist. The optimal technique of anaesthesia is the subject of debate.

- **Spinal or epidural block:** There is a concern that spinal or epidural block may introduce the virus into the CNS with resultant meningitis or encephalitis. Camann and Toumala advised against regional block for at least 2 weeks after the onset of varicella symptoms [2]. However, **regional anaesthesia has been advocated as the technique of choice in parturients with acute varicella due to the high risk of pneumonia** [3]. Brown et al suggested that the use of a pencil point needle may reduce the risk of introduction of viral material into the CNS [4]. **It would be prudent to avoid inserting a spinal /epidural needle through skin lesions.**
- **General anaesthesia:** General anaesthesia may be required to avoid extensive lesions on the back [4]. The main concern with the use of general anaesthesia is a risk of postoperative pneumonia. There is evidence that general anaesthesia produces a decrease in immune function response. Nitrous oxide, inhalational agents e.g. isoflurane, sevoflurane, desflurane have all been implicated [5].

9. Other Recommendations

- On occasion a family member or sibling has varicella around the time mother and newborn baby are due for discharge from hospital. If the mother is immune to varicella there is no risk to the newborn. However, if she is not immune the newborn should be given VZIG.
- All reasonable steps should be taken to isolate individuals, including health care professionals, with VZ infection, from pregnant women attending hospital or general practitioner surgeries. (Guidelines re Infection Control manual. Staff should liaise with Occupational Health.
- Staff who are thought (or known by previous testing) to be "not immune" should avoid contact with pregnant women with chickenpox. However, those who are exposed, should be tested for varicella antibodies, and if found to be susceptible should be warned they may develop varicella. The incubation period is between 1- 3 weeks.

10. Management of VZV occurring in a clinical area

Please refer to the 'Trust Policy'

11. Management of other rashes in pregnancy

Please refer to the flowchart in appendix A

12. Monitoring Compliance and Effectiveness

As per agreed business unit audit forward programme

13. References

RCOG Guideline No 13 Chickenpox in pregnancy January 2015

Department of Health: The Green Book: Chapter 34: Varicella. Available from: https://www.gov.uk/government/publications/varicella-the-green-book-chapter-34.

UK Health Security Agency. Guidelines on post exposure prophylaxis (PEP) for varicella/shingles (January 2023). Guidelines on post exposure prophylaxis for varicella or shingles (publishing.service.gov.uk)

See also the pathology shared care guideline

Varicella-Zoster Virus (VZV) - post exposure prophylaxis (UHDB Guideline on KOHA)

