Prevalence, Natural History and Risk Factors of Neonatal Prolonged Icterus of Newborns in a Preventive Setting in Flanders

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Keywords
Prolonged jaundice ; prolonged icterus ; biliary atresia ; screening ; preventive child care ; stool discoloration.

Abstract
Background
Prolonged jaundice is a symptom that requires further investigation. Early diagnosis of severe underlying causes can prevent harm and improve outcomes. Currently, there are no known data on the prevalence, risk factors, outcomes, and prognosis of children with prolonged jaundice in Flanders. This study aimed to provide more information on the natural history, prevalence and risk factors of prolonged icterus in order to optimize newborn screening.

Methods
We reviewed the records of 65497 newborns who consulted Kind & Gezin, a preventive public health service in Flanders. Neonates from the Brussels-Capital region and one with an error in gestational age were excluded. Jaundice was assessed visually by care providers. Prolonged jaundice was defined as jaundice persisting beyond the fourteenth day of life. Stool colour was assessed using a stool colour card.

Results
On day 15, 21.1% of the children were found to have jaundice, with a progressively decreasing frequency thereafter. A significant association was found between prolonged jaundice and male sex ($p<0.001$), prematurity ($p<0.001$), breastfeeding ($p<0.001$), maternal country of origin ($p<0.001$), lower socioeconomic status ($p<0.001$), and the province of residence ($p<0.001$). Multivariate logistic regression revealed that gender ($p<0,001$), prematurity ($p<0,001$), breastfeeding at 2 weeks ($p<0,001$), maternal country of origin ($p<0,001$), province of residence ($p=0,007$) and socioeconomic status ($p= 0,025$) are all independent risk factors for prolonged jaundice.

Conclusions
Prolonged jaundice in neonates born in Flanders is prevalent and is mainly linked to established risk factors for neonatal jaundice. However, only 5.8% of the variance in prolonged jaundice could be explained by the studied variables. Therefore, population screening is recommended regardless of the presence of underlying characteristics.

Background

The term 'icterus' refers to the yellow discolouration of the skin and mucous membranes caused by the accumulation of bilirubin in these tissues, a condition known as hyperbilirubinemia. Approximately 60% of term-born and 80% of preterm infants develop jaundice within the first week of life. In most cases, this jaundice is physiological and not indicative of an underlying disease (1).

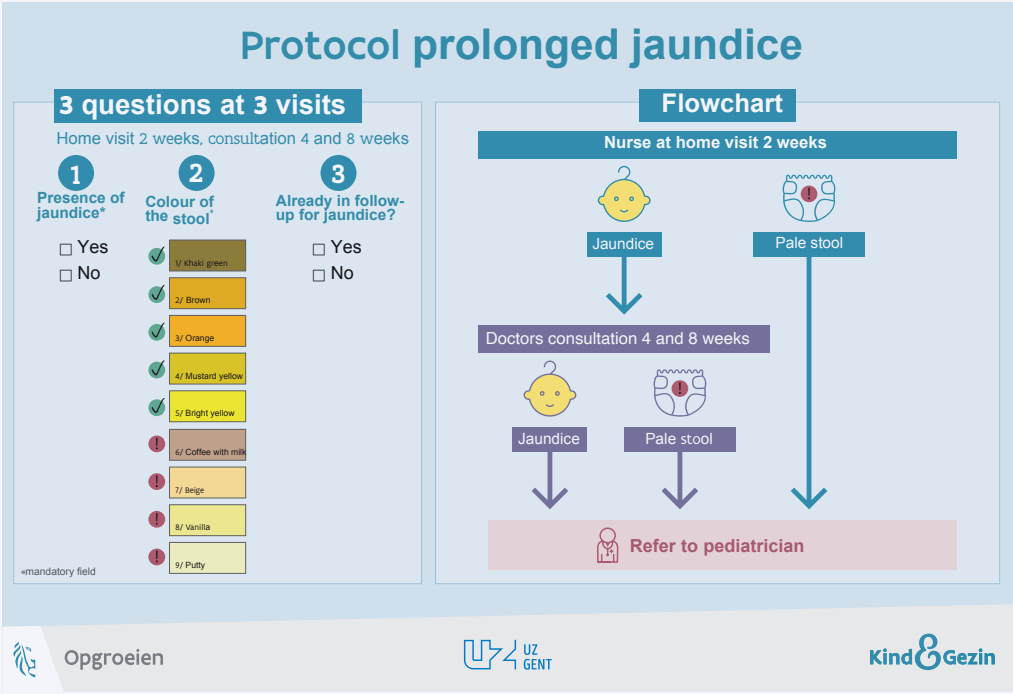
If jaundice persists beyond the second week in term infants and beyond the third week in preterm infants, it is classified as 'prolonged jaundice' (1,2). Although often a self-limiting benign condition affecting up to 15% of newborns, further investigation is warranted (1,3,4). Prolonged icterus may result from unconjugated (indirect) hyperbilirubinemia, which is physiological in many infants, or conjugated (direct) hyperbilirubinemia, which is always pathological and requires urgent diagnostic evaluation. Early detection of prolonged jaundice is crucial to exclude treatable causes of cholestasis, such as biliary atresia, to prevent life-threatening complications like vitamin K-deficient haemorrhage, and to identify pathological forms of indirect hyperbilirubinemia (5). Biliary atresia, a serious liver disease due to fibrotic obliteration of the bile ducts, requires early Kasai portoenterostomy, ideally before 6 weeks of age (4,6-9). Untreated, it leads to progressive liver failure. A stool card, to detect pale stool, a key sign of biliary atresia, is used successfully as a screening tool in some countries (10-12).

