Occupational Hazards Associated with Exposure to Anesthetic Gases on Reproductive Health in Operating Theatre Staff in Three Hospitals in Khartoum State, Sudan

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Contents

Dedication 1

Acknowledgement 2

Abbreviations 3

Abstract 4

Chapter One: Introduction 5

Chapter Two: Literature Review 7

Waste Anesthetic gases 8

Adverse health effects of occupational exposure to anesthetic gases 10

Reproductive toxicology of anesthetic gases 11

Recommendations and regulatory limits of anesthetic gas exposure 13

Methods of assessing exposure to anesthetic gases in the work place 13

The anesthetic machine 15

General workplace controls 16

Scavenging system and ventilation 18

Chapter Three: Methodology 20

Chapter Four: Results 22

Chapter Five: Discussion

Chapter Six: Conclusion and Recommendations 38

Appendix 16

References 40

Dedication

Dedicated to all working mothers....

..... especially my dear mother.....

..... for the sake of healthy babies.....

Acknowledgement

To participate in our COMERRM111'dy by highly hiring important notices and research, the need for encouragement and tolerance is a priority which was given and very grateful to my family and friends. I am very thankful to my skilful supervisor Dr. Ahmed P1111 Khaleol for his guidance, helpful thoughts and remarkable support 11 needed. Special thanks for the statistician who had been very patient and cooperative, as well as EhHam Mohammed and Hadya Mohammed; the librarians in the Ministry of Health who had helped me a Hot. H greatly appreciate Shaza, the secretary and her friends for their help and support. Thanks to everyone who has been at my side during this bumpy journey.

Abbreviations

ACGIH: American Conference of Governmental Industrial Hygienists

APL: Adjustable Pressure-Limiting

ASA: American Society of Anesthesiologists

COSHH: Control of Substances Hazardous to Health Regulations

CPC: Chemical Protective Clothing

DISS: Diameter Indexed Safety System

ECRI: Emergency Care Research Institute

ETT: Endotracheal Tube

FDA: Food and Drug Administration

HVAC: Heating, Ventilating and Air Conditioning

LMA: Laryngeal Mask Airway

NIOSH: National Institute for Occupational Safety and Health

OES: Occupational Exposure Standards

OR: Operating Room

OSHA: Occupational Safety and Health Administrations

PACU: Post Anesthesia Care Unit

PEEP: Pulmonary End Expiratory Pressure

PEL: Permissible Exposure Limits

PISS: Pin Index Safety System

ppm: Parts Per Million

psig: Pressure Square Inch Gauze

PVA: Polyvinyl Alcohol

REL: Recommend Exposure Limit

TFA: Trifluoroacetic Acid

TLV: Threshold Limit Value

TWA: Time-Weighted-Average

WAGs: Waste Anesthetic Gases

Abstract

Objective: To assess the occupational hazard of unscavenged waste anesthetic gases on reproductive health (infertility, abortions, preterm delivery and congenital anomalies) in personnel working in operating rooms.

Methods: The study was conducted by a questionnaire-based survey of 99 operating room personnel and 118 non exposed personnel from the general wards in Omdurman Military Hospital, Omdurman Teaching Hospital and Bahri Teaching Hospital. Controls selected by matching age, gender and job grade, 68 were eligible for analysis, 38 males & 30 females. Single personnel and those working less than five years were excluded from the study.

Results: Incidence of infertility in operating room personnel was 7.35% compared to 1.47% in non-exposed health workers (relative risk RR 4.93, 95% confidence interval: 0.6-41.7). There was a higher incidence of abortion in OR personnel in the first ten years of work (43.3%) with (RR=3, (95% CI 0.8-11.93) while 14.29% in non-exposed health workers. Longer durations of exposure were associated with having fewer children (0.05). Incidence of preterm delivery was similar in both groups (10% Vs 13.3%), but higher by about two-fold the general population (5%). Incidence of congenital anomalies in offspring was similar in both groups (1.47%).

Conclusion: There is a reproductive health risk of exposure to anesthetic gases. Adequate hazard control can be achieved by well-designed anesthetic equipment and high standards in scavenging and general ventilation and continuous training for good work practices. All staff working with anesthetic agents and contemplating pregnancies should limit exposure to toxic substances to the lowest level achievable.

Keywords: Occupational hazard; Waste anesthetic gases; Reproductive health

Chapter 1

Introduction

Health care is one of the largest industries and fastest growing occupations. Health care workers face many work place hazards; in addition to physical injuries such as needle stick injuries, back injuries and work place stressors, they also run the risk of exposure to anesthetic waste gases, sterilant gases, solvents and disinfectants [1].

Anesthetic gases (such as nitrous oxide, halothane (Fluothane), Enflurane (Ethane), Isoflurane (Forane) can be released into work areas of the health care facility: operating rooms, recovery rooms, labor and delivery rooms, dental operatories and veterinary clinics [2]. The anesthetic gases dispersed in operating rooms ORs are considered as pollutants. They are dispersed into the environment through problems in the equipment and from the exhalation of the patient [3]. Although healthcare workers are exposed to much lower anesthetic concentrations than the patients, this exposure often extends over many years. The decisive factors as concerns the adverse health effects of exposure to anesthetic gases are mainly the type of gases used, the length of exposure, and the gas concentrations [4]. Occupational exposure to anesthetic gases has a wide range of health effects, including neurological, renal and hepatic disease also reduction in mental performance and mental dexterity [5]. The harmful effects to personnel from excessive exposure to anesthetic gases have been documented in various literatures. Much serious disorders such as reduced fertility and problems during pregnancy are mentioned [4]. Scientific evidence obtained from human and animal studies suggest that chronic exposure to anesthetic gases increases the risk of spontaneous abortions and congenital abnormalities in the offspring of female workers and wives of male workers [6].

To prevent unnecessary exposure to WAGs, protocols and guidelines for workplace control have been developed in the USA, UK and most European countries by setting recommendations and regulatory limits. It is also important to have good engineering control by scavenging systems and HVAC systems in the hospital ORs. Unfortunately, in most of the hospital ORs in Sudan there are no scavenging systems, and therefore there are minimal measures to prevent occupational exposure to WAGs. As there are no published studies covering this area of concern, this study was conducted to assess the reproductive effect of WAGs on healthcare personnel working in unscavenged ORs, including risk of infertility, misscarriage, preterm delivery and congenital malformations of the offspring. Unfortunately, the levels of anestheic gases were not measured in the operating rooms, but hopefully in further studies in the future it would be possible.

Chapter 2

Literature Review

Waste Anesthetic Gases

Definition

Waste inhalation anesthetic gases and vapours are those which are released into work areas (operating room, recovery room, delivery room, or other areas where workers may be subject to job-related exposure) associated with, and adjacent to, the administration of a gas for anesthetic purposes, and include both gaseous and volatile liquid agents. Waste gases and vapours are here in referred to as waste anesthetic gases WAGs [7]. The waste anesthetic gases and vapours that create health effects from over-exposure include nitrous oxide and halogenated agents such as halothane, isoflurane, enflurane, trichloroethylene and chloroform [1].

General Information

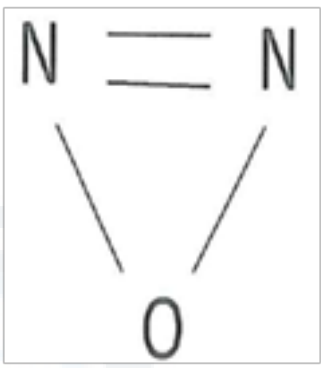
Surgical inhalation anesthesia was first used in the US when diethyl ether was administered to a patient in 1842. Since then, many chemical compounds have been used to anesthetize patients to keep them free from pain during surgical procedures. Many of the earlier inhalation anesthetics, such as diethyl ether and cyclopropane, are flammable and explosive and have been largely replaced by non-explosive, non flammable agents such as halothane and methoxyflurane [7,8].

It is estimated that more than 200,000 health care professionals; including anesthesiologists, nurse anesthetists, surgical and obstetric nurses, operating room technicians, surgeons, anesthesia technicians, post anesthesia care nurses, dentists, dental assistants, dental hygienists, veterinarians and their assistants, emergency room staff, and radiology department personnel, are potentially exposed to waste anesthetic gases and are at risk of occupational illness.

Health-care workers in the recovery room encounter occupational exposure to WAGs from the patients which are eliminated by their respiratory system into the ambient environment [8]. Nitrous oxide will continue to be exhaled by the patient for up to one hour after the surgery is finished [3]. Exposure measurements taken in operating rooms during the clinical administration of inhaled anesthetics indicate that waste gases can escape into the room air from various components of the anesthesia delivery system. In general, the detection of halogenated anesthetic agents by their odour would indicate the existence of very high levels, as these agents do not have a strong odour at low concentrations. Hallen et al. [7] found that fewer than 50% of the population can detect the presence of halothane until concentrations are 125 times the NIOSH REL (National Institute for Occupational Safety and Health, REL Recommended exposure limit) [8,9].

a. Nitrous oxide

i. Physical and chemical properties: Nitrous oxide (N_20; laughing gas) is the only inorganic anesthetic gas in clinical use (Structure 1). It is colorless and essentially odourless. Although non explosive and nonflammable, nitrous oxide is capable as oxygen of supporting combustion. Unlike the potent volatile agents, nitrous oxide is a gas at room temperature and ambient pressure. It can be kept as a liquid under pressure because its critical temperature lies above room temperature [10] (Table 1).



Structure 1: Structure of Nitrous oxide.

Table 1: Physical properties of nitrous oxide [11].

Molecular formula	N_20
Molar mass	44.013 g/mol
Appearance	colorless gas
Density	1.977 g/L (gas)
Melting point	—90.86 °C (182.29 K)
Boiling point	—88.48 °C (184.67 K)
Solubility in water	0.15 g/100 ml (15 °C)
Solubility	soluble in alcohol, ether, sulfuric acid
Vapour pressure	5150 l<Pa (20 °C)

Nitrous oxide gives rise to nitric oxide (NO) on reaction with oxygen atoms, and this NO in turn reacts with ozone. As a result, it is the main naturally occurring regulator of stratospheric ozone. It is also a major greenhouse gas and air pollutant.

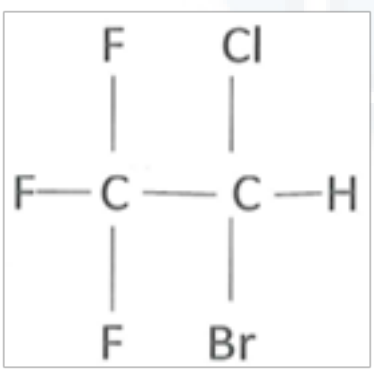
ii. Other uses: Nitrous oxide, in addition to its use as general anesthetic, is also used as an oxidizer in rocket motor racing to increase the power output of engines. It is also approved as a food additive (E942), specifically as an aerosol spray propellant. Its most common uses in this context are in aerosol whipped cream, canisters, cooking sprays, to inhibit bacterial growth, when filling packages of potatoes chips and other similar foods WI'.

iii. Biotransformation and toxicity: During emergence, almost all nitrous oxide is eliminated by exhalation. A small amount diffuses out through the skin. Biotransformation is limited to the less than 0.01% that undergoes reductive

metabolism in the gastrointestinal tract by anaerobic bacteria. Nitrous oxide inhibits enzymes that are vitamin B12 dependent by irreversibly oxidizing the cobalt atom in vitamin B12. These enzymes include methionine synthetase, which is necessary for myelin formation, and thymidylate synthetase, which is necessary for DNA synthesis. Prolonged exposure to anesthetic concentration of nitrous oxide can result in bone marrow depression (megaloblastic anemia) and even neurological deficiencies (peripheral neuropathies and pernicious anemia). However, administration of nitrous oxide for bone marrow harvest does not appear to affect the viability of bone marrow mononuclear cells. Because of possible teratogenic effects, nitrous oxide is often avoided in patients who are pregnant. Nitrous oxide may also alter the immunological response to infection by affecting chemotaxis and motility of polymorphonuclear leukocytes [10].

b. Halothane

i. Physical properties: Halothane is a halogenated alkane (Structure 2). The carbon-fluoride bonds are responsible for its nonflammable and non-explosive nature. Thymol preservative and amber-colored bottles retard spontaneous oxidative decomposition. Halothane is the least expensive volatile anesthetic, and because of its safety profile, continues to be used worldwide.

