

Pregnant Oral and Maxillofacial Patient - Catch 22 Situation

Lakshmi Shetty, Anagha Shete, Archana Anshuman Gupta* and Supriya Kheur

Dr.D.Y. Patil Dental College and Hospital, Pune, Maharashtra, India

Abstract

There have been many advances in both gynecology and oral maxillofacial fields but one issue for discussion is the pregnant oral and maxillofacial surgery patient. This places the surgeons in a Catch 22 situation whether to operate or not. The lives of two individuals, mother and her fetus are at risk. This narrative literature review data is based on searches without restriction on dates of publication from MEDLINE®, PubMed, Cochrane Library, Embase and various other relevant databases using the search terms "pregnant", "drugs" and "oral and maxillofacial surgery". The treatment for the pregnant oral and maxillofacial patient depending on the trimester of pregnancy has been dealt in depth in this informative review. The evaluation of the risk for the two lives and taking the best possible decision for the clinical situation based on the current evidence is the only solution for any 'Catch 22 situation'.

Keywords: Pregnancy; Trimester; Oral and maxillofacial surgery; Risk management

Introduction

Pregnancy is a beautiful yet a complex state of physiological change in a woman's life. The perioperative management of a pregnant patient is of utmost concern for a patient going in for surgical treatment and the drug interactions which happen between the mother and the fetus. The knowledge of the physiological changes from a non-gravid woman to a gravid woman is of utmost importance to the oral and maxillofacial surgeon in his or her ability to manage this patient population. The hormonal and anatomical changes during gestation result in alterations of the major organ systems [1]. The rate of spontaneous abortion in the gravid woman is 15% to 40% [2]. The conditions that a pregnant patient may present with a number of acute oral surgery diseases. Conditions such as maxillofacial trauma, infections, or oral cancer require timely surgical and therapeutic management to ensure maternal health and fetal wellbeing. The whole rainbow of physiological changes in a pregnant patient puts the surgeon in a catch 22 situation whether to perform surgery or not. There are many myths regarding the gravid patient, some true and some false (Figure 1).

This is an extensive review describing the challenges faced by the maxillofacial surgeon in treating a pregnant patient and the various ways to answer the surgeon's dilemma. This review of literature was based on search in knowledge based resources without any restriction in dates of the publication in PubMed, Embase, MEDLINE, and Cochrane Database of Systematic reviews. The search terms were "pregnancy", "drugs" and "oral and maxillofacial surgery". In addition the text books, case reports, studies published in English were reviewed. Our goal was to be as comprehensive as possible in order to focus last 5-6 years i.e., the information which will be useful since new landmarks are set with earlier original researches.

Ethical issues and considerations

The treatment of the pregnant patient has the potential to affect two individuals; hence ethical consideration is very important. The best support of the fetus is the mother. Biologically, we know fetal incubator is the uterus of mother. In certain pathologic conditions, such as placental abruption, the pregnant uterus fails to meet fetal needs [3]. The oral and maxillofacial surgeon should consult an obstetrician or other medical specialist in a given clinical situation. Mazze and Kallen have recorded an increased risk of low birth weight, preterm births, and neonatal deaths in women who had undergone surgery during pregnancy [4]. In the literature search Stepp et al. have identified first-trimester surgery, peritonitis, procedure length, and surgery at 24 weeks

gestation as factors associated with pre-viable or preterm delivery [5].

Pregnancy State

Neuroendocrine changes play a vital role in systemic alterations of gestation and are critical in directing fetal growth and development. The duration of the average pregnancy is approximately symptoms 275 days which is divided into 3 trimesters. The clinical symptoms in the first trimester are cessation of the menstrual flow, nausea, vomiting and breast enlargement [6]. There is also a tendency towards postural hypotension, fatigue and syncope [2]. The successful implantation organogenesis begins and continues for the following 60 gestational days. During this period, the embryo is highly sensitive to exogenous insults and may undergo major morphological changes. In the second trimester, abdominal enlargement becomes increasingly noticeable due to enlargement of the uterus. The uterine dimension in a non-pregnant and pregnant state reveals a solid organ of 50 to 70 g expanding to reach 800 to 1200 g at term. In the second trimester the fetus becomes less sensitive to morphological alterations, but changes in functional capacity such as intellect, reproduction, or aging may occur. During the third trimester, breast and abdominal enlargement, fetal movement and heart sound are pronounced; the fetus is more prone to trans-placental carcinogens. In the final days of gestation, labor begins by painful contractions. The uterus contracts throughout pregnancy; however these contractions are irregular in timing and intensity and are totally painless. The contractions appear 2 to 3 min and last approximately 1 min. The active phase of labor begins with intense increase and frequent painful contractions with 3 to 4 cm cervical dilation [2].

Physiology of Gestation

Cardiovascular system

The cardiovascular system undergoes profound changes during

***Corresponding author:** Archana Anshuman Gupta, BDS, MSc, Department of Oral Pathology and Microbiology, Dr. D.Y. Patil Dental College and Hospital, Chinchwad, Pune, Maharashtra, India-411033, Tel: +917276072737, +917276072735; E-mail: archana.gupta@dpu.edu.in

Received August 05, 2015; **Accepted** August 20, 2015; **Published** August 29, 2015

Citation: Shetty L, Shete A, Gupta AA, Kheur S (2015) Pregnant Oral and Maxillofacial Patient - Catch 22 Situation. Dentistry 5: 329. doi:10.4172/2161-1122.1000329

Copyright: © 2015 Shetty L, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

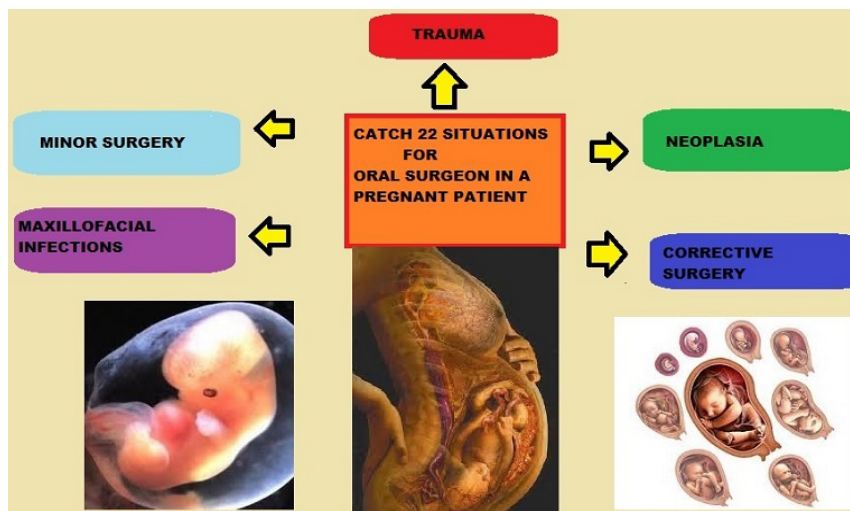


Figure 1: 13 patients received conventional treatment with a Hyrax-RME. 15 additional patients received previous surgical weakening. 7 patients received conventional treatment with Hybrid-RME.

pregnancy with an increase in the total blood volume and cardiac output. There is a decrease in blood pressure, and the potential occurrence of the supine hypotensive syndrome. The volume of blood increases by 40% to 50% by the 32nd week of gestation, caused primarily by a 40-50% increase in plasma volume [7,8]. In addition to an increase in the plasma volume there is also a 30% increase in the red cell volume contributing to the increase of the total blood volume [8]. An increase in cardiac output by 30-50% occurs between the 25th and the 33rd week of pregnancy secondary to an increase in stroke volume [9]. Supine hypotensive syndrome is a condition that affects up to 8% of pregnant women and occurs mainly after the later part of second trimester [10]. When the pregnant woman is in the supine position, there is impaired venous return to the heart due to compression of the inferior vena cava by the fetus. The resulting decrease in the stroke volume stimulates the baroreceptors as a normal compensatory mechanism to maintain cardiac output which leads to hypotension, nausea, dizziness, and fainting [11].

