

Efficacy And Quality Application of Sedation and Anesthetics in Pregnant Women in Dentistry

Wamiq Musheer Fareed¹, Monadil H. Ali¹, Zakher Eid T Alrayes², Mohammad Nasser A Alabdan², Saif Tirad M Aldhafeeri², Mohammad Dahlawi³, Sahar Burmah⁴, Mohammed Nasir K Inamdar¹, Abdullah Abdulaziz Saeidi⁵

¹College of Dentistry and Pharmacy, Buraydah Colleges, P.O. Box 31717, Buraydah, 51418, Saudi Arabia

²College of Dentistry, Mustaqbal University, Qassim, Saudi Arabia

³College of Dentistry, Batterjee Medical College, Jeddah, Saudi Arabia

⁴Pediatric Dentistry Specialists at the Ministry of Health, Yanbu, Saudi Arabia

⁵Department of Oral and Maxillofacial Diagnostic Sciences, College of Dentistry, Taibah University, Madinah

Cite this paper as: Wamiq Musheer Fareed, Monadil H. Ali, Zakher Eid T Alrayes, Mohammad Nasser A Alabdan, Saif Tirad M Aldhafeeri, Mohammad Dahlawi, Sahar Burmah, Mohammed Nasir K Inamdar, Abdullah Abdulaziz Saeidi, (2025). Efficacy And Quality Application of Sedation and Anesthetics in Pregnant Women in Dentistry. *Journal of Neonatal Surgery*, 14 (20s), 514-527

ABSTRACT

It is crucial to maintain good dental health when pregnant. New medications have pushed the limits of the kind of anesthesia that can be delivered in emergency rooms by medical specialists. Conscious/procedural sedation is a field that is always evolving since doctors are constantly conducting qualitative research to come up with much more effective and satisfying ways to sedate patients. By giving out medications and painkillers, it is possible to address sensitivity during a procedure and anxiety brought on by a provoking diagnostic image. Despite the superiority of clinical discernment, sometimes what seems easy can actually be highly complicated; an injury, trauma, or lesion that seems minor or painless ends up being quite severe and intolerable for the patient. In a dental emergencies procedural sedation may benefits pregnant woman perceiving pain, nervousness, fears, apprehensions and anxiety. This article deals with efficacy and importance of analgesic sedation its safety, quality and physiological changes in a pregnant dental patient

Keyword: *Pregnancy, Efficacy, Anesthetics, Sedation, Analgesia, Dentistry*

1. INTRODUCTION

A multi-state study highlights negligence of women of any age regarding health issue and so it's obviously the same attitude during pregnancy especially for dental illness [1]. Dental wellbeing is ignored by 50% of expecting women even after having dental problem [2]. A woman reluctance to take dental treatment during normal status is the proofs indicators why they ignore it during pregnancy, and a conscious woman will thoroughly check the wellbeing of the oral treatment. Ignored dental disease can be harmful for both the mother and the unborn [3]. Probability to get dental infections during pregnancy is higher than normal days; it increases the chances of having low birth weight or premature birth [4], than in woman who has no teeth and gum infections [5, 6].

Tooth decay is well known to increase during pregnancy. Teeth are inconvenient, and tooth loss is obvious [7,8]. There is no scientific evidence that there is a fetal need for calcium, which is required for intrauterine growth, can be obtained from a variety of sources. Mother's teeth and tooth loss is a normal part of pregnancy. This phenomenon can be justified by nausea and vomiting seen in 70% of pregnancies. Vomiting can cause tooth erosion or have a negative impact on oral hygiene a layer of enamel on the mother's teeth. There is a decrease in blood flow during pregnancy. Calcium has accumulated in the body. In terms of ionized matter, however, there is no difference in Ca levels before and after pregnancy. Bone turnover, on the other hand, doubles during pregnancy. Tooth decay can be avoided by improving oral hygiene habits during pregnancy [9]. The degradation of dental and oral health during pregnancy causes as some women may have a high craving for specific meals, particularly carbs, during the initial months of pregnancy, and tooth brushing may be overlooked after they ingest these things [10]. Vomiting makes the mouth more acidic, especially during the first few months of pregnancy. The mother may not give much thought to oral hygiene in the first few months after vomiting. If teeth are not brushed correctly, an acidic environment develops in the mouth [11]. Pregnant women bleed more easily due to the effects of pregnancy hormones (estrogen, progesterone) and may put off brushing their teeth. As a result, bacterial plaque builds up [12].

Many dentists believe that as long as the pregnant woman's doctor grants her permission, minor operations can be performed [13]. The majority of dental operations are significant in the first three months and the last three months in terms of the

stresses to which the mother and the newborn will be exposed [14]. During the first trimester, effective dental treatment should be avoided. This is a particularly critical period since it is the stage of organogenesis [15]. (Figure 1)

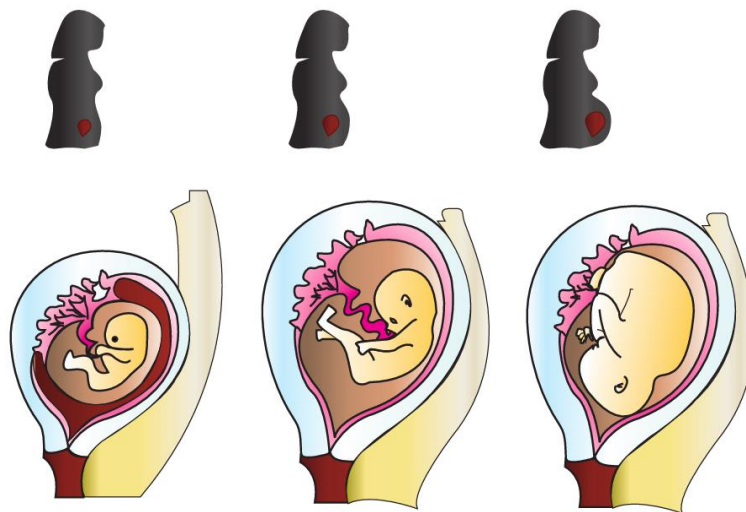


Figure 1: Stages of embryonic development a) 1st Trimester b) 2nd Trimester c) 3rd Trimester

Unnecessary intervention can lead to abortions. However, if there is pain or delaying therapy might do further injury, the teeth must be treated right away. Unbearable condition due to pregnancy fractures, exposed wounds, pericoronitis, oral abscess, also give rise to the need of procedural sedation [16]. Where neuromuscular blockade or unconsciousness is not applied, in those case Procedural sedation and analgesia (PSA) technique is suitable/applied [17]. Currently, PSA is applied in cardiology, dentistry, gastroenterology radiology, dermatology, as well in situation like emergencies [18]. PSA is now a standard parameter practice in most countries to assist, support performance as well as activity of a variety of analysis and therapy procedures.

Sedatives have been shown to be useful and safe for anxiety management during dental treatment. This article will address the pharmacological and therapeutic factors that regulate the appropriate use of sedatives [19].