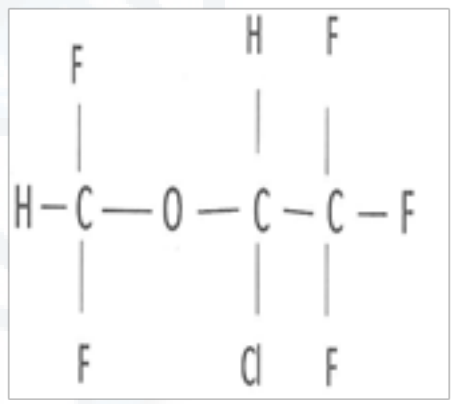


Structure 2: Structure of Halothane (Fluothane).

ii. Biotransformation and toxicity: Halothane is oxidized in the liver by a particular isozyme of cytochrome P450 (2E1) to its principle metabolite, trifluoroacetic acid. Bromide, another oxidative metabolite, has been incriminated in but is an improbable cause of post anesthetic changes in mental status. In the absence of oxygen, reductive metabolism may result in a small amount of hepatotoxic end products that covalently bind to tissue macromolecules. This is more apt to occur following enzyme induction by Phenobarbital. Elevated fluoride levels signal significant anaerobic metabolism. Postoperative hepatic dysfunction has several causes: viral hepatitis, impaired hepatic perfusion, preexisting liver disease, hepatocyte hypoxia, sepsis, hemolysis, benign postoperative intrahepatic cholestasis, and drug induced hepatitis. Halothane hepatitis is extremely rare (1 per 35, 000 cases). Patients exposed to multiple halothane anesthetics at short intervals, middle-aged obese women, and persons with a familial predisposition to halothane toxicity or a personal history of toxicity are considered to be at increased risk.

c. Isoflurane

i. Physical properties: Isoflurane is a nonflammable volatile anesthetic with a pungent ethereal odor. Although it is a chemical isomer of enflurane, it has different physicochemical properties (Structure 3).



Structure 3: Isoflurane (Forane) structure.

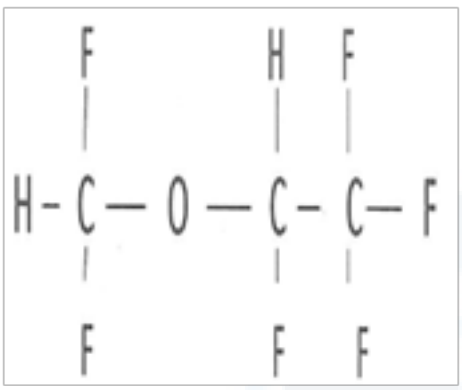
ii. Biotransformation and toxicity: Isoflurane is metabolized to trifluoroacetic acid. Although serum fluoride fluid levels may rise, nephrotoxicity is extremely unlikely even in the presence of enzyme inducers.

d. Desflurane

i. Physical properties: The structure of desflurane is very similar to that of isoflurane, with the only difference of substitution of a fluorine atom for isoflurane's chlorine atom. That "minor" change has profound effects on the physical properties of the drug. The vapor pressure of desflurane at 20°C is 681 mmHg, so at high altitudes it boils at room temperature; this problem necessitated the development of a special desflurane vaporizer. Furthermore, the low solubility of desflurane in blood and body tissues causes a very rapid washing and washout of anesthetic. Desflurane is roughly one-fourth as potent as the other volatile agents it is 17 times more potent than nitrous oxide (Structure 4).

ii. Biotransformation and toxicity: Desflurane undergoes minimal metabolism in humans.

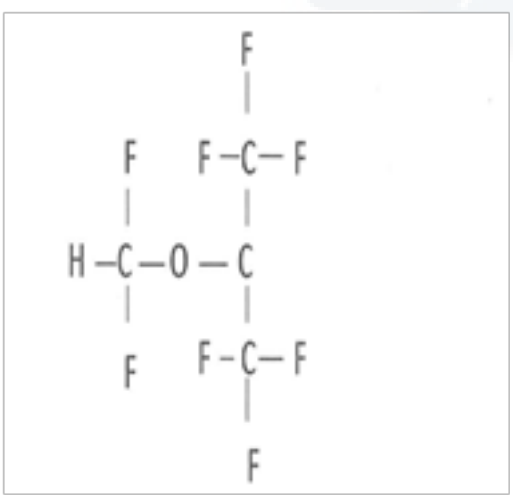
Serum and urine inorganic fluoride levels following desflurane anesthesia are essentially unchanged from preanesthetic levels. There is insignificant percutaneous loss. Desflurane, more than other volatile anesthetics, is degraded by desiccated carbon dioxide absorbent (particularly barium hydroxide lime, but also sodium and potassium hydroxide) into potentially clinically significant levels of carbon monoxide.



Structure 4: Desflurane (Suprane)

e. Sevoflurane

i. Physical properties: Like desflurane, sevoflurane is halogenated with fluorine. Sevoflurane combines a solubility in blood slightly greater than desflurane (Structure 5). Nonpungency and rapid increases in alveolar anesthesia concentration make sevoflurane an excellent choice for smooth and rapid inhalation induction in pediatric and adult patients.



Structure 5: Sevoflurane (Ultane) Structure.

Biotransformation and toxicity: The liver microsomal enzyme P450 (specifically the 2E1 isoform) metabolizes sevoflurane at a rate one-fourth that of halothane (5% versus 20%), but 10 to 25 times that of isoflurane or desflurane. The potential nephrotoxicity of the resulting rise in inorganic fluoride (F). Serum fluoride concentrations exceed 50pmol/L in approximately 7% of patients who receive sevoflurane, yet clinically significant renal dysfunction has not been associated with sevoflurane anesthesia. The overall rate of sevoflurane metabolism is 5%, or 10 times that of isoflurane. Nonetheless, there has been no association with peak fluoride levels following sevoflurane and any renal concentrating abnormality. Sevoflurane can also be degraded into hydrogen fluoride by metal and environmental impurities present in manufacturing equipment, glass bottle packaging, and anesthesia equipment. Hydrogen fluoride can produce an acid burn on contact with respiratory mucosa [10].

Adverse Health Effects of Occupational Exposure to Anesthetic Gases

Even in the early days of anesthesia, the dangers of inhaled anesthetics to both patients and operating room (OR) personnel were recognized. Patients occasionally suffered serious toxicity, such as hepatic failure, after the use of chloroform, whereas OR personnel were at risk for fires and explosions with the use of ether and cyclopropane [12]. Occupational exposures to anesthetic gases involve concentrations much smaller than those administered to patients in surgery. However, the side effects of anesthetic gases on patients are of interest for purposes of preventing adverse health effects on health care workers who are generally exposed to these gases over many years while working in OR, recovery rooms, or in outpatient clinics [4].

a. Central Nervous System: The effects of sedation and analgesia sought for the patient may lead to undesirable effects in the personnel exposed, especially when the concentrations exceed current occupational exposure limits. The following symptoms have been described, among others: fatigue, headache, dizziness, nervousness, nausea, concentration impairment and lacking fitness [4,12].

b. Peripheral Nervous System: Peripheral neuropathy with sensitivity impairments, parasthesias, and muscular weakness has been observed after occupational exposure to nitrous oxide, but only at very high concentrations of several thousand ppm. Peripheral neuropathy due to nitrous oxide can also be explained by the inactivation of the methionine synthase. When the concentration is less than 400 ppm, no significant inhibition of this enzyme is observed.

c. Hematopoietic System: Nitrous oxide oxidizes the cyanocobalamin (vitamin B12) cobalt complex and thereby irreversibly inhibits the methionine synthase activity that requires vitamin B12 in reduced form as coenzyme. This effect is dose-dependent. Nitrous oxide can thus cause medullary depression with megaloblastic anemia, leucopenia and thrombocytopenia. In patients, such hematological side effects are observed only for nitrous oxide concentration at or above 20% by volume. They have been observed mainly in cases

of prolonged or intermittent use of nitrous oxide (e.g. sedation of patients suffering from tetanus with intermittent administration of nitrous oxide to facilitate physiotherapy). However, damage to the hematopoietic system from occupational exposure to nitrous oxide in the operating room is improbable. The other anesthetic gases don't induce any hematological changes in exposed personnel.

d. The Immune system: Changes in the immune system such as a reduction in the number of B-lymphocytes and natural killer cells have been observed in exposed personnel after exposure to high concentrations of nitrous oxide (100 to 1500ppm) and halothane (1 to 40ppm) [4]. In a study on anesthetists exposed to low levels of anesthetic gases (nitrous oxide and isoflurane) percentages of T cells (CD3) decreased significantly and natural killer cells increased [13].

e. The Liver: In nearly 20% of patients, halothane causes an increase in hepatic enzymes that is usually not clinically apparent, but which can exceptionally evolve toward a clinically manifest toxic hepatitis. Severe cases of hepatitis with massive liver cell necrosis were even observed (with an incidence of 1:35,000). This is probably an antigen-antibody reaction involving trifluoroacetic acid (TFA) adducts and hepatocyte proteins as antigens. Cases of hepatitis due to halothane have also been described in personnel after months or years of occupational exposure [4]. Buring et al. [14] reviewed 17 published reports. There was an approximately 50-percent increase in liver disease among men and women working in the OR and a 30% increase in kidney disease among women [14]. Enflurane exceptionally prompts liver cell necroses in patients in cases of overdosing and severe hypoxia. Cases of toxic hepatitis in patients have also been attributed to exposure to isoflurane. But no hepatic disorder due to isoflurane or Enflurane has been found in exposed personnel. No sign of hepatotoxicity has been observed for desflurane or sevoflurane.

f. The Kidneys: Methoxyflurane has a nephrotoxic effect and is therefore no longer used in human medicine. There is no data hinting that commonly used anesthetic gases have nephrotoxic effects.

g. The Respiratory Tract: Bronchial asthma has been reported after repeated exposure to Enflurane. The diagnosis could be established by specific bronchial provocation tests with enflurane.

h. The Skin: Airborne allergic contact eczema has been described after occupational exposure to halothane and isoflurane.

i. Metabolic effects: Sevoflurane causes an increase in plasmatic fluorides in patients, but this effect seems to have no relevance in subjects occupationally exposed to sevoflurane.

j. Genotoxic effects (Mutagenicity): Studies on the genotoxic effects of occupational exposure to anesthetic gases (chromosome aberrations, sister chromatid exchange, micronucleus assay) yield contradictory results. Some, including recent ones, bring out a partly dose-dependent increase in sister chromatid exchange and micronucleic in the lymphocytes of exposed personnel, while others find no effect either in patients or exposed personnel [4]. Despite these encouraging results, tests of body fluids and blood cells from OR personnel have given variable results and are difficult to interpret. Results from these studies could be related to other factors in the operating room environment and not necessarily to exposure to trace concentrations of anesthetic gases [12].

k. Carcinogenic effects: Some epidemiological surveys bring out an increased incidence of leukemia, neoplasia of the lymphatic system, and other malignant tumors in exposed personnel. When evaluating these surveys, though, other factors such as exposure to ionizing radiation should be taken into account. Considering the methodological lacks of older studies, the lack of data indicating increased carcinogenic risk in the recent studies and the lack of conclusive data on any carcinogenic risk in the frame work of animal experiments, a cancer risk due to occupational exposure to anesthetic gases seems unlikely, though it cannot be entirely excluded [4].