Clinical relevance: To prevent supine hypotensive syndrome in the dental chair, the pregnant woman should have the right hip elevated 10-12 cm or rolled to the left side to lift the uterus off the inferior vena cava [12]. The physiological increase in cardiac output compensates for the decreased oxygen capacity of maternal blood, decrement in cardiac output from any source may result in maternal hypoxia and compromise fetal wellbeing.

Respiratory system

The respiratory system in a pregnant woman during gestation undergoes various anatomical changes. The mucosa in the upper airways may also become more edematous and friable. The functional residual capacity reduces by 20% because of elevated diaphragm by the gravid uterus. There is an increase in estrogen production capillaries in the mucosa of the nasopharynx to become engorged, which results in edema, nasal congestion and predisposition to epistaxis [13]. There is an increase in xerostomia and patient is more prone for caries. There is a decrease in functional residual capacity. Maternal oxygen intake increases by 20% and oxygen reserve decreases, which causes mother and fetus risk of hypoxia [14].

The effect of hyperventilation is respiratory alkalosis. The ventilation

pattern and position of pregnant patient is of utmost priority in order to avoid hypoxemia.

Clinical relevance: A pregnant woman has an impaired ability to tolerate episodes of apnea, pulmonary congestion, or excess nasopharyngeal secretions. The inspired oxygen content should be increased before intubation and tracheal suctioning. To prevent hypoxia, it is recommended that the anesthesiologist allow adequate preoxygenation for 3-5 minutes of 100% oxygen.

Hematological alterations

Hematologic changes in the gravid patient include an increase in the number of erythrocytes and leukocytes, erythrocyte sedimentation rate, and most of the clotting factors, causing a hypercoagulable state [15,16]. There is decrease in blood hemoglobin concentration. The plasma volume and erythrocyte volumes increase in the gravid patient, the increase in volume of the plasma exceeds that of the erythrocyte, which leads to a physiologic anemia [11]. It is assumed that increased levels of circulating catechol amines and cortisol contribute to the leukocytosis seen in pregnancy [11,15]. Also all coagulation factors except XI and XIII are increased. This increase in the levels of clotting factors is responsible for hypercoagulable state of the women during pregnancy. These factors can cause deep vein thrombosis and pulmonary edema. Before carrying out any minor surgeries involving oral tissue or any procedure involving loss of blood, it is very important to observe the hemoglobin level and the red blood cell count of the pregnant woman to prevent any further complications.

Clinical relevance: The pregnant woman is at risk of thromboembolic events. Approximately 0.10% of pregnant patients have thrombus formation, up to 20% of these women develop pulmonary embolism, with a 12% to 15% mortality rate [17]. Low molecular weight heparin is preferred because it does not cross placenta, and has been demonstrated to be more effective than heparin for prophylaxis and less likely to cause spontaneous bleeding [17,18]. The supine position should be avoided because compression of the venacava increases venous stasis and enhances the risk of clot formation.

Gastrointestinal system

Increased estrogen production during pregnancy causes the

capillaries in the mucosa of the nasopharynx to become engorged, which results in edema, nasal congestion and predisposition to epistaxis. The increase in progesterone levels during pregnancy causes a decrease in lower esophageal tone and gastric and intestinal motility. Heartburn, nausea, vomiting are common symptoms seen in most pregnant women in the first trimester. These symptoms make the pregnant woman very uncomfortable to carry out dental procedures. The tone of the lower half of the esophagus falls during the last two trimesters and becomes more pronounced at 36 weeks. Pyrosis occurs in approximately 30-50% of pregnant woman. Reflux also occurs as result of an increased intragastric pressure due to the enlarging fetus, slow gastric emptying rate and decreased lower esophageal sphincter resting pressure [19].

Clinical relevance: The gravid patient is at risk for esophageal incompetence and reflux esophagitis in the third trimester. During general anesthesia appropriate management involves prevention of gastric aspiration. The patients should be advised to avoid citrus drinks or fatty foods as they may cause gastric upset or delay gastric emptying [20].

Renal changes

There is an increase in progesterone levels in first trimester which result in dilation of uterus, renal pelvis and calyces. There is increase in glomerular filtration rate and renal plasma flow to levels of 30-50% above those in the non-gravid women. There is an increase in the renal plasma flow is due to generalized increase in blood volume. Creatinine clearance is increased with uric acid and urea excretion resulting in a slight decline in serum creatinine and blood urea nitrogen levels [8,21].

Clinical relevance: Urinary stasis may help to explain why pregnant woman with asymptomatic bacteria develop pyelonephritis. A value of increased renal hemodynamics may allow commonly used perioperative medications to undergo a rapid excretion. Human chorionic gonadotropin may be involved in the osmoregulatory changes of pregnancy [22].

Oral and facial considerations

Pregnancy being a set of complex events, affects each tissue and organ system of the body. Hence, it also leads to a few changes in the orofacial region. Various gingival and periodontal manifestations are seen. They include pregnancy gingivitis, gingival hyperplasia, pyogenic granuloma (pregnancy tumor) and periodontitis. This results on account of elevated circulating estrogen which causes increased capillary permeability and inflammation affecting the marginal and interdental papillae in the first trimester. Pregnancy worsens pre-existing gingivitis and periodontitis [23]. Mineral changes in the lamina dura, disturbances in the periodontal ligament attachments and vitamin C deficiency contribute to teeth mobility [24]. Few studies also suggest the relation between periodontal disease and preterm labor and low birth weight; the former being the independent risk factor. It can be decreased by good oral hygiene and periodontal treatment [25].

1-5% of pregnant females demonstrate occurrence of pyogenic granuloma which is also called as pregnancy tumor. It is due to increased estrogen levels in gingival crevicular fluid causing increased angiogenesis and inflammation when local irritating factors like dental plaque are present [26]. The common location is the labial aspect of the interdental papilla. The interproximal papillae are red, edematous and tender to palpation, and they bleed easily if subjected to trauma. This gradually progresses to pyogenic granuloma. It is observed in the first and second trimester and usually regresses after child birth [27].

Larger and resistant lesions require surgical excision. On account of chronic vomiting, erosion of teeth on lingual and palatal surfaces of incisors may be seen [28]. In normal pregnancy, there is 30-40% increase in cardiac output which is mediated by an increase in both the stroke volume and heart rate. This along with hormonal changes sometimes results in formation of arteriovenous malformations in the head and neck region, though these are very rare [29,30]. Trauma and infection are the predisposing factors [31-33]. Intraorally it results in bluish gingival or mucosal mass [34]. Expecting mothers often suffer from reduced salivary secretion and hence, xerostomia. The flow, composition, pH and hormone levels of saliva are affected leading to a reduced whole stimulated salivary flow rate in pregnant women as seen by some cross-sectional studies [27]. There is a decrease in salivary sodium, its pH, and an increase in potassium, protein, and estrogen levels [27,35]. In many cases of preterm labor, salivary estrogen levels were increased than in women having normal term deliveries [36,37]. Hence, salivary estrogen level is suggested as a screening test to detect the risk potential for preterm labor.

