

Intrahepatic Cholestasis of pregnancy

DATA COLLECTION FORM

STUDY - IDENTIFICATION NUMBER: **ICP000**

**BACKGROUND INFORMATION**

Intrahepatic Cholestasis of Pregnancy (ICP) affects 0.1–2% of pregnant women. Its incidence is higher in some countries, such as Chile and Norway (1). ICP is diagnosed in women with gestational pruritus and increased levels of serum bile acids, and can be complicated by preterm labor, fetal asphyxia, meconium-stained amniotic fluid, and stillbirth (2). It is associated with maternal discomfort because of pruritus and it can be associated with insomnia and general symptoms (3). According to retrospective studies, the increased risk of stillbirth is associated with high maternal serum bile acid concentrations (4). A large 2019 meta-analysis demonstrated that bile acid levels above 100 micmol/L were associated with a significant increased risk of stillbirth, 30-50 times higher than when bile acid levels were <100 micmo/L (5). The risk of stillbirth increases with increasing gestational age. The meta-analysis showed no increase in stillbirth compared to the background population before 39 weeks gestation when bile acids were <100 micmol/L. However, it is important to notice that the high number of iatrogenic preterm birth may have biased these numbers. It seems that ursodeoxycholic acid (UDCA) is effective against pruritus (6), but it is not clear whether ursodeoxycholic acid reduces neonatal morbidity and mortality. The recent PITCHES study (a double-blind, multicenter, randomized placebo-controlled trial at 33 hospital maternity units in England and Wales) showed that the treatment with UDCA does not reduce adverse perinatal outcomes, in women affected by ICP, and suggest reconsidering its routine use for this condition (7). There is no standard management for ICP (8): there is no strong evidence that monitoring by US or cardiotocogram can reduce adverse fetal outcomes (2). There is no consensus on bile acid level dosage, or on the right gestational age for termination of the pregnancy (8, 9, 10). As a result of the above key points, there is scope for improvement in the outcome of ICP through a better understanding and awareness of the problem

With this study we want to investigate intermediate (bile acids 40-99 micmol/L) and severe (bile acids ≥ 100 micmol/L) ICP in Belgium: to determine the incidence of this pregnancy complication, the diagnosis and management in Belgian hospitals and the maternal and fetal outcomes of pregnancies complicated with ICP. Further, we want to compare Belgian incidence, management and outcome of ICP with our neighbouring countries.

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**CASE DEFINITION**

Every pregnant woman identified as having

**Intermediate** (bile acids 40-99micmol/L) or **Severe**  (bile acids ≥ 100micmol/L)

**Intrahepatic Cholestasis of Pregnancy (ICP)**

Defined as:

* Pruritus without rash associated with elevated serum bile acid levels ≥ 40 micmol/L
* At any stage of the pregnancy,
* Not explained by other pathologies,
* Disappearing after the delivery.

**Exclusion criteria:**

* Serum bile acid levels less than 40 micmol/L
* Other hepatic/infectious/dermatologic/pregnancy disease, which could explain the symptoms

**DATA COLLECTION FORM**

### Section 1. Woman’s details

* 1. Year of birth: (YYYY) 0000
	2. Country in which patient was born
	3. Is the mother single?

[ ] Yes

[ ] No

[ ] Not known

* 1. Did the patient or her partner have a steady income during pregnancy (excluding social security)

[ ] Yes

[ ] No

[ ] Not known

* 1. Height at 1st visit:      cm
	2. Weight at 1st visit:      kg
	3. ~~Calculate BMI:~~ ~~kg/m~~~~2~~
	4. Did the patient smoke during pregnancy? (answer yes, even if she quit during pregnancy)

[ ] Yes

[ ] No

[ ] Not known

* 1. What was the highest education of the patient?

|  |
| --- |
| [ ] no formal schooling |
| [ ] Less than primary schooling |
| [ ] Primary school |
| [ ] Secondary school |
| [ ] Higher: bachelor, master, university |
|  |

### Section 2. Previous Obstetric History

* 1. Gravidity.
		1. Number of current pregnancy (number)
		2. Number of completed pregnancies of ≥ 22 weeks (number)
	2. Please indicate if any of the following were present in previous pregnancies:

|  |
| --- |
| [ ] Gestational diabetes |
| [ ] Pre-eclampsia |
| [ ] HELLP syndrome |
| [ ] ICP |

* 1. If the patient had previous ICP
		1. At which gestational age did it appear? (number of weeks)
		2. At wich gestational age did she deliver (number of weeks)
		3. Did she experience (tick all that apply)

|  |
| --- |
| [ ]  Spontaneous preterm labour [ ]  Fetal asphyxia [ ]  Meconium-stained amniotic fluid [ ]  Stillbirth  |

* 1. Did the woman have any other previous pregnancy problems?