Reproductive Toxicology of Anesthetic Gases

Data from animal experiments

Nitrous oxide is the only inhaled anesthetic that has been convincingly shown to be directly teratogenic in experimental animals. High concentrations (50% to 75%) delivered to pregnant rats for 24 hour periods during the period of organogenesis and low concentrations (0.1%) delivered to rats throughout pregnancy result in an increased incidence of fetal resorption and visceral and skeletal abnormalities [14]. Nitrous oxide causes a reduction in the testicular weight in the male rat, with a decrease in sperm count, anomalies in spermatozoa form, and a drop in fertility. Fertility is also reduced in the female rat, nitrous oxide is embryotoxic and increases the incidence of resorption as well as malformations of the skeleton and soft tissues. Minimum concentrations of nitrous oxide causing a significant drop in methionine synthase correspond approximately to those with fetotoxicity (between 50 and 1000ppm) was observed, which seems to indicate a relationship between these two phenomena [4]. Any teratogenic effects observed are caused by the severe and uncorrected physiological changes associated with the administration of the anesthetics rather than by the anesthetic themselves [12]. Halothane also has dose-dependent teratogenic effects in animal experiments. For Enflurane and isoflurane, animal experiments bring out no embryo or fetotoxic effects except in cases of exposure at very high doses [4].

Effects on fertility

A retrospective study conducted in the United States on female dental assistants showed a significant relationship

between high exposures to nitrous oxide and a decrease in fertility [2,4]. For exposures between 200 and 7000ppm for more than five hours per week, the probability to become pregnant was reduced by 60% compared with persons with little or no exposure. So it is likely that high exposures to nitrous oxide will impair fertility [4].

Unfavorable effects on progress of pregnancy

Numerous studies [15-21] have documented an increased risk of spontaneous abortions among female personnel, including anesthetists, OR nurses and dental assistants (referenced by Boivin [22]. In 1966, Vaisman [23] surveyed by questionnaire 303 Russian anesthesiologists (193 men and 110 women), 98% reported using diethyl ether; 59% ;nitrous oxide, 28%; halothane, and 21%, other agents. Scavenging of waste anesthetic gases was not practiced and concentration levels were not presented. The authors noted that 18 of 31 pregnancies of anesthesiologists who were between the ages of 24 and 38 ended in spontaneous abortions. In addition, there were two premature births and one child was born with a congenital malformation. The anesthesiologists with abnormal pregnancies had exposures of 25 hrs/week or more while those with normal pregnancies did not exceed 15 hrs/week.

Askrog and Harrald [24] reported the results of a 1970 questionnaire survey of 578 nurses in anesthesia departments and of 174 females and male anesthetists. The survey was intended to determine if long- term, low dosage of inhalation of anesthetics had a teratogenic effect. The abortion frequency was significantly higher during employment (20%) than before (10%), not only for exposed female personnel but also for the wives of anesthesiologists. Though not statistically significant, the number of male children born in all groups was decreased.

In 1971, Cohen et al. [16] presented the results of a double survey among California nurses and female physicians. The first study consisted of personally interviewing 67 female operating room nurses and 92 female general duty nurses (control). The second study was a questionnaire survey in which responses were obtained from 50 female anesthesiologists and 82 female physicians in specialties other than anesthesia who were used as controls. The results from the nurses showed that 29.7% of pregnancies in operating room nurses ended in spontaneous miscarriage compared with 8.8% in the control group, which is statistically significant (p=0.045). For the period 1965-1970, the anesthetists showed a 37.8% spontaneous miscarriage rate compared with 10.3% in the control group, which is statistically significant (p=0.0035). The anesthetic as concentration and the type of gases to which the study group was exposed were not reported [7]. The 1974 national study supported by the American Society of Anesthesiologists (ASA) on the effects of trace levels of WAGs on the health of OR personnel. Compared with unexposed women, women exposed to WAGs were reported to have increased risk of spontaneous abortion, cancer, hepatic disease, and renal disease, and their offspring were reported to have an increased risk of congenital abnormalities. Exposed male anesthesiologists were reported to have increased risk of hepatic disease and their offspring to have an increased risk of congenital abnormalities [12]. Later, the ASA commissioned a group of epidemiologists and biostatisticians to evaluate the significance of epidemiological study of possible health hazards associated with exposure to WAGs. The report of the group appeared in 1985. Buring et al. [14] reviewed 17 published reports. Results indicated a 30% increase risk of spontaneous abortion for women working in the OR and a similar but less consistent increase in congenital anomalies among offspring of exposed physicians. The investigators noted that all the studies reviewed had weaknesses, including low response rates, inadequate information on non responders, anesthetic exposure levels and confounding variables and a lack of verification of outcome events [12].

Most of the studies took place before scavenger systems for recovering of waste gas were installed, and the current opinion holds that, with proper functioning scavengers and ventilators, the risk of over-exposure is greatly reduced [2]. A recent met-analysis showed that occupational exposure to inhaled anesthetics is associated with an increased risk for spontaneous abortion (relative risk (RR)=1.48, 95% confidence interval (CI)=1.40 to 1.58) [22], On the other hand, several researchers have shown that exposure to inhaled anesthetics among veterinarians is not associated with an increased risk for adverse pregnancy outcome [25,26]. On the basis of epidemiological evidence and the data supporting the current occupational exposure limits, it can be considered that, if the recommended preventive measures are applied and the occupational exposure limits complied with, i.e., when the occupational hygiene principles are followed, there is probably no increased risk of spontaneous abortion except in cases of exposure to halothane [4].

Developmental effects

Most retrospective studies, as well as one recent prospective study, have shown no evidence of significant increase in malformations in the offspring of parents occupationally exposed to anesthetic gases. However, a small number of studies have shown a relationship between the malformation rate and exposure of the parents [4]. A study on Ontario female veterinary staff exposed to inhaled anesthetics and/or radiation did not seem to be at increased risk for major malformation above baseline risk [30]. Under the conditions that currently prevail in operating room rooms, though, it seems that risk of malformation in the off-spring of parents occupationally exposed to anesthetic gases is not increased. Because of the neurotoxic effects of halothane and the high sensitivity of the human embryo's brain, central nervous system disorders in the case of in utero exposure to this anesthetic can nonetheless not be excluded. However, such effects cannot readily be evidenced [4].

Recommendations and Regulatory Limits of Anesthetic Gas Exposure

National Institute for Occupational Safety and Health (NIOSH) Recommendations

Modified 1977 NIOSH criteria recommend the following time-weighted-average (TWA) exposure limits as measured over the period of anesthetic administration:

a) Halogenated anesthetics: 2ppm when used alone, and 0.5ppm when used in combination with nitrous oxide.

b) Nitrous oxide: 25ppm [6].

OSHA Recommendations

There are no Occupational Safety and Health Administration OSHA permissible exposure limits (PEL) governing exposures to either halogenated anesthetics or nitrous oxide [6]. No worker should be exposed to a concentration of WAGs>2ppm of any halogenated anesthetic agent based on personnel and area sampling methods. When such agents are used in combination with nitrous oxide, levels of 0.5ppm are achievable. Nitrous oxide, when used as the sole anesthetic agent, should be controlled so that no worker is exposed eight-hour time-weighted-average concentration >25ppm during anesthetic administration [12].

The American Conference of Governmental Industrial Hygienists (ACGIH)

The ACGIH has established Threshold Limit Values (TLV) of 5Oppm, measured as a eight-hour TWA for both the halogenated anesthetic (halothane) and nitrous oxide. There are no TLVs established for other halogenated anesthetics such as isoflurane or sevoflurane (Table 2).

Table 2: Summary of the REL of anesthetic gas.

Anesthetic gas (ppm)	OSHA PEL	NIOSH REL (PPM)	ACGIH TLV-TWA (ppm)
Nitrous oxide Isoflurane	-	25*	50
Isoflurane	-	Ceiling 2**	none
Halothane	-	Ceiling 2	50
Desflurane	-	Ceiling 2	none
Sevoflurane	-	Ceiling 2	none
Enflurane	-	Ceiling 2	75
Methoxyflurane	-	Ceiling 2	none

PEL: Permissible exposure limit; REL: Recommended exposure limit measured as a time-weighted-average (TWA) during the period of anesthetic administration, not to exceed one hour;

TLV-TWA: Threshold Limit Value-Time-weighted-average. This value refers to an eight- hour work-day and a forty-hour work week;

ppm: parts per million.

*: measured as a TWA over the period of anesthetic administration.

**: ceiling limit concentration of no greater than 2ppm over a period not to exceed one hour.

British government health services advisory committee

In 1996, the British Government Health Services Advisory Committee published its recommendations, Anesthetic Agents: Controlling Exposure under the Control of Substances Hazardous to Health Regulations 1994 (COSHH) in which occupational exposure standards (OES) were issued. The OES are for an eight-hour time-weighted-average reference period for trace levels of WAGs and are shown below:

a. 100ppm for nitrous oxide

b. 5Oppm for enfiurane and isoflurane 1Oppm for halothane

Other Euopean countries

The Netherlands has a limit of 25ppm for nitrous oxide. Italy, Sweden, Norway and Denmark set 100ppm as their upper limit exposure level for nitrous oxide. The difference illustrate the difficulty in setting standards without adequate data [14].

Methods of Assessing Exposure to Anesthetic Gases in the Work Place

Analysis of data from the literature

Many studies have been published over recent years on the risks related to anesthetic gases. These data can be used to identify the risks on a case-by-case basis after checking that the working conditions described do correspond

precisely enough to the situation actually encountered in the field by comparing specific parameters which influence exposure:

i. The anesthetic method used the type of surgery practiced, the working technique, the anesthetic apparatus, the exhaust device, as well as quality assurance measures.

ii. Mode of room ventilation, organizational measures and quality assurance measures.

iii. The concentration of anesthetic gas that develops in the room depends on the room size, the length of anesthesia, and the intensity of the ventilation.

Air monitoring

There are various techniques for measuring anesthetic gas concentrations in the air:

A. Direct-reading systems.

B. Air sampling with equipment such as adsorbent tubes or cuffs, followed by analysis using gas chromatography or an infrared technique.

C. Diffusion sampler and analysis.

Calculation methods

Occupational exposure to anesthetic gases can be estimated by mathematical modeling of exposure in the workplace on the basis of all intervening factors. The same process can be applied for evaluating past occupational exposure (e.g., when assessing occupational disease) or fore casting exposure at future workplaces (e.g., when planning protective measures). To do so, full information is needed concerning the product in question, the emission source, the room dimensions and ventilation conditions and work methods, and it must be possible to document the calculations precisely.

The simplest calculation assumes that a homogenous as mixture forms in the room and a steady-state regime is established.

The dangerous product concentration is computed using the following formula:

$$X_D = \dot{M}_D / \dot{V}_L$$

In which:

X_D = concentration of dangerous product in the air [mg / m³].

M_D = dangerous product mass flow [mg/hr].

V_L = fresh air flow.

However, to calculate the concentration more precisely, other factors need to be taken into account such as the length of anesthesia, room size and air exchange rate in the operating room. The following complex formula is then used:

$$\bar{X}_D = \left[\frac{\dot{M}_D}{\dot{V}_L} + X_{D,ex}\right] \cdot \left[1 - \frac{1 - e^{-\lambda.\Delta t}}{\lambda.\Delta t}\right] + X_{D,0.} \frac{1 - e^{-\lambda.\Delta t}}{\lambda.\Delta t}$$

In which:

$\bar{X}_D$ = mean concentration of dangerous product in the air [mg/m³].

$\dot{M}_D$ =dangerous product mass flow [mg/hr].

V_L = fresh air flow.

$X_{D,ex}$ = concentration of dangerous product in fresh air [mg/m³].