Xerostomia may lead to difficulty and discomfort during mastication, speech and deglutition. This along with unawareness and poor maintenance of oral hygiene causes increased evidence of dental caries. Salivary estrogen also increases the proliferation and desquamation of the oral mucosa and an increase in subgingival crevicular fluid levels. The desquamating cells provide a suitable environment for bacterial growth by providing nutrition predisposing the pregnant woman to dental caries [27]. Increase in estrogen and progesterone levels also result in bilateral brown patches of facial pigmentation in the malar region. It is called as melasma or the 'mask of pregnancy'. This is noted in 73% of pregnant females and is common in the first trimester [38]. It usually resolves after parturition [39]. All of the stated factors need to be considered during the dental treatment of the pregnant patient and precautionary measures should be taken to avoid complications and complex forms of treatment.

Pregnancy Radiodiagnostics and Therapeutics

The pregnant patient cannot be denied the necessary radiographic investigations. While taking radiographs for the pregnant patients, the dental staff must practice ALARA (As Low as Reasonably Achievable) principle. Radiographs should be obtained only if they help significantly in the diagnosis and treatment plan [40]. According to many studies, if the total radiation exposure is less than 5-10 cGy [41], there is no increased risk of congenital anomalies or intrauterine growth retardation. A full-mouth series of dental radiographs results in only 8×10^{-4} cGy, with E-speed film and a rectangular collimated beam [42]. Bitewing and panoramic radiography generates about one third the radiation exposure associated with a full-mouth series [43]. If protective measures like the use of high speed (E-speed) films, rectangular collimated beams, lead apron and thyroid collar are used, dental radiography is absolutely safe for the pregnant patients. The efficacy of lead apron in providing radiation protection is still debatable. Computed Tomography (CT) scanning delivers up to 4.0 cGy of radiation, which is lower than the recommended safe cumulative dose of 5-10 cGy during pregnancy [44]. Magnetic Resonance Imaging does not use ionising radiation, hence is safer than CT in pregnant patients [45].

Effects of radiation on the fetus

The fetus is exposed to 9 cGy of radiation by head and neck irradiation when abdominal and pelvic shields are used [46]. Radiation exposure secondary to brachytherapy is lower. At the peri-implantation

and immediate post-implantation stages radiation levels above safety limits have an all or none effect resulting in embryonic death or normal development [47]. Mental retardation and microcephaly are the common central nervous system side effects in an established foetus [48]. All such effects vary with the gestational age. Radiation might have wider effects on the fetus. Intracellular ionisation and consequent DNA damage cause cell death, mitotic delay, and disturbance of cell migration. During periods of organogenesis these result in structural malformation and organ dysfunction. Growth retardation, teratogenesis and fetal death also occur. Long-term effects may also be seen such as childhood cancers, germ cell mutations and sterility. Fetal exposure to radiation is mediated by the size of the radiation field, the target dose given, the distance of the fetus from the edge of the radiation field, the specific radiation machine used, the leakage from the machine, and the use of shielding techniques [44,49]. Secondary maternal effects like tissue stiffness limiting head and neck movements, oral ulceration and osteoradionecrosis may develop compromising the child care by mothers. There is a risk of carcinogenesis in radiation-damaged tissues raising the possibility of another primary tumor developing later in life [49].

Dental radiography during pregnancy produces negligible radiation exposure to the fetus in utero, around 1/50000 of the direct exposure to the head [50]. The risk of teratogenesis from dental exposure is nil with a threshold safety factor of 10000x [51]. The first 10 days after the conception carry the greatest risk to the fetus for teratogenicity and death. The most critical period of fetal development is between 4 and 18 weeks after conception. The chance of fetal teratogenicity with an exposure of 0.01Gy is about 0.1% and radiation doses of up to 0.05Gy or less are not associated with significant increase in teratogenicity [52]. The National Commission for Radiation Protection (NCRP) recommends that the cumulative fetal dose should not exceed 0.005 Gy [53]. The ADA endorses US Food and Drug Administration (FDA) selection criteria for dental X-ray exposures. It states that “Dental radiographs for pregnant patients may be prescribed according to the usual and customary selection criteria” [54]. Table 1 gives the average radiation exposure to the human body by various radiographs in Gray (Gy) [12,43,52].

Drugs and Pregnancy Present Status

Drugs should be prescribed with great caution to the pregnant women as some drugs are known to cause miscarriage, teratogenicity and low birth weight of the fetus. The Table 2 describes the FDA pregnancy risk category medications during pregnancy. The demographic studies suggest that the female patients are exposed to many classes of antibiotics during the course of their pregnancy [55].

Analgesics

Aspirin should be avoided at any cost as it can lead to constriction of ductus arteriosus of the fetus if prescribed during the third trimester of pregnancy. Analgesics like acetaminophen are commonly prescribed during pregnancy as it is proved to be safe and effective pain killer. Acetaminophen is the most widely used analgesic agent in pregnancy. It has not been associated with increased risk of congenital anomalies [56]. Low-dose aspirin has been used to prevent pre-eclampsia, with no identifiable cardiac defects [57]. Ibuprofen, naproxen, and ketoprofen have been used most frequently in pregnancy. Use of these drugs in early pregnancy has been associated with an increased risk of cardiac septal defects [58]. By inhibiting prostaglandin synthesis, they also may cause dystocia and delayed parturition.

Antibiotics

Penicillin and cephalosporins are the most common antibiotics prescribed for oral infections. These drugs are found to be safe when used in pregnancy. For patients who are allergic to penicillin, macrolides such as erythromycin and clindamycin can be prescribed. Metronidazole used against anaerobic bacteria has previously been shown to be carcinogenic and mutagenic in certain bacteria. In more than 17,000 fetuses exposed to metronidazole in the first trimester, however, there was no increase in the rate of congenital anomalies [59,60]. The use of metronidazole is justified in maxillofacial infections.

Radiographs	Exposure in Gy
Full mouth series (18 intraoral, D film, lead apron)	1×10^{-5}
Panoramic film	15×10^{-5}
Daily radiation (Cosmic)	4×10^{-4}
Skull	4×10^{-3}
Chest	8×10^{-3}

Table 1: Radiation exposure to human body through various radiographs.

Agent	FDA category/ During Pregnancy
Analgesics and Anti - Inflammatories	
Acetaminophen	B/ Safe
Aspirin	C/D / Avoid
Codeine	C / Caution
Glucocorticoids (Dexamethasone, Prednisone)	C Avoid
Hydrocodone	C/ Caution
Ibuprofen	C/D/ Avoid
Oxycodone	B / Caution
Antibiotics	
Amoxicillin	B/ Safe
Cephalexin	B/ Safe
Chlorhexidine (topical)	B/ Safe
Clindamycin	B/ Safe
Doxycycline	D/ Avoid
Erythromycin	B/ Safe
Metronidazole	B/ Safe
Penicillin	B/ Safe
Tetracycline	D/ Avoid
Local Anesthetics	
Articaine	C/ Caution
Bupivacaine	C/ Caution
Lidocaine	B/ Safe
Prilocaine	B/ Safe
Benzocaine (topical)	C/ Caution
Lidocaine (topical)	B/ Safe
Sedatives	
Benzodiazepines	D/X/ Avoid
Zaleplon	C/ Caution
Zolpidem	C/ Caution
Emergency Medications	
Albuterol	C / Caution
Diphenhydramine	B/ Safe
Epinephrine	C/ Caution
Flumazenil	C/ Caution
Naloxone	C/ Caution
Nitroglycerin	C/ Caution

Table 2: Key medications consideration during pregnancy.