[ ] Yes

[ ] No

If yes, please specify

[ ]  Recurrent miscarriages (3 or more)

[ ]  Amniocentesis

[ ]  Amniotic fluid embolism

[ ]  Baby with a major congenital abnormality

[ ]  Haemorrhage

[ ]  Infant requiring intensive care

[ ]  Neonatal death

[ ]  Ovarian hyperstimulation syndrome

[ ]  Placenta praevia

[ ]  Placental abruption

[ ]  Post-partum haemorrhage requiring transfusion

[ ]  Pre-eclampsia (hypertension and proteinuria)

[ ]  Premature rupture of membranes

[ ]  Partus prematurus

[ ]  Partus immaturus

[ ]  Puerperal psychosis

[ ]  Severe infection e.g. pyelonephritis

[ ]  Stillbirth

[ ]  Surgical procedure in pregnancy

[ ]  Other, please specify

### Section 3. Previous personal and familiar medical history

* 1. Was there a previous or pre-existing maternal medical condition?

[ ] Yes

[ ] No

[ ] Not known

If yes, please specify

[ ]  Cardiac disease (congenital or acquired)

[ ]  Diabetes

[ ]  Epilepsy

[ ]  Endocrine disorders e.g. hypo or hyperthyroidism

[ ]  Essential hypertension

[ ]  Haematological disorders e.g. sickle cell disease

[ ]  Inflammatory disorders e.g. inflammatory bowel disease

[ ]  I.V. drug use

[ ]  Lung disease

[ ]  Myeloproliferative disorders e.g. essential thrombocythaemia, polycythaemia vera

[ ]  Neoplasia

[ ]  Paraplegia

[ ]  Psychiatric disorders

[ ]  Renal disease e.g. nephrotic syndrome

[ ]  Systemic lupus erythematosus

[ ]  Other, please specify

* 1. Any previous surgery (including caesarean section)

[ ] Yes

[ ] No

[ ] Not known

If yes, please specify

* 1. Please indicate whether any of the following specific problems: (tick all that apply)

[ ] Hepatitis C infection
[ ]  Hepatitis B infection
[ ]  Hepatitis A infection
[ ]  Ebstein Barr Virus infection
[ ]  Cytomegalovirus infection
[ ]  Autoimmune Hepatitis
[ ]  Primary biliary cirrhosis

[ ]  Primary sclerosing cholangitis
[ ]  Gallstone
[ ]  Cyclical itch/cholestasis
[ ]  Other episode of cholestasis, like drug induced

* 1. Did anybody of the family experienced ICP during a previous pregnancy?

[ ] Yes

[ ] No

[ ] Not known

If yes specify relation to the patient

### Section 4: This pregnancy

* 1. The number of foetuses in current pregnancy (≥ 22 weeks)
	2. Gestational age in completed weeks at booking (first antenatal visit)
	3. Beginning of the pregnancy

[ ]  Spontaneous
[ ]  Hormonal

[ ]  IVF/ICSI

[ ] Not known

* 1. Is this pregnancy complicated by

[ ]  Gestational Diabetes
[ ]  Pregnancy Induced Hypertension

[ ]  Preeclampsia
[ ]  Hyperemesis of the first trimester

* 1. Gestational age at the diagnosis of ICP (number of completed weeks)
	2. Did the mother suffer from the following symptoms

 (at the time of diagnosis or any time following diagnosis)

|  |  |  |
| --- | --- | --- |
|  | Yes | GA at onset |
| Pruritus  |[ ]        |
| Vomiting |[ ]        |
| Abdominal pain |[ ]        |
| Insomnia  |[ ]        |
| Jaundice  |[ ]        |
| Steatorrhea  |[ ]        |
| Hypoglycaemia |[ ]        |

* 1. Was abdominal US performed

[ ] Yes

[ ] No

If yes, what were the findings

* 1. Were other imaging techniques performed?