$X_{D,0}$ = concentration of dangerous product in room studied at beginning of calculation [mg/m³].

λ = air exchange = $\dot{V}_L$ / room volume [L/h].

Δt = time interval over which the calculation is made.

The conclusions that can be drawn from the calculation results depend essentially on the quality of the available data input on the relevant factors. Calculation methods have been published by the German BIA-Occupational safety institute of the institutions for statutory accident insurance and prevention (Report 3/2001).

Biological monitoring

Concentration of anesthetic gases or their metabolites can be determined in the biological material to complement the air monitoring data, notably in cases if intermittent exposure or when establishing a cumulative exposure over several days. An important biotransformation has been experimentally proven for all volatile anesthetics. Of the absorbed and liver-metabolized halothane portion, 18-20% is found in urine as bromide and 12% as trifluoracetic acid. Enflurane undergoes a smaller biotransformation and is eliminated by the lungs for as much as 83%, the remaining percentage being eliminated with urine only 2.4% of the absorbed portion is found as non-volatile metabolites: methoxidifluoracetic acid, oxalic acid, fluorides and chlorides. Nitrous oxide is a substance with little solubility in the blood and only partially metabolized by the body; it is quickly eliminated by the lungs at the end of the exposure and very small quantities are excreted unaltered in urine. Biological compartments usually chosen or proposed for biological monitoring of anesthetics absorbed through the respiratory system are:

a) The alveolar compartment (middle expiratory compartment).

b) The blood compartment (venous).

c) The urinary compartment.

Sought substances are the non metabolized compounds and some of the well-known and analyzable biotransformation products. Biological monitoring carried out on alveolar air (middle expired air) or venous blood samples can be performed in different moments, and in general:

a) During the exposure.

b) Immediately after the exposure.

c) At the end of the working week.

The values thus obtained are concentration instant values that must be referred to environmental instant concentration values (if the sampling took place during exposure) or to environmental average concentration values (if the sampling took place after the exposure) of the last period of exposure or of the last day or the last few days of exposure. On the contrary, urinary concentration values are not instant, but well pondered (Table 3).

The Anesthetic Machine

An anesthetic machine is an assembly of various components and devices that include medical gas cylinders in machine hanger yokes, pressure regulating and measuring devices, valves, flow controllers, flow meters, vaporizers, carbon dioxide absorbers, canisters, and breathing circuit assembly. The basic two-gas anesthesia machine has more than 700 individual components. The anesthesia machine is a basic tool of the anesthesiologist and serves as the primary work station. It allows the anesthesia provider to select and mix measured flows of gases, to vaporize controlled amounts of liquid anesthetic agents and thereby to administer safely controlled concentrations of oxygen and anesthetic gases and vapours to the patient via breathing circuit. The anesthesia machine also provides a working surface for placement of drugs and devices for immediate access and drawers for storage of small equipment, drugs, supplies and equipment instruction manuals. Finally, the machine serves as a frame and source of pneumatic and electric power for various accessories such as a ventilator, and monitors that observe or record vital patient functions.

Gas flow in the anesthesia machine and breathing system

The internal piping of a basic two-gas anesthesia machine has many connections and potential sites for leaks. Both oxygen and nitrous oxide may be supplied from two sources: a pipeline supply source (central piping system from bulk storage) and a compressed gas cylinder supply source. In hospitals, the pipeline supply source is the primary gas source for the anesthetic machine. Pipeline supplied gases are delivered through wall outlets at pressure of 50-55psig through diameter indexed safety system (DISS) fittings or through quick-connect couplings that are gas specific within each manufacturers' patented system. Because pipeline system can fail and because the machines may be used in locations where piped gases are not available, anesthesia machines are fitted with reserve cylinder of oxygen and nitrous oxide. The oxygen cylinder source is regulated from approximately 2200psig in the tanks to approximately 45psig in the machine high pressure system, and the nitrous oxide cylinder source is regulated from 745psig in the tanks to approximately 45psig in the machine high-pressure system.

Table 3: Biological exposure limit of inhalation anesthetics.

Anesthetic	Biological Marker
Halothane	Hematic trifluoracetic acid:2.5 mg/L blood (taken at the end of the week and at the end of the exposure)
Halothane	Alveolar halothane: 0.5ppm (measured in operating-theatre at the end of the exposure)
Isoflurane	Isoflurane urinary: 18nM/L urine (measured in urine at the end of the exposure)
Nitrous oxide	Nitrous oxide urinary: 27mcg/L (measured in the urine at the end of the exposure; biological equivalent value to 50ppm of environmental concentration).
Nitrous oxide	Nitrous oxide urinary: 55 mcg/L (measured in the urine taken at the end of the exposure; biological equivalent value to 100ppm of environmental concentration).

Compressed gas cylinders of oxygen, nitrous oxide and other medical gases are attached to the anesthesia machine through the hanger yoke assembly. Each hanger yoke is equipped with the pin index safety system (PISS), a safeguard introduced to eliminate interchanging and the possibility of accidentally placing the incorrect gas tank in a yoke designed for another gas tank. Oxygen from the wall outlet or cylinder pressurizes the anesthesia delivery system. Compressed oxygen provides the needed energy for a pneumatically powered ventilator, if used, and it supplies the oxygen flush valve used to supplement oxygen flow to the breathing circuit. Oxygen also powers an in-line pressure-sensor shut off valve for other gases to prevent their administration if the oxygen supply pressure in the oxygen high pressure system falls below a threshold valve.

Once the flows of oxygen, nitrous oxide and other medical gases (if used) are turned on at their flow control valves, the gas mixture flows into the common manifold and through a concentration-calibrated agent-specific vaporizer where a potent inhaled volatile anesthetic agent is added. The

mixture of gases and vaporized anesthetic agent then exits the anesthesia machine low pressure system through the common gas outlet and flows to the breathing system. The circle system is the breathing system most commonly used in operating rooms. It is so named because its components are arranged in a circular manner. The essential components of a circle breathing system include:

a) A site for inflow of fresh gas, A carbon dioxide absorber canister (containing soda lime or barium hydroxide lime) where CO_2 is absorbed,

b) A reservoir bag,

c) Inspiratory and expiratory unidirectional valves,

d) Flexible corrugated breathing tubing,

An adjustable pressure-limiting (APL) or "pop off" valve for venting excess gas,

e) A Y-piece that connects to a face mask, tracheal tube, laryngeal mask airway LMA or other airway management device.

Once inside the breathing system, the mixture of gases and vapours flows to the breathing systems inspiratory uni-directional valve, then on toward the patient. Exhaled gases pass through the expiratory unidirectional valve and enter the reservoir bag. When the bag is full, excess gas flows through the APL valve and into the scavenging system that removes the waste gases. On the next inspiration, gas from the reservoir bag passes through the carbon dioxide absorber prior to joining the fresh gas from the machine on its way to the patient. The general use of fresh gas flow rates into anesthetic systems in excess of these required to compensate for uptake, metabolism, leaks, or removal of exhaled carbon dioxide results in variable volumes of anesthetic gases and vapours exiting the breathing system through the APL valve. When an anesthetic ventilator is used, the ventilator bellows functionally replaces the circle system reservoir bag and becomes part of the breathing circuit. The APL valve in the breathing circuit is either closed or excluded from the circuit using a manual/automatic circuit selector switch. The ventilator incorporates a pressure-relief valve that permits release of excess anesthetic gases from the circuit at end-exhalation. These gases should be scavenged.

Sources of leaks within the anesthesia machine and breathing system

No anesthetic machine system is totally leak-free (Emergency Care Research Institute 1991). Leakage may originate from both the high-pressure and low-pressure systems of the anesthesia machine.

High pressure system: It consists of all piping and parts of the machine that receive gas at cylinder or pipeline supply pressure. It extends from the high-pressure gas supply to the flow control valves. Leaks may occur from the high pressure connectors where the supply hose connects to the wall outlet or gas cylinder and where it connects to the machine inlet. Therefore, gas-supply hoses should be positioned to prevent strain on the fittings and constructed from supply-hose materials designed for high-pressure as flow and minimal kinking. High pressure leakage may also occur within the anesthesia machine itself. Other potential sources of leak include quick-connect fittings, cylinder valves, absent or warn gaskets, missing or worn yoke plugs in a dual yoke assembly, and worn hoses.

The low pressure system: In the low pressure system, the pressure is slightly above atmospheric, it consists of components downstream of the flow-control valves. It includes flow meter tubes, vaporizers, common gas outlet, and breathing circuit. Leaks may occur from the connectors and components anywhere between the anesthesia gas flow control valves and the airways; loose-fitting connections, defective and worn seals and gaskets, worn or defective breathing bags, hoses, and tubing, loosely assembled or deformed slip joints and threaded connections, also leakage may occur from the moisture drainage port of the CO_2 absorber which may be in the "open" position, at the gas analysis sensor and gas sampling sites, from the face mask, the tracheal tube (especially in paediatric patients where a leak is around the uncuffed tracheal tube), laryngeal mask airway; connection points for accessory devices such as humidifiers, temperature-probe, or PEEP valve, inappropriate installation of a calibrated vaporizer or misalignment of a vaporizer on its manifold (ECRI 1991) can also contribute to anesthetic gas leakage.

Checking anesthesia machines: Prior to induction of anesthesia, the anesthesia machine and its components should be made ready for use. All parts of the machine should be in good working order with all accessory equipment and necessary supplies on hand. The waste gas disposal system should be connected, hoses visually inspected for obstructions or kinks, and proper operation determined.

The anesthesia breathing system should be tested to verify that it can maintain positive pressure. Leaks should be identified and corrected before the system is used. Several check-out procedures exist. The 1993 Food and Drug Administration (FDA) Anesthesia Apparatus Check out Recommendations Document is based on guidelines developed by the FDA, as advised by anesthesiologists and manufacturers (Appendix).

General Workplace Controls

Occupational exposures can be controlled by the application of a number of well-known principles which may be applied at or near the hazard source, to the general workplace environment, or at the point of occupational exposure to individuals. Controls applied at the source of the hazard, including engineering and work practice controls, are generally the preferred and most effective means of control. To minimize WAGs concentration in the operating room the recommended air exchange rate (room dilutional ventilation) is a minimum total of 15 air changes per hour with a minimum air changes of outdoor air (fresh air) per hour (American Institute of Architects (1996-1997).

In anesthetizing locations and PACUs, where employees are at risk of exposure to waste anesthetic gases, exposure may be controlled by some or all of the following:

a) Effective anesthetic gas scavenging systems that remove excess anesthetic gas at the point of origin,

b) Effective general or dilutional ventilation,

c) Good work practices on the part of health-care workers, including the proper use of controls,

d) Proper maintenance of equipment to prevent leaks.

e) Periodic personnel exposure and environmental monitoring to determine the effectiveness of the overall waste anesthetic gas control program.

Engineering controls

The collection and disposal of WAGs in ORs and non-operating room settings is essential for reducing occupational exposures. Engineering controls such as an appropriate anesthetic gas scavenging system are the first line defence and the preferred method of control to protect employees from exposure to anesthetic gases. The heating, ventilating and air conditioning (HVAC) system also contributes to the dilution and removal of waste gases not collected by the scavenging system or from other sources such as leaks in the anesthetic apparatus or improper work practices. The exhalation of residual gases by patients in the PACU may result in significant levels of waste anesthetic gases when appropriate work practices are not used at the conclusion of the anesthetic or inadequate ventilation exists in the PACU. A non-recirculating ventilation system can reduce waste anesthetic gas levels in this area.

Work practices

This involves the way in which a task is performed. OSHA has found that appropriate work practices can be a vital aid in reducing the exposures of OR personnel to waste anesthetic agents. Improper anesthetizing techniques can contribute to increased waste gas levels, which can include:

a) Improperly selected and fitted face mask,

b) Insufficiently inflated tracheal tube cuff,

c) Improperly positioned laryngeal mask or other airway,

d) Careless filling of vaporizers and spillage of liquid anesthetic agents.