Antifungal and antiviral drugs

The use of topical agents for treatment of superficial fungal infections is safe and effective. Amphotericin B remains the drug of choice for the treatment of deep and life-threatening fungal infections in pregnancy [61]. Drugs such as griseofulvin, ketoconazole may be associated with fetal malformations Acyclovir and valacyclovir are antiviral antibiotics that can be used to treat herpetic infections. These antiviral agents may be used when a significant benefit is expected [62].

Local anesthetics

Local anesthetics used in dentistry cross the placental barrier primarily through passive diffusion [63]. The main concern in a pregnant patient is overdose with increased vascular volume and permeability. Lidocaine is one of the most common local anesthetic used during dental treatment. Lidocaine along with epinephrine when used in the correct dosage is safe during pregnancy [11]. Articaine, Bupivacaine, prilocaine are listed by the FDA as class C during pregnancy (Table 2). Topical anesthetics such as benzocaine, lidocaine, tetracaine are associated with rare, but serious health concern for both mother and fetus with a condition called methemoglobinemia. The risk factors for developing acquired methemoglobinemia include the use of oxidative drugs, patients with glucose-6-phosphate dehydrogenase and use of local anesthetics [64,65]. Epinephrine-containing local anesthetics in accidental intravascular injection results in uterine artery vasoconstriction and decreased uterine blood flow. Levonordefrin, another vasoconstrictor used in local anesthetic solutions, in concentrations of 1:20,000 which is 5 times more than concentrations of epinephrine (1:100,000) [66]. The judicious use of vasoconstrictor with local anesthesia would be the dictum for pregnant patient.

Steroids

Corticosteroids are used to reduce inflammation in oral region. Prednisone and prednisolone have been used clinically in pregnant women, especially for treatment of severe asthma, without adverse effects on the fetus [67]. Triamcinolone and beclomethasone are teratogenic in animals but have not been associated with fetal defects in humans [68]. They are safe locally but systemic use can harm the mother and the fetus and thus should be avoided during pregnancy [11]. Pregnancy specific complications that arise are premature rupture of embryonic membranes, hypertension and gestational diabetes mellitus [69] The American College of Obstetricians and Gynecologists Committee on Obstetric Practice supports a single course of corticosteroids to all pregnant women between 24 and 34 weeks of gestation who are at risk to preterm delivery within 7 days [70].

Conscious sedation and general anesthetics

The use of diazepam and midazolam are particularly hazardous and must be avoided in the first trimester and last month of the third trimester of pregnancy [71]. Barbiturates and benzodiazepines are categorized by FDA class D drugs and hence must be avoided during pregnancy. The use of nitrous oxide in pregnancy is still contentious and so must be avoided during pregnancy till proper evidence is gained regarding its safety [11]. It has not been classified into any category by the FDA. Nitrous oxide also causes vasoconstriction and may reduce uterine blood supply. Chronic exposure of pregnant dental health workers to nitrous oxide for more than 3 hours without the use of scavengers has resulted in decreased fertility and spontaneous abortions [72]. A review suggests nitrous oxide is safe for use in parturient women, their newborns, and healthcare workers in attendance during its administration [73].

The National Institute of Occupational Safety and Health recommends that proper ventilation (10 or more room air exchanges per hour), scavenging systems (vacuum up to 45 L/min), appropriate mask sizes, regular air sampling, and low exposure of 25 parts per million to be used when pregnant health care workers are involved [74,75]. Pregnant patients demonstrate a 30% reduction in the minimum alveolar concentrations of volatile anesthetic agents [76]. Superimposed upon the increase in alveolar MV, this leads to rapid induction of anesthesia if an inhalation induction technique is used. Similarly, neural tissue demonstrates increased sensitivity to the effects of local anesthetic drugs. Both therapeutic doses and toxic plasma levels are reduced by approximately 30% in pregnancy [77]. The total volume of the epidural and subarachnoid spaces is reduced in pregnancy as inferior venacaval compression produces engorgement of the epidural venous plexus. This leads to more extensive spread of local anesthetic agents administered during central neuraxial blockade. The response of the autonomous nervous system to hemodynamic changes is biphasic. In the first trimester, there is a shift toward increased vagal tone and decreased sympathetic activity in association with the increase in blood volume. A gradual transition in the second trimester leads to lower vagal tone and increased sympathetic activity by the third trimester, which helps overcome the mechanical effects of both aortocaval compression and low-resistance parallel placental circulation (Figure 2) [78]. The hypoventilation or hyperventilation could bring negative effects and hence the surgeon should be cautious and vigilant while administering under general anesthesia [79].

Intubation can be difficult in pregnant as there is a risk of epistaxis from nasal tubes due to friable mucous membrane. Supine position should be avoided and lateral decubitus position is preferable. Thiopental and propofol are safe induction agents. Halothane, isoflurane, enflurane and desflurane are safe during pregnancy in appropriate doses.

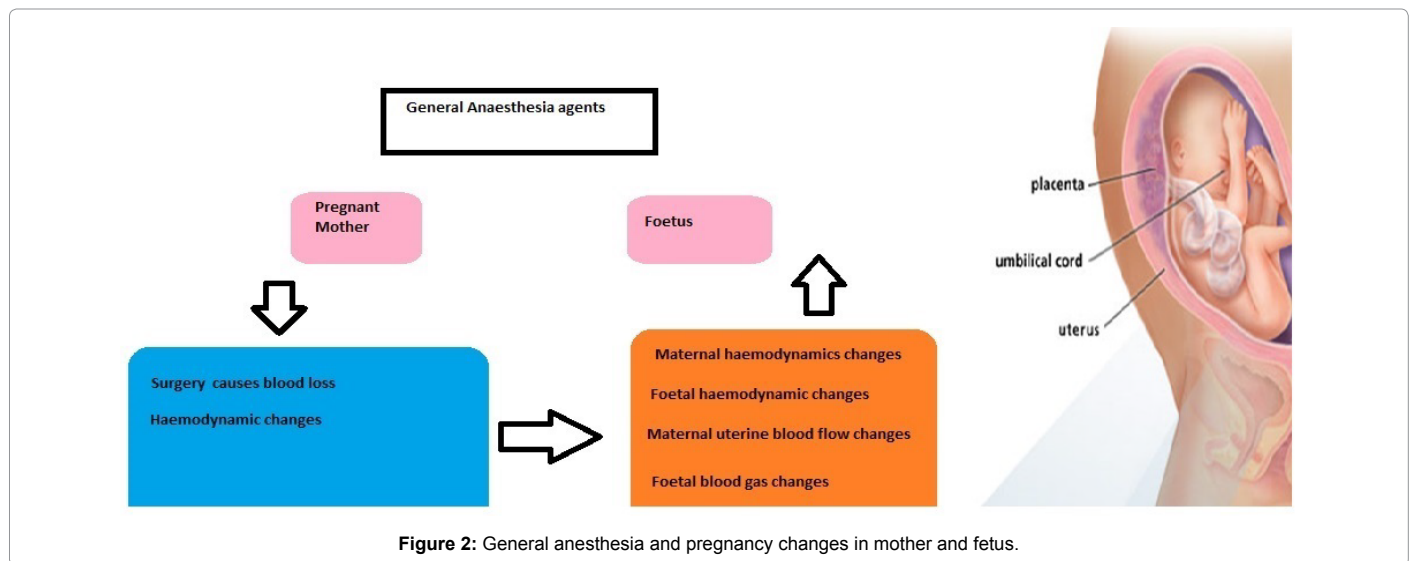
Teratogenicity of drugs

Several categories of drugs that are known to be teratogenic (i.e., drugs that can cause either structural or functional birth defects), include alcohol, tobacco, cocaine, thalidomide, methyl mercury, anticonvulsant medications, warfarin compounds, angiotensin-converting enzyme (ACE) inhibitors, retinoid, and certain antimicrobial agents. Alcoholic women who consume eight or more drinks daily throughout pregnancy have a 30-50% risk of delivering a child with all of the features of fetal alcohol syndrome [80]. Tobacco has been associated with cleft lip and palate in many individuals who carry polymorphism in the transforming growth factor gene [80].