1.1 Sedation:

Sedation is the reduction of irritability or agitation by administering sedative drug. It is a condition of diminished fervor or anxiety or uneasiness that is incited by the sedative agents [20]. Minor injuries including fractures, sprains, or open wounds happen between 6% and 7% of all pregnant women. Local anesthetic or procedural sedation may be obligatory to treat these unpleasant disorders [16].

Procedural sedation and analgesia previously (and improper) referred to as conscious sedation, short term painkillers and sedative drugs, permit the practitioner execute method/steps sufficiently at the same time keeping surveillance on the patient towards unwanted negative impact. Maternal oxygen demand increases during pregnancy, but functional residual capacity decreases, both of which can contribute to the rapid decline in maternal PaO₂ even during brief apnea. Maternal hyperventilation and a reduction in PaCO₂ are also present, however these effects are minimized by procedural sedation and/or general anesthesia [16].

Deeper sedation is a drug causing depression of consciousness amid which patients cannot be easily instigated but reacts purposefully to a repeated or painful stimulation. The capability to maintain ventilatory function freely may be impaired, and has similar risks as general anesthesia, requiring an equivalent level of care. Reflex i.e., natural reaction towards a painful stimulus, action or incitement is not considered a purposeful or wanted response [16]. The three level of sedation has been described in Table1.

Analgesia or painkiller is an absence of the sense of pain without loss of consciousness, usually induced and impelled by group of drugs including nitrous oxide. They perform locally (interfering nerve functions) or at large (suppressing sense of pain in the central nervous system of the body) [17].

General anesthesia is a treatment that includes set of medicines that is inhaled or given through a needle to the vein causing unconscious, it creates a state having no purposeful response to any stimuli. It suppresses normal automatic functions of the body like breathing, heartbeat, blood circulation, digestive system, protective reflexes. So, anesthesiologists must keep

balance of medicine, at the same time keep a close watch on the body vital function. An endotracheal tube is used to give inhaled anesthesia and oxygen to control and assist breathing [18].

Table 1: The continuum quality of sedation and sedation end points[18]

	Minimal sedation /Anxiolysis	Moderate sedation /Analgesia "Conscious sedation"	Deep sedation /Analgesia	General anesthesia
Responsiveness	Responds to verbal stimuli	Purposeful response to verbal or tactile stimuli	Purposeful response only after repeated or painful stimuli	Unable
Airway	Unaffected	No intervention required	Intervention may be required	Intervention Often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired

1.2 Scale of perceptiveness of sedation:

Subjective scales to assess agitation and sedation has been classified in the following:

Minimal sedation or negligible calmness during this, the body vital physical functions like ventilatory cardiovascular are unaffected and a patient reacts normally to verbal instructions. Only brain and physical co-ordination might get disturbed [18].

Moderate sedation is a drug causing depression of consciousness. The patient maintains ability to respond accordingly to a verbal instruction, alone or accompanied by soft tactile and controlled stimulation. Intervention is not required to maintain the patient's airway as spontaneous ventilation is adequate and cardiovascular functions is usually maintained (Reflex withdrawal to a painful stimulus is not considered as a purposeful response [18, 19].

Conscious sedation is a technique in which, variety of drugs, including propofol brings a state of depression to the central nervous system, letting treatment to happen at the same time verbal communication with the patient is maintained. The drugs and techniques used here must carry enough safety measures to render loss of consciousness differently, besides drugs it may accompany local anesthesia. The level of sedation retains defensive reflexes and is able to react to verbal orders, the patient remains alert and conscious. Sedation crossing this level of consciousness must be considered as general anesthesia and is then subjected to different regulation, and if at all intervention is required in exceptional situation [19].

Table 2: Scale of perceptiveness of sedation: characterization of general anesthesia and stages or planes of sedation/analgesia [18,21].

	Airway	Responsiveness	Spontaneous	Cardiovascular function
Minimal Sedation/ Anxiolysis	Unaffected	Typical reaction to verbal incitement	Ventilation	Unaffected
Moderate Sedation/ Absence of pain ('Cognizant Sedation')	No intervention required	Deliberate reaction to verbal or material incitement	Unaffected	Usually maintained
Profound Sedation/	Intervention may be needed	Purposeful response	Satisfactory May be insufficient	Usually maintained

Absence of pain		following repeated or painful stimulation		
-----------------	--	---	--	--

Non-Dissociative Sedation:

Non dissociative sedative drugs like opioids, benzodiazepines, barbiturates, etomidate and propofol performs according to sedation dose, resulting in response needed and expected. On increasing the dose, the effect of sedation raises leading airway and cardiovascular adjustments, missing protective reflexes and general anesthesia (GA) [21].

2. DISSOCIATIVE SEDATION

Ketamine causes dissociative sedation almost like being hypnotized state of mind. Define with deep analgesia, amnesia, sedation at the same holding protective response, voluntary breathing and cardiovascular movement [22].

1. Physiological alteration in pregnant women and application of sedation and/or anesthetic:

Physiological changes happen throughout pregnancy to fulfill the fetus's increased metabolic demands, to allow for efficient embryonic growth, and to strengthen the body for childbirth. The alterations start in the first trimester, peak around the due date or during labor, and then revert to pre-pregnancy levels within a few weeks following delivery. In healthy females, these changes are well endured, but they may worsen or reveal a from before the disease or pregnancy-related pathology [23]. Patients should be assessed/analyzed with respect to the American Society of Anesthesiologists (ASA) Physical Status Classification System (Table 3)

At 6 to 8 weeks of pregnancy, blood volume increases to a maximum of roughly 20% by the mid-third trimester. The renin-angiotensin system is activated by a wide pulse pressure and a low mean arterial pressure, which causes salt and water absorption. This causes a 40–50 percent increase in plasma volume. The end-diastolic volume of the left ventricle is increased while the end-systolic volume remains unaltered, resulting in an increase in ejection fraction. The pressures in the central venous and pulmonary capillary wedges are unaltered [24]. During epidural anesthesia and analgesia, abscess of the epidural venous plexus can affect the possibility of bloody tap and intravascular catheter implantation. In the incidence of hypotension, higher concentrations of vasopressors such phenylephrine are necessary due to suppression of adrenergic receptors [24].

During second and third trimesters, a decrease in blood pressure and cardiac output can occur while patient is in supine position due to decreased venous return to heart due to compression of inferior vena cava by fetus. These leads to postural supine hypotension. The compression can be relieved by placing a small pillow under the right hip or turning the patient left laterally to avoid the nausea and vomiting from hypotension [24]. (Figure 2)

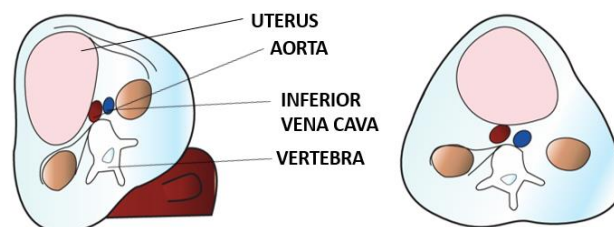


Figure 2: Management of postural supine hypotension to avoid compression of inferior vena cava

During a brief apnea in pregnancy, it is noticed that maternal oxygen consumption increases, with the decline in functional residual strength limit, and both of this helps fast reduction in maternal Pao₂ [24]. At the same time moderate maternal hyperventilation and lessened maternal pao₂ is witnessed an effect which is balanced during general anesthesia or procedural sedation. Due to dynamic physical changes at the airway route during pregnancy, there is a high risk of difficult intubation lack of airway control is one of the major causes of maternal mortality due to anesthesia [24].