General wok practices recommended for anesthetizing locations include the following: A complete anesthesia apparatus check out procedure should be performed each day before the first case. An abbreviated version should be performed before each subsequent case. The FDA Anesthesia Apparatus Checkout Recommendations (Appendix) should be considered in developing inspection and testing procedures for equipment checkout prior to administering an anesthetic.

If a face mask is to be used for administration of inhaled anesthetics, it should be available in a variety of sizes to fit each patient properly. The mask should be pliable and provide as effective a seal as possible against leakage into the surrounding air. Tracheal tubes, laryngeal masks and other airway devices should be positioned precisely and the cuffs inflated adequately. Vaporizers should be filled in a well-ventilated area and in a manner to minimize spillage of the liquid agent. This can be accomplished by using a specialized “key-fill” spout to pour the anesthesia into the vaporizer instead of pouring from a bottle into a funnel-fill vaporizer. Vaporizers should be filled at the location where the anesthetic will be administered and, when filled electively, with the fewest possible personnel present in the room. Vaporizers should be turned off when not in use. Spills of liquid anesthetic agents should be cleaned up promptly.

Before extubating the patients’ trachea or removing the mask or other airway management device, one should administer non-anesthetic gases/agents so that the washed-out anesthetic gases can be removed by the scavenging system. In most patients, a circle absorption system is used and can be easily connected to a waste gas scavenging system. In paediatric anesthesia, systems other than those with a circle absorber may be used. Choice of the breathing circuit that best meets the needs of paediatric patients may alter a clinician’s ability to scavenge waste gas effectively. Breathing circuits frequently chosen for neonates, infants, and small children are usually valveless, have low resistance, and limit rebreathing. The Mapleson D system and the Jackson-Rees modification of the Ayre’s T-piece are examples of limited rebreathing systems that require appropriate scavenging equipment. The following work practices may be employed with any of the above breathing circuits:

a) Empty the contents of the reservoir bag directly into the anesthetic gas scavenging system and turn off the flow of nitrous oxide and any halogenated anesthetic agent prior to disconnecting the patient circuit.

b) Turn off the flow of nitrous oxide and the vaporizer, if appropriate, when the patient circuit is disconnected from the patient.

c) Test daily for low-pressure leaks throughout the entire anesthesia system. All leaks should be minimized before the system is used.

d) Work practices performed by biomedical engineer and technicians also contribute significantly to the efficacy of managing waste gas exposure. It is, therefore, important for this group of workers to do the following:

e) Monitor airborne concentrations of waste gases by sampling, measuring, and reporting data to the institution administration. Air monitoring for waste anesthetic gases should include both personnel sampling (i.e., in a health-care workers’ breathing zone) and area sampling.

Assist in identifying sources of waste/leaking gases and implementing corrective action.

f) Determine if the scavenging system is designed and functioning properly to remove the waste anesthetic gases from the breathing circuit, and ensure that the gases are vented from the work-place in such a manner that occupational re-exposure does not occur.

g) Ensure that operatory and PACU ventilation systems provide sufficient room air exchange to reduce ambient waste gas levels.

Good techniques that help avoid harm to anesthesia personnel from WAGs include good mask fitting, avoiding unscavenged techniques when possible, preventing flow from the breathing system into room air (gases turned on only when mask is on face), washout anesthetic (into the breathing circuit at the end of anesthesia, avoiding spill of liquid agent, using low flows, using cuffed ETT when possible, checking machine for leaks regularly, disconnecting nitrous oxide pipeline connection at the end of the day and use of total intravenous anesthesia.

Administrative controls

For workers potentially exposed to waste anesthetic gases, the program administrator should establish and implement policies and procedures to:

a) Institute a program of routine inspection and regular maintenance of equipment in order to reduce anesthetic gas leaks and to have the best performance of scavenging equipment and room ventilation. Preventive maintenance should be performed which includes inspection, testing, cleaning, lubrication and adjustment of various components and should be performed by trained individuals.

b) Implernent a monitoring program to measure airborne levels of waste gases in the breathing zone or immediate work area of those most heavily exposed (eg. Anesthesiologist, nurse anesthetist, oral surgeon) in each anesthetizing location and PACU. Periodic monitoring of waste gas concentrations is needed to ensure that the anesthesia delivery equipment and engineering/environmental controls work properly and that the maintenance program is effective. Monitoring may be performed effectively using conventional time-weighted-average air sampling or real-time air sampling techniques.

c) Encourage or promote the use of scavenging systems in all anesthetizing locations where inhaled agents are used.

d) Innplement an information and training program for employees exposed to anesthetic agents.

e) Define and implement appropriate work practices to help reduce employee exposure.

f) Implement a medical surveillance program for all workers exposed to waste gases.

g) Ensure proper use of personal protective equipment during clean-up and containment of major spills of liquid anesthetic agents.

h) Manage disposal of liquid agents, spill containments, and air monitoring for waste gases following a spill.

Personal protective equipment

Personal protective equipment should not be used as a substitute for engineering, work practice, and/or administrative controls in anesthetizing locations and PACUs. Air-supplied respirators with self-contained air source are ideal for eliminating exposure but are not a practical alternative. When selecting gloves and chemical protective clothing (CPC), some of the factors to be considered include material chemical resistance, physical strength and durability, and overall product integrity. Among the most effective types of gloves and body protection are those made from Viton°, neoprene, and nitrile. Polyvinyl alcohol (PVA) is also effective but it should not be exposed to water or aqueous solutions [8].

Scavenging System and Ventilation

Scavenging systems

Scavenging is the collection and removal of vented anesthetic gases from the OR. Since the amount of anesthetic gas supplied usually far exceeds the amount necessary for the patient, OR pollution is decreased by scavenging. If a fresh gas flow-size volume enters the breathing circuit each minute, the same flow must leave it, or barotrauma will result. Scavenger and OR ventilation efficiency are the two most important factors in reduction of WAGs.

Types: Scavenging may be active (suction applied) or passive (waste gases proceed passively down corrugated tubing through the room ventilation exhaust grill of the OR). Active systems require a means to protect the patients airway from the application of suction, or build up of positive pressure. Passive systems require that the patient be protected from positive pressure build-up only. Another important distribution is that scavenger interfaces may be open (to the atmosphere) or closed (gases within the interface may communicate with the atmosphere only through valves; the other type). The different types of interface have clinical implications.

Clearly, Open interface: Has no valves, and is open to the atmosphere (allows both negative and positive pressure relief). Should be used only with active systems. While safer for the patient (no hazard of positive or negative pressure being applied to the airway as a result of scavenger failure), the risk of occupational exposure for providers ignorant of their proper use is higher with the open interface. Open interfaces are found on most new gas machines (e.g., Fabius GS, Narkomed 6000, ADU).

Closed interface: Communicates with atmosphere only through valves. Vacuum should be adjusted so that reservoir bags neither nor over-distends. Aestiva may have an open or closed interface.

Components of the scavenger system

a) Gas collection assembly, (tubes connected to APL and vent relief valve),

b) Transfer tubing (19 or 30mm, sometimes yellow color-coded),

c) Scavenging interface: Which is the most important component. It protects the breathing circuit from excess positive or negative pressure.

Hazards of scavenging

i. Obstruction distal to interface causes barotrauma or excess negative pressure (action: disconnect gas collection tubing from back of pop off valve (APL) or turn off suction at scavenger interface)

ii. Occupational exposure.

iii. Barotrauma or inability to ventilate.

Effectiveness: Unscavenged or show 10-70ppm halothane and 400-3000ppm nitrous oxide. Minimal scavenging brings these levels down to 1 and 60 ppm respectively; adding careful attention to leaks and technique can yield levels as low as 0.005 and 1ppnn [27].

Ventilation

The American Institute of Architects, in its 1992 Guidelines for Construction and Equipment of Hospitals and Medical Facilities, established recommendations for ventilation systems in OR (15-21 air exchanges per hour, of which must be fresh outside air) and PACU's (6 air exchanges per hour, of which 3 must be fresh outside air) [28].

HVAC systems: HVAC systems used in health-care facilities are of two types: Non recirculating and recirculating. Nonrecirculating systems (single-pass systems), take in fresh air from the outside and circulate filtered and conditioned air through the room. Whatever volumes of fresh air are introduced into the room are ultimately exhausted to the outside. WAG can be efficiently disposed via this nonrecirculating system. When a nonrecirculating ventilation system serves through large-diameter tubing and terminating the tubing at the room's ventilation exhaust as the disposal route for excess anesthetic gases, disposal involves directing the waste gases grille. The sweeping effect of the air flowing into the grille carries the waste gases away.

Concern for fuel economy has increased the use of systems that recirculates air. Recirculating HVAC/ventilation systems return part of the exhaust air back into the of anesthetic exposure, air which is to be recirculated must not contain anesthetic gases.

Under certain circumstances a separate duct for venting anesthetic gases directly outside the building without the use of a fan, may be an acceptable alternative. By this technique, excess anesthetic gases may be vented through the wall, window, ceiling, or floor, relying only on the slight positive pressure of the gases leaving the gas collection assembly to provide the flow. However, several limitations are apparent. A separate line would be required for each OR to prevent the cross-contamination with anesthetic gases among the ORs. A safe disposal site would be necessary. The possible effects of variations in wind velocity and direction would require a means for preventing a reverse flow in the disposal system. Occlusion of the outer portion of such a passive system by insect or bird nest is also possible.

Adsorbers: Adsorbers can also trap most excess anesthetic gases. Canisters of varying shapes and capacities filled with activated charcoal have been used as waste gas disposal assemblies by directing the gases from the gas disposal tubing through them. Activated charcoal canisters will effectively adsorb the vapours of halogenated anesthetics but not nitrous oxide. The efficiency of adsorption depends on charcoal brand, type of inhaled volatile anesthetic, on the rate of gas flow through the canister. The disadvantages are that they are expensive and must be changed frequently.

General or dilutional ventilation: An effective room HVAC system when used in combination with an anesthetic gas scavenging system should reduce, although not entirely eliminate, the contaminating anesthetic gases. If excessive concentrations of anesthetic gases are present, then airflow should be increased in the room to allow for more air mixing and further dilution of the anesthetic gases. Supply register louvers located in the ceiling should direct fresh air toward the floor and toward the health-care workers to provide dilution, and removal of the contaminated air from the operating or PACU. They should be located usually low on the wall near the floor level in the room to provide adequate air distribution. They should not be located near the supply air vents so as not to short-circuit the airflow and prevent proper air mixing and flushing of the contaminants from the room [8]. In order for all routine techniques to be carried out in an OR without exceeding the occupational exposure limits, it is recommended that the minimum fresh air supply be 800 to 1200 m3/h, or more than 15 fresh air changes per hour, as recommended by various rational regulations [4].

Chapter 3

Methodology

Study design was a retrospective cohort study conducted in three hospitals in Khartoum state; Omdurman Military Hospital, Omdurman Teaching Hospital and Bahri Teaching Hospital. The study was designed to evaluate the relation of long-term exposure of OR personnel to WAGs on reproductive health including fertility, miscarriage, premature birth and congenital anomalies of the offspring by comparison with the non-exposed group of health-care personnel working outside the OR in the same hospital.

Study population were randomly selected from OR personnel working in different departments i.e. General surgery, ENT, Ophthalmology, Obstetrics and Gynaecology, Orthopaedics and Dentistry. 99 personnel included different job grades; surgeons, anesthesiologists, assistants, technicians and OR nurses. 118 health-care personnel from the general wards including physicians, general practitioners, medical officers, technicians and nurses. They presented the non-exposed group. By matching age, sex and job grade; 136 were eligible for analysis. 68 exposed and 68 non-exposed to anesthetic gases. Only individuals working more than five years and married were included in the study.