Warfarin compounds, such as Coumadin, cause a dose-dependent risk of fetal damage. Ginsberg and Hirsh performed an analysis of 186 studies involving 1325 exposed pregnancies [81]. Although mercury is not currently used as a drug, environmental exposures to methyl mercury have resulted in a range of birth defects, from developmental delay to microcephaly and severe brain damage [3]. Thalidomide, the proven teratogen even if used for immunomodulation should be avoided. Clefts develop almost ten times more often in fetuses of women who have epilepsy than in general population. The high serum levels of antiepileptic medications and use of multiple anticonvulsants increase the risk of fetal malformations. ACE inhibitors should be avoided as they may cause renal ischemia, renal tubular dysgenesis, and anuria [3].

Oral Maxillofacial Surgery and Pregnant Patient

The oral and maxillofacial surgery in a pregnant patient should be undertaken only in emergency situations as the concern is between two lives mother and fetus.



Dentoalveolar surgery

Elective dentoalveolar surgery should be carried out only in second trimester. Dentoalveolar surgery should be directed toward the relief of pain, elimination of infection and neoplasia, and repair of traumatic injuries. The patient should be positioned in the left lateral decubitus position, with the right hip elevated approximately 15° (6-12 inches) above the surface of the chair [17]. Aortocaval compression, which occurs specifically in the supine position, leads to supine hypotensive syndrome, which is characterized by symptoms and signs such as lightheadedness, weakness, sweating, restlessness, tinnitus, pallor, decrease in blood pressure, syncope and, in severe cases, unconsciousness and convulsions [40]. The position of the patient is very important in terms of cardiopulmonary resuscitation.

Trauma and Pregnancy

Motor vehicular accidents can be the cause of trauma in 50% of the patients. They are responsible for 82% of fetal deaths caused by trauma [82]. Injury in a pregnant patient may be accidental, intentional causing maternal death. Fildes et al., stated 50% of maternal deaths are due to trauma [83]. 6-7% of all pregnancies are complicated by trauma, and 0.4% of pregnant patients require hospitalization in order to treat traumatic injuries [84]. The actual number of injured pregnant women is underestimated because many of them are unreported, especially those due to domestic violence. Major blunt and penetrating trauma is more likely to affect both a pregnant woman and her fetus, complications limited to the pregnancy itself, such as abruption placenta and fetal injuries, can occur after relatively minor trauma to the abdomen from falls, domestic abuse, and low-speed motor vehicle accidents.

The possibility of a pregnancy must be considered in all injured women between the ages of 10 and 50 years [85]. Various causes for trauma causing injury and death are motor vehicle collisions, violence and assault, gunshots, stabbing, strangulation, falls, suicide, drug overdose, poisoning, burns. The penetrating injuries to the gravid uterus from spears, sticks, and animal horns have been observed from ancient times. An estimated 33% of abused women have anxiety and depression, and 26% of female suicide attempts are by women experiencing interpersonal violence, but this number is underestimated, as these injuries are unreported, especially in the pregnant patients.

Emergency care should be given to the pregnant women considering them as high risk, if they have one or more of following conditions

- rib or pelvic fracture,
- unexplained hypotension,
- vaginal blood loss,
- hematuria,
- altered sensorium due to drugs, alcohol, or brain injury.

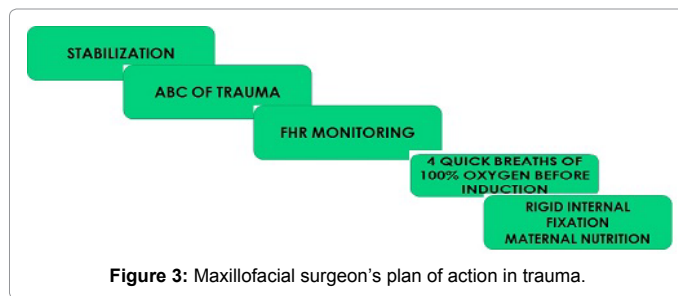
There are several factors associated with risk to the fetus [85]. The most common factors are maternal death, maternal hypotension, maternal traumatic brain injury, high injury severity score, pelvic fracture, ejection of pregnant woman from a vehicle, and severe abdominal injury to pregnant women.

The predictive factors associated with maternal mortality include amniotic fluid embolism, deep venous thrombosis and pulmonary embolism, and infections [86]. Gunshot wounds are the next common type of traumatic injury sustained by the parturient. In general, a multidisciplinary approach involving maternal and fetal medicine, neonatology, anesthesiology, and intensive care medicine is essential for optimizing outcomes in cases of severe trauma [87]. The oral and maxillofacial surgeon is often the first fraternity to evaluate these patients and should identify appropriately. The oral surgeon should refer victims of domestic violence to prevent future injuries [88]. Rigid internal fixation should be advisable and decided based on the status of the gravid mother and fetus. The closed reduction of the fracture till completion of gestation and labor is another option for treatment of trauma. Maxillofacial surgeon's plan of action is described (Figure 3).

Maxillofacial Infections and Pregnancy

Maxillofacial infections should be managed aggressively in the gravid patient. There is a mild degree of immunosuppression in pregnancy, and sepsis is known to occur more frequently in pregnant than non-pregnant women. Primary concern should be given to airway stability. Mucosal and skin changes are commonly seen during pregnancy and are secondary to hormonal alterations. Ludwig's angina is life threatening because of both septicemia

and asphyxia [89]. The treatment is summarized in (Figure 4).



Septicemia is certainly the cause for death in Ludwig's angina after airway obstruction [90].

Neoplasia and Pregnancy

Neoplasia or cancer may affect pregnancy. The early pregnancy could be terminated if within 28 days. There is no specific treatment for cancer. Metastasis to the placenta and/or the fetus is rare complications of malignant melanoma and lymphoma [44]. Head and neck cancers not only have physical and physiological effects in pregnancy, they also impact psychologically. More often social changes place women in position to have children late in life and hence become the high risk age group for neoplasia. Maternal deformity secondary to tumor or surgery is a source of additional psychological burden.

In the case of cancer during late pregnancy, three treatment options exist [91,92]:

- standard treatment after induced delivery in an attempt to save the infant, with or without fetal lung maturation; this entails a high risk of complications, including hyaline membrane disease or sepsis of the baby, because of immaturity at birth
- no-treatment of the tumor until after natural birth; it gives priority to full time delivery of the fetus over the mother's risks
- starting cancer therapy during pregnancy with corresponding risks regarding both fetal viability and teratogenicity.