[ ] Yes

[ ] No

[ ] Not known

If yes, what type of imaging technique?

If yes, what were the findings

* 1. Was a liver biopsy performed?

[ ] Yes

[ ] No

[ ] Not known

If yes, what were the findings

* 1. Please note if any other problems of the pregnancy occurred?

[ ]  Amniocentesis

[ ]  Antenatal haemorrhage

[ ]  Ovarian hyperstimulation syndrome

[ ]  Placenta praevia

[ ]  Placental abruption

[ ]  Premature rupture of membranes

[ ]  Puerperal psychosis

[ ]  Severe infection e.g. pyelonephritis

[ ]  Surgical procedure in pregnancy

[ ]  Other, please specify

### Section 5. Biochemistry before delivery

**5.1.** Please mark the level at diagnosis, the worst recorded level and the level at delivery

|  |  |  |  |
| --- | --- | --- | --- |
|  | At diagnosis | Worst level + GA at worst level | At delivery |
| Serum bile acids (micmol/L) |       |       |       |        |
| AST (U/L) |       |       |       |        |
| ALT(U/L) |       |        |       |        |
| Bilirubin (mg /dL) |       |        |       |        |
| GGT (U/L) |       |        |       |        |
| Creatinine (mg/dL) |       |        |       |        |
| Platelets (x103 mm3) |       |        |       |        |
| PT (%) |       |        |       |        |
| APTT (s) |       |        |       |        |
| WBC count (x103 mm3) |       |        |       |        |

* 1. Please note how the sample type of bile acid level was taken

|  |
| --- |
| [ ]  Fasten [ ]  Random[ ]  Not known |

### Section 6. Treatment

* 1. Was treatment with ursodeoxycholic acid (UDCA) started?

[ ] Yes

[ ] No

* 1. If yes please give the dose (total daily dose in mg)       and gestational age (in completed weeks) at start treatment
	2. Did symptoms improved with UDCA?

[ ] Yes , Please specify which symptoms:

[ ] No

[ ] Not known

* 1. How often were bile acids measured?

 [ ] More than 1xweek

 [ ] Weekly

 [ ] Every two weeks

 [ ] Less than every two weeks

* 1. How long does it take for the results of bile acids to come back in your maternity?

[ ] Less than 24 hours

 [ ] 24 to 48 hours

 [ ] More than 48 hours

* 1. How do you usually control bile acids in pregnant patients in your maternity unit?

[ ] Fasted

[ ] Random

* 1. Was treatment with K vitamin started?

[ ] Yes

[ ] No

* 1. Did the woman receive treatment for fetal lung maturation?

[ ] Yes

[ ] No

If yes at what GA? (number of completed weeks)

* 1. Was any other treatment started?

[ ] Yes

[ ] No

If yes, please specify

### Fetal monitoring

* 1. How often was a fetal US performed?

[ ] More than once per week

[ ] Once per week

[ ] Once every 2 weeks

[ ] Less than once every 2 weeks

* 1. Were any foetal US abnormalities recorded?

[ ] Yes

[ ] No

If yes, Please specify

* 1. How often was a cardiotocography performed

[ ] More than once per day

[ ] Once per day

[ ] More than once per week

[ ] Once per week

[ ] Less than once per day

[ ] None

* 1. Were any CTG abnormalities recorded?

[ ] Yes

[ ] No

[ ] N/A

If yes, Please specify

* 1. Were any other monitoring strategy employed? (eg. Home monitoring, Kick chart, …)

[ ] Yes

[ ] No

If yes please specify

* 1. Was the patient admitted to the hospital in this pregnancy (besides hospitalisation for delivery)?

[ ] Yes

[ ] No

If yes, at what GA was she admitted (number of completed weeks)?

If yes, was she admitted for fetal monitoring because of ICP

[ ] Yes

[ ] No

If no, please specify the reason for admission:

### Section 8. End of pregnancy

* 1. Gestational age in completed weeks at the end of the pregnancy
	2. What was the planned mode of delivery?

[ ] Vaginal

[ ] Caesarean section

* 1. Was delivery induced?

