UKOSS

UK Obstetric Surveillance System

Haemophagocytic Lymphohistiocytosis (HLH) or Macrophage Activation Syndrome (MAS) 02/24

Data Collection Form - CASE

Please report any woman delivering on or after the 01/10/2024 and before 01/10/2029

Case Definition:

Any pregnant or recently pregnant (< 6 weeks since delivery) woman with a diagnosis or suspected diagnosis of haemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS).

Case ID Number: | | | | | | | |

Royal College of Obstetricians and Gynaecologists

Bringing to life the best in women's health care

Please return the completed form to:

ukoss@npeu.ox.ac.uk

UKOSS
National Perinatal Epidemiology Unit
University of Oxford, Old Road Campus, Oxford, OX3 7LF

Phone: 01865 617764 / 617774

Reporting Month: _____

Reporting Hospital: _____

OXFORD POPULATION HEALTH
UNIVERSITY OF OXFORD
NPEU

Instructions

1. Please do not enter any personally identifiable information (e.g. name, address or hospital number) on this form.
2. Please record the ID number from the front of this form against the woman's name for your own reference on the 'UKOSS - Reported cases' document.
3. Fill in the form using the information available in the woman's case notes.
4. Tick the boxes as appropriate. If you require any additional space to answer a question please use the space provided in section 7.
5. Please complete all dates in the format DD/MM/YY, and all times using the 24hr clock e.g. 18.37
6. If codes or examples are required, some lists (not exhaustive) are included on the back page of the form.
7. If the woman has not yet delivered, please complete the form as far as you are able, excluding delivery and outcome information, and return to the UKOSS Administrator. We will send these sections again for you to complete two weeks after the woman's expected date of delivery.
8. If you do not know the answers to some questions, please indicate this in section 7.
9. If you encounter any problems with completing the form please contact the UKOSS Administrator or use the space in section 7 to describe the problem.

Section 1: Woman's details

FOR OFFICE USE ONLY

1.1 Year of birth Y Y Y Y

1.2 Ethnic group[1]* *(enter code, please see back cover for guidance)*

1.3 Was the woman in paid employment at booking? Yes ☐ No ☐

If Yes, what is her occupation _____

If No, what is her partner's (if any) occupation _____

1.4 Height at booking ☐☐☐ cm

1.5 Weight at booking ☐☐☐.☐ kg

1.6 Smoking status

never ☐ gave up prior to pregnancy ☐

current ☐ gave up during pregnancy ☐

1.7 Vaping status

never ☐ gave up prior to pregnancy ☐

current ☐ gave up during pregnancy ☐

Section 2: Previous Obstetric History

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2.1 Gravidity

Number of completed pregnancies beyond 24 weeks ☐☐

Number of pregnancies less than 24 weeks ☐☐

If no previous pregnancies, *please go to section 3.*

2.2 Did the woman have any previous pregnancy problems?[2]* Yes ☐ No ☐

If Yes, please specify _____

2.3 Are the woman's parents first degree relatives? Yes ☐ No ☐

*For guidance please see back cover

Section 3: Previous Medical History

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3.1 Has the woman ever had any of the following diagnoses/conditions?

Malignancy Yes ☐ No ☐

If Yes, please specify type(s) _____

Severe infection and/or Sepsis Yes ☐ No ☐

If Yes, please specify principal infection site _____

AND

Organism _____

Autoimmune rheumatic disease Yes ☐ No ☐

(eg. systemic lupus erythematosus, adult onset Still's disease, juvenile idiopathic arthritis)

If Yes, please specify _____

Previous admission to critical care Yes ☐ No ☐

If Yes, what was the reason for admission? _____

HLH or MAS? Yes ☐ No ☐

3.2 Did the woman have any other pre-existing medical problems?[3*] Yes ☐ No ☐

If Yes, please specify _____

Section 4: This Pregnancy

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4.1 Final Estimated Date of Birth (EDB)?[4*] D D / M M / Y Y

4.2 Was this a multiple pregnancy? Yes ☐ No ☐

If Yes, please specify number of fetuses ☐☐

4.3 Were there any problems in this pregnancy?[2*] Yes ☐ No ☐

If Yes, please specify _____

_____

4.4 Were any of the following conditions felt to have contributed to the woman's HLH and/or noted to be active during the pregnancy?