There are no specific clinical signs to confirm or exclude underlying pathology in prolonged icterus, highlighting the need for cost-effective screening and structured diagnostic guidelines. Belgium currently lacks national guidelines on this subject. The existence of guidelines in other countries, such as the NICE, NHSGCC, and NVK guidelines, underscores their importance (1,4,13). In Flanders, a screening protocol for prolonged jaundice (figure 1) was initiated within Kind en Gezin (Child and Family), part of the agency Op-

groeien (Growing Up). Kind en Gezin conducts routine health assessments for children up to 3 years of age, focusing on early detection of health and social concerns, administering the Flemish immunization program, and providing parental support. In this protocol children with pale stools were referred at the three time points (consultation 2 weeks, 4 weeks and 8 weeks) and children with prolonged icterus were referred at consultation 4 weeks and 8 weeks.

The 'prolonged jaundice' protocol aims to optimize early detection and ensure a prompt transition from preventive to curative care for neonates with prolonged jaundice. All data in this study were extracted from the data collected under this protocol.

FIGURE 1: Visual presentation of the Flemish protocol "prolonged jaundice", version September 2021.



The aim of this study was to examine the general characteristics of children with prolonged icterus and to identify potential risk factors as an initial step towards developing a national guideline on prolonged neonatal jaundice.

Methods

Data sources

We reviewed the health records of all Flemish children born between 1/10/2021 and 30/09/2022. Parameters collected at scheduled visits at 2, 4, and 8 weeks included age, gender, gestational age, feeding type, maternal country of origin, province and region of residence, socioeconomic status, and stool colour. The presence of icterus was clinically assessed by evaluating the colour of the skin and sclerae by Kind & Gezin healthcare providers. Stool colour was assessed using a stool colour card, indicating which colours required referral ('suspect') and which were normal ('normal') (figure 2). The card was created for the 'prolonged jaundice' protocol based on international guidelines (4, 14-17).

This study was approved by the Ethics Committee of UZ Ghent, ensuring compliance with all ethical standards and guidelines.

Study population

The study population consisted of 68679 Flemish newborns. We excluded 3181 newborns from the Brussels-Capital region due to the mix of Flemish and Walloon services offered there, given that Kind & Gezin is an exclusively Flemish organization. One additional patient was excluded due to a potential registration error (gestational age of 45 weeks), resulting in 65497 newborns included. To examine the characteristics of newborns with prolonged neonatal icterus, we selected data from the fifteenth day of life.

Variables were grouped for consistency. Regions of residence were categorized as urban, transitional, and rural. Urban areas included 'centre cities,' 'provincial small towns,' 'large cities,' 'Brussels

FIGURE 2: Stool colour card.

agglomeration,' and 'structural towns.' Transitional areas included 'transition area,' 'metropolitan fringe,' and 'regional agglomeration.' Maternal country of origin was grouped by continent: Europe (including Belgium; Northern, Western, Eastern and Southern Europe; and the Eastern bloc), Asia (including Turkey and the other Asian countries), Africa (including the Maghreb and other African countries), and America (including South and Central America). "Rich OESO countries" and "other countries" were excluded from the analysis when this variable was categorized by continent due to insufficient data for continental classification.

