

Correlation between Neonatal Jaundice in Normal Vaginal Delivery and Cesarean Section under General Anesthesia with Isoflurane and Sevoflurane

Ahmed Samir Abukhomra¹, Hadeel Abdulameer Shamkhi Alshlah², Aqeel Muslim Al-Jadi³,
Adnan Mansour Jasim⁴

^{1,4}College of Veterinary Medicine, AL-Qasim green University, Babylon 51001, IRAQ.

²FICMS FICOG department of Gynecology and Obstetrics, College of Medicine, University of Al-Ameed

³Al-Furat Al-Awsat Technical University - AL-Mussaib Technical College, Department of Animal Production Technologies

Email address: ²hadeel-Alshlah@alameed.edu.iq, ³akeel.moslem@atu.edu.iq

Abstract—Background: Neonatal jaundice is a highly prevalent and always benign physiological condition in newborns, clinically characterized by an icterus of the skin and the whites of the sclera of eyes. In medical terms, this condition is named as neonatal jaundice. For neonates with darker skin pigmentation, the icterus may be less noticeable. **Objectives:** This investigation aims to determine the relationship between the mode of delivery, specifically comparing infants born via normal vaginal delivery (NVD) versus those Cesarean Section (CS) delivery under General Anesthesia (GA) with isoflurane and sevoflurane. **Materials and Methods:** Forty birth cases were systematically analyzed, including both natural deliveries and those done under GA. The cases were collected from Babylonian Hospital, where the study was conducted. **Results:** The study establishes that GA influence on neonatal jaundice incidence, highlighting a crucial need to examine the pharmacological role of the administered anesthetic agents, is associated with an increased incidence of jaundice in newborns. This effect was showed in both physiological parameters and levels of liver enzyme, suggesting a significant influence on neonatal health. **In conclusion,** the use of GA, especially sevoflurane, has been related with higher percentages of neonatal jaundice. These findings necessitate the need for further research to identifying and exploring alternative GA that demonstrably has a no adverse effect on neonatal bilirubin homeostasis and subsequent icterus levels.

Keywords— Isoflurane, sevoflurane, jaundiced infant, caesarian section.

I. INTRODUCTION

Hyperbilirubinemia, a condition named Jaundice as, is a significant factor in hospital readmittance for newborns. Although many studies to identify infants at risk for elevated hyperbilirubinemia, detecting the condition is very difficult [1]. According to hospital data, 80% of preterm babies and 60% of full-term babies and undergo jaundice in the first days after birth. Despite the fact that icterus is already harmless, newborns should be further checked in order to prevent progress serious hyperbilirubinemia as well as acute encephalopathy [2]. Bilirubin-induced neurotoxicity can be either temporary or reversible. While infrequent, kernicterus is a rare but is an uncommon but hazardous of hyperbilirubinemia. Potentially life-threatening consequence of uncontrolled [3]. Numerous researchers have been done to determine the different influencing hyperbilirubinemia in neonates [4]. The results showed that a different of risk factors have been recorded as drivers of icterus, involving maternal and neonatal threat factors like the Rh- blood group, age of newborn's, weighting of mother at birth, and type of nutrition [5]. The severity of jaundice is also affected by the manner of delivery. Risk factors also include unnecessary delivery treatments, including caesarean sections, and the overuse of oxytocin during labour [6].

Different research have been done to confirm the factors that influencing hyperbilirubinemia in newborns [7].

Moreover, Beyazit and Çetinkaya (2022) ultimately confirmed it and Bravo et al. (2022) that natural neonate's delivery had higher bilirubin levels as compared with infants born by caesarean section (CS). The factors that have contributed to the increase in the prevalence of newborn jaundice in recent years have not yet been fully studied. Bilirubin level partition is the main step for the clinical assessment of jaundice. Free hyperbilirubinemia, if left without treatment, may reach to toxic levels. Primary disorders for hepatobiliary, thus infectious, toxicity, genetic defect, and metabolic diseases, May confirmed with hyperbilirubinemia conjugated type. A well-structured and fast diagnostic evaluation is paramount, as it facilitates the early and accurate identification of treatable underlying disorders. Nevertheless, the clinical challenge resulting from cholestatic liver disease after medical management and their drugs complications.

Early surgery related to biliary atresia and big steps forward in transplantation of hepatocyte have made it possible for babies with liver diseases that used to be fatal to live for a long time. The current study was created to look into how the factors listed above affect neonatal jaundice. This was done because the results on elements affecting neonatal icterus, like way of delivery and anaesthesia, have been inconsistent, and the number of caesarean sections is steadily rising [8]. A Cesarean section is a surgical operation involving an incision in the mother's abdomen to deliver the baby [9, 10]. Global rates of this procedure have risen sharply, jumping from 7% in 1990 to 21% in 2011, according to the WHO. This trend is

projected to continue, with the global rate expected to reach 29% by 2030 [11]. Consequently, this surge means that while some areas still have unmet needs, a significant number of women and children worldwide are being needlessly exposed to short- and long-term health risks when CS is performed without a clear medical justification [12].