The minimum alveolar concentration of volatile anesthetic decreases by up to 30%. Intravenous induction and sedative substances are physiologically more sensitive in pregnant women [25]. Since the conclusion of the first trimester, the spinal dose of local anesthetics (LA) has decreased by 25–40%, indicating that changes in epidural space anatomy are not the main cause. Following sympathetic blockade caused by neuraxial anesthesia, pregnant women are more susceptible to hypotension and hemodynamic instability [26].

During pregnancy hemodynamic alteration includes, decrease in systemic circulatory pressure arising from progesterone

induced vasodilation and low safety placenta, systemic hypotension (particularly in the prostrate position) due to aortocaval packing by the gravid uterus, a critical increment in cardiovascular yield and a fall in maternal hematocrit [24, 26].

Mild hypothermia is prevalent after moderate sedation or general anesthesia, and it's often accompanied with shivering and pain. Temperature drops that are considerably lower can have an even greater number of negative consequences [27]. The body temperature drops in three phases after general anesthesia. The first half hour, or phase 1, sees the most significant reduction. The body's heat is generally distributed unevenly, with core tissue temperatures 2 to 4 degrees Celsius higher than the skins. After anesthetic induction, vasodilation paired with a reduced hypothalamic cold sensitivity leads for a translocation of body heat from core tissues to skin, where heat is lost often through radiating. Phase 2 commences after about an hour, when internal temperature starts to fall more slowly and develops in a linear fashion as heat loss from the body surpasses heat generation. Phase 3 begins when a balance is struck between heat loss and heat generation, and thermoregulated vasoconstriction continues to work [26-28].

Table 3: Physical Status Classification System [29]

Class I	A normally healthy patient
Class II	A patient with mild systemic disease and no functional incapacity
Class III	A patient with severe systemic disease that limits activity, but is not incapacitating
Class	A patient with severe systemic disease that is a constant threat to life
Class V	A moribund patient not expected to survive 24 hours with or without an operation
"E"	An emergency procedure is denoted by the letter E following the class number

3. PHARMACOLOGY DURING PREGNANCY

Pregnancy affects pharmacokinetics of drugs in terms of distribution, degradation, and elimination of drugs and, therefore, under certain circumstances and pharmacodynamics as well [30].

Drug absorption and bioavailability are negatively impacted by the digestive system's decreased generation of hydrochloric acid. The activation of prodrugs, the process of absorption, biotransformation, and offset can all be affected by changes in the synthesis of liver enzymes, on the other hand. An illustration of this phenomena is the conversion of codeine to morphine by the cytochrome CYP2D6, whose activity is elevated during pregnancy [30]. In pregnant women, codeine quickly relieves pain, but it also has a higher toxicity [30, 31]. Pregnant patients have an increase in body mass and volume, which results in a higher drug volume of distribution and elimination [14]. Pregnancy increases both clearance and distribution volume, so it is impossible to estimate how a drug's half-life would change; instead, each drug should be examined separately. The placenta is a semipermeable membrane that allows cross of substances, similar to the blood–brain barrier. Generally, all substances that can pass the blood–brain barrier can also pass into the placenta [32, 33].

4. DRUGS DURING PREGNANCY

The Food and Drug Administration (FDA) classification reflects the potential risk that consuming medications while pregnant poses for birth abnormalities. Drugs have been categorized by the FDA into five groups based on the validity of the available scientific data and the cost-benefit analysis [33][Table 4].

Table 4: FDA Pregnancy risk factor definition [33]

Category	Definition
A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of risk in later trimester), and the possibility of fetal harm appears remote.
B	Either animal reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant woman or animal reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confined in controlled studies in women in the first trimester (and there is no evidence of risk in later trimesters).
C	Either studies in animals have revealed adverse effects on the fetus (teratogenic, embryocidal or other) and there are no controlled studies in women or studies in women and animals are not available.

	Drugs should be given only if the potential benefit justifies the potential risk to the fetus.
D	There is positive evidence of human fetal risk, but the benefits of use in a pregnant woman may be acceptable despite the risk (for example, if the drugs are needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
X	Studies in animals or human being have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

4.1 Local Anesthetics:

Both regional and general anesthesia have been associated to serious side effects [30, 32]. When a localized anesthetic is used, combative behavior, changed pain perception, and ephedrine-resistant hypotension may develop [32]. Low doses of phenylephrine, titrated to effect, usually restore normal blood pressure. So, use of anesthetic is critical, especially in pregnancy [33].

Most local anesthetics are thought to be quite safe for use in dentistry because they have not been proven to be teratogenic in humans. In experiments on animals, injections of high doses of lidocaine, bupivacaine, or mepivacaine near the umbilical artery can cause fetal bradycardia [33].

The administration of local anesthetics during pregnancy requires careful dose optimization to mitigate risks of fetal exposure. Current guidelines emphasize limiting anesthetic doses to the minimum necessary for effective pain control, as all local anesthetics can cross the placenta and potentially cause fetal central nervous system depression [34]. Nonsteroidal anti-inflammatory drugs (NSAIDs) and opioid analgesics may serve as safer alternatives for postoperative pain management in pregnant individuals, particularly when reducing reliance on bupivacaine—even at submaximal doses—is warranted [35].

Certain anesthetics, such as prilocaine and benzocaine, carry specific risks; both agents are associated with methemoglobinemia, a condition that reduces oxygen delivery to fetal tissues [36]. Lidocaine, when combined with vasoconstrictors like epinephrine (adrenaline), demonstrates a favorable safety profile. The addition of epinephrine prolongs the anesthetic's duration of action and reduces systemic toxicity by slowing absorption through vasoconstriction [37]. This results in a gradual rise in maternal blood lidocaine levels, avoiding toxic peaks and allowing slower placental transfer to the fetus. Consequently, fetal exposure remains within a wider safety margin [38].

Lidocaine 2% with epinephrine 1:100,000 is widely regarded as a relatively safe option for use during pregnancy. Studies indicate minimal fetal effects even at doses below the maximum recommended threshold, provided careful monitoring is maintained [39,40]. Table 4 depicts some FDI recommended local anesthetics in pregnancy.

Table 5: FDI recommendation of local anesthetics in pregnancy [41]

DRUG Local Anesthetics	During Pregnancy (prescription drug)	During Breastfeeding	FDA Category
Lidocaine	Yes	Yes	B
Mepivacaine	Use with alert counsel doctor	Yes	C
Prilocaine	Yes	Yes	B
Bupivacaine	Use with alert counsel doctor	Yes	C
Etidocaine	Yes	Yes	B
Procaine	Use with alert counsel doctor	Yes	C

4.2 Specific drugs

The medications most ordinarily/commonly utilized as a step during procedural anesthesia are midazolam, remifentanyl, propofol, ketamine, and nitrous oxide [42].