The added knowledge required is encompassed within a triangle of effects: the effect of pregnancy on cancer, and the effect of diagnostic and treatment modalities on pregnancy.

Osteomyelitis can occur in the pregnant patient with a history of local irritant which can induce inflammation. Pregnancy results in an increase in the concentration of circulating parathyroid hormone by up to 50% [93]. This mobilizes calcium from bone and may have contributed to the rapid lysis of the mandible [94].

Arteriovenous malformation (AVM) may present in any body tissue and over half occur in the head and neck [95]. They are rare in the oral and maxillofacial regions. Trauma, infection, and hormonal changes are predisposing factors [89]. Although changes in the hormonal balance during pregnancy are thought to cause progression [32,96] experimental evidence is lacking. There are several ways of treating AVM of the head and neck, including embolization, sclerotherapy, resection, and a combination of two or more methods [97]. The local compression and cauterization was done for mandibular AVM as reported by Sasaki et al., till completion of pregnancy [34].

Fetal Monitoring

Fetal heart rate (FHR) variability is a useful indicator of fetal wellbeing and can be monitored from 25 to 27 weeks' gestation onward. Anesthetic agents reduce both baseline FHR and FHR variability, so

readings must be interpreted in the context of administered drugs. The human fetus may respond to a number of environmental stimuli including noise, pressure, pain, and cold temperature. Noxious stimuli produce an autonomic response and a rise in stress hormones. The value of intraoperative FHR monitoring is that it detects early compromise, allowing optimization of maternal hemodynamics and oxygenation with appropriate fluid therapy, vasopressors, blood product administration, hyperventilation, or position adjustment [98].

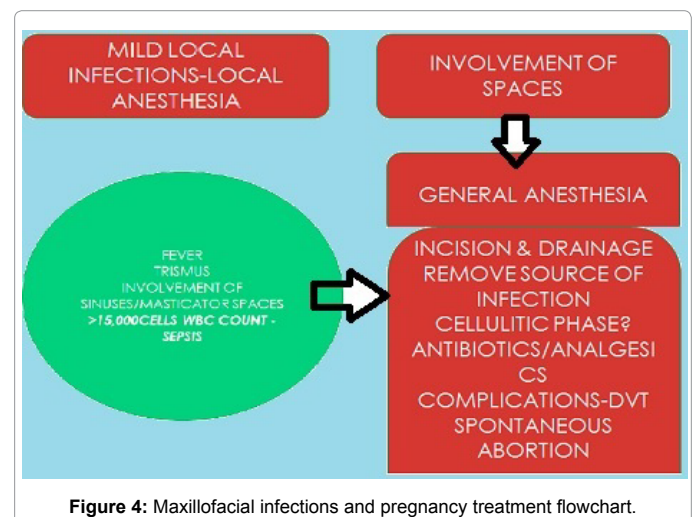
Orthognathic and cosmetic procedures should be postponed till delivery since it is elective procedure.

Complications

The common complications during pregnancy are spontaneous abortion and preterm labor. In the first trimester there is spontaneous abortion occurs in 10-15% of all pregnancies [99]. Minor contractions without bleeding (Braxton Hicks contractions) which subside spontaneously or contractions when a patient shifts position do not indicate an emergency [100]. Oxygen should be administered. The patients should lie on the left lateral side if presents with vaginal bleeding with or without powerful contractions. Preterm labor comprises of back pain or discomfort, pelvic and or abdominal pressure, or vaginal discharge [101,102]. If the patient presents with spontaneous labor in the maxillofacial department the emergency care of monitoring the patient for vital signs and proper positioning should be followed. The medical assistance and the obstetrician should be consulted in this situation

Conclusion

The pregnant woman and the fetus she is bearing are a huge challenge to the oral and maxillofacial surgeon for effective surgical management. The acute presentation of the patient suffering with any ailment can be treated with minimal risks to mother and the fetus. All elective procedures should be delayed to the postpartum period. The routine dental health should be maintained before conception in planned pregnancies and during the second trimester all elective and dentoalveolar procedures should be undertaken [103]. The key is to emphasize particular attention in obtaining an obstetric consultation and to understanding the physiologic changes of gestation.



