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Research Paper

# Intraoperative Awareness During Cesarean Delivery Under General Anesthesia

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**Running Title** Awareness During General Anesthesia and Cesarean Delivery

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## ABSTRACT

**Background:** General anesthesia (GA) for caesarean section (CS) has distinctive characteristics that may increase the risk of awareness during GA (AGA).

**Objectives:** The aim of this study was to investigate the incidence of unintended awareness during GA (AGA) in CS.

**Materials & Methods:** This cross-sectional descriptive study was performed in Alzahra Hospital in Rasht City, Iran. Eligible women with term pregnancy candidates for CS under GA were enrolled in this survey from May 2018 to August 2021. After delivery, a questionnaire including demographic data and questions related to different stages of anesthesia was completed via a face-to-face interview. The collected data were analyzed using repeated measurement, the Chi-square, Fisher exact, and t-test in SPSS v. 21.

**Results:** The data from 174 women were analyzed, and 12 (6.9%) experienced AGA. Among them, dreaming and feeling the manipulation of the surgical area (27.8%) were the most common reported awareness states. Body mass index had a significant (P=0.034) relationship with AGA, but age (P=0.843), the level of education (P=0.714), history of anesthesia (P=0.552), 5-minute Apgar score (P=0.49), and surgery time (P=0.686) had no significant relationship with AGA.

**Conclusion:** The incidence of AGA during CS was almost close to the high limit established by the credible evidence, and a significant number of the women were not in completely acceptable conditions. Therefore, the management of GA for CS should be revised in this academic hospital.

**Keywords:** Intraoperative awareness, General anesthesia, Cesarean section

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## Highlights

• Cesarean section is associated with a high risk for intra-operative awareness as no anesthetic agent or opioids can be administrated for premedication until after delivery.

• In this study, the incidence of awareness during general anesthesia in the cesarean section was almost close to the maximum reported range, indicating the need to revise the general anesthesia management for cesarean section.

## Introduction

Awareness during general anesthesia (AGA) is defined as the postoperative recall of any event that occurred during surgery. It indicates the failure to achieve the primary goals of anesthesia and has been reported as auditory perception, pain, panic, loss of motor function, and helplessness [1]. AGA is a serious problem with long-term psychological complications such as post-traumatic stress disorder, flashbacks, a tendency to avoid future medical visits and care, sleep disorders, lack of concentration, nightmares, and irritability. Studies have demonstrated that pain during general anesthesia (GA) which is a major risk factor for long-term psychological disorders, is associated with the use of muscle relaxants (MRs). Furthermore, despite immobility, AGA occurs during surgery in patients who receive large doses of opioids without receiving MRs [2, 3].

One of the main reasons for AGA is the use of neuromuscular blocking agents. Light anesthesia is another major cause of awareness. In general, the overall prevalence of intraoperative awareness is 0.1%-0.2%. However, in cases of significant trauma, cardiac surgery, and cesarean section, the prevalence is higher, reaching 0.1% to 7% in CS [4].

Spinal anesthesia (SA) is considered the choice of anesthesia for CS. Preventing the fetus from being exposed to anesthetic agents, early onset, and ease of performance are some advantages of this method compared to GA [5-7]. The risk of pulmonary aspiration, failed intubation, increased blood loss, higher degrees of postoperative pain, chronic pain, increased risk of postpartum depression, and oxygen toxicity are GA-related risks in CS [8-10]. However, in emergencies or any contraindication to SA, GA should be considered [11].

It has long been well known that CS is one of the primary surgeries at risk of AGA. Because no anesthetic agent is administrated as premedication, opioids are not allowed until after delivery. Being afraid of fetal depression and uterine atony, anesthesiologists limit the concentrations of volatile anesthetics (VA) in CS. In addition, the risk of awareness increases with rapid sequences of induction of anesthesia and surgical incision immediately after that [12].

When surgery begins, there may be insufficient time to produce the appropriate analgesic and hypnotic effects of VA. Furthermore, a single dose of induction drug is rapidly redistributed. Nitrous oxide is also rapidly uptaken, but it is a weak anesthetic. It should also be noted that the minimum alveolar anesthetic concentration in CS is reduced by 25%-40% [13, 14].