Malignancy Yes ☐ No ☐

If Yes, please specify type(s) _____

Severe infection and/or Sepsis Yes ☐ No ☐

If Yes, please specify principal infection site _____

AND

Organism _____

Autoimmune rheumatic disease Yes ☐ No ☐

(eg. systemic lupus erythematosus, adult onset Still's disease, juvenile idiopathic arthritis)

If Yes, please specify _____

HIV Yes ☐ No ☐

Other Yes ☐ No ☐

If Yes, please specify _____

*For guidance please see back cover

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4.5 **What date and time did the woman present with symptoms?**

D D / M M / Y Y h h : m m (24hr)

4.6 **What date and time was the diagnosis of HLH/MAS made?**

D D / M M / Y Y h h : m m (24hr)

4.7 **Which of the following diagnostic criteria for HLH/MAS did the woman have at time of diagnosis?**

Criteria

Known underlying immunosuppression (e.g., HIV positive, or receiving long-term immunosuppressive therapy) Yes ☐ No ☐

Maximum temperature

- < 38.4 °C ☐
- 38.4-39.4 °C ☐
- > 39.4 °C ☐
- Not known ☐

Organomegaly

- No organomegaly ☐
- Hepatomegaly or splenomegaly ☐
- Hepatomegaly and splenomegaly ☐
- Not known ☐

Number of cytopaenias
(i.e., Hb ≤ 92 g/L, platelets ≤110 x 10^9 /L, white cell count ≤ 5)

- 1 lineage ☐
- 2 lineages ☐
- 3 lineages ☐
- Not known ☐

Ferritin

- < 2000 µg/L ☐
- 2000-6000 µg/L ☐
- > 6000 µg/L ☐
- Not known ☐

Triglycerides

- < 1.5 mmol/L ☐
- 1.5-4 mmol/L ☐
- > 4 mmol/L ☐
- Not known ☐

Fibrinogen

- ≤ 2.5g/L ☐
- > 2.5 g/L ☐
- Not known ☐

continues overleaf

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Criteria

Serum aspartate aminotransferase (AST) or serum alanine aminotransferase (ALT)

- < 30 IU/L ☐
- ≥ 30 IU/L ☐
- Not known ☐

Haemophagocytosis features on bone marrow aspirate Yes ☐ No ☐ Not known ☐

4.8 **Was the woman assigned an HScore (a diagnostic score derived from diagnostic criteria[*8]) when making the diagnosis?** Yes ☐ No ☐

If Yes, please give the score: ☐☐☐

4.9 **Did any of the following symptoms, physical signs or organ defects affect the woman during the course of her illness with HLH/MAS?** *(please tick all that apply)*

Fever ☐	Skin rash ☐	Lymphadenopathy ☐
Arthritis ☐	Diarrhoea ☐	Hypotension (blood pressure <90/60mmHg) ☐
Confusion and/or delirium ☐	Hypoxia (oxygen saturation <94%) ☐	Tachycardia (heart rate >100bpm) ☐
Kidney failure support (eg. Haemodialysis, haemofiltration) ☐	Respiratory failure support (eg. O^2, intubation, NIV) ☐	None ☐

4.10 **Please provide the following levels during the course of the woman's illness (from symptom onset) with HLH/MAS** *(indicate if not tested)*

Test	Result	Date	Not tested
Haemoglobin (lowest level)	_____ g/L	D D / M M / Y Y	☐
Creatinine (highest level)	_____ mmol/L	D D / M M / Y Y	☐
C-reactive protein (highest level)	_____ mg/L	D D / M M / Y Y	☐
Procalcitonin (highest level)	_____ ng/mL	D D / M M / Y Y	☐
Urea (highest level)	_____ mmol/L	D D / M M / Y Y	☐
Platelet count (lowest level)	_____ x10^9/L	D D / M M / Y Y	☐
Neutrophil (lowest level)	_____ x10^9/L	D D / M M / Y Y	☐
Neutrophil (highest level)	_____ x10^9/L	D D / M M / Y Y	☐

continues overleaf

Test	Result	Date	Not tested
Fibrinogen (lowest level)	_____ g/L	D D / M M / Y Y	☐
Soluble CD25 (highest level)	_____ U/ml	D D / M M / Y Y	☐
Rheumatoid factor (give titer)	_____	D D / M M / Y Y	☐
Serum triglycerides (highest level)	_____ mmol/L	D D / M M / Y Y	☐
Serum ferritin (highest level)	_____ ng/mL	D D / M M / Y Y	☐
Serum ALT or AST or SGOT (highest level)	_____ iu/L	D D / M M / Y Y	☐
Anti-nuclear antibodies (state if positive or negative and titres)	_____ / _____	D D / M M / Y Y	☐
Any positive autoantibodies (eg. Positive anti-Ro, anti-La, anti-RNO, anti-Sm, anti-dsDNA, anti-Jo1, anti-centromere, anti-cardiolipin IgG/IgM, anti-beta2glycoproten 1 IgM/IgG, lupus anticoagulant)	List positive results: _____ _____ _____ _____ _____	D D / M M / Y Y	☐

Microbiology

4.11 Were there any microbiologically confirmed infections? Yes ☐ No ☐

If Yes, please indicate

Microbiologically confirmed infections		If Yes, please specify organism and site
Bacterial	Yes ☐ No ☐	Organism: _____ Site: _____
Viral	Yes ☐ No ☐	Organism: _____ Site: _____
Fungal	Yes ☐ No ☐	Organism: _____ Site: _____

4.12 Did the woman have any imaging? Yes ☐ No ☐

If Yes, what was the type of scan? *(please tick all that apply)*

CT scan ☐ MRI scan ☐ Echocardiogram ☐

If Yes, were there any abnormal findings on imaging?