Those who were single were excluded from the study whether they were not married, divorced or widowers. During the data collection there were 9 who refused to fill the questionnaire.

Data collection was conducted by a questionnaire in both Arabic and English languages (Appendix), filled personally. Confidentiality was taken into consideration. Data management and analysis was done by computer program SPSS version 5,11, and were presented as tables and figures, with reference p value of 0.05 as the level of significance. chi-square was used for categorical variables.

Chapter 4

Results

Cases selected from the OR were 68 from three different hospitals in Khartoum state; Omdurman Military Hospital (OMH), Omdurman Teaching Hospital (OTH) and Bahri Teaching Hospital (BTH), they were matched by age, sex and job grade, with 68 personnel chosen from the general medicine wards in each hospital (Table 4). The number of male personnel was 38 and 30 females (Table 5). The majority of personnel involved in the study were aged between thirty's and fifty's; 44.1% aged (41-50) and 30.9% aged (31-40) (Table 6). Different job grades included in the study are shown in Table 4.

Table 4: Percentage of cases and control in three hospitals in Khartoum state.

Hospital	Cases	Control	Percent
OMH	23	23	33.8
OTH	20	20	29.4
BTH	25	25	36.8
Total	68	68	100

Table 5: The males and females involved in the study.

Hospital	Cases	Control	Percent
Male	38	38	55.90%
Female	30	30	44.10%
Total	68	68	100%

Table 6: The age groups of individuals in the study.

Age	Cases	Control	Percent
<31	3	3	4.40%
31-40	21	21	30.90%
41 - 50	30	30	44.10%
51-60	14	14	20.60%

The incidence of individuals with no children in the group of OR personnel exposed to waste anesthetic gases was higher (7.35%) than in non-exposed personnel (1.47%) but not statistically significant; RR=5 (95% Confidence interval CI=0.6-41.7) as shown in table 5. When studying female health workers; 13.3% had no children which was statistically significant (p5.0.05) shown in Figure 1, relative risk was 0.87 (95% confidence interval 0.75 to 1.00). However, in male health workers, the incidence was the same (2.63%) in both exposed and non-exposed to WAGs shown in Figure 2.

When duration of working years was studied, 22.1% of personnel working for more than 15 years in the OR had no children which had a statistically significant difference with personnel working outside the OR for the same duration (W.05) Table 6. It is noticed in Figure 3 that female health workers not exposed to WAGs had more than six children (6.6%) while exposed females didn't. In male health workers the number of children was almost the same in both exposed and non-exposed personnel shown in Figure 4.

The OR nurses had the highest percentage of childlessness (9.7%) among the other OR personnel, while the surgical team had limited children of less than six (Figure 5).

Exposed personnel had similar numbers of male children as non-exposed personnel did, except that 10% of non-exposed workers had more than five boys while only 2% of exposed workers did (Figure 6). Female children in both groups were similar (Figure 7). In the health care workers, incidence of abortion was the same (39.7%) in both exposed and non-exposed to WAGs (Table 5). Percentage of abortion was slightly higher (36.8%) in males exposed to WAGs while it was 34.2% in non-exposed personnel (Figure 2). It was noticed that there was a significantly higher incidence of abortion (43.3%) in exposed workers who have been working for a duration of 5 to 15 years compared to 14.3% in non-exposed workers of the same duration, RR=2 (95% confidence interval 0.04 to 0.52) (Figure 8). When details of the cause of abortion were taken in consideration, the percent of individuals with unknown cause of abortion and weren't investigated was 92.6% in OR personnel, while 63% in non-exposed personnel. The incidence was 67.6 in exposed workers which was significantly higher than that in non-exposed 11.8%, RR=5.8 (95% confidence interval 0.12 to 0.25) (Table 7).

Incidence of preterm delivery in exposed personnel was 8.8%, while it was 13.23% in non-exposed personnel (Table 5). In the study the incidence of a congenital anomaly in the offspring was the same (1.47%) in exposed and non-exposed workers (Table 5). In Omdurman Military Hospital OMH, infertility seemed to be high in exposed personnel (13%) compared to personnel working in Omdurman Teaching Hospital OTH and Bahri Teaching Hospital BTH (Figure 9). Incidence of abortion in BTH among exposed workers was high (52%), the RR was 1.3 (95% confidence interval 0.32-0.72) (Table 8-11). However, in OTH the incidence of preterm delivery was high (20%) in exposed personnel, while it was less than 5% in both BTH and OMH (Figure 10). Incidence of congenital anomaly of the offspring was found to be 5% only in OTH, in both exposed and non-exposed personnel (Figure 9).

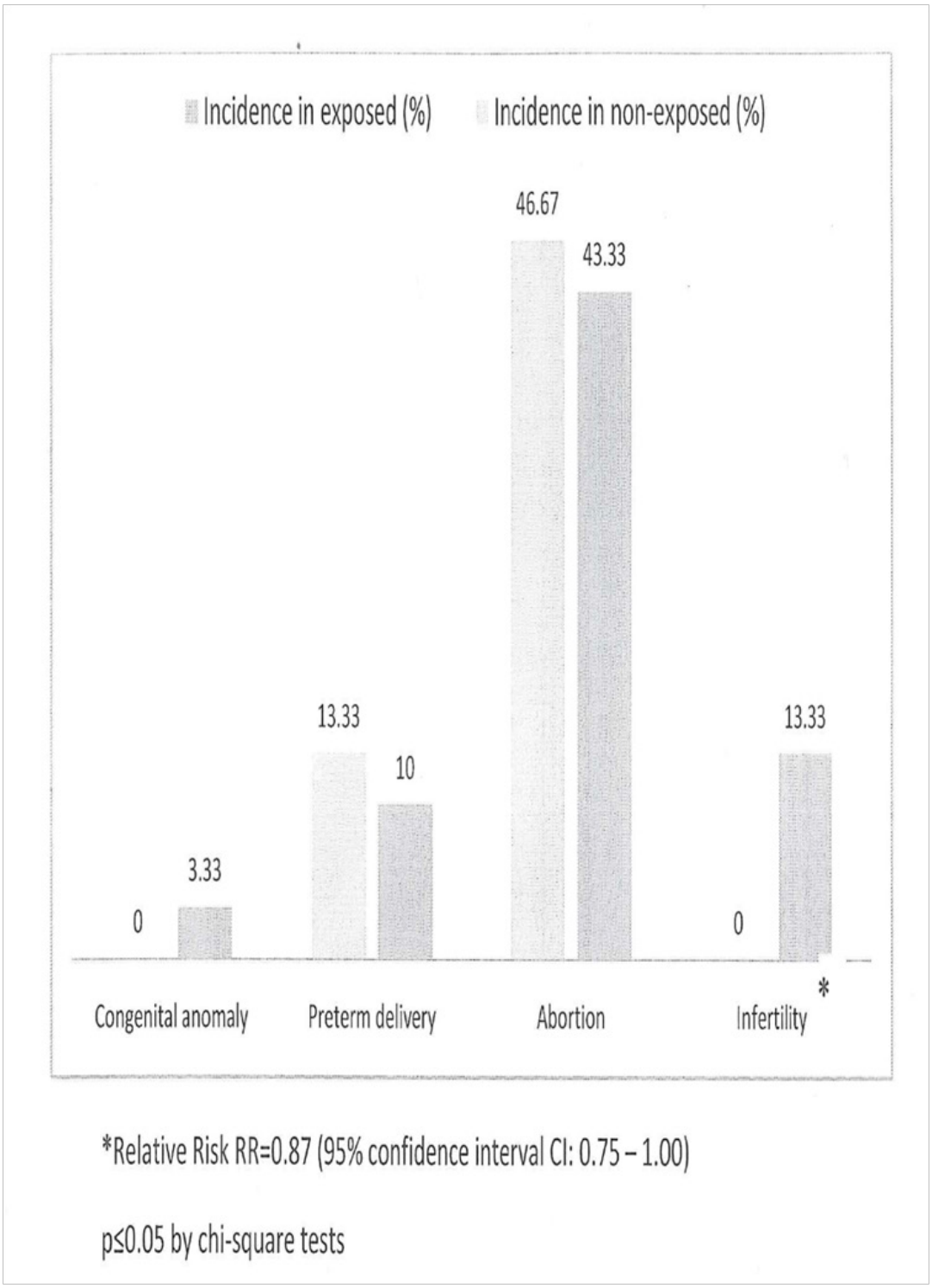


Figure 1: Comparison of incidence of each adverse reproductive health effect in female healthcare workers exposed and non-exposed to waste anesthetic gases.

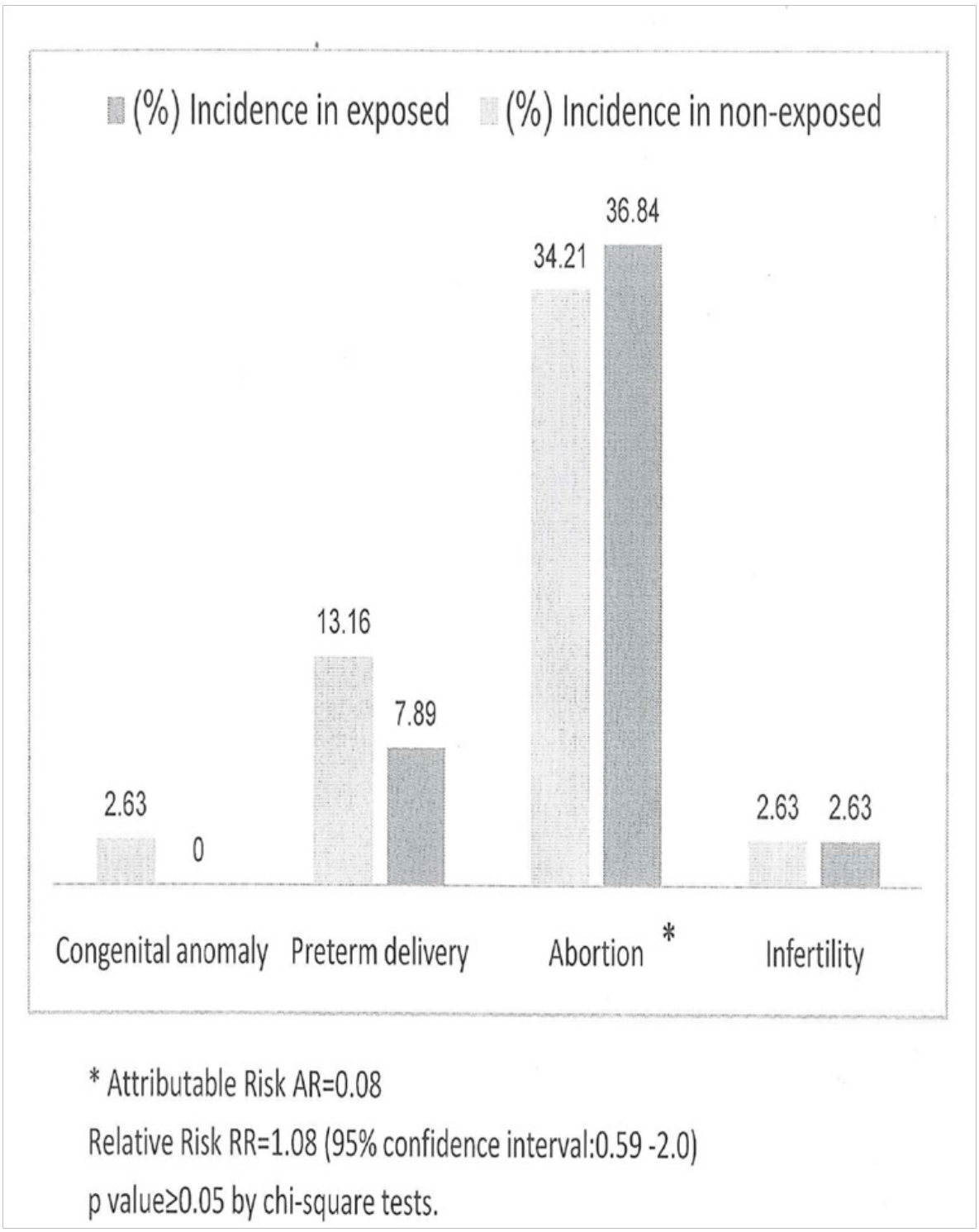


Figure 2: Incidence of adverse reproductive health effects on male health workers and non-exposed to waste anesthetic gases.