In this regard, anesthesiologists play an essential role in balancing the appropriate depth of anesthesia and fetal drug transmission. Studies have shown various choices for GA induction in CS, different agents, and dosages. However, the first choice and an acceptable standard regime to prevent maternal awareness while maintaining fetal safety have not been introduced [15]. Given the adverse consequences of intraoperative awareness, all anesthesiologists and anesthesia departments should consider strategies to limit the rate of AGA. To achieve this goal, the first step is to realize the current situation. To the best of our knowledge, similar studies are few in Iran, let alone in our province. In this study, the prevalence of unintended AGA in CS in an academic and referral hospital affiliated with Guilan University of Medical Sciences was investigated

## Materials and Methods

This cross-sectional descriptive study was performed in Alzahra Hospital, an academic hospital affiliated with Guilan University of Medical Sciences (GUMS), Rasht City, Iran, from May 2018 to August 2021.

The inclusion criteria were women with a term pregnancy aged between 18 and 45 years, ASA (American Society of Anesthesiology physical status classifications) class I or II, candidates for non-emergent CS under GA, and without chronic drug abuse.

The exclusion criteria were patients who disagreed to participate, uncooperative patients with psychological disorders, and a history of awareness in previous surgeries.

After sufficient explanations about the study process and obtaining informed consent, eligible women were enrolled in the survey. The anesthesia and surgery protocols were the same for all women.

Entering the operating room, standard monitoring including electrocardiogram (ECG), heart rate (HR), pulse oximetry ($SPO_2$), non-invasive arterial pressure, mean arterial pressure (MAP), and end-tidal $CO_2$ ($ETCO_2$) gas analyzer were performed for all patients. To reduce the fetus's exposure to anesthetic drugs, before induction of anesthesia, skin preparation and draping were done. Firstly, the patient was pre-oxygenated with 100% oxygen, and then propofol (2 mg/kg) and succinylcholine (1-2 mg/kg) were administrated, and tracheal intubation was performed. Anesthesia was maintained with isoflurane and nitrous oxide in oxygen ($N_2O/O_2$). After delivery, fentanyl (3 µg/kg) and midazolam (0.01 mg/kg) were administrated.

At the end of the surgery, to reverse the effects of MRs, neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg) were injected, and the patient was transferred to the recovery ward. Hemodynamic parameters, including MAP and HR, were recorded by the responsible medical student at four time points: before induction of anesthesia (T0), immediately after intubation (T1), 20 minutes after induction (T2), and at the end of surgery (T3). After delivery, when the patients were completely awake and cooperative, a questionnaire, including demographic data (age, level of education, BMI, history of anesthesia, gestational age, 1-minute Apgar score, and surgery duration) and 14 specific questions about the first memory after emergence from anesthesia and the last memory before anesthesia and determining the status of AGA during anesthesia was filled out via a face-to-face interview. The mentioned questionnaire was taken from the study of Noor Mohammad Arefian [16], and its content validity index (CVI) and content validity ratio (CVR) were also calculated in our center. In this regard, 30 patients filled out the questionnaire, and 10 expert faculty members of the Obstetrics and Anesthesia Department examined the questions. The value of the CVR for all questions was higher than 0.72. The reliability of the questionnaire was measured by Dorney's similarity coefficient (the Cronbach alpha), and the content validity coefficient was 0.79.

There are different grades of AGA. Grade 0 refers to unconsciousness and indicates no recall and no signs neither immediately nor in more than one month, and the highest grade 5 points to consciousness, indicating explicit recall with distress and pain, awareness with an emotional squeal [17].

### Statistical analysis

The collected data were analyzed by repeated measurement, the Chi-square test, and the Fisher exact and t-test in SPSS v. 21 (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, v. 21 (Armonk, NY: IBM Corp).

## Results

During the study period, a total of 195 women were screened, and the data from 174 cases were analyzed.

The mean values of age, BMI, gestational age, number of gravidae, number of abortions, the history of receiving GA, the 1st and 5th minute Apgar scores, and duration of surgery were summarized in Table 1.

The changes in MAP and HR from T0 to T3 were significant (P<0.0001), and the highest HR values were recorded at T1. In terms of MAP values, unlike HR, it did not increase at T1 compared to the baseline (T0) (Table 2).

About the last event that was remembered before the induction of anesthesia, 15.5% of women experienced unpleasant conditions. Of them, 17 (9.8%) reported pain before being unconscious, and 10 cases (5.7%) experienced anxieties about surgery and anesthesia and fear of death. Seventy-eight cases (44.8%) remembered face masks and saying take a deep breath as the last memory recalled before anesthesia. About the first event mothers remembered immediately after emergence from anesthesia, 36.2% of them had acceptable conditions and the rest complained of severe pain, suffocation, suctioning, and inability to move. Two cases of slapping in the face and one feeling of the endotracheal tube were also reported. Vague and incomprehensible noise and crowds around was the most frequently recalled event after emergence from anesthesia by 45 cases (25.9%) (Table 3).