If Yes, please specify _____

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4.13 **Was a bone marrow aspirate performed?** Yes ☐ No ☐

If Yes, was there evidence of another condition from the bone marrow biopsy? Yes ☐ No ☐

If Yes, please specify _____

4.14 **Were genetic studies performed?** Yes ☐ No ☐

If Yes, was there an identified gene mutation? Yes ☐ No ☐

If Yes, please specify _____

4.15 **Please indicate which of the following treatments the woman received from symptom onset**

Anti-infective drugs			Steroids		
Antibiotics	Yes ☐	No ☐	Dexamethasone	Yes ☐	No ☐
Antifungal	Yes ☐	No ☐	Hydrocortisone	Yes ☐	No ☐
Antivirals	Yes ☐	No ☐	Prednisolone (inc methylprednisolone)	Yes ☐	No ☐

Cytotoxics			Others		
Cyclophosphamide	Yes ☐	No ☐	Anakinra	Yes ☐	No ☐
Cyclosporin	Yes ☐	No ☐	Immunoglobulins	Yes ☐	No ☐
Doxorubicin	Yes ☐	No ☐	Rituximab	Yes ☐	No ☐
Etoposide	Yes ☐	No ☐	Tocilizumab	Yes ☐	No ☐
Methotrexate	Yes ☐	No ☐			
Vincristine	Yes ☐	No ☐			

4.16 **Were any other drugs or agents used to treat the HLH/MAS?** Yes ☐ No ☐

If Yes, please specify _____

4.17 **Was the woman referred for bone marrow transplantation?** Yes ☐ No ☐

Section 5: Delivery

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5.1 **Did this woman have a miscarriage?** Yes ☐ No ☐

If Yes, please specify date D D / M M / Y Y

5.2 **Did this woman have a termination of pregnancy?** Yes ☐ No ☐

If Yes, please specify date D D / M M / Y Y

If Yes to 5.1 or 5.2, please now complete sections 6a, 7 and 8.

5.3 **Is this woman still undelivered?** Yes ☐ No ☐

If Yes, will she be receiving the rest of her antenatal care from your hospital? Yes ☐ No ☐

If No, please indicate name of hospital providing future care:

_____ ☐

Will she be delivered at your hospital? Yes ☐ No ☐

If No, please indicate name of delivery hospital, then *go to Section 7*

_____ ☐

5.4 **Was delivery induced?** Yes ☐ No ☐

If Yes, please state indication _____ ☐

Was vaginal prostaglandin used? Yes ☐ No ☐

5.5 **Did the woman labour?** Yes ☐ No ☐

If Yes, please provide date of onset of labour D D / M M / Y Y

5.6 **Was delivery by caesarean section?** Yes ☐ No ☐

If Yes, please state

Grade of urgency[5]* ☐

Indication for caesarean section _____ ☐

Method of anaesthesia: Regional ☐ General anaesthetic ☐

5.7 **What was the date and time of childbirth?** D D / M M / Y Y h h : m m (24hr)

5.8 **Mode of birth**

Spontaneous vaginal ☐ Ventouse ☐ Forceps ☐ Breech ☐

Pre-labour caesarean section ☐ Caesarean section after onset of labour ☐

*For guidance please see back cover

Section 6: Outcomes

Section 6a: Woman

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6a.1 **Was the woman admitted to ITU (critical care level 3)?** Yes ☐ No ☐

If Yes, please specify:

Duration of stay ☐☐ days

Or Tick if woman is still in ITU (critical care level 3) ☐

Or Tick if woman was transferred to another hospital ☐

6a.2 **Did any other major maternal morbidity occur?**[6*] Yes ☐ No ☐

If Yes, please specify _____ ☐

6a.3 **Did the woman die?** Yes ☐ No ☐

If Yes, please specify date of death D D / M M / Y Y

What was the primary cause of death as stated on the death certificate?

(Please state if not known) _____ ☐

Was a post mortem examination undertaken? Yes ☐ No ☐ Not known ☐

If Yes, did the examination confirm the certified cause of death/diagnosis? Yes ☐ No ☐ Not known ☐

Section 6b: Infant 1

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NB: If more than one infant, for each additional infant, please photocopy the infant section of the form **(before filling it in)** and attach extra sheet(s) or download extra copies of the form.

