

PAPERS AND ORIGINALS

Factors influencing the incidence of neonatal jaundice

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British Medical Journal, 1978, 1, 1235-1237**Summary and conclusions**

A retrospective study of 12 461 single births confirmed an association between maternal oxytocin infusion and neonatal jaundice. The effect of oxytocin on jaundice was independent of gestational age at birth, sex, race, epidural anaesthesia, method of delivery, and birth weight, each of which was significantly associated with neonatal jaundice.

The effect of oxytocin was, however, small, producing a calculated mean increase in peak plasma bilirubin concentration of 8.6 $\mu\text{mol/l}$ (0.5 mg/100 ml); this excess was independent of sex and less than the effect of the baby being born one week earlier.

Introduction

Although mild jaundice of the newborn is accepted as normal, severe or prolonged jaundice is a potential cause of mental or motor impairment.¹ Several workers have suggested recently that the incidence of considerable neonatal jaundice has increased.²⁻³ Changes in obstetric practice have been blamed for this increase, particularly the increased use of oxytocin for inducing labour.⁴⁻⁵ But this increased incidence of neonatal jaundice is largely based on clinical impression, and the role of oxytocin in producing the increase is difficult to confirm since oxytocin use is associated with other icterogenic factors such as preterm delivery, instrumental delivery, and epidural anaesthesia. We therefore analysed neonatal jaundice rates in one obstetric hospital over five years. The rates were examined for

the factors associated with neonatal jaundice, and we measured the relative contribution of the icterogenic factors identified.

Methods

The study population was drawn from the 15 932 live births at Queen Charlotte's Hospital in 1971-5. Cases of multiple birth, rhesus incompatibility, ABO incompatibility, and G6PD deficiency were excluded, as were those in which the infant did not remain in hospital for seven days or more after delivery (in whom jaundice may have developed after discharge). The study group was thus composed of 12 461 infants without haematological predisposition to neonatal jaundice who were observed in hospital for the first week after birth. The date of delivery, sex, race, birth weight, gestational age, and method of delivery were recorded as were presence or absence of amniotomy, oxytocin infusion (whether for induction or acceleration of labour), epidural anaesthesia, and general anaesthesia. When plasma bilirubin had been measured the peak plasma bilirubin concentration in the first seven days after delivery was recorded.

The proportion of neonates with significant jaundice (a peak plasma bilirubin concentration of 205 $\mu\text{mol/l}$ (12 mg/100 ml) or greater) was calculated for each variable. Statistical differences between groups were calculated using the χ^2 test. Each factor showing a relationship with jaundice was also studied using a linear discriminant function (0 = no jaundice, 1 = bilirubin $\geq 205 \mu\text{mol/l}$ (12 mg/100 ml)) to determine whether the factor had an influence dependent on or independent of other factors. A multiple regression analysis was carried out to determine the numerical influence of each independent variable on the peak neonatal bilirubin concentration, assigning an arbitrary peak plasma bilirubin value of 77 $\mu\text{mol/l}$ (4.5 mg/100 ml) to those infants who had not had their bilirubin concentrations measured because they had had no clinical sign of jaundice.

Results and comments**SERIAL FIGURES**

The proportions of neonates with peak plasma bilirubin concentrations of 205 $\mu\text{mol/l}$ (12 mg/100 ml) or 291 $\mu\text{mol/l}$ (17 mg/100 ml) or greater over the five years are shown in fig 1. The incidence of jaundice was lowest in 1971 and remained steady thereafter.

INDIVIDUAL FACTORS

The seven factors that were associated with a significantly different incidence of jaundice are shown in table 1. Four other factors

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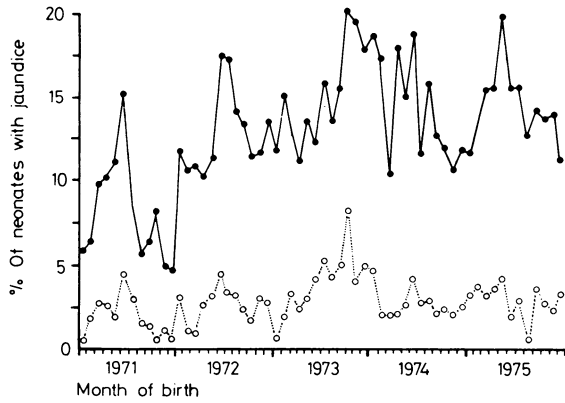


FIG 1—Percentage of neonates with plasma bilirubin concentrations of $\geq 205 \mu\text{mol/l}$ (12 mg/100 ml) (●) and $\geq 291 \mu\text{mol/l}$ (17 mg/100 ml) (○) month by month over five years.