A CS conceptions maternal health, leading to higher percentages of mortality and boost risk for confusion both during the initial recovery and in all future pregnancies. Specifically, women delivered by CS are confirmed to be high susceptible to life-threatening Occurrences such as major hemorrhage, severe acute infection, and shock. The history of surgical operation also give a predisposition for critical complications in subsequent pregnancies, involving rupture of uterine and placenta Previa [13]. CS method of delivery than vaginal has been linked with the progressive of endometriosis later in life [14]. On a global scale, around 10% of women and girls of reproductive age are affected by endometriosis. However, it is currently unclear how much of this incidence may be attributed to caesarean section (CS). Furthermore, multiple research have discovered a substantial correlation between endometriosis and a heightened probability of acquiring diverse types of cancer, such as ovarian cancer, endometrial cancer, and breast cancer [15]. In addition to the direct health consequences, CS (Caesarean sections) are linked to higher healthcare costs. As the rate of CS continues to rise, it is expected to place additional strain on the healthcare system, particularly in low- and middle-income countries (LMICs), which could have negative effects. [12, 16]. Isoflurane is a inhalation anesthetic agent, which is widely utilized to patients undergoing surgical operation [17]. The metabolism of drug characterized by minimal metabolites, so it's remain responsible hepatotoxicity [18]. The recent report by Noori and his coauthors confirmed that isofluran induce oxidative stress resulting hepatic necrosis and apoptosis [19]. Sevoflurane, a new generation of anesthetic agent , has bronchodilator and may offer better protection against reperfusion injury after one-lung ventilation in thoracic surgery [20] [21].

Elevated bilirubin levels are known to negatively influence brain function, increasing its vulnerability to anesthetic agents including etomidate, desflurane, and isoflurane. Research has shown that jaundiced patients exhibit prolonged recovery times, higher rates of bradycardia and hypotension post-anesthesia administration, and greater sensitivity to isoflurane when compared to non-jaundiced patients [22]. Consequently, initial research suggests that isoflurane induces hepatotoxicity through its regulation of IGF-1 expression, and that supplementation with IGF-1 may potentially prevent isoflurane-induced liver injury. RetryClaude can make mistakes.

II. MATERIALS AND METHODS

During this experiment, a number of birth cases were taken under general anesthesia and natural birth. This study included forty cases distributed among the hospitals from which we took them, namely Al-Zahraa Maternity Hospital (Babylon), Imam Sadiq Hospital (Turkish) (Babylon), and Al-Mahawil General

Hospital (Babylon). The study also included cases from Al-Qasim Hospital in Babylon and the Women's and Children's Teaching Hospital in Diwaniyah.

III. RESULTS AND DISCUSSION

The findings presented in Table 1 demonstrate that total bilirubin concentrations in the blood serum of neonates born via cesarean section showed a statistically significant elevation among jaundiced infants whose mothers received isoflurane as a general anesthetic, with levels reaching 8.10 ± 0.4 . This was notably higher compared to infants whose mothers were administered sevoflurane (5.6 ± 0.41), while neonates delivered through normal vaginal birth without surgical intervention exhibited physiological bilirubin levels of 1.68 ± 0.21 . Moreover, table (1) refer to the levels of infants' total creatinine in t the blood serum of infants after cesarean sections indicated significant increase in its levels in infants with jaundice in whom the general anesthetic isoflurane or sevoflurane (0.56 ± 0.08 and 0.58 ± 0.15) respectively while the levels were normal for infants'. After giving birth, the surgical procedure was not performed and the birth was normal to record rates (0.23 ± 0.01).

TABLE 1. Infants' serum total bilirubin in normal parturition and Caesarean section women

Groups	Total bilirubin mg/dl (mean ±SE)	Total creatinine mg/dl
Healthy (Normal parturition)	$1.68 \pm 0.21a$	$0.23 \pm 0.01b$
Caesarean section with isoflurane admins.	$8.10 \pm 0.4b$	$0.56 \pm 0.08a$
Caesarean section with sevoflurane admins.	$5.6 \pm 0.41c$	$0.58 \pm 0.15a$
P value	<0.0001	0.062