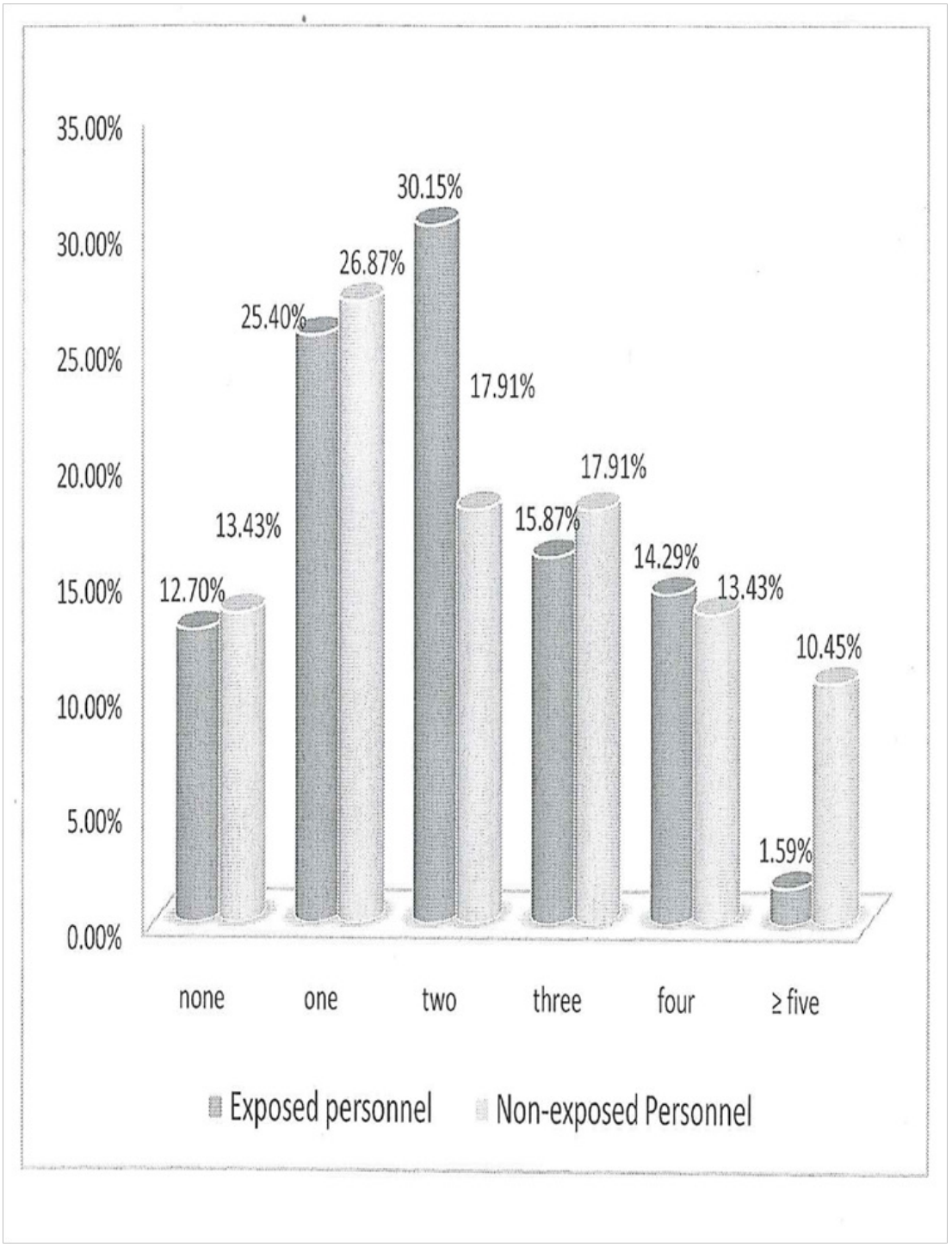


Figure 3: Comparison of male sex outcomes of personnel exposed and non-exposed to WAGs.

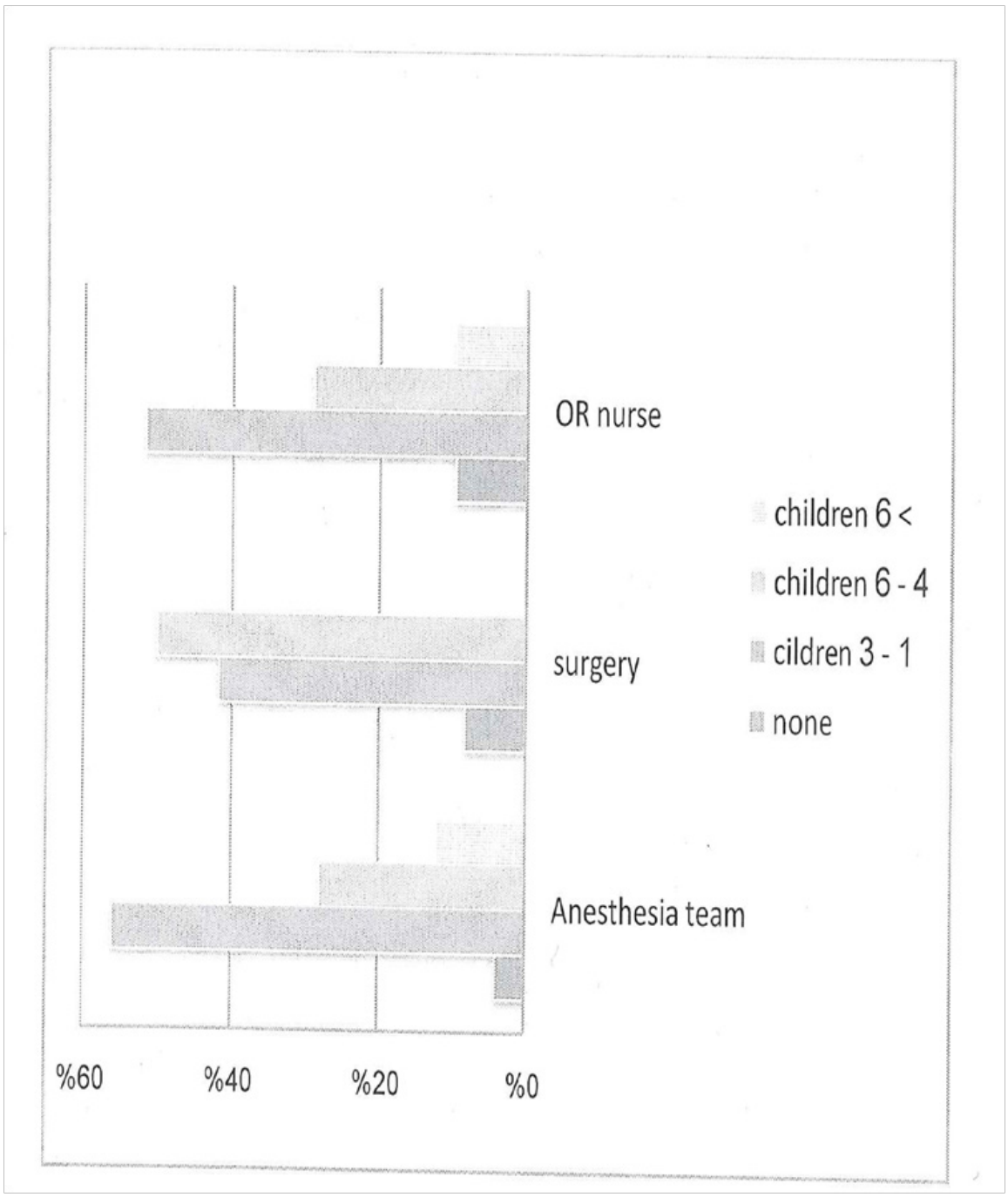


Figure 4: Percentage of children outcome of operating room personnel.

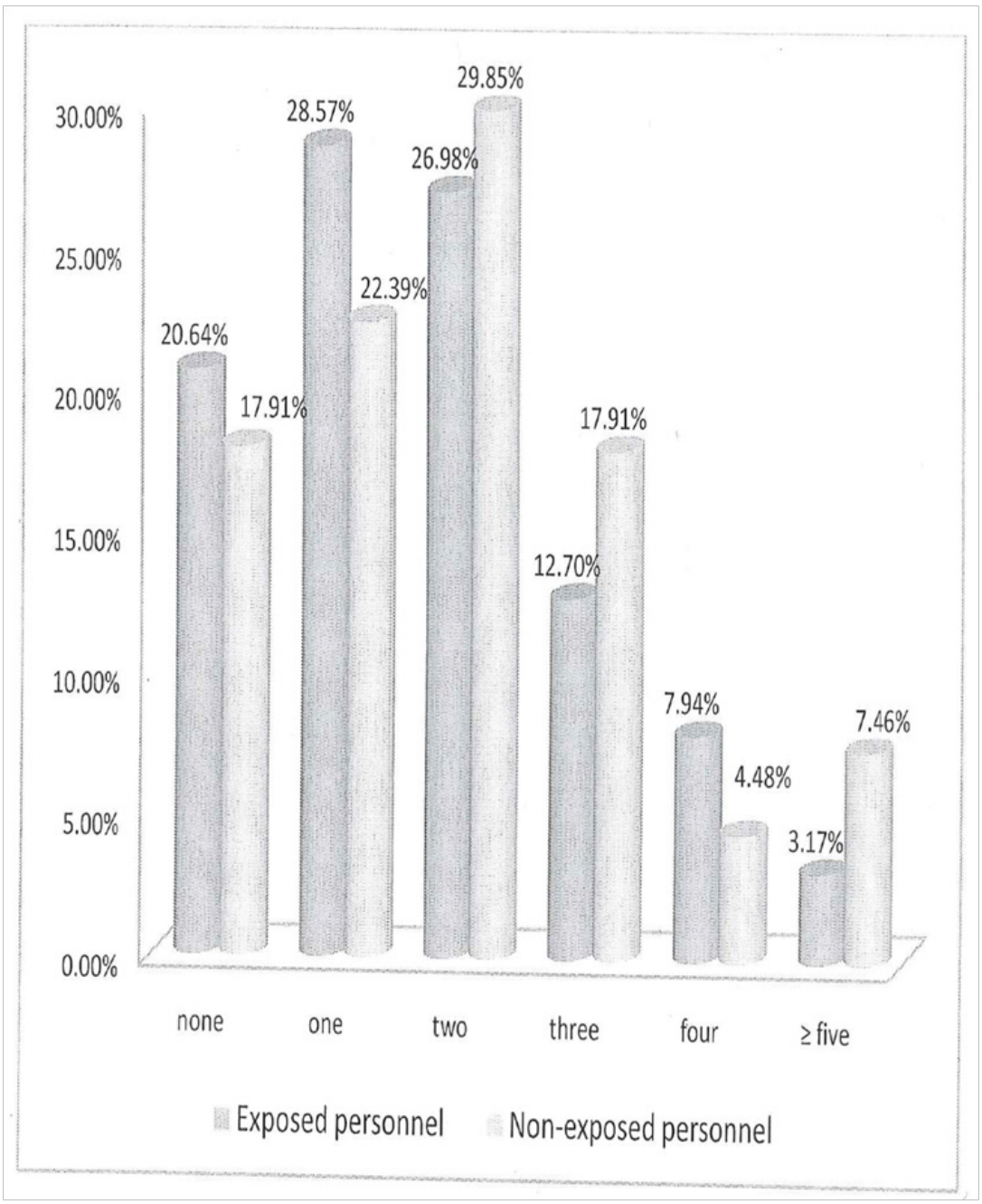


Figure 5: Comparison of female sex outcomes of personnel exposed and non-exposed to WAGs.