TABLE 1: number of examined cases and missing values for each test done is this survey.

	Examined	Missing
Icterus per age	44 743	20 754
Prolonged jaundice and gender	59 229	6 268
Prolonged jaundice and prematurity	58 967	6 530
Prolonged jaundice and breastfeeding at 2 weeks	45 068	20 429
Prolonged jaundice and breastfeeding at 4 weeks	43 344	22 153
Prolonged jaundice and breastfeeding at 8 weeks	42 283	23 214
Prolonged jaundice and maternal country of origin	59 229	6 268
Prolonged jaundice and socioeconomic status	54 189	11 308
Prolonged jaundice and province of residence	59 229	6 268
Prolonged jaundice and region of residence	59 229	6 268
Prolonged jaundice and stool colour	58 197	7 300
Logistic regression	41 156	24 341

Statistical analysis

Data cleaning involved verifying potential duplications and variable characteristics. Descriptive statistics included frequencies, measures of central tendency, and measures of variability for nominal and ordinal variables.

The Chi-square test was used to assess significant differences in jaundice between 2 categories of a variable. Due to the substantial amount of missing data in various variables from lack of registration, the Chi-square test was performed on each newborn for whom we had information on jaundice and the variable of interest. Consequently, each test had its own study population, with the amount of missing data, both shown in Table 1. Logistic regression analysis determined which variables significantly affected prolonged icterus.

All tests were conducted using SPSS Statistics 29 (SPSS Inc, Chicago, IL, USA).

Used terminology

Socioeconomic status (SES) was based on an index calculated by Kind & Gezin nurses and family support workers, considering variables such as monthly income, parental education, children's level of stimulation, parental work situation, housing and health. Families with living conditions below a pre-set minimum in 3 or more areas were classified as having low SES (18).

Results

General patient characteristics

Of the 65 497 newborns studied, 33516 (51.2%) were boys and 31981 (48.8%) were girls. The median gestational age was 39 weeks (range 23 to 43 weeks). A total of 4832 (7.5%) of the newborns were born prematurely (under 37 weeks), of which 1143 (23.7%) were early preterm (born under 34 weeks of gestational age). The first visit (usually planned around 2 weeks of age), the second visit (usually planned around 4 weeks of age) and the third visit (usually planned around 8 weeks of age) were performed at a mean age of 13,04 days (range 1 to 425 days), 34,68 days (range 8 to 194 days) and 62,61 days (range 39 to 206 days), respectively. Table 2 provides an overview of the feeding type, country of origin of the mother, socioeconomic status, and the province and region of residence.

Icterus per age

On the 5th day of life, 40.7% of the children who visited Kind & Gezin at that age had jaundice, which was the maximum rate, and it decreased from there. On the 15th of life, 21.1% of the children visiting at that age were still jaundiced. Figure 3 shows the proportion of newborns presenting with jaundice at Kind & Gezin respective to the age (in days) at the time of consultation.

Characteristics of newborns with prolonged neonatal icterus

We examined the data of 59 229 newborns who consulted Kind & Gezin after the age of 14 days. Of these, 6 436 (10.9%) had prolonged jaundice. The counts, expected counts and p-values of the different variables in the prolonged icterus group are presented in table 3.

FIGURE 3: Figure 3: Proportion of newborns presenting with jaundice at each age (in days) that they consulted Kind & Gezin. The X-axis represents the age in days. The dark blue bars show the proportion of jaundiced newborns visiting at each age to the total number of newborns visiting Kind &Gezin at that specific age.