Furthermore, Table 2 presents clinical parameters revealing that both heart rate and respiratory rate displayed abnormalities with significant increases in cesarean-delivered, jaundiced infants. Those exposed to isoflurane recorded values of 173.05 ± 2.4 and 67.25 ± 0.68 , respectively, while sevoflurane exposure resulted in rates of 170.5 ± 2.02 and 67.12 ± 1.07 , respectively. No statistically significant difference was observed between these two anesthetic groups. In contrast, neonates born via normal delivery exhibited typical heart and respiratory rates of 102.8 ± 5.64 and 51.11 ± 2.71 , respectively. The current study also showed in table (3) a significant decrease in infant weights after cesarean section under the use of general anesthesia under isoflurane and sevoflurane to recorded mean value (2.33 ± 0.17 and 2.45 ± 0.24) respectively as compared with normal parturition to show range at 3.48 ± 0.2 . kg On the other aspect data refer that Liver malformation percent was 20% in infant weights after cesarean section while percent was 11.7 down syndrome in infants under general anesthetic isoflurane table (4). While percent of jaundice in sevoflurane was 10% in liver malformation and down syndrome.

Statistical significance between any two group means is denoted by the presence of different superscript letters adjacent to the values.

TABLE 2. Infants' heart and respiratory rate in normal and Caesarean section women

Groups	Heart rate/min	Respiratory rate/min
Healthy (Normal parturition)	102.8±5.64a	51.11±2.71a
Cesarian section with isoflurane admins.	173.05±2.4b	67.25±0.68b
Cesarian section with sevoflurane admins.	170.5±2.02b	67.12±1.07b
P value	<0.0001	<0.0001

A variance is considered statistically significant when the probability value (P) is less than 0.05.

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TABLE 3. Weight of infants in normal parturition and caesarian section women under isoflurane and sevoflurane

Groups	Infants weight in kg
Healthy (Normal parturition)	3.48±0.2a
Cesarian section with isoflurane admins.	2.33±0.17b
Cesarian section with sevoflurane admins.	2.45±0.24b
P value	0.001

Different superscript letters between any two means denote a statistically significant difference at $P < 0.05$.

TABLE 4. Infant malformation normal and Caesarian section women under isoflurane or sevoflurane anesthesia.

Groups	Total No.	Liver malformation	Down synd.
Healthy (Normal parturition)	10	0(0)	0(0)
Cesarian section with isoflurane admins.	20	3(15)	0(0)
Cesarian section with sevoflurane admins.	10	1(10)	1(10)
P value		0.488*	0.247*

* No significant variation at $P < 0.05$

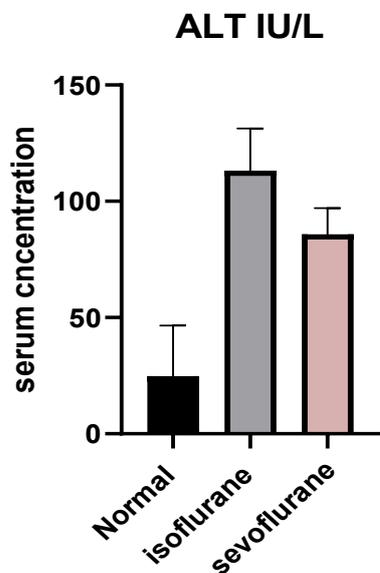


Fig. 1. Serum ALT levels increased in isoflurane and sevoflurane groups compared to normal controls, with the highest level in the isoflurane group.

Both anesthetic agents caused an increase in figure (1, 2) ALT, and AST levels respectively as compared to the normal range, indicating liver stress. Isoflurane, however, was associated with the most significant elevation of ALT while sevoflurane resulted in only a moderate increase. This pattern clearly suggests that isoflurane has a greater hepatotoxic effect (impact on the liver) than sevoflurane.

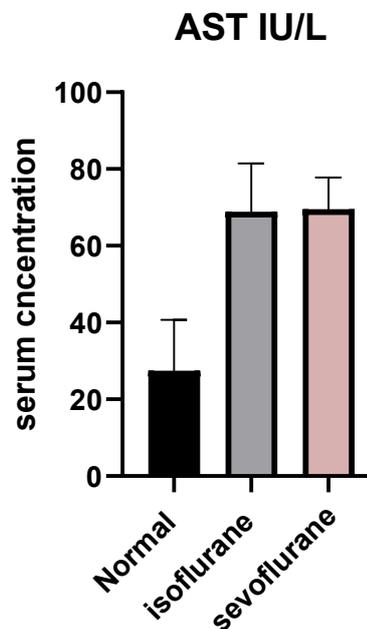


Fig. 2. Serum AST levels increased in isoflurane and sevoflurane groups compared to normal controls.