A total of 12 women (6.9%) experienced AGA. Among them, 18 cases of different awareness states were identified. "Dreaming during surgery and anesthesia," as well as "feeling the manipulation of the surgical area," each by 27.8%, were the most common types of awareness state. The frequency distribution of various awareness states is shown in Table 4.

**Table 1.** Demographic and clinical data of women undergoing cesarean section under general anesthesia

| Feeling Awareness | Items of the Last Feeling Awareness | Mean±SD/No.(%) |
|---|---|---|
| Age (y) (20-46) | | 32.76±5.74 |
| Level of education | Illiterate | 2(11) |
| | Elementary or middle school | 27(15.5) |
| | High school | 26(14.9) |
| | Diploma | 78(44.8) |
| | University degree | 41(23.6) |
| BMI (kg/m²) (22-35) | | 28.84±2.85 |
| History of anesthesia | Yes | 71(40.8) |
| | No | 103(59.2) |
| Number of abortions (0-4) | | 1.49±0.71 |
| Gestational age (wk) (37-40) | | 37.85±0.87 |
| Number of gravida (1-6) | | 2.39±1.31 |
| Apgar 1st minute (5-9) | | 7.68±0.69 |
| Apgar 5th minute (7-10) | | 8.84±0.47 |
| Surgery time (min) (45-60) | | 50.63±4.0 |

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Comparing the demographic data of women with and without AGA, showed a significant association between higher BMI and the occurrence of AGA (P=0.034) but not in terms of age (P=0.843), level of education (P=0.714), history of anesthesia (P=0.552), gestational age (P=0.11), 1-minute Apgar score (P=0.347), 5-minute Apgar score (P=0.49), and surgery duration (P=0.686) (Table 5).

No statistically significant difference was found between MAP (P=0.477) and HR values (P=0.457) at 4 time points between the two groups of with and without AGA (Table 6).

## Discussion

This study revealed that 12 pregnant women (6.9%) suffered from AGA during CS, which is close to the maximum reported range [4].

About the last event that was remembered before anesthesia, 15.5% of women experienced unpleasant conditions. Seventeen cases (9.8%) reported pain before being unconscious, while the anesthesia sequence should be managed such that the surgical incision be made after the appropriate depth of anesthesia. Ten people (5.7%) experienced anxiety related to surgery and anesthesia and fear

**Table 2.** The changes in mean arterial pressure (map) and heart rate (hr) values at four time points

| Variables | Mean±SD | | | | P |
|---|---|---|---|---|---|
| | Before Induction | Immediately After Intubation | Twenty min After Induction of anesthesia | At the End of Surgery | |
| MAP (mm Hg) | 92.29±2.79 | 90.95±2.72 | 89.39±2.67 | 85.98±2.95 | 0.0001 |
| HR (min) | 84.61±17.21 | 103.42±17.09 | 88±14.62 | 85.06±10.17 | 0.0001 |

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**Table 3.** Frequency of the last memory recalled before anesthesia and the first memory after emergence from anesthesia

| Feeling Awareness | Items of the Last Feeling Awareness | No. (%) |
|---|---|---|
| The last memory before anesthesia | Putting a face mask and saying take a deep breath | 78(44.8) |
| | The voice of operating room staff talking | 50(28.7) |
| | Prayer and supplication to God | 3(1.7) |
| | Pain | 17(9.8) |
| | Feeling of fear and anxiety about surgery, anesthesia, and death | 10(5.7) |
| | Feeling Suffocated | 0(0) |
| | Washing and sterilizing the abdomen | 8(4.6) |
| | I do not remember anything during a smooth induction | 8(4.6) |
| The first memory after emergence from anesthesia | Hearing: Swallow your saliva and take a deep breath / your surgery is over / open your eyes | 24(13.8) |
| | Asking about my baby's health and gender | 39(22.4) |
| | Severe pain | 33(19) |
| | Vague and incomprehensible noise and crowds around me | 45(25.9) |
| | Feeling suffocated, cold, or hot | 19(10.9) |
| | Slap in my face | 1(0.6) |
| | Suctioning and the presence of a tube in my mouth | 1(0.6) |
| | Inability to move | 12(6.9) |

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of death, which emphasizes the need for proper communication between the patient and physicians involved, including gynecologists and anesthesiologists, to reduce perioperative anxiety. Regarding the first event mothers remembered immediately after emergence from anesthesia, 36.2% of them had acceptable conditions, and the rest complained of severe pain, suffocation, suctioning, and inability to move. All the mentioned distressing situations could be managed properly. For example, primitive pain control could be considered before emergence from anesthesia which is an effective modality [18].