Maintaining a semi seated posture and keeping a planned safety from uncontrolled sedation is needed to avoid feelings and

anxiety. (Figure 3) Conscious sedation is the last possible option in the third trimester. The best treatments of these female patients are with well-equipped arrangement general anesthesia [41].

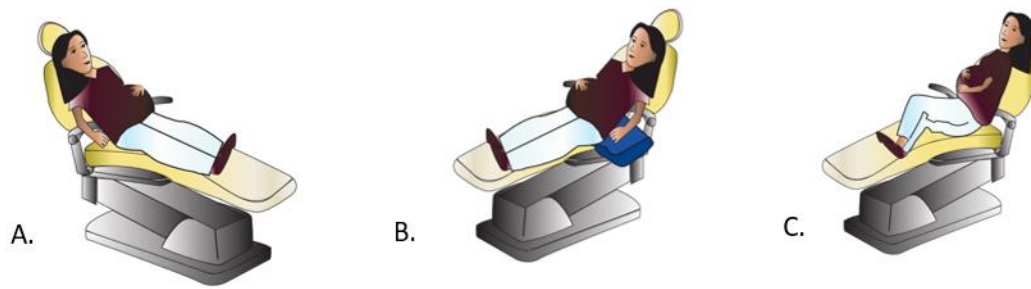


Figure 3: Schematic presentation of correct positioning for pregnant patients

Midazolam:

Midazolam, a quick relief substitute of imidazobenzodiazepine, it promotes aminobutyric burning (GABA) stimulate reaction inside central nervous system. Midazolam is firmly established as perfect soother, utilized in patients going through dental operations. Besides midazolam having settled narcotic and amnesia impact, there is difference in opinion on whether it has torment relieving impact. In the process that midazolam sedation has pain relieving impact [43]. There is critical effect during clinical observation of pain handling and cooperation from the patient. At the junction when intense pain is common, midazolam sedation can be used as an aid to control pain. This can maybe reduce pain along with better patient consent for the treatment. The utilization of benzodiazepines close term was indicated to be identified with the "floppy baby syndrome disorder," particularly in higher doses [44, 45].

Ketamine:

Ketamine is a rapid and short-acting general anesthetic, producing an anesthetic state characterized by profound analgesics. The ruling part of the medical drug settings is reachable as a racemic combination/mixture. The variety of role and cardiovascular safety in ketamine make it unique, costly expert for agonizing procedures. It stimulates a state of cortical segregation, with vital absence of pain, sedation and amnesia and is commonly suggested as a sedo-analgesic for patients [46].

Ketamine sometimes is linked to unwanted developments restricting its utilization, when all other treatment like MRI, CT scans are exercised. On the other side various tranquilizer has respective preservation on airway reflexes and tone. Ketamine strengthens excretion of saliva and tracheobronchial. Preventive conduction of an anti-sialagogue (atropine or glycopyrrolate) is exploited to minimize exasperating negative effects. Maternal pulse and heart rate is said to be intensified 30% to 40% by Ketamine [47]. Therefore, should be avoided by ladies experiencing hypertension from before. Neonatal depression and sufferings are additional concern when ketamine is induced-injected close to delivery. To sum up the restricted accessible human information suggest usage of ketamine to a minimum throughout pregnancy, although different treatments may be/considered perfect [48, 49].

Propofol:

An intravenous anesthetic drug frequently used is propofol. It is the preferred anesthetic for quick surgical procedures since it is quickly removed from the circulation and has a short half-life. Propofol was not found to be teratogenic in investigations on animals [16, 50].

Propofol can cause maternal hypotension, which is a typical side effect, but a study found that the drug also maintains healthy umbilical blood flow because it has a dilating effect on fetal placental blood vessels [51-53].

Although there have been concerns concerning neonatal sedation and depression, multiple investigations have demonstrated that low dose propofol, spinal anesthesia, or barbiturates all produce identical Apgar scores and neurological and adaptive capacity ratings [54-57]. Neonatal sedation and depression have drawn attention, although investigations have revealed identical Apgar ratings and neurological and adaptive capacities. Given peripartum, high-dose propofol may momentarily impair infant neurobehavioral function [16, 58].

In conclusion, there is no evidence that propofol is teratogenic in either humans or animals, but there are worries regarding neonatal depression when it is taken just before delivery, especially at high doses.

Nitrous oxide:

The usage of nitrous oxide has to be limited or constrained to cases where main or subordinate analgesics are weak. In such a situation meeting with the pre-natal worker is judged. Satisfying defensive measures should be taken to encounter hypoxia, hypotension, and aspiration [59]. Since pregnancy comes with astonishing changes in life structure, and physiology having disturbed sleep, disturbance, resulting high level of danger for both mother and the unborn. Considering all these facts, anesthetist prefers local sedatives for pregnant woman. A lower level of nitrous oxide is sufficient to acquire sedation in pregnancy. Rehabilitation standard drug dosage for experienced sedation under (MAC) intravenous and sedation are much less in pregnancy. If the pregnant ladies are given regular measurements of drugs for mental sedation, she might get senseless. An Oximeter for heartbeat is necessary in pregnancy accepting MAC. Similarly maternal oxygen supply should be 95% or more to ensure enough oxygen supply to the unborn [60, 61].

Due to delay in gastric clearance and distorted lower esophageal sphincter a pregnant lady is considered to dependably have full stomach. Pregnant women are at high risk for breathlessness or aspiration, so prophylactic measures to anticipate goal is used, specifically during the third trimester. Woman with multiple incubation faces are a huge threat and danger because of strong emotions and or anxiety during the middle second semester due to enlarge uterus. For individuals who are phobic or apprehensive, it is secure and provides great sedation [62-64]. Pregnant women frequently experience increased anxiety [62]. Nitrous oxide is the drug of choice if the patient's anxiety levels are so high that they are impeding their ability to cooperate and sedation is ineffective in controlling their fear [63, 64]. As far as possible, prolonged exposure should be avoided.

4.3 Analgesics:

Analgesics can be administered during pregnancy if the treatment is unavoidable (Table 5), however dental specialist suggest shelving of selected dental procedure [65]. Many studies clearly state no increase in inborn abnormalities at the time of childbirth after anesthesia during pregnancy, however this does not proof that analgesic specialist are not teratogenic on human, from the very first trimester anesthesia increases the danger of spontaneous or unwanted premature delivery and low birth weight [Table 5]. Due to the possibility of postpartum hemorrhage, acetylsalicylic acid is not advised. Paracetamol is preferred because it also results in less stomach irritation [66].

Additionally, NSAIDs should not be used during the first trimester of pregnancy as some authors have noted an increased incidence of septal heart abnormalities in neonates delivered to moms who took NSAIDs such ibuprofen, naproxen, diclofenac, and ketoprofen. Celecoxib and rofecoxib, two novel types of cyclooxygenase inhibitors, have been placed in category C. Additionally, since these medications pose the risk of prematurely closing an arterial duct during the first trimester, they should be avoided [67-72].