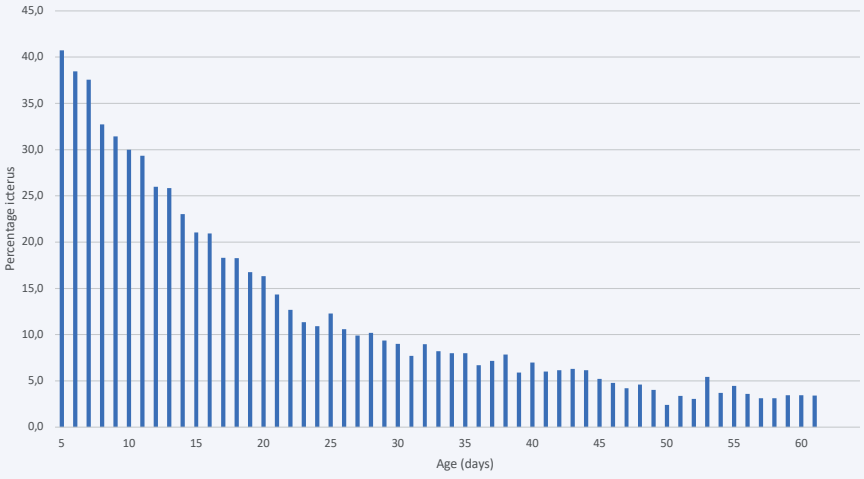


TABLE 2: General information (feeding type, country of origin of the mother, SES, province and region of residence) of the newborns who visited Kind & Gezin.

	Frequencies	Percent
Feeding type first consultation		
Breastfeeding	31 977	48,8%
Non-breastfeeding	15 084	23%
Missing	18 436	28,1%
Feeding type second consultation		
Breastfeeding	28 505	43,5%
Non-breastfeeding	16 572	25,3%
Missing	20 420	31,2%
Feeding type third consultation		
Breastfeeding	22 756	34,7%
Non-breastfeeding	21 201	32,4%
Missing	21 540	32,9%
Maternal country of origin		
Belgium	41 431	63,3%
Northern and Western Europe	1 975	3%
South Europe	819	1,3%
Eastern Europe and Eastern Bloc	3 064	4,7%
Eastern Bloc (non-EU)	1 936	3%
Rich OESO-countries (non-EU)	292	0,4%
Turkey	1 068	1,6%
Maghreb	2 862	4,4%
South and Central America	571	0,9%
Other African countries	2 608	4%
Other Asian countries	3 678	5,6%
Other countries	65	0,1%
Missing	5 128	7,8%
Europe	49 225	82%
Africa	5 470	9,1%
Asia	4 746	7,9%
America	571	1%
Socioeconomic status (SES)		
Belgian and low SES	1 976	3%
Belgian and high SES	38 245	58,4%
Non-Belgian and low SES	5 083	7,8%
Non-Belgian and high SES	13 050	19,9%
Missing	7 143	10,9%
Province of residence		
East Flanders	15 189	23,2%
West Flanders	11 032	16,8%
Limburg	7 885	12%
Antwerp	19 855	30,3%
Flemish Brabant	11 536	17,6%
Region of residence		
Centre cities	8 781	13,4%
Metropolitan fringe	3 100	4,7%
Large cities	9 901	15,1%
Small-town provincial	6 675	10,2%
Transition area	14 202	21,7%
Countryside	9 307	14,2%
Regional urban fringe	3 615	5,5%
Urban area around Brussels	3 074	4,7%
Structure support	6 842	10,4%
Urban area	35 313	53,9%
Transition area	20 877	31,9%
Rural area	9307	14,2%

a. Gender and prolonged icterus

58.1% of the newborns with prolonged jaundice were male compared to 50.3% in the group without jaundice (p<0.001). Of all boys 12.3% had prolonged jaundice compared to 9.3% of girls.

b. Prematurity and prolonged icterus

13% of the newborns with prolonged jaundice were born prematurely compared to 6,3% in the group without jaundice (p<0.001). Of all prematurely born babies who consulted Kind & Gezin after 14 days of life, 20,1% had prolonged jaundice compared to 10,2% of the babies born at term.

When categorizing prematurity into early prematurity (<34 weeks) and late prematurity (34-37 weeks), 15,6% of the early premature group had prolonged icterus compared to 21,3% of the late premature group (p<0.001).

c. Breastfeeding and prolonged icterus

85,4%, 81,7% and 71,1% of the newborns with prolonged jaundice were breastfed at 2, 4 and 8 weeks respectively compared to 67,5%, 62,9% and 51,2% in the group without jaundice.

Of all babies who consulted Kind & Gezin after 14 days of life and were breastfed at 2 weeks, 14% had prolonged jaundice compared to 5,5% of the babies who were not breastfed at that time (p<0,001).

d. Maternal country of origin and prolonged icterus

Among babies consulting Kind en Gezin after 14 days of life, 10.7% of those born to mothers born in Belgium had prolonged jaundice, compared to 11.4% of those born to mothers born in other countries (p=0,014).