Nineteen cases (10.9%) complained of suffocation, feeling cold or hot. Of them, 12 (6.9%) complained of inability to move, indicating that MRs were not completely reversed at the end of the surgery, which is a flaw in the anesthesia process. In standard anesthesia sequence, the effects of hypnotics should not wear off before MRs.

**Table 4.** Frequency of various awareness states during general anesthesia in cesarean section

| A Variety of Awareness | No. (%) |
|---|---|
| Inability to move during anesthesia | 1(5.5) |
| Hearing during anesthesia | 4(22.2) |
| Dreaming during anesthesia | 5(27.8) |
| Feeling pain during anesthesia | 3(16.7) |
| Feeling the manipulation of the surgical area during anesthesia | 5(27.8) |

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**Table 5.** Comparing demographic data of women with and without awareness during general anesthesia

| Variables | Status | Awareness During Anesthesia | No Awareness During Anesthesia | P |
|---|---|---|---|---|
| | | No. (%)/Mean±SD | | |
| Age (y) | ≤35 | 6(5.6) | 102(94.4) | 0.372 |
| | >35 | 6(9.1) | 60(90.9) | |
| | | 33.08±5.71 | 32.74±5.76 | 0.843 |
| Education level | Illiterate | 0(0) | 2(100) | 0.714 |
| | Elementary or middle school | 1(3.7) | 26(96.3) | |
| | High school | 3(11.5) | 23(88.5) | |
| | Diploma | 6(7.7) | 72(92.3) | |
| | Academic degree | 2(4.9) | 39(95.1) | |
| BMI (kg/m$^2$) | | 27.16±3.06 | 28.96±2.8 | 0.034 |
| History of anesthesia | Yes | 6(8.5) | 65(91.5) | 0.552 |
| | No | 6(5.8) | 97(94.2) | |
| Gestational age (wk) | 37-38 weeks | 7(5.2) | 127(94.8) | 0.11 |
| | 39-40 weeks | 5(12.5) | 35(87.5) | |
| 1-min Apgar score | Less or equal to 7 | 4(10.3) | 35(89.7) | 0.347 |
| | More than 7 | 8(5.9) | 127(94.1) | |
| 5-min Apgar score | Less or equal to 7 | 0(0) | 6(100) | 0.49 |
| | More than 7 | 12(7.1) | 156(92.9) | |
| Surgery time (min) | | 50.83±4.17 | 50.61±4 | 0.686 |

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Lots of noise and overcrowding could also be easily prevented by capable and responsible management of the operating room. Two cases of face slapping and one feeling of the endotracheal tube were reported, which were not acceptable. In our study, AGA was detected based on the mother's statements, and no intraoperative monitoring device was used. However, there is strong evidence that it could not be a limitation of this study.

Studies using the isolated forearm technique (IFT) reported the incidence of AGA up to 40% [11]. Interestingly, none of these cases could recall any intraoperative events. This may be because anesthetics are potent amnesiacs even at sub-anesthetic doses [19]. Fortunately, to date, there is no evidence that awareness detected solely based on these monitors and without patients' recall has significant adverse psychological consequences [20].

Supporting them, Zand et al. demonstrated that the bispectral index (BIS) was not a reliable monitor for detecting light anesthesia in CS [21]. In addition, a recent review article explained that the routine use of depth of anesthesia monitoring was not recommended [22].

Therefore, it seems that the results of this study, which were obtained by direct postoperative questioning, are reliable. However, a major concern is a difficulty of distinguishing between intra-operative events and the emergence phenomena. Baby crying, pain, and voices are related to postoperative events that the mother may report as AGA [23]. Dreaming during GA may also be due to light anesthesia or a part of emergence time. It should be noted that there is no consensus on the idea that only unpleasant dreams are linked to AGA [24].