[ ] Yes

[ ] No

If yes:

* + 1. Please specify the reason for the induction
		2. The method of the induction (more than one option possible)

[ ] Amniotomy

[ ] Oxytocin

[ ] Prostaglandin IV

[ ] Prostaglandin vaginal/intra-cervical

[ ] Catheter balloon

[ ] Double balloon

* 1. Did the woman labour?

[ ] Yes

[ ] No

If yes :

* + 1. Was labour augmented?

[ ] Yes

[ ] No

If yes, please specify augmentation methods:

[ ]  Amniotomy was performed for augmentation

[ ]  Oxytocin was used for augmentation

* + 1. What type of monitoring was performed?

[ ] Continuous cardiotocography

[ ] STAN monitoring

[ ] Intermittent cardiotocography

Were any CTG abnormalities / STAN events recorded during labor?

[ ] Yes

[ ] No

[ ] N/A

If yes, please describe

* + 1. If yes please specify:

The length of the 1st stage of labour (number of hours)

The length of the 2nd stage of labour (number of minutes)

* 1. Mode of delivery 1st neonate

[ ] Spontaneous cephalic

[ ] Breech

[ ] Instrumental vaginal delivery

[ ] Pre-labour caesarean section

[ ] Secondary caesarean section

In case of caesarean section, please specify

* + 1. Reason for caesarean section

[ ] Maternal

[ ] Fetal
[ ] Elective

Please specify

* + 1. Grade of urgency



[ ]  Category I

[ ]  Category II

[ ]  Category III

[ ]  Category IV

* 1. Type of analgesia

[ ] General

[ ] Loco-regional

[ ] None

* 1. In case of twin pregnancy – based on question 4.1
		1. Mode of delivery 2nd neonate

[ ] Spontaneous cephalic

[ ] Breech

[ ] Instrumental vaginal delivery

[ ] Pre-labour caesarean section

[ ] Secondary caesarean section

* + 1. In case of caesarean section, please specify reason for caesarean section

[ ] Maternal

[ ] Fetal
[ ] Elective

Please specify

* + 1. Grade of urgency



[ ]  Category I

[ ]  Category II

[ ]  Category III

[ ]  Category IV

* 1. Type of analgesia

[ ] General

[ ] Loco-regional

[ ] None

* 1. How was the placenta delivered?

[ ] Spontaneous
[ ]  Manual

* 1. Was the placenta analysed?

[ ] Yes , Please specify diagnosis:

[ ] No

[ ] N/A

### Section 9. Maternal outcomes

* 1. Did any major maternal morbidity occurred:

[ ]  Post-partum haemorrhage

If yes: estimated blood loss in ml

If yes: number of Packed Cells transfused

[ ]  Severe pre-eclampsia (See list 4: definition of severe preeclampsia)



[ ]  Admission to Intensive care unit / high depency unit

If yes: how many days
If yes: reason for admission

* 1. Did the mother die

[ ] Yes

[ ] No (Please go straight to section 10)

* + 1. If yes, please specify the timing of death following birth

[ ]  < 24 hours

[ ]  < 7 days

[ ]  < 42 days

[ ]  > 42 days

* + 1. If yes, what was the cause of death?
		2. If yes, was postmortem performed

[ ] Yes

[ ] No

*If yes*, please specify diagnosis

### Section 10. Infant outcomes

 (please complete one section for each infant)

* 1. Birthweight       grams
	2. Percentile
	3. Sex of the infant

[ ] male

[ ] female

[ ] indeterminate

* 1. Was the infant stillborn

[ ] Yes

[ ] No (Please go straight to 10.4.2)

* + 1. **If yes** : please complete this part 10.4.1 and go to Section 11

Cause of death (if known):

Gestational age at diagnosis       completed weeks

Last US before diagnosis of stillbirth       days before

Last cardiotocography before diagnosis of stillbirth       days before

Was postmortem performed

[ ] Yes , please specify diagnosis

[ ] No

Please add any other relevant details:

* + 1. **If not stillborn** :
1. min Apgar

Was the infant admitted to neonatal unit?

[ ] Yes

[ ] No

If yes, please complete

How many days?

Indication for admission

Was there meconium-staining of the amniotic fluid, placenta or membranes?