According to the current research, neonates delivered spontaneously had a no risk of jaundice than neonates delivered via cesarean section. The degree of jaundice and the method of delivery were positively correlated. As a matter of fact, infants delivered via cesarean section were less likely than those vaginal delivered to experience severe jaundice. Chang et al. (2011) demonstrated that newborns delivered spontaneously had low concentration of serum bilirubin levels than neonates delivered via cesarean section, which is consistent with the current findings.

Additionally, the likelihood of supplements being given to neonates born via cesarean section increases, which lessens the degree of jaundice [23]. Jaundice and mode of birth did not significantly correlate, according to research by Poorzanjani (2007) and Boskabadi et al. (2011) [24]. In a similar vein, Sharifzade et al. (2012) discovered no connection among the manner of delivery and degree of icterus. Conversely, a statistically significant link was discovered by Temoke et al. (2004) between the route of birth and the degree of jaundice [25].

The contradictory findings of the correlation between the manner of delivery and icterus could perhaps be attributed to variations in the variation used, the conditions under investigation, and the size of the sample. According to the current study, oxytocin usage during vaginal delivery may have an impact on the positive correlation that has been shown

among the degree of icterus and oxytocin utilize for reinforcement or induction of labor.

The results presented by [26] and were in agreement with the current findings [27]. Infants' red blood cells retain water due to the hypoosmotic effects of oxytocin, which also reduces the capacity of cells to undergo cellular transformation. Additionally, oxytocin promotes the lysis of red blood cells as they travel through the arteries, which results in hyperbilirubinemia. Corticosteroids are necessary for the hepatic enzymes that release bilirubin into the bloodstream. Adrenocorticosteroids also play a significant role in priming the liver of the baby for the removal of bilirubin from its body. Actually, because normal childbirth results in the absence of developed hepatic enzymes, the administration of oxytocin may be linked to neonatal jaundice. In current data, there was highly a significant correlation among infants jaundice, type of delivery and type of anesthesia. Demiraran, Albayrak [28] confirm that local (anesthesia technique spinal and epidural) was related with a reduced level of total serum bilirubin in infants, as versus to GA (24). Nevertheless, Eskicioğlu et al. (2014) showed no significant correlation among jaundice and variants types of anesthesia [29]. In addition, apoptosis (programmed cell death) has been regarded as a primary mechanism of liver injury that occurs following anesthetic administration [30] and may result in mass apoptosis [31]. Therefore, the present study speculated that the liver injury induced by isoflurane anesthesia and sevoflurane as well as increase cases of jaundice in infants after cesarean section.

Cesarean sections (CS) are performed for numerous medical reasons, including prolonged or obstructed labor, fetal distress, high maternal blood pressure or glucose, multiple gestations, and abnormal presentation of the baby [32]. For decades, this surgical procedure has proven beneficial, significantly lowering both maternal and neonatal illness and death when clinically indicated. However, CS poses risks when performed unnecessarily. A growing trend shows that not all CS are medically justified; the rate of procedures lacking clinical indication, often referred to as "cesarean on maternal request," is rapidly increasing [33]. Today, a huge elevation of percentages of cesarean section due to nonmedical reasons. In fact, it involves high maternal demand because of fearing from pain from vaginal delivery and anxiety or desire to have a baby on a specific day [34].

IV. CONCLUSION

The results of the current study demonstrated the impact of all studied parameters on infants, highlighting the role of general anesthetics in increasing neonatal jaundice rates, particularly with the use of sevoflurane. This outcome, demonstrated at both the systemic (physiological) level and via changes in liver enzyme profiles, underscores the necessity for targeted research to identify and validate safer anesthetic alternatives that minimize adverse effects on neonatal well-being.

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Ali H ilal Imran: Funding Acquisition, Curation and Writing

Ethics approval

This is to certify that the research project entitled "Correlation between Neonatal Jaundice in Normal Vaginal Delivery and Cesarean Section Under General Anesthesia with Isoflurane and Sevoflurane" submitted by: Principal Investigator (Student/Researcher): Adnan Mansour jasim, Department of physiology, pharmacology, and biochemistry/ College of Veterinary Medicine, has been reviewed and approved by the Research Ethics Committee of Al-Qasim Green University. The Committee confirms that the study complies with institutional and national ethical standards for NUMBER OF YEARS research involving:

Human participants and biological samples

Certificate No.: qgec/13 /2025

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Consent to participate

For all research involving human participants, freely-given, informed consent is a mandatory prerequisite for study involvement, which must be obtained from the participant or, for minors under the age of sixteen, from a parent or legal guardian and a statement to this effect should appear in the manuscript.

Example statement:

"Informed consent was obtained from all individual participants included in the study."

"Written informed consent was obtained from the parents."

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