**Table 6.** Comparison of mean arterial pressure (MAP) and heart rate (HR) values of women with and without awareness during general anesthesia

| Variables | Awareness During Anesthesia | Mean±SD | | | | Intragroup Statistical Estimation | Intergroup Statistical Estimation |
|---|---|---|---|---|---|---|---|
| | | Before Induction of Anesthesia | Immediately After Intubation | Twenty Minutes After Induction of Anesthesia | At the End of Surgery | | |
| MAP (mm Hg) | Yes | 91.25±3.64 | 89.75±3.51 | 88±2.82 | 84.58±3.6 | P=0.0001 | P=0.477 |
| | No | 92.37±2.75 | 91.04±2.64 | 89.5±2.64 | 86.09±2.88 | P=0.0001 | |
| HR (min) | Yes | 92.33±19.61 | 111.75±18.21 | 95.33±17.38 | 90.5±9.94 | P=0.0001 | P=0.457 |
| | No | 84.04±16.95 | 102.8±16.9 | 87.46±14.31 | 84.66±10.1 | P=0.0001 | |

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Odor et al. investigated the rate of AGA in CS. They found that 0.47% of the mothers had specific awareness. Similar to our study, the evaluating tool was a direct postoperative interview. Paralysis was reported in 5 (41.7%) and pain by 2 (16.7%); distressing memories were reported in 9 cases (75%) during induction and emergence [25]. Khanjani et al. compared the rate of AGA in two groups of propofol and isoflurane in CS. They found that when anesthesia was maintained with propofol, the occurrence of AGA was significantly higher compared to isoflurane (0.97%, and 6.7%, respectively) [26].

Yu Z et al. reported that in GA for CS, the administration of dexmedetomidine provided better Apgar scores and reduced catecholamine release compared to remifentanil which was associated with better hemodynamic stability. None of the women recalled perioperative or intraoperative events [27].

Hadavi et al. evaluated the incidence of AGA in CS at an academic hospital. They reported that the current anesthesia technique for CS provided a proper depth of anesthesia, and none of their cases experienced AGA. Good Apgar scores were also reported in their study. They recommended future studies with higher dosages of anesthetics [28].

The reason for this discrepancy among studies is justified by differences in methods. Indeed, the measurement tools, the time of interview and evaluation, the studied populations, and the chosen anesthetics were not the same among the studies. As mentioned above, studies have reported contradictory results [29, 30].

The diagnosis of AGA based on symptoms related to sympathetic activation, such as hemodynamic parameters and objective signs such as lacrimation, sweating, and movement, is not reliable enough and differs from monitoring such as electroencephalogram (EEG) changes [31], IFT [32], or BIS [33]. In such studies, which are designed based on patients' statements, the time of the interview is important, and in the long period after surgery, the possibility of forgetting the details should be considered. In addition to the monitoring, choosing the anesthetic agents differ according to the mother's medical conditions and her co-morbidities, the availability, and the price of the drugs, which affects the outcomes. For example, the prevalence of AGA is significantly higher when propofol is used than isoflurane [34]. In another study, Altıparmak et al. examined the effects of magnesium sulfate on postoperative pain and depth of anesthesia in pregnant women undergoing CS under GA. They found promising effects from this intervention [35].

Intraoperative awareness has long been known as one of the patients' main concerns. Despite the current literature to prevent this adverse event, the issue has remained complex and with several unanswered questions. Although the low incidence of AGA in CS may be inevitable, successful defense is not easily possible. Therefore, to reduce the litigation, it is suggested to discuss the possibility of AGA in high-risk patients, and in case of awareness, it should be fully documented in patients' medical records. In these cases, an apology may prevent the physicians from being sued. On the contrary, denial can make the situation worse [36].

## Conclusion

This study revealed that the prevalence of AGA in CS was almost close to the highest reported by the current evidence. It was also found that the effects of MRs were not completely reversed when the hypnotics' effects

ended. A noticeable percentage of our cases did not experience acceptable conditions either before induction of anesthesia or during emergence. Therefore, it seems that the sequence of GA for CS should be critically revised in our hospital.

### Study limitations

The study was single-centered. Women with the experience of AGA were not followed up for the adverse consequences.

## Ethical Considerations

### Compliance with ethical guidelines

All study procedures followed the ethical standards outlined in the Helsinki Declaration (2013). The study protocol was approved by the Research Ethics Committee of the Guilan University of Medical Sciences and registered (Code: IR.GUMS.REC.1399.390).

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### Authors contributions

Study concept and design: Gelareh Biazar and Mandana Mansour Ghanaie; Drafting of the manuscript: Fatemeh Hosseinzadeh and Mahin Tayefeh Ashrafiyeh; Acquisition of data: Haniye Dalir and Zahra Rafiei Sorouri; Statistical analysis: Soheil Soltanipour; Analysis and interpretation of data: Zahra Hamidi Madani; Critical revision of the manuscript for important intellectual content: Gelareh Biazar; Study supervision: Mandana Mansour Ghanaie.

### Conflict of interest

The authors declared no conflict of interest.

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