References

- Barron WM (1984) The pregnant surgical patient: medical evaluation and management. *Ann Intern Med* 101: 683-691.
- Creasy RK, Resnik R (1989) *Maternal-Fetal Medicine: Principles and Practices*. (2nd edn), WB Saunders, Philadelphia.
- Flynn TR, Susarla SM (2007) Oral and maxillofacial surgery for the pregnant patient. *Oral Maxillofac Surg Clin North Am* 19: 207-221.
- Mazze RI, Källén B (1989) Reproductive outcome after anesthesia and operation during pregnancy: a registry study of 5405 cases. *Am J Obstet Gynecol* 161: 1178-1185.
- Stepp KJ, Sauchak KA, O'Malley DM, Mercer B (2002) Risk factors for adverse outcomes after intraabdominal surgery during pregnancy. *Obstet Gynecol* 99: 23S.
- Pradel EC (1998) The pregnant oral and maxillofacial surgery patient. *Oral Maxillofac Surg Clin N Am* 10: 471-488.
- Theunissen IM, Parer JT (1994) Fluid and electrolytes in pregnancy. *Clin Obstet Gynecol* 37: 3-15.
- Duvekot JJ, Peeters LL (1994) Renal hemodynamics and volume homeostasis in pregnancy. *Obstet Gynecol Surv* 49: 830-839.
- Barron WM, Lindheimer MD (1995) *Medical disorders during pregnancy*. (2nd edn), Mosby, St. Louis.
- Lanni SM, Tillinghast J, Silver HM (2002) Hemodynamic changes and baroreflex gain in the supine hypotensive syndrome. *Am J Obstet Gynecol* 187: 1636-1641.
- Suresh L, Radfar L (2004) Pregnancy and lactation. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 97: 672-682.
- Little JW, Falace DA, Miller CS, Rhodus NL (2002) *Dental management of the medically compromised patient*. (6th edn), Mosby, St. Louis.
- Gordon MC (2002) Maternal physiology in pregnancy. In: Gabbe SG, Niebyl JR, Simpson J (eds). *Obstetrics: normal and problem pregnancies*. (4th edn), Churchill Livingstone, New York.
- Thornburg KL, Jacobson SL, Giraud GD, Morton MJ (2000) Hemodynamic changes in pregnancy. *Semin Perinatol* 24: 11-14.
- Branch DW (1992) Physiologic adaptations of pregnancy. *Am J Reprod Immunol* 28: 120-122.
- Hamaoui E, Hamaoui M (2003) Nutritional assessment and support during pregnancy. *Gastroenterol Clin North Am* 32: 59-121.
- Turner M, Aziz SR (2002) Management of the pregnant oral and maxillofacial surgery patient. *J Oral Maxillofac Surg* 60: 1479-1488.
- Barbour LA (1997) Current concepts of anticoagulant therapy in pregnancy. *Obstet Gynecol Clin North Am* 24: 499-521.
- Richter JE (2003) Gastroesophageal reflux disease during pregnancy. *Gastroenterol Clin North Am* 32: 235-261.
- Koch KL, Frissora CL (2003) Nausea and vomiting during pregnancy. *Gastroenterol Clin North Am* 32: 201-234.
- Sifakis S, Pharmakides G (2000) Anemia in pregnancy. *Ann N Y Acad Sci* 900: 125-136.
- Davison JM, Shiells EA, Philips PR, Lindheimer MD (1988) Serial evaluation of vasopressin release and thirst in human pregnancy. Role of human chorionic gonadotrophin in the osmoregulatory changes of gestation. *J Clin Invest* 81: 798-806.
- Tilakaratne A, Soory M, Ranasinghe AW, Corea SM, Ekanayake SL, et al. (2000) Periodontal disease status during pregnancy and 3 months post-partum, in a rural population of Sri-Lankan women. *J Clin Periodontol* 27: 787-792.
- Little JW, Falace DA, Miller CS, Rhodus NL (2008) *Dental management of the medically compromised patient*. (7th edn), Mosby, St. Louis.
- López NJ, Smith PC, Gutierrez J (2002) Periodontal therapy may reduce the risk of preterm low birth weight in women with periodontal disease: a randomized controlled trial. *J Periodontol* 73: 911-924.
- Yuan K, Wing LY, Lin MT (2002) Pathogenetic roles of angiogenic factors in pyogenic granulomas in pregnancy are modulated by female sex hormones. *J Periodontol* 73: 701-708.
- Laine M, Tenovuuo J, Lehtonen OP, Ojanotko-Harri A, Vilja P, et al. (1988) Pregnancy-related changes in human whole saliva. *Arch Oral Biol* 33: 913-917.
- Evans RD, Briggs PF (1994) Tooth-surface loss related to pregnancy-induced vomiting. *Prim Dent Care* 1: 24-26.
- Ueland K, Novy MJ, Peterson EN, Metcalfe J (1969) Maternal cardiovascular dynamics. IV. The influence of gestational age on the maternal cardiovascular response to posture and exercise. *Am J Obstet Gynecol* 104: 856-864.
- Robson SC, Hunter S, Boys RJ, Dunlop W (1989) Serial study of factors influencing changes in cardiac output during human pregnancy. *Am J Physiol* 256: H1060-1065.
- McMahon MJ, Hansen WF, O'Meara AT (1997) Mandibular arteriovenous malformation in pregnancy. *Am J Perinatol* 14: 619-621.
- De Riu G, Sanna MP (1999) Mandibular arteriovenous malformation in pregnancy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 87: 396-397.
- Werner JA, Dünne AA, Folz BJ, Rochels R, Bien S, et al. (2001) Current concepts in the classification, diagnosis and treatment of hemangiomas and vascular malformations of the head and neck. *Eur Arch Otorhinolaryngol* 258: 141-149.
- Sasaki R, Okamoto T, Komiya C, Uchiyama H, Ando T, et al. (2008) Mandibular gingival arteriovenous malformation in pregnancy. *Br J Oral Maxillofac Surg* 46: 675-676.
- Salvolini E, Di Giorgio R, Curatola A, Mazzanti L, Fratto G (1998) Biochemical modifications of human whole saliva induced by pregnancy. *Br J Obstet Gynaecol* 105: 656-660.
- Mauldin JG, Newman RB (2001) Preterm birth risk assessment. *Semin Perinatol* 25: 215-222.
- Heine RP, McGregor JA, Goodwin TM, Artal R, Hayashi RH, et al. (2000) Serial salivary estriol to detect an increased risk of preterm birth. *Obstet Gynecol* 96: 490-497.
- Kauh YC, Zachian TF (1999) Melasma. *Adv Exp Med Biol* 455: 491-499.
- Neville BW, Damm DD, Allen CM, Bouquot JE (2002) *Oral & Maxillofacial Pathology*. (3rd edn), WB Saunders, Philadelphia.
- Giglio JA, Lanni SM, Laskin DM, Giglio NW (2009) Oral health care for the pregnant patient. *J Can Dent Assoc* 75: 43-48.
- Katz VL (2003) Prenatal care. In: Scott JR, Gibbs RS, Karlan BY, Haney AF (eds). *Danforth's obstetrics and gynecology*. (9th edn), Lippincott, Williams and Wilkins, Philadelphia.
- National Council on Radiation Protection and Measurements (1987) *Recommendations on limits for exposure to ionizing radiation*. NCRP, Bethesda, NCRP report no. 91.
- Freeman JP, Brand JW (1994) Radiation doses of commonly used dental radiographic surveys. *Oral Surg Oral Med Oral Pathol* 77: 285-289.
- Lishner M (2003) Cancer in pregnancy. *Ann Oncol* 14: 31-36.
- Wong GC (2002) Management of haematologic malignancies in pregnancy. *Ann Acad Med Singapore* 31: 303-310.
- Podgorsak MB, Meiler RJ, Kowal H, Kishel SP, Orner JB (1999) Technical management of a pregnant patient undergoing radiation therapy to the head and neck. *Med Dosim* 24: 121-128.
- Weisz B, Schiff E, Lishner M (2001) Cancer in pregnancy: maternal and fetal implications. *Hum Reprod Update* 7: 384-393.
- Greskovich JF Jr, Macklis RM (2000) Radiation therapy in pregnancy: risk calculation and risk minimization. *Semin Oncol* 27: 633-645.
- Bradley PJ, Raghavan U (2004) Cancers presenting in the head and neck during pregnancy. *Curr Opin Otolaryngol Head Neck Surg* 12: 76-81.
- Richards AG (1968) Dental x-ray protection. *Dent Clin North Am* .
- International Commission on Radiological Protection (1991) *1990 Recommendations of the International Commission on Radiological Protection*. Ann ICRP 21: 1-201.
- Brent RL (1983) The effects of embryonic and fetal exposure to X-ray, microwaves, and ultrasound. *Clin Obstet Gynecol* 26: 484-510.
- National Council on Radiation Protection (1998) *Radionuclide Exposure of the Embryo/Fetus*. NCRP, Bethesda, NCRP report no. 128.