TABLE 1—Proportion of neonates with jaundice (peak bilirubin $\geq 205 \mu\text{mol/l}$ (12 mg/100 ml)) according to various factors

Factor	Neonates with factor		Neonates without factor		P value (χ^2 test)
	Total No	% with jaundice	Total No	% with jaundice	
Asiatic race*	220	24.1	12 241	12.6	<0.001
Breech delivery	265	22.6	12 196	12.6	<0.001
Ventouse extraction	502	21.3	11 959	12.5	<0.001
Oxytocin	2 820	15.3	9 641	12.1	<0.001
Epidural anaesthesia	5 915	15.0	6 546	10.8	<0.001
Male sex	6 140	14.9	6 296	10.6	<0.001
Negro race	911	7.0	11 550	13.3	<0.001

*Asians of Chinese or Japanese origin excluding Indian race.
Conversion: SI to traditional units—Bilirubin: $1 \mu\text{mol/l} \approx 0.058 \text{ mg } 100 \text{ ml}$.

investigated—caesarean section, forceps delivery, general anaesthesia, and amniotomy—were not associated with significantly different rates of jaundice. Linear discriminant function analysis, where the numerical factors birth weight in grams and gestational age in weeks were also included, gave slightly different results. The analysis confirmed an independent influence of six of the factors previously noted—Asiatic race, ventouse extraction, oxytocin, male sex, epidural anaesthesia, and Negro race—but did not definitely confirm breech delivery ($P = 0.09$) and introduced general anaesthesia as an independent factor ($P = 0.005$). Gestational age in weeks was the most important of all factors considered. Birth weight was also significantly related to neonatal jaundice as a factor independent of gestational age. The proportion of variation in the incidence of jaundice explicable in terms of the nine factors totalled 7.6%.

A second multiple regression analysis in which the bilirubin concentration of $77 \mu\text{mol/l}$ (4.5 mg/100 ml) was assigned to non-jaundiced infants gave nearly identical results. The partial regression coefficients of this equation are shown in table II; these values can be equated to the mean increase in peak bilirubin concentration in $\mu\text{mol/l}$ attributable to each of the independent variables or a unit increase in that variable.

SMALL-FOR-DATES INFANTS

An interesting relationship between birth weight, gestational age, and neonatal jaundice was noticed. When mean peak bilirubin

TABLE II—Influence of various factors on peak neonatal plasma bilirubin concentrations ($\mu\text{mol/l}$) calculated by multiple regression analysis

Factor	Partial regression coefficient	Significance (F value)
Asiatic race	+20.5	25.36 ($P < 0.001$)
Ventouse extraction	+15.4	32.01 ($P < 0.001$)
Negro race	-13.0	38.48 ($P < 0.001$)
Oxytocin	+8.6	39.72 ($P < 0.001$)
Female sex	-8.6	60.43 ($P < 0.001$)
Epidural anaesthesia	+6.8	35.66 ($P < 0.001$)
General anaesthesia	-6.2	10.87 ($P < 0.01$)
Gestational age (weeks)	-9.4	603.79 ($P < 0.001$)
Birth weight (kg)	-3.4	8.00 ($P < 0.01$)

concentration was plotted against gestational age the expected negative correlation was seen. But when the relationships for infants of different birth weights were considered separately (fig 2) an unexpected pattern was seen for infants of gestational age less than 36 weeks. The lighter infants had a lower mean bilirubin concentration than those of heavier weight. This is contrary to what might have been expected and may represent another example of accelerated physiological maturity in small-for-dates infants.

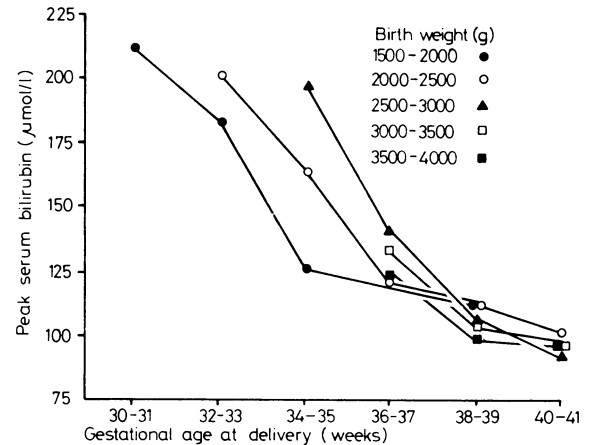


FIG 2—Mean peak neonatal serum bilirubin values according to gestational age for groups of infants with different birth weights. Points have been omitted where fewer than 20 infants fitted the category.