6b.1 **Birthweight** ☐☐☐☐ *g*

6b.3 **Sex of infant** Male ☐ Female ☐ Indeterminate ☐

6b.4 **Was the infant stillborn?** Yes ☐ No ☐

If Yes, was this Ante-partum ☐ ***OR*** Intra-partum ☐

If Yes, *go to section 7*

6b.5 **5 min Apgar** ☐☐

6b.6 **Was the infant admitted to the neonatal unit?** Yes ☐ No ☐

If Yes, please specify details _____ ☐

6b.7 **Did any other major infant complications occur?**[7*] Yes ☐ No ☐

If Yes, please specify details _____ ☐

6b.8 **Did this infant die?** Yes ☐ No ☐

If Yes, please specify date of death D D / M M / Y Y

What was the primary cause of death as stated on the death certificate?

(Please state if not known) _____ ☐

*For guidance please see back cover

Section 7:

Please use this space to enter any other information you feel may be important

Section 8:

Name of person completing the form _____

Designation _____

Today's date D D / M M / Y Y

You may find it useful in the case of queries to keep a copy of this form.

Definitions

1. UK Census Coding for ethnic group

WHITE
- 01. English, Welsh, Scottish, Northern Irish or British
- 02. Irish
- 03. Gypsy or Irish Traveller
- 04. Roma
- 05. Any other white background

MIXED
- 06. White and black Caribbean
- 07. White and black African
- 08. White and Asian
- 09. Any other mixed or multiple ethnic background

ASIAN OR ASIAN BRITISH
- 10. Indian
- 11. Pakistani
- 12. Bangladeshi
- 13. Chinese
- 14. Any other Asian background

BLACK OR BLACK BRITISH
- 15. Caribbean
- 16. African
- 17. Any other black, black British or Caribbean background

OTHER ETHNIC GROUP
- 18. Arab
- 19. Any other ethnic group

2. Previous or current pregnancy problems, including:

3 or more miscarriages
Amniocentesis
Baby with a major congenital abnormality
Gestational diabetes
Haemorrhage
Hyperemesis requiring admission Infant requiring intensive care Neonatal death
Placenta praevia
Placental abruption
Post-partum haemorrhage requiring transfusion
Pre-eclampsia (hypertension and proteinuria)
Premature rupture of membranes
Preterm birth or mid trimester loss
Puerperal psychosis
Thrombotic event
Severe infection e.g. pyelonephritis
Stillbirth
Surgical procedure in pregnancy

3. Previous or pre-existing maternal medical problems, including:

Cardiac disease (congenital or acquired) Diabetes
Epilepsy
Endocrine disorders e.g. hypo or hyperthyroidism
Essential hypertension
Haematological disorders e.g. sickle cell disease, diagnosed thrombophilia
Inflammatory disorders e.g. inflammatory bowel disease
Psychiatric disorders
Renal disease

4. Estimated date of birth (EDB):

Use the best estimate (ultrasound scan or date of last menstrual period) based on a 40 week gestation

5. RCA/RCOG/CEMACH/CNST Classification for urgency of caesarean section:

1. Immediate threat to life of woman or fetus
2. Maternal or fetal compromise which is not immediately life-threatening
3. Needing early delivery but no maternal or fetal compromise
4. At a time to suit the woman and maternity team

6. Major maternal morbidity, including:

Adult respiratory distress syndrome
Cardiac arrest
Cerebrovascular accident
Disseminated intravascular coagulopathy
HELLP
Mendelson's syndrome Persistent vegetative state
Renal failure
Required ventilation Septicaemia
Thrombotic event

7. Fetal/infant complications, including:

Chronic lung disease
Exchange transfusion
Intraventricular haemorrhage
Jaundice requiring phototherapy
Major congenital anomaly
Necrotising enterocolitis
Neonatal encephalopathy
Respiratory distress syndrome
Severe infection e.g. septicaemia, meningitis

8. HLH Diagnostic Criteria/HScore:

Fever >38.5 deg C
Splenomegaly
Peripheral blood cytopaenia affecting >2 of 3 lineages: Hb <90g/L; Platelet <100x109, Neutropaenia <1x109 micro/L
Hypertriglyceridaemia and/or hypofibrinogenaemia fasting triglycerides >3.0 mmol/L (>265 mg/dl) OR fibrinogen <1.5 g.L
Haemophagocytosis in bone marrow, spleen or lymph nodes
Low or absent NK activity (using local laboratory reference ranges)
Ferritin >500 ug/L
Soluble CD25 (ie. soluble 1L-2 receptor) >2,400 U/ml

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