Table 6: Analgesic used in pregnancy [65]

Analgesic	Use in pregnancy	FDI category
acetaminophen	Yes	B
Codeine	Low dose, short duration acceptable	C
propoxyphene	Low dose, short duration acceptable	C
Oxycodone	Low dose, short duration acceptable	B
Meperidine	Low dose, short duration acceptable	B
Diflunisal	Do not use in 3 rd trimester	C/D
Aspirin	Do not use in 3 rd trimester	C/D
Naproxen	Do not use in 3 rd trimester	B//D
Etodolac	Do not use in 3 rd trimester	B/D
Flurbiprofen	Do not use in 3 rd trimester	B/D
Ibuprofen	Do not use in 3 rd trimester	B/D
Ketorolac	Do not use in 3 rd trimester	B/D

2. Teratogenicity by Anesthetic Agent:

Basically, all drugs usually have teratogenic/ harmful property on specific animal category, when conducted in required quantity during a particular pregnancy interval amid vital timing and when entering the placenta. When considering the possible teratogenicity of various anesthetic agents, several important points must be kept in mind. First, the background incidence of congenital anomalies in humans is approximately 3%. Second, physiologic derangements such as hypoxemia, hypercarbia, stress and hypotension may be teratogenic themselves. These problems can occur during anesthesia and surgery and sometimes exist pre-operatively. This requires for narcotic experts along with their adjuvants, and its demonstration is mostly single and in small period. Generally, drugs like painkiller, used for sedation enters into placenta due to low sub-atomic weight, high lipid solvency, low level of ionization and low protein binding [67, 72]. Teratogenic characteristics of a medicine when circulating in a placenta depends on the developing stage of the fetus. In the middle of origination and implantation, put-down to the incipient organism can bring about its passing and premature delivery or in place survival. At this "all or none" arrange, the incipient organism is undifferentiated and repair is conceivable through duplication of the still omnipotent cells. Organogenesis, from 18 to 58 days after origination, is the time of greatest affectability to teratogenicity. Harm to tissue is irreparable as they divide quickly, leading deviation in structure. Once organogenesis is completed, teratogenic exposure will interfere in development of the fetus organ size and functionality. Till today no sedative drug has been declared precisely, teratogenic on human [73].

Teratogenicity of common anaesthetic drugs such as N₂O inhibits methionine synthetase, an enzyme necessary for DNA synthesis. Teratogenic effects are shown in animals after administering high concentrations for prolonged periods. However, such high required doses are not encountered in clinical practice. However, some recommend avoiding nitrous oxide in pregnant women [67].

Most other anesthetic medications, including barbiturates, propofol, opioids, muscle relaxants, and local anesthetics have been widely used during pregnancy with a good safety record. Nonetheless, delicate associations cannot be ruled out [73].

Ladies experience some astonishing changes while being pregnant, however tooth loss ought not one of them. There is no histologic, substance, or radiographic proof to help pregnancy creating calcium resorption inside teeth that would prompt tooth loss. There are some biologic changes that may prompt an expanded danger of dental contamination, for example, increment in hunger, increment in longings for surprising nourishment, corrosive disintegration of teeth (morning infection/ esophageal reflux), xerostomia (dry mouth), and hormonal/ vascular changes that may misrepresent a provocative reaction [1].

Oral wellbeing ought to be a necessary part of pre-birth mental peace. Although we have known for quite a while that oral wellbeing is vital, some pregnant ladies are not accepting oral health awareness benefits prenatal workers / midwives can play a critical part in to educate on the importance and significance of oral wellbeing. Enhancing oral wellbeing in pregnancy improves the general strength of ladies as well as helps enhancing the morale of their children.

5. CONCLUSION

Procedural sedation and analgesia administered to patient with urgent dental intolerable pain due to injury, trauma, or lesion that seems minor or painless ends up being quite severe with a thorough risk-benefit analysis, timing, proper selection of sedative agents used to provide conscious or moderate procedural sedation as well ensure vigilant monitoring. Comprehensive approach and adherence to protocols, healthcare providers can safely manage sedation in a pregnant patient which will have favorable outcomes. At the same many studies do not conclude that these drugs do not have teratogenic effect on human. From the very conception it can cause abortion, low birth weight, compounds in PSA might have the potential to cross the placental barrier which can have a negative impact on mother and fetal health. Future research should focus on identifying the barriers that prevent using of sedation in pregnant women, seeking to explore the safety and efficacy of the use of procedural sedation and analgesia (PSA). Additionally, more studies are needed in exploring and expanding our knowledge in these areas, for betterment, pain less, comfortable and promising new treatment modalities in sedation for pregnant women.

Authors' Contributions:

Wamiq Musheer Fareed conceived and designed the study, Mohammed Nasir K Inamdar organized, Monadil and Wamiq Musheer Fareed wrote the initial and final drafts of the article. Sahar Burmah and Abdullah Abdulaziz Saeidi critically reviewed the manuscript. Zakher Eid T Alrayes , Mohammad Dahlawi, Mohammad Nasser A Alabdan and Saif Tirad M Aldhafeeri have critically reviewed approved the final draft and are responsible for the content and similarity index of the manuscript.

Conflict of Interest: The authors have no conflict of interest to declare.

ACKNOWLEDGEMENTS

We would like to express our sincere gratitude to Dr. Ziyad Almushayti, Department of Radiology, College of Medicine, Qassim University, Al Mula'ida, Buraydah and Dean of the College of Dentistry and Pharmacy at Buraydah Colleges and for providing the resources and facilities essential to the completion of this study