[ ] Yes

[ ] No

[ ] N/A

Was the umbilical arterial or venous pH measured?

[ ] Yes

[ ] No

If yes please complete the values:

Arterial pH       BE
Venous pH       BE

Did any major neonatal complication occur? (see list number 5)

[ ] Yes

[ ] No

If yes please specify (list 5)

[ ]  Chronic lung disease

[ ]  Exchange transfusion

[ ]  Intraventricular haemorrhage

[ ]  Jaundice requiring phototherapy

[ ]  Necrotising enterocolitis

[ ]  Neonatal encephalopathy

[ ]  Respiratory distress syndrome

[ ]  Severe infection e.g. septicaemia, meningitis

[ ]  Other, please specify

Did the infant have any congenital anomaly?

[ ] Yes

[ ] No

If yes please specify (free text)

Did the infant die?

[ ] Yes

[ ] No (Please go straight to section 11)

If yes please specify:

Timing of death

[ ] <24 h

[ ] < 7d

[ ] < 28d)

Was postmortem performed

[ ] Yes , please specify diagnosis

[ ] No

### Section 11. Post partum

* 1. Were the serum bile acid levels controlled after the delivery?

[ ] Yes

[ ] No

If yes, how many weeks after?

Value of BA in the Post partum?      micmol/L

* 1. Was there further follow-up of this woman by a liver specialist ?

[ ] Yes

[ ] No

If yes, please specify findings if any

* 1. Did the patient receive any contraception after the delivery?

[ ] N/A

[ ] Yes

[ ] No

[ ] Not known

If yes, please specify:

[ ] Oral estrogen-progestin pills
[ ] Oral progestin pills
[ ] Progestin IUD
[ ] Non-hormonal IUD
[ ] Progestin implant
[ ] Other EP methods
[ ] Barrier methods

### Section 12. Any other remarks

* 1. Please note any other remarks you have regarding this case:

[ ] Finished

Please check this box when you are finished with this form.

##### **List 1: Previous or current pregnancy problems, including**

1. Recurrent miscarriages (3 or more)
2. Amniocentesis
3. Amniotic fluid embolism
4. Baby with a major congenital abnormality
5. Gestational diabetes
6. Haemorrhage
7. Hyperemesis requiring admission/ Dehydration
8. Infant requiring intensive care
9. Neonatal death
10. Ovarian hyperstimulation syndrome
11. Placenta praevia
12. Placental abruption
13. Post-partum haemorrhage requiring transfusion
14. Pre-eclampsia (hypertension and proteinuria)
15. Premature rupture of membranes
16. Partus prematurus
17. Partus immaturus
18. Puerperal psychosis
19. Severe infection e.g. pyelonephritis
20. Stillbirth
21. Surgical procedure in pregnancy
22. Other, please specify

##### **List 2: Previous or pre-existing maternal medical problems, including**

1. Cardiac disease (congenital or acquired)
2. Diabetes
3. Epilepsy
4. Endocrine disorders e.g. hypo or hyperthyroidism
5. Essential hypertension
6. Haematological disorders e.g. sickle cell disease
7. Inflammatory disorders e.g. inflammatory bowel disease
8. I.V. drug use
9. Lung disease
10. Myeloproliferative disorders e.g. essential thrombocythaemia, polycythaemia vera
11. Neoplasia
12. Paraplegia
13. Psychiatric disorders
14. Renal disease e.g. nephrotic syndrome
15. Systemic lupus erythematosus

##### **List 3: Previous or pre-existing maternal medical problems, including**



##### **List 4: Severe Pre-eclampsia criteria:**

Clinical

1. SBP ≥160 mm Hg/ DBP ≥ 100 mm Hg
2. Neurological or visual signs
3. Epigastric or RUQ pain
4. Pulmonary oedema

Biological

1. Serum creatinine >135 mg/dl
2. Low platelets < 100.000/mcL
3. Abnormal LFTs double of normal values

##### **List 5: Infant complications, including:**

1. Chronic lung disease
2. Exchange transfusion
3. Intraventricular haemorrhage
4. Jaundice requiring phototherapy
5. Major congenital anomaly
6. Necrotising enterocolitis
7. Neonatal encephalopathy
8. Respiratory distress syndrome
9. Severe infection e.g. septicaemia, meningitis
10. Other, please specify