10,8% of the children of mothers born in European countries had prolonged icterus, 8,2% of the children of mothers born in African countries, 14,2% of the children of mothers born in Asian countries and 10,8% of the children of mothers born in American countries (p<0,001).

e. Socioeconomic status (SES) and prolonged icterus

Of the neonates born in a family with low SES who consulted Kind & Gezin after 14 days of life, 9,4% had prolonged jaundice compared to 11,1% of the neonates born in a family with high SES (p<0,001).

f. Province of residence and prolonged icterus

Of the newborns living in East Flanders who consulted Kind & Gezin after 14 days of life, 10,7% had prolonged jaundice compared to 10,7% of the newborns living in West Flanders, 11,5% in Limburg, 10,3% in Antwerp, 11,8% in Flemish Brabant (p<0,001).

g. Region of residence and prolonged icterus

Of the newborns living in an urban area who consulted Kind & Gezin after 14 days of life, 11% had prolonged jaundice compared to 10,6% of the newborns living in a transition area and 10,8% in a rural area (p=0,394).

Stool colour

Across all visits, 88 newborns had a suspicious stool colour. There were 18 newborns with suspicious stool colour at the

TABLE 3: counts, expected counts and p-values, of the different variables in the prolonged icterus group.

Variable		Count	Expected count	p-value
Gender	Boy	3737	3292,3	<0,001
	Girl	2699	3143,8	
Prematurity	At term	5583	5967,4	<0,001
	Premature	836	451,6	
	Early premature	129	166,4	<0,001
	Late premature	707	669,6	
Breastfeeding at 2 weeks	No	755	1569,7	<0,001
	Yes	4405	3590,3	
Breastfeeding at 4 weeks	No	864	1657,0	<0,001
	Yes	3866	3073,0	
Breastfeeding at 8 weeks	No	1258	2037,1	<0,001
	Yes	3096	2316,9	
Country of origin of the mother	Belgian	4041	4124,1	= 0,014
	Non-Belgian	1967	1883,9	
	Europe	4855	4870,1	<0,001
	Africa	419	553,3	
	Asia	639	489,1	
	America	55	55,6	
Socioeconomic status	Low	610	707,5	<0,001
	High	5290	5192,5	
Province where the child is domiciled	East Flanders	1492	1510,2	<0,001
	West Flanders	1059	1080,2	
	Limburg	850	800,4	
	Antwerp	1891	1989,6	
	Flemish Brabant	1144	1055,6	
Region where the child is domiciled	Urban area	3502	3452,0	=0,394
	Transition area	2031	2073,7	
	Rural area	903	910,3	
Stool colour	Normal	6386	6390,3	=0,140
	Abnormal	14	9,7	

first visit (around 2 weeks), 27 at the second visit (around 4 weeks) and 45 at the third visit (around 8 weeks). 2 children had persistent abnormal stool colour the second and third visit. 23 newborns had abnormal stool categorized as type 6 (coffee with milk), 35 as type 7 (beige), 20 as type 8 (vanilla) and 12 as type 9 (putty). Of the 18 newborns with abnormal stool colour at the first visit, 11 had jaundice, of which 2 had prolonged jaundice. 4 of the 27 newborns with abnormal stool colour at the second visit had (prolonged) icterus and 4 of the 45 newborns with abnormal stool colour at the third visit.

Of the newborns with abnormal stool colour who consulted Kind & Gezin after 14 days of life, 15,9% had prolonged jaundice compared to 11% of the newborns with normal stool colour (p= 0,140). There were 14 of the 88 children with abnormal stool colour and prolonged icterus, both at least at one of the visits.

Risk assessment by logistic regression model

Univariate logistic regression explored the association between the different variables (gender, prematurity, feeding type, maternal country of origin categorized by continent, socioeconomic status, province and region of residence, stool colour) and prolonged jaundice. A statistically significant effect of gender, prematurity, breastfeeding at 2, 4 and 8 weeks of age, maternal country of origin, socioeconomic status (p<0,001) and province of residence (p=0,001) was found.