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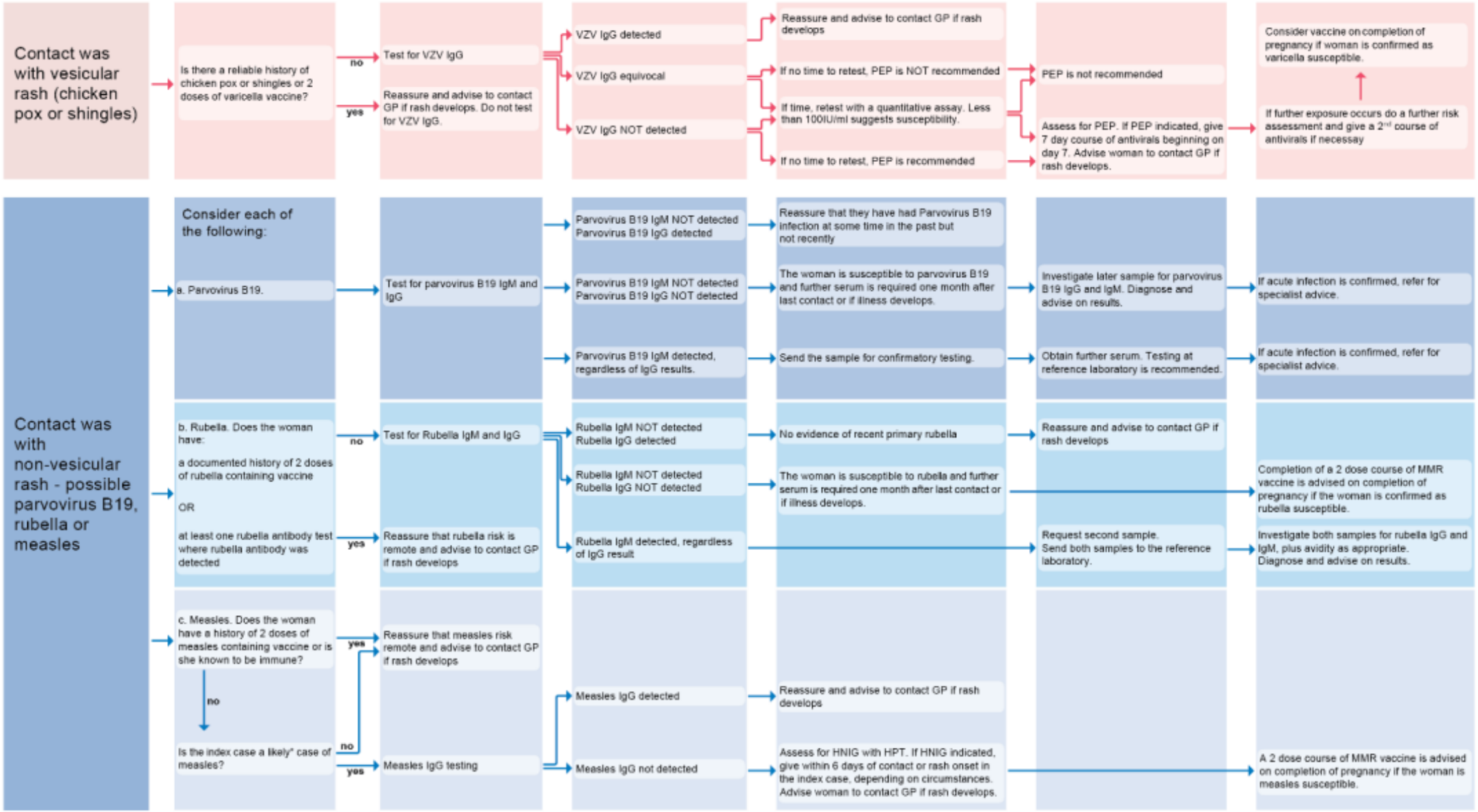

*Contact the local HPT to establish the likelihood of measles in the index case

Documentation control

Reference Number: UHDB/07:23/C3	**Version:** **UHDB version 2**		**Status: FINAL**	
Version Amendment	Version	Date	Author	Reason
	1	November 2001	Maternity Development Committee	
	2	January 2012	Dr S.Dixit - SpR Obstetrics and Gynaecology Miss S Rajendran – Consultant Obstetrician	Review
	3	August 2016	Miss S.Dixit – Consultant Obstetrician Dr A Richardson – SpR O&G	Review
UHDB	1	June 2020	Miss S.Dixit – Consultant Obstetrician Dr Cariad Evans – Consultant Virologist	Review & Merge
	2	April 2023	Miss S.Dixit – Consultant Obstetrician Dr Cariad Evans – Consultant Virologist	Review
Intended Recipients: All staff with responsibility for caring for women in the Antenatal period				
Training and Dissemination: Cascaded through lead midwives/doctors / Published on Intranet NHS mail circulation / Article in BU newsletter				
To be read in conjunction with:				
Consultation with:	Obstetricians, Maternity Staff			
Business Unit Sign off:	02/05/2023: Maternity Guidelines Group: Miss S Rajendran – Chair 19/06/2023: Maternity Governance Group - Mr R Deveraj			
Notification Overview sent to TIER 3 Divisional Quality Governance Operations & Performance: 20/06/2023				
Implementation date:	04/07/2023			
Review Date:	July 2026			
Key Contact:	Joanna Harrison-Engwell			