REFERENCES

- [1] Gaffield, M. L., Gilbert, B. J., Malvitz, D. M., & Romaguera, R. (2001). Oral health during pregnancy: an analysis of information collected by the pregnancy risk assessment monitoring system. *Journal of the American Dental Association* (1939), 132(7), 1009–1016.
<https://doi.org/10.14219/jada.archive.2001.0306>
- [2] Boggess, K. A., Urlaub, D. M., Massey, K. E., Moos, M. K., Matheson, M. B., & Lorenz, C. (2010). Oral hygiene practices and dental service utilization among pregnant women. *Journal of the American Dental Association* (1939), 141(5), 553–561. <https://doi.org/10.14219/jada.archive.2010.0228>
- [3] Hilgers, K. K., Douglass, J., & Mathieu, G. P. (2003). Adolescent pregnancy: a review of dental treatment guidelines. *Pediatric dentistry*, 25(5), 459–467.
- [4] Massoth, C., Chappell, D., Kranke, P., & Wenk, M. (2022). Supine hypotensive syndrome of pregnancy: A review of current knowledge. *European journal of anaesthesiology*, 39(3), 236–243. <https://doi.org/10.1097/EJA.0000000000001554>
- [5] Haerian-Ardakani, A., Eslami, Z., Rashidi-Meibodi, F., Haerian, A., Dallalnejad, P., Shekari, M., Moein Taghavi, A., & Akbari, S. (2013). Relationship between maternal periodontal disease and low birth weight babies. *Iranian journal of reproductive medicine*, 11(8), 625–630.
- [6] Michalowicz, B. S., DiAngelis, A. J., Novak, M. J., Buchanan, W., Papapanou, P. N., Mitchell, D. A., Curran, A. E., Lupo, V. R., Ferguson, J. E., Bofill, J., Matseoane, S., Deinard, A. S., Jr, & Rogers, T. B. (2008). Examining the safety of dental treatment in pregnant women. *Journal of the American Dental Association* (1939), 139(6), 685–695. <https://doi.org/10.14219/jada.archive.2008.0250>
- [7] Lim, Hae. (2007). Anesthesia and Sedation. *Journal of the Korean Medical Association*. 50. 1065. [10.5124/jkma.2007.50.12.1065](https://doi.org/10.5124/jkma.2007.50.12.1065).
- [8] Hagai, A., Diav-Citrin, O., Shechtman, S., & Ornoy, A. (2015). Pregnancy outcome after in utero exposure to local anesthetics as part of dental treatment: A prospective comparative cohort study. *Journal of the American Dental Association* (1939), 146(8), 572–580. <https://doi.org/10.1016/j.adaj.2015.04.002>
- [9] Yenen, Z., & Ataçağ, T. (2019). Oral care in pregnancy. *Journal of the Turkish German Gynecological Association*, 20(4), 264–268. <https://doi.org/10.4274/jtgga.galenos.2018.2018.0139>
- [10] Marão Martins, Rafiza Felix., Paiva de Azevedo, Juliana Aires., Leite Dourado, Carolina Raiane., Costa Ribeiro, Cecília Cláudia., Coelho Alves, Cláudia Maria., & Abreu Fonseca Thomaz, Erika Bárbara. (2014), "Oral Health Behaviors and Dental Treatment During Pregnancy: A Cross-Sectional Study Nested in a Cohort in Northeast Brazil." *Pesquisa Brasileira em Odontopediatria e Clínica Integrada*, Vol. 14, núm.1, pp.5-11
- [11] Tamannur, T., Das, S. K., Nesa, A., Nahar, F., Nowshin, N., Binti, T. H., . . . Rahman, M. M. (2024). Mothers' knowledge and practices towards oral hygiene of their children aged 5-9 years old: a cross-sectional study in Dhaka. *medRxiv*, 2024.2004.2005.24305403. doi: 10.1101/2024.04.05.24305403
- [12] Wu, M., Chen, S. W., & Jiang, S. Y. (2015). Relationship between gingival inflammation and pregnancy. *Mediators of inflammation*, 2015, 623427. <https://doi.org/10.1155/2015/623427>
- [13] Favero, V., Bacci, C., Volpato, A., Bandiera, M., Favero, L., & Zanette, G. (2021). Pregnancy and Dentistry: A Literature Review on Risk Management during Dental Surgical Procedures. *Dentistry Journal*, 9(4), 46. <https://doi.org/10.3390/dj9040046>
- [14] urien, S., Kattimani, V. S., Sriram, R. R., Sriram, S. K., Rao V K, P., Bhupathi, A., Bodduru, R. R., & N Patil, N. (2013). Management of pregnant patient in dentistry. *Journal of international oral health : JIOH*, 5(1), 88–97.
- [15] Vt, H., T, M., T, S., Nisha V, A., & A, A. (2013). Dental considerations in pregnancy-a critical review on the oral care. *Journal of clinical and diagnostic research : JCDR*, 7(5), 948–953. <https://doi.org/10.7860/JCDR/2013/5405.2986>
- [16] Neuman, G., & Koren, G. (2013). Safety of procedural sedation in pregnancy. *Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC*, 35(2), 168–173.

[https://doi.org/10.1016/S1701-2163\(15\)31023-9](https://doi.org/10.1016/S1701-2163(15)31023-9)

- [17] Benzoni T, Cascella M. Procedural Sedation. [Updated 2023 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK551685/>
- [18] South African Society of Anaesthesiologists., Guidelines for the safe use of procedural sedation and analgesia for diagnostic and therapeutic procedures in adults: 2010. *S S Afr J Anaesthesiol Analg*, 16(4)(Supplement 1):S1-S24, Accessed on 26/03/25.
- [19] Bean T, Aruede G. Conscious Sedation in Dentistry. [Updated 2023 Apr 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK592406/>
- [20] Elo, J. A., & Sun, H.-H. (2016). Anesthesia and Sedation. InTech. doi: 10.5772/63539
Smith G, D'Cruz JR, Rondeau B, et al. General Anesthesia for Surgeons. [Updated 2023 Aug 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK493199/>
- [21] Tobias, J. D., & Leder, M. (2011). Procedural sedation: A review of sedative agents, monitoring, and management of complications. *Saudi journal of anaesthesia*, 5(4), 395–410. <https://doi.org/10.4103/1658-354X.87270>
- [22] Gitlin, J., Chamadia, S., Locascio, J. J., Ethridge, B. R., Pedemonte, J. C., Hahm, E. Y., Ibala, R., Mekonnen, J., Colon, K. M., Qu, J., & Akeju, O. (2020). Dissociative and Analgesic Properties of Ketamine Are Independent. *Anesthesiology*, 133(5), 1021–1028. <https://doi.org/10.1097/ALN.0000000000003529>
- [23] Gangakhedkar, G. R., & Kulkarni, A. P. (2021). Physiological Changes in Pregnancy. *Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine*, 25(Suppl 3), S189–S192. <https://doi.org/10.5005/jp-journals-10071-24039>
- [24] Melaku L. (2022), Physiological Changes in the Pregnancy and Anesthetic Implication during Labor, Delivery, and Postpartum . *Open Anesthesia J*, 16: e258964582207130. <http://dx.doi.org/10.2174/25896458-v16-e2207130>
- [25] Ebert, T. J., & Lindenbaum, L. (2011). Clinical pharmacology of inhaled anesthetics. In A. S. Evers, M. Maze, & E. D. Kharasch (Eds.), *Anesthetic Pharmacology: Basic Principles and Clinical Practice* (pp. 397–419). chapter, Cambridge: Cambridge University Press.
- [26] Bhatia, P., & Chhabra, S. (2018). Physiological and anatomical changes of pregnancy: Implications for anaesthesia. *Indian journal of anaesthesia*, 62(9), 651–657. https://doi.org/10.4103/ija.IJA_458_18
- [27] Díaz, M., & Becker, D. E. (2010). Thermoregulation: physiological and clinical considerations during sedation and general anesthesia. *Anesthesia progress*, 57(1), 25–34. <https://doi.org/10.2344/0003-3006-57.1.25>
- [28] Saad, H., & Aladawy, M. (2013). Temperature management in cardiac surgery. *Global cardiology science & practice*, 2013(1), 44–62. <https://doi.org/10.5339/gcsp.2013.7>
- [29] Hendrix, J. M., & Garmon, E. H. (2025). American Society of Anesthesiologists Physical Status Classification System. In StatPearls. StatPearls Publishing.
- [30] Krauer, B., Krauer, F. Drug Kinetics in Pregnancy. *Clin Pharmacokinet* 2, 167–181 (1977). <https://doi.org/10.2165/00003088-197702030-00002> (Accessed on 13/03/2025).
- [31] Research C for DE and Drug Safety and Availability—FDA Drug Safety Communication: FDA Restricts Use of Prescription Codeine Pain and Cough Medicines and Tramadol Pain Medicines in Children; Recommends Against Use in Breastfeeding Women. Available from: <https://www.fda.gov/Drugs/DrugSafety/ucm549679.htm> (accessed on 1 July 2024)
- [32] Ansari, J., Carvalho, B., Shafer, S. L., & Flood, P. (2016). Pharmacokinetics and Pharmacodynamics of Drugs Commonly Used in Pregnancy and Parturition. *Anesthesia and analgesia*, 122(3), 786–804. <https://doi.org/10.1213/ANE.0000000000001143>.
- [33] Law, R., Bozzo, P., Koren, G., & Einarson, A. (2010). FDA pregnancy risk categories and the CPS: do they help or are they a hindrance?. *Canadian family physician Medecin de famille canadien*, 56(3), 239–241.
- [34] American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics

- (2019). ACOG Practice Bulletin No. 209: Obstetric Analgesia and Anesthesia. *Obstetrics and gynecology*, 133(3), e208–e225. <https://doi.org/10.1097/AOG.0000000000003132>.
- [35] Smith J, Fernandes L, Dowswell T. (2018), NSAIDs for Peripartum Pain: A Systematic Review., *J Matern Fetal Neonatal Med.*, 31(6), 787–794.
- [36] Andrew C. Faust, Emily Guy, Nidhu Baby, Anthony Ortegon (2018), Local Anesthetic–Induced Methemoglobinemia During Pregnancy: A Case Report and Evaluation of Treatment Options, *The Journal of Emergency Medicine*, 54(5), 681–684. <https://doi.org/10.1016/j.jemermed.2018.01.039>.
- [37] Brown, D. L., Ransom, D. M., Hall, J. A., Leicht, C. H., Schroeder, D. R., & Offord, K. P. (1995). Regional anesthesia and local anesthetic-induced systemic toxicity: seizure frequency and accompanying cardiovascular changes. *Anesthesia and analgesia*, 81(2), 321–328. <https://doi.org/10.1097/00000539-199508000-00020>.
- [38] Santos, A. C., & Pedersen, H. (1994). Current controversies in obstetric anesthesia. *Anesthesia and analgesia*, 78(4), 753–760. <https://doi.org/10.1213/00000539-199404000-00024>.
- [39] Johnson RF, Herman NL, Johnson HV, et al. (1999), Effects of Fetal Lidocaine Exposure on Cerebral Oxygenation and Blood Flow, *Anesthesiology*, 90(2), 437–444.
- [40] Kuczkowski K. M. (2003). Labor analgesia for the drug abusing parturient: is there cause for concern?. *Obstetrical & gynecological survey*, 58(9), 599–608. <https://doi.org/10.1097/01.OGX.0000082148.97981.30>.
- [41] Lee, J. M., & Shin, T. J. (2017). Use of local anesthetics for dental treatment during pregnancy; safety for parturient. *Journal of dental anesthesia and pain medicine*, 17(2), 81–90.
- [42] Tobias, J. D., & Leder, M. (2011). Procedural sedation: A review of sedative agents, monitoring, and management of complications. *Saudi journal of anaesthesia*, 5(4), 395–410. <https://doi.org/10.4103/1658-354X.87270>
- [43] Ornoy, A., Arnon, J., Shechtman, S., Moerman, L., & Lukashova, I. (1998). Is benzodiazepine use during pregnancy really teratogenic?. *Reproductive toxicology (Elmsford, N.Y.)*, 12(5), 511–515. [https://doi.org/10.1016/s0890-6238\(98\)00035-5](https://doi.org/10.1016/s0890-6238(98)00035-5).
- [44] McElhatton P. R. (1994). The effects of benzodiazepine use during pregnancy and lactation. *Reproductive toxicology (Elmsford, N.Y.)*, 8(6), 461–475. [https://doi.org/10.1016/0890-6238\(94\)90029-9](https://doi.org/10.1016/0890-6238(94)90029-9)
- [45] Dolovich, L. R., Addis, A., Vaillancourt, J. M., Power, J. D., Koren, G., & Einarson, T. R. (1998). Benzodiazepine use in pregnancy and major malformations or oral cleft: meta-analysis of cohort and case-control studies. *BMJ (Clinical research ed.)*, 317(7162), 839–843. <https://doi.org/10.1136/bmj.317.7162.839>.
- [46] Jelen, L. A., Young, A. H., & Stone, J. M. (2021). Ketamine: A tale of two enantiomers. *Journal of psychopharmacology (Oxford, England)*, 35(2), 109–123. <https://doi.org/10.1177/0269881120959644>
- [47] J.G Bovill, J.W Dundee, D.L Coppel, J Moore (1971), Current status of ketamine anaesthesia. *Lancet*, 297(7712), 1285–88. [https://doi.org/10.1016/S0140-6736\(71\)91794-6](https://doi.org/10.1016/S0140-6736(71)91794-6).
- [48] Tang Y, Liu R, Zhao P. Ketamine: An Update for Obstetric Anesthesia (2017), *Transl Perioper & Pain Med*, 4(4):1-12. DOI: 10.31480/2330-4871/058
- [49] Pacilio, R. M., Lopez, J. F., Parikh, S. V., Patel, P. D., & Geller, J. A. (2024). Safe Ketamine Use and Pregnancy: A Nationwide Survey and Retrospective Review of Informed Consent, Counseling, and Testing Practices. *The Journal of clinical psychiatry*, 85(3), 24m15293. <https://doi.org/10.4088/JCP.24m15293>
- [50] Hudaib, M., Malik, H., Zakir, S.J. et al. (2024), Efficacy and safety of ciprofol versus propofol for induction and maintenance of general anesthesia: a systematic review and meta-analysis. *J Anesth Analg Crit Care* 4(25). <https://doi.org/10.1186/s44158-024-00160-8>
- [51] Mongardon, N., Servin, F., Perrin, M., Bedairia, E., Retout, S., Yazbeck, C., Faucher, P., Montravers, P., Desmonts, J. M., & Guglielminotti, J. (2009). Predicted propofol effect-site concentration for induction and emergence of anesthesia during early pregnancy. *Anesthesia and analgesia*, 109(1), 90–95. <https://doi.org/10.1213/ane.0b013e3181a1a700>.
- [52] Alon, E., Ball, R. H., Gillie, M. H., Parer, J. T., Rosen, M. A., & Shnider, S. M. (1993). Effects of propofol and thiopental on maternal and fetal cardiovascular and acid-base variables in the pregnant ewe. *Anesthesiology*, 78(3), 562–576. <https://doi.org/10.1097/00000542-199303000-00020>.