Multivariate logistic regression (variables gender, prematurity, feeding type, maternal country of origin categorized by continent, socioeconomic status and province of residence) revealed that gender, prematurity, breastfeeding at 2 weeks of age, maternal country of origin (p<0.001), province of residence (p=0,007) and socioeconomic status (p=0,025) are all independent risk factors for prolonged jaundice. The p-values and odds ratios of the logistic regression model for the various variables are presented in table 4.

Number needed to screen

The number needed to screen in the general population to diagnose one newborn with biliary atresia is determined by its prevalence, which de Vries et al. described to be 1 in 18 619 live births in the Netherlands (9).

To determine the number needed to screen, the requirement for liver transplantation within four years following portoenterostomy was identified as the adverse event to be prevented. The publication of de Vries et al. described that of those who had a portoenterostomy at less than 60 days of age, 56% were living with their own liver 4 years later compared to 34% of those who underwent surgery after 60 days of age (9).

Based on these publications we calculated a number needed to screen of 84 631,8 children in the general population to prevent one child with biliary atresia from requiring a liver transplant within the first 4 years after portoenterostomy.

Discussion

Prolonged icterus can be physiological but may also indicate significant underlying diseases; therefore, timely referral of these newborns is crucial. As an initial step in the diagnostic approach, measuring the total and conjugated fractions of bilirubin is essential to identify cholestasis, which is always pathological, defined as the conjugated fraction exceeding 20% of the total bilirubin. Once cholestasis is diagnosed, a structured, step-by-step diagnostic approach is necessary to enable timely treatment, if available, and to prevent complications. A time-critical illness in the differential diagnosis of cholestasis is biliary atresia, where the prognosis is significantly better if surgery is performed before the age of 60 days (4,6-8). Newborns with biliary atresia often lack specific signs indicating the underlying disease (1,4,13,19). This underscores the importance of a robust screening program, leading to the initiation of the 'prolonged jaundice' protocol in Flanders.

This study aimed to provide more information on the natural history, prevalence, and risk factors of prolonged icterus to optimize screening for newborns.

TABLE 4: p-values and B-values of the logistic regression model for the different variables.

Variable (reference value)	P-value	Exp(B)
Gender (girl)	<0,001	0,718
Prematurity (premature)	<0,001	2,582
Breastfeeding at 2 weeks (yes)	<0,001	3,016
Maternal country of origin	<0,001	
Africa (Europe)	<0,001	0,636
Asia (Europe)	<0,001	1,202
America (Europe)	=0,117	0,759
Socioeconomic status (high)	=0,025	1,130
Province of residence	=0,007	
West Flanders (East Flanders)	=0,200	1,067
Limburg (East Flanders)	=0,095	1,095
Antwerp (East Flanders)	=0,546	0,947
Flemish Brabant (East Flanders)	=0,008	1,141

In this cohort study, we found that 10.9% of the children consulting Kind & Gezin had prolonged jaundice, which is slightly less than the prevalence reported in the literature, ranging between 15-32.2% (3,20).

By examining risk factors, we aimed to make a better selection of the population for screening for prolonged jaundice. Consistent with published evidence, we found that boys, prematurely born babies, and breastfed infants are more at risk for prolonged icterus (3,21-23). The increased incidence of prolonged jaundice in preterm infants can be explained by an increased bilirubin production due to elevated red blood cell turnover, a decreased bilirubin clearance and conjugation, resulting from hepatic immaturity and an enhanced enterohepatic circulation of bilirubin. An increased intrahepatic circulation of bilirubin is considered a contributing factor in breast milk jaundice. The reason why prolonged jaundice is more common in male infants remains unclear.

The higher incidence of prolonged jaundice in late preterm babies compared to early preterm babies is likely due to the older age at the visits of early preterm babies.

Surprisingly, we found that children born into families with low socioeconomic status have a lower risk of prolonged icterus compared to those from high socioeconomic status families. The reason for this difference is currently unknown, and we could not identify confounders to explain this result. We observed significant differences in the occurrence of prolonged jaundice based on the mother's country of origin and the province where the child resides. Consistent with the literature, we found more prolonged jaundice in children with Asian mothers compared to those with American and European mothers (24). Conversely, we found a lower incidence of prolonged jaundice in children with African mothers compared to those with American and European mothers. These findings should be interpreted with caution, as published literature suggests that visual assessment of jaundice may be less reliable across different skin tones if only the skin colour is considered and not the sclerae (1,25). This study also found more prolonged icterus in children living in Limburg and Flemish Brabant and less in Antwerp compared to East and West Flanders. The reason for this difference is currently unknown, and we could not identify confounders to explain this result.