Discussion

The serial figures for the incidence of neonatal jaundice show a possible increase in 1971 and a stable rate thereafter. Among several reports quoting a recent increase in neonatal jaundice only two include serial incidence rates. Sims and Neligan² quote an increase from 2.2% to 5.5% in the proportion of infants with bilirubin concentrations of 15 mg/100 ml [$257 \mu\text{mol/l}$] or greater between 1972 and 1973. Campbell *et al*³ quoted a progressive increase in yearly jaundice rates between 1969 and 1973. They also used data from Queen Charlotte's Hospital but their method of sampling was not as rigorous as ours since they included all infants born in the hospital except those with rhesus disease. If neonatal jaundice had genuinely increased in recent years as a result of some obstetric innovation then the present incidence (about 12.9% of neonates have a peak bilirubin value of $205 \mu\text{mol/l}$ (12 mg/100 ml) or greater) should be greater than figures quoted in earlier reports. These surveys are few but Trolle⁶ measured plasma bilirubin concentrations in a sample of 1469 untreated infants in 1968. Altogether 15.8% had serum bilirubin concentrations of $205 \mu\text{mol/l}$ or more.

A recent postal survey of neonatal paediatricians in Europe and the USA confirmed that most had seen no evidence of an increased incidence of neonatal jaundice since either 1970 or 1965.⁷ Jaundice rates may fluctuate according to the interest taken in the condition and hence the measurements made of bilirubin concentrations. The availability of phototherapy and the continuing controversy over the role of oxytocin in jaundice may have led paediatricians to suspect significant jaundice more often.

We have analysed certain factors suggested to have been associated with this "increase" in neonatal jaundice, notably oxytocin and epidural anaesthesia.^{4,5} The technique of multiple regression analysis enables these factors to be examined independently of their frequent association with one another and with other known icterogenic factors such as prematurity and instrumental delivery. Our results show that both oxytocin and epidural anaesthesia have a small effect, which probably explains

why some authors have found these factors to be associated with jaundice^{2 4 5 8} while others have not.^{9 10}

The mechanism of the icterogenic effect of these drug treatments is obscure. Neither bupivacaine, the local anaesthetic used in epidural blocks, nor oxytocin has any direct effect on glucuronidation of bilirubin *in vitro*.¹¹ The hypo-osmotic effect of oxytocin has been implicated,¹² as has the increased placental transfusion of fetal blood resulting from oxytocin.¹³ So far as oxytocin induction is concerned this relationship may be due to an association between the use of induction in chronologically mature but physiologically immature infants who fail to initiate parturition.

The finding that premature, small-for-dates infants were protected from jaundice by their low weight suggests that hepatic glucuronyl transferase is prematurely developed in small-for-dates infants. This development recalls the accelerated surfactant production by the lung in small-for-dates infants, which has been attributed to intrauterine stress.¹⁴ A teleological explanation would be that early maturation of liver and lung enzymes may prepare small-for-dates infants for premature delivery.

Neonatal jaundice is undoubtedly a time-consuming clinical problem. Severe physiological jaundice is associated with mild brain damage,^{1 15 16} although classical kernicterus is rare. Our results indicate that the problem is unlikely to be resolved by changes in obstetric practice, for even elimination of epidural anaesthesia and oxytocin use would have little impact. These considerations may suggest to paediatricians that they should look again at prophylactic prenatal drug treatment for neonatal jaundice. Though phenobarbitone is effective,⁶ its adverse effects may be greater than the morbidity and medical costs of a

significant rate of neonatal jaundice; other enzyme-inducing agents might be found with fewer side effects.

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High prevalence of hyperuricaemia and gout in an urbanised Micronesian population

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Summary and conclusions

The prevalence of hyperuricaemia and gout was investigated in the Micronesian inhabitants of the highly urbanised central Pacific island of Nauru. Sixty-four per cent of men and 60% of women aged 20 years and over had hyperuricaemia—the highest prevalence rates yet reported for a population. The hyperuricaemia in men was accompanied by a high prevalence of clinical gout (6.9%).

While the hyperuricaemia is probably genetic, the high prevalence of gout may be related to the environmental change from the traditional island style of living to one of almost complete Westernisation.

Introduction

As the Third World nations change from subsistence to cash economies, drastic changes have occurred in the social, cultural, and health aspects of their societies. With the shedding of the traditional lifestyle for the seemingly more glamorous Western style of living and eating, there has been a dramatic rise in the prevalence of chronic degenerative diseases such as diabetes mellitus, hypertension, heart disease, and gout—conditions previously unknown or rare in these populations.¹⁻⁴ Nowhere have these changes been more apparent than in the developing countries of the Pacific.

Nevertheless, while diabetes, hypertension, and heart disease are rare in populations maintaining traditional lifestyles and appear only in their urbanised counterparts,⁵ hyperuricaemia has been reported in Pacific islanders both affected and unaffected by Western influences.¹ Thus, while the clinical expression of hyperuricaemia may be influenced by the change to a modern lifestyle, the actual metabolic abnormality is present in both environments.

In one particular Micronesian population the results of Western influence have been disastrous. In a recent survey of the population of the urbanised central Pacific island of Nauru we found that 34.4% of the people aged 15 years and over had diabetes.³ This figure is comparable with that of the American Pima Indians—a population with the highest prevalence of diabetes ever reported.⁶

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