- [53] C Celleno, D., Capogna, G., Tomassetti, M., Costantino, P., Di Feo, G., & Nisini, R. (1989). Neurobehavioural effects of propofol on the neonate following elective caesarean section. *British journal of anaesthesia*, 62(6), 649–654. <https://doi.org/10.1093/bja/62.6.649>.
- [54] Soares de Moura, R., Silva, G. A., Tano, T., & Resende, A. C. (2010). Effect of propofol on human fetal placental circulation. *International journal of obstetric anesthesia*, 19(1), 71–76. <https://doi.org/10.1016/j.ijoa.2009.01.019>.
- [55] Abboud, T.K., Zhu, J., Richardson, M., Silva, E.P.D. and Donovan, M. (1995), Intravenous propofol vs thiamylal-isoflurane for caesarean section, comparative maternal and neonatal effects. *Acta Anaesthesiologica Scandinavica*, 39: 205-209. <https://doi.org/10.1111/j.1399-6576.1995.tb04044.x>
- [56] C Capogna, G., Celleno, D., Sebastiani, M., Muratori, F., Costantino, P., Cipriani, G., Passarelli, F., & Varrassi, G. (1991). Propofol and thiopentone for caesarean section revisited: maternal effects and neonatal outcome. *International journal of obstetric anesthesia*, 1(1), 19–23. [https://doi.org/10.1016/0959-289x\(91\)90025-l](https://doi.org/10.1016/0959-289x(91)90025-l).
- [57] G Gin, T., O'Meara, M. E., Kan, A. F., Leung, R. K., Tan, P., & Yau, G. (1993). Plasma catecholamines and neonatal condition after induction of anaesthesia with propofol or thiopentone at caesarean section. *British journal of anaesthesia*, 70(3), 311–316. <https://doi.org/10.1093/bja/70.3.311>.
- [58] Eziefule, A. A., Elshatanoufy, S., Thakur, M., & Rocha, F. G. (2016). Propofol-Related Infusion Syndrome in the Peripartum Period. *AJP reports*, 6(4), e368–e371. <https://doi.org/10.1055/s-0036-1593405>.
- [59] Becker, D. E., & Rosenberg, M. (2008). Nitrous oxide and the inhalation anesthetics. *Anesthesia progress*, 55(4), 124–132. <https://doi.org/10.2344/0003-3006-55.4.124>.
- [60] Mazze, R. I., & Källén, B. (1989). Reproductive outcome after anesthesia and operation during pregnancy: a registry study of 5405 cases. *American journal of obstetrics and gynecology*, 161(5), 1178–1185. [https://doi.org/10.1016/0002-9378\(89\)90659-5](https://doi.org/10.1016/0002-9378(89)90659-5).
- [61] Aldridge, L. M., & Tunstall, M. E. (1986). Nitrous oxide and the fetus. A review and the results of a retrospective study of 175 cases of anaesthesia for insertion of Shirodkar suture. *British journal of anaesthesia*, 58(12), 1348–1356. <https://doi.org/10.1093/bja/58.12.1348>.
- [62] Khouj, M. A., Albasri, S., Albishri, A. A., Softa, S. M., Almaslamani, A. S., & Ahmad, H. M. (2022). Prevalence of Stress, Anxiety, and Depression Among Pregnant Women in Jeddah. *Cureus*, 14(7), e27174. <https://doi.org/10.7759/cureus.27174>.
- [63] Manouchehrian, N., & Bakhshaei, M. H. (2014). Nitrous oxide effect on relieving anxiety and pain in parturients under spinal anesthesia for caesarean section. *Anesthesiology and pain medicine*, 4(2), e16662. <https://doi.org/10.5812/aapm.16662>.
- [64] Vallejo, M. C., Phelps, A. L., Shepherd, C. J., Kaul, B., Mandell, G. L., & Ramanathan, S. (2005). Nitrous oxide anxiolysis for elective cesarean section. *Journal of clinical anesthesia*, 17(7), 543–548. <https://doi.org/10.1016/j.jclinane.2005.01.009>
- [65] Kurien, S., Kattimani, V. S., Sriram, R. R., Sriram, S. K., Rao V K, P., Bhupathi, A., Bodduru, R. R., & N Patil, N. (2013). Management of pregnant patient in dentistry. *Journal of international oral health : JIOH*, 5(1), 88–97.
- [66] Favero, V., Bacci, C., Volpato, A., Bandiera, M., Favero, L., & Zanette, G. (2021). Pregnancy and Dentistry: A Literature Review on Risk Management during Dental Surgical Procedures. *Dentistry Journal*, 9(4), 46. <https://doi.org/10.3390/dj9040046>.
- [67] Burdan, F., Szumilo, J., Dudka, J., Korobowicz, A., & Klepacz, R. (2006). Congenital ventricular septal defects and prenatal exposure to cyclooxygenase inhibitors. *Brazilian journal of medical and biological research = Revista brasileira de pesquisas medicas e biologicas*, 39(7), 925–934. <https://doi.org/10.1590/s0100-879x2006000700011>
- [68] Dos Santos, C. S., Silva, P. V., Castelo, R., & Tiago, J. (2021). Premature closure of ductus arteriosus after a single dose of diclofenac during pregnancy. *BMJ case reports*, 14(6), e243485. <https://doi.org/10.1136/bcr-2021-243485>
- [69] Bakas, A. M., Healy, H. M., Bell, K. A., Brown, D. W., Mullen, M., & Scheid, A. (2020). Prenatal duct closure leading to severe pulmonary hypertension in a preterm neonate-a case report. *Cardiovascular diagnosis and therapy*, 10(5), 1691–1695. <https://doi.org/10.21037/cdt-20-123>
- [70] Antonucci, R., Zaffanello, M., Puxeddu, E., Porcella, A., Cuzzolin, L., Pilloni, M. D., & Fanos, V. (2012).

Use of non-steroidal anti-inflammatory drugs in pregnancy: impact on the fetus and newborn. *Current drug metabolism*, 13(4), 474–490. <https://doi.org/10.2174/138920012800166607>

- [71] Li, D. K., Liu, L., & Odouli, R. (2003). Exposure to non-steroidal anti-inflammatory drugs during pregnancy and risk of miscarriage: population based cohort study. *BMJ (Clinical research ed.)*, 327(7411), 368. <https://doi.org/10.1136/bmj.327.7411.368>
- [72] Burdan, F., Pliszczynska-Steuden, M., Rozylo-Kalinowska, I., Chalas, A., Rozylo, T. K., Staroslawska, E., Klepacz, R., & Szumilo, J. (2011). Developmental outcome after exposure to cyclooxygenase inhibitors during pregnancy and lactation. *Reproductive toxicology (Elmsford, N.Y.)*, 32(4), 407–417. <https://doi.org/10.1016/j.reprotox.2011.09.012>
- [73] Brakke, B. D., & Sviggum, H. P. (2023). Anaesthesia for non-obstetric surgery during pregnancy. *BJA education*, 23(3), 78–83. <https://doi.org/10.1016/j.bjae.2022.12.001>
- ..
-