54. ADA Council on Scientific Affairs (2001) An update on radiographic practices: information and recommendations. ADA Council on Scientific Affairs. *J Am Dent Assoc* 132: 234-238.
55. Broe A, Pottegård A, Lamont RF, Jørgensen JS, Damkier P (2014) Increasing use of antibiotics in pregnancy during the period 2000-2010: prevalence, timing, category, and demographics. *BJOG* 121: 988-996.
56. Thulstrup AM, Sørensen HT, Nielsen GL, Andersen L, Barrett D, et al. (1999) Fetal growth and adverse birth outcomes in women receiving prescriptions for acetaminophen during pregnancy. EuroMap Study Group. *Am J Perinatol* 16: 321-326.
57. Di Sessa TG, Moretti ML, Khoury A, Pulliam DA, Arheart KL, et al. (1994) Cardiac function in fetuses and newborns exposed to low-dose aspirin during pregnancy. *Am J Obstet Gynecol* 171: 892-900.
58. Ofori B, Oraichi D, Blais L, Rey E, Bérard A (2006) Risk of congenital anomalies in pregnant users of non-steroidal anti-inflammatory drugs: A nested case-control study. *Birth Defects Res B Dev Reprod Toxicol* 77: 268-279.
59. Piper JM, Mitchel EF, Ray WA (1993) Prenatal use of metronidazole and birth defects: no association. *Obstet Gynecol* 82: 348-352.
60. Burtin P, Taddio A, Ariburnu O, Einarson TR, Koren G (1995) Safety of metronidazole in pregnancy: a meta-analysis. *Am J Obstet Gynecol* 172: 525-529.
61. Moudgal VV, Sobel JD (2003) Antifungal drugs in pregnancy: a review. *Expert Opin Drug Saf* 2: 475-483.
62. Raborn GW, McGaw WT, Grace M, Tyrrell LD, Samuels SM (1987) Oral acyclovir and herpes labialis: a randomized, double-blind, placebo-controlled study. *J Am Dent Assoc* 115: 38-42.
63. Donaldson M, Goodchild JH (2012) Pregnancy, breast-feeding and drugs used in dentistry. *J Am Dent Assoc* 143: 858-871.
64. Wilburn-Goo D, Lloyd LM (1999) When patients become cyanotic: acquired methemoglobinemia. *J Am Dent Assoc* 130: 826-831.
65. Annabi EH, Barker SJ (2009) Severe methemoglobinemia detected by pulse oximetry. *Anesth Analg* 108: 898-899.
66. Fayans EP, Stuart HR, Carsten D, Ly Q, Kim H (2010) Local anesthetic use in the pregnant and postpartum patient. *Dent Clin North Am* 54: 697-713.
67. Fitzsimons R, Greenberger PA, Patterson R (1986) Outcome of pregnancy in women requiring corticosteroids for severe asthma. *J Allergy Clin Immunol* 78: 349-353.
68. Dombrowski MP, Brown CL, Berry SM (1996) Preliminary experience with triamcinolone acetonide during pregnancy. *J Matern Fetal Med* 5: 310-313.
69. Committee on Clinical Guidelines (1996) Guidelines for monitoring drug therapy in rheumatoid arthritis. American College of Rheumatology Ad Hoc Committee on Clinical Guidelines. *Arthritis Rheum* 39: 723-731.
70. Committee on Obstetric Practice (2002) ACOG committee opinion: antenatal corticosteroid therapy for fetal maturation. *Obstet Gynecol* 99: 871-873.
71. Silk H, Douglass AB, Douglass JM, Silk L (2008) Oral health during pregnancy. *Am Fam Physician* 77: 1139-1144.
72. Rowland AS, Baird DD, Shore DL, Weinberg CR, Savitz DA, et al. (1995) Nitrous oxide and spontaneous abortion in female dental assistants. *Am J Epidemiol* 141: 531-538.
73. Rosen MA (2002) Nitrous oxide for relief of labor pain: a systematic review. *Am J Obstet Gynecol* 186: S110-126.
74. Haas DA, Pynn BR, Sands TD (2000) Drug use for the pregnant or lactating patient. *Gen Dent* 48: 54-60.
75. McGlothlin JD, Jensen PA, Fischbach TJ, Hughes RT, Jones JH (1992) Control of anesthetic gases in dental operator. *Scand J Work Environ Health* 18 Suppl 2: 103-105.
76. Gin T, Chan MT (1994) Decreased minimum alveolar concentration of isoflurane in pregnant humans. *Anesthesiology* 81: 829-832.
77. Sanson BJ, Lensing AW, Prins MH, Ginsberg JS, Barkagan ZS, et al. (1999) Safety of low-molecular-weight heparin in pregnancy: a systematic review. *Thromb Haemost* 81: 668-672.
78. Kuo CD, Chen GY, Yang MJ, Lo HM, Tsai YS (2000) Biphasic changes in autonomic nervous activity during pregnancy. *Br J Anaesth* 84: 323-329.
79. Stewart MK, Terhune KP2 (2015) Management of pregnant patients undergoing general surgical procedures. *Surg Clin North Am* 95: 429-442.
80. Shaw GM, Velie EM, Schaffer D (1996) Risk of neural tube defect-affected pregnancies among obese women. *JAMA* 275: 1093-1096.
81. Ginsberg JS, Hirsh J (1989) Anticoagulants during pregnancy. *Annu Rev Med* 40: 79-86.
82. Mattox KL, Goetzl L (2005) Trauma in pregnancy. *Crit Care Med* 33: S385-389.
83. Fildes J, Reed L, Jones N, Martin M, Barrett J (1992) Trauma: the leading cause of maternal death. *J Trauma* 32: 643-645.
84. Lavery JP, Staten-McCormick M (1995) Management of moderate to severe trauma in pregnancy. *Obstet Gynecol Clin North Am* 22: 69-90.
85. Petrone P, Asensio JA (2006) Trauma in pregnancy: assessment and treatment. *Scand J Surg* 95: 4-10.
86. Petroni P, Marini CP (2015) Trauma in pregnant patient. *Curr Probl Surg*.
87. Cole DE, Taylor TL, McCullough DM, Shoff CT, Derdak S (2005) Acute respiratory distress syndrome in pregnancy. *Crit Care Med* 33: S269-278.
88. Le BT, Dierks EJ, Ueek BA, Homer LD, Potter BF (2001) Maxillofacial injuries associated with domestic violence. *J Oral Maxillofac Surg* 59: 1277-1283.
89. Abramowicz S, Abramowicz JS, Dolwick MF (2006) Severe life threatening maxillofacial infection in pregnancy presented as Ludwig's angina. *Infect Dis Obstet Gynecol* 2006: 51931.
90. Osunde O, Bassey G1, Ver-Or N2 (2014) Management of Ludwig's Angina in Pregnancy: A Review of 10 Cases. *Ann Med Health Sci Res* 4: 361-364.
91. Garcia AG, Lopez JA, Gandara Rey JM, Camean MP (2001) Squamous cell carcinoma of the maxilla during pregnancy: report of case. *J Oral Maxillofac Surg* 59: 456-461.
92. Koike T, Uehara S, Kobayashi H, Kurashina K, Yamazaki T (2005) Squamous cell carcinoma of tongue during pregnancy experiences in two year treatments. *Oral Oncol Extra* 41: 7-11.
93. Wilson SG, Retallack RW, Kent JC, Worth GK, Gutteridge DH (1990) Serum free 1,25-dihydroxyvitamin D and the free 1,25-dihydroxyvitamin D index during a longitudinal study of human pregnancy and lactation. *Clin Endocrinol (Oxf)* 32: 613-622.
94. Clover MJ, Barnard JD, Thomas GJ, Brennan PA (2005) Osteomyelitis of the mandible during pregnancy. *Br J Oral Maxillofac Surg* 43: 261-263.
95. Persky MS (1986) Congenital vascular lesions of the head and neck. *Laryngoscope* 96: 1002-1015.
96. Geary M, McParland P (1996) Multiple and massive arteriovenous malformations in pregnancy. *Eur J Obstet Gynecol Reprod Biol* 64: 147-150.
97. Lee BB, Do YS, Yakes W, Kim DI, Mattassi R, et al. (2004) Management of arteriovenous malformations: a multidisciplinary approach. *J Vasc Surg* 39: 590-600.
98. Ní Mhuireachtaigh R, O'Gorman DA (2006) Anesthesia in pregnant patients for nonobstetric surgery. *J Clin Anesth* 18: 60-66.
99. Daya S (2003) Recurrent spontaneous early pregnancy loss and low dose aspirin. *Minerva Ginecol* 55: 441-449.
100. Tarsitano BF, Rollings RE (1993) The pregnant dental patient: evaluation and management. *Gen Dent* 41: 226-234.
101. Sinclair C (1996) Handbook of obstetrical emergencies. (1st edn), WB Saunders, Philadelphia.
102. Lumley J (2003) Defining the problem: the epidemiology of preterm birth. *BJOG* 110 Suppl 20: 3-7.
103. Kurien S, Kattimani VS, Sriram RR, Sriram SK, Rao VKP, et al. (2013) Management of pregnant patient in dentistry. *J Int Oral Health* 5: 88-97.