Based on the regression model, only 5.8% of the variance in prolonged jaundice could be explained by the variables used. Therefore, we cannot define risk groups that need prioritization for screening. This highlights the importance of population-based screening programs, such as the existing guidelines from the National Institute for Health and Care Excellence (NICE), the National Health Service Greater Glasgow and Clyde (NHSGCC), the Dutch Society for Paediatrics (NVK), the American Academy of Paediatrics (AAP), and the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition, and the North American Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN/NASPGHAN) (1,4,13,19, 26, 27). The study by Tan et al. demonstrated that a stepwise regional protocol for prolonged icterus in Perak, Malaysia, led to fewer visits, fewer investigations, and improved quality of care for neonates (28). The study by Hsiao et al. showed that universal screening with a stool colour chart led to earlier portoenterostomy, resulting in better outcomes for children with biliary atresia (10).

Using guidelines for prolonged jaundice is an appropriate course of action to improve public health based on Wilson & Jungner's principles of screening (table 5) (29). We previously demonstrated that biliary atresia is an important health problem with a known natural history, screening possibilities, and available and accepted diagnostic and therapeutic options. Currently, we have insufficient information about the cost of case-finding in Belgium to assess the cost-effectiveness of an early screening program that leads to early diagnosis and treatment, potentially avoiding liver transplantation. In the current screening program for prolonged jaundice in Flanders, visual and clinical assessments of all newborns are embedded in regular visits to Kind & Gezin, making this a low-cost step. Based on this study's data, a total of 6 524 newborns (10% of all screened

TABLE 5: Wilson & Jungner's principles of screening. Source: 29.

Wilson & Jungner's principles of screening		
1.	The condition should be an important health problem.	+
2.	There should be an accepted treatment for patients with recognized disease.	+
3.	Facilities for diagnosis and treatment should be available.	+
4.	There should be a recognizable latent or early symptomatic phase.	+
5.	There should be a suitable test or examination.	+
6.	The test should be acceptable to the population.	+
7.	The natural history of the condition, including development from latent to declared disease, should be adequately understood.	+
8.	There should be an agreed policy on whom to treat as patients.	+
9.	The cost of case-finding (including a diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.	?
10.	Case-finding should be a continuous process and not a "once and for all" project.	+

newborns) would be referred annually to a paediatrician for further examinations. We currently lack information on the number of newborns requiring more specialized examinations, which would incur higher costs. A study by Hoshino et al. showed that the greatest cost in treating biliary atresia is liver transplantation (annual costs about $166 808 in the USA) (30). Although it is not possible to avoid all liver transplants, early diagnosis can at least reduce the need for transplantation within the first 4-10 years after portoenterostomy (8,9). In this study, we found a high number needed to screen in the general population to prevent one liver transplant within 4 years after portoenterostomy, highlighting the rarity of biliary atresia.

Table 5 presents Wilson and Jungner's principles of screening. In the right column, we applied these criteria to screening for biliary atresia.

The main strength of this study is the large sample size and good representation of the population in Flanders. However, the study has several limitations. We could not follow the newborns over time, so we only have information from the 3 time points they were seen at Kind & Gezin. Our results are based on public health data that are not linked to curative health care records. Consequently, we do not have access to the clinical diagnoses of the screened children. Moreover our database contains a significant amount of missing data, likely due to registration issues.

Conclusion

Currently, there is no national Belgian screening protocol for prolonged icterus, despite international consensus. It has been proven that a screening protocol leads to earlier referral for children with underlying diseases, resulting in better prognosis through earlier treatment and prevention of complications.

The risk factors for neonatal jaundice are well known and were consistently identified in this study. Nevertheless, this study found that only 5.8% of the variance in prolonged jaundice could be explained by the studied variables. Therefore, population screening is recommended regardless of the presence of underlying characteristics.

Future and long-term studies are required to evaluate the efficacy and cost-effectiveness of the screening program and to further investigate the causes of prolonged icterus in Flemish or Belgian newborns. Establishing a robust national guideline for prolonged jaundice in Belgium is imperative for advancing patient care and ensuring consistent, high-quality medical practice.

The authors have no conflicts of interest in relation to the subject matter of this manuscript.

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