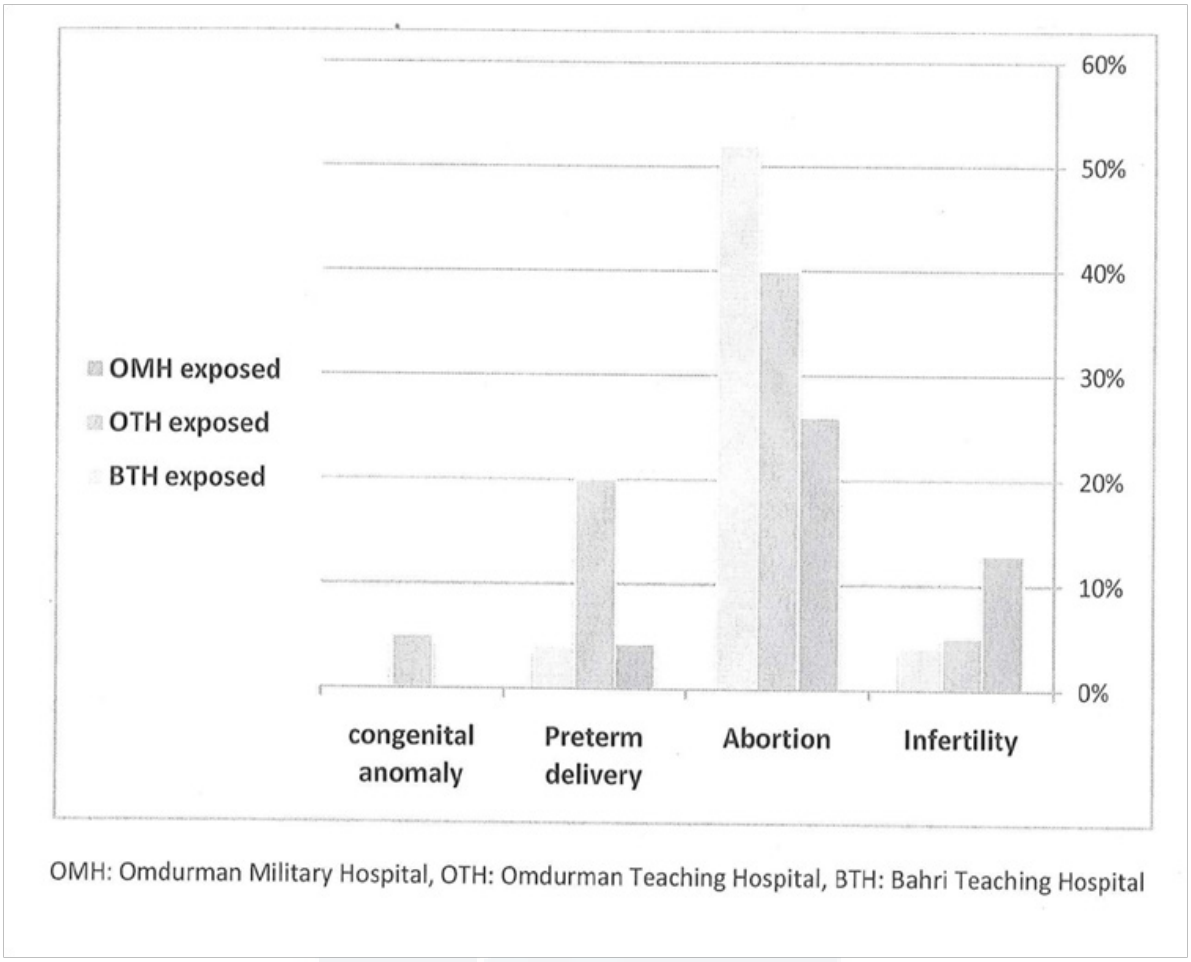


Figure 6: incidence of adverse reproductive effects in health-workers exposed and not exposed to WAGs in each of the three hospitals OMH, OTH and BTH in Khartoum state.

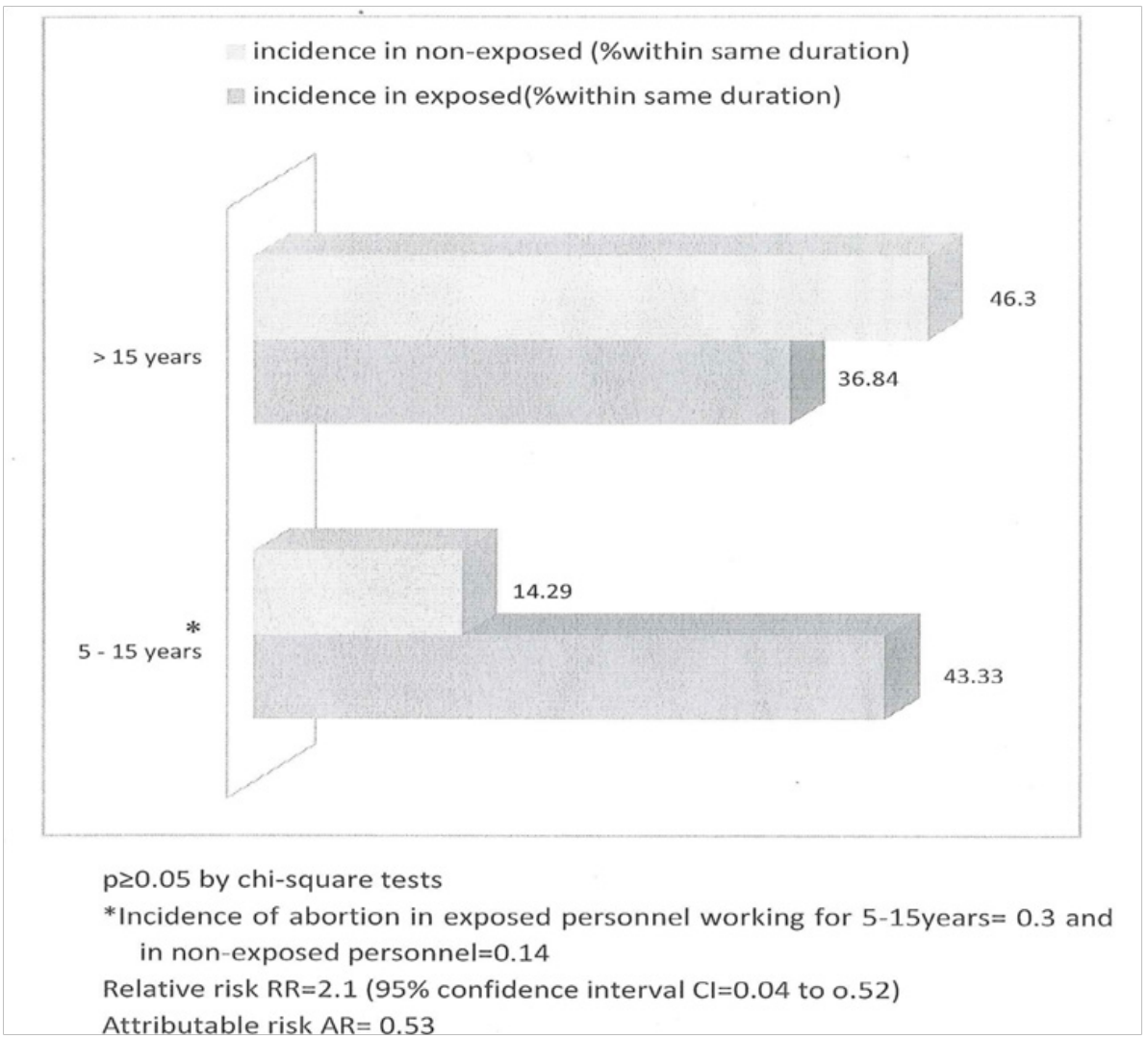


Figure 7: comparision of percentage of abortion in healthcare workers exposed and not exposed to WAGs according to duration of work.

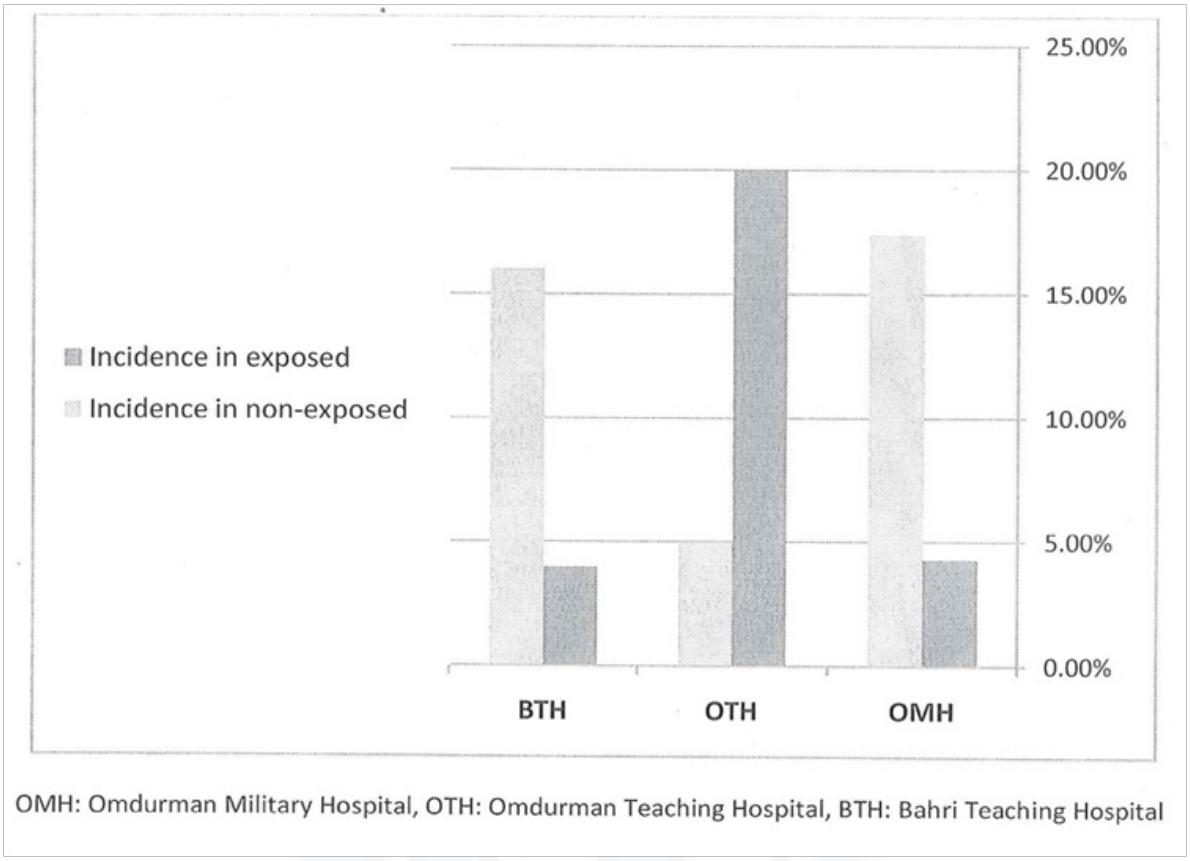


Figure 8: Incidence of preterm delivery in health personnel exposed and not exposed to WAGs in each of the three hospitals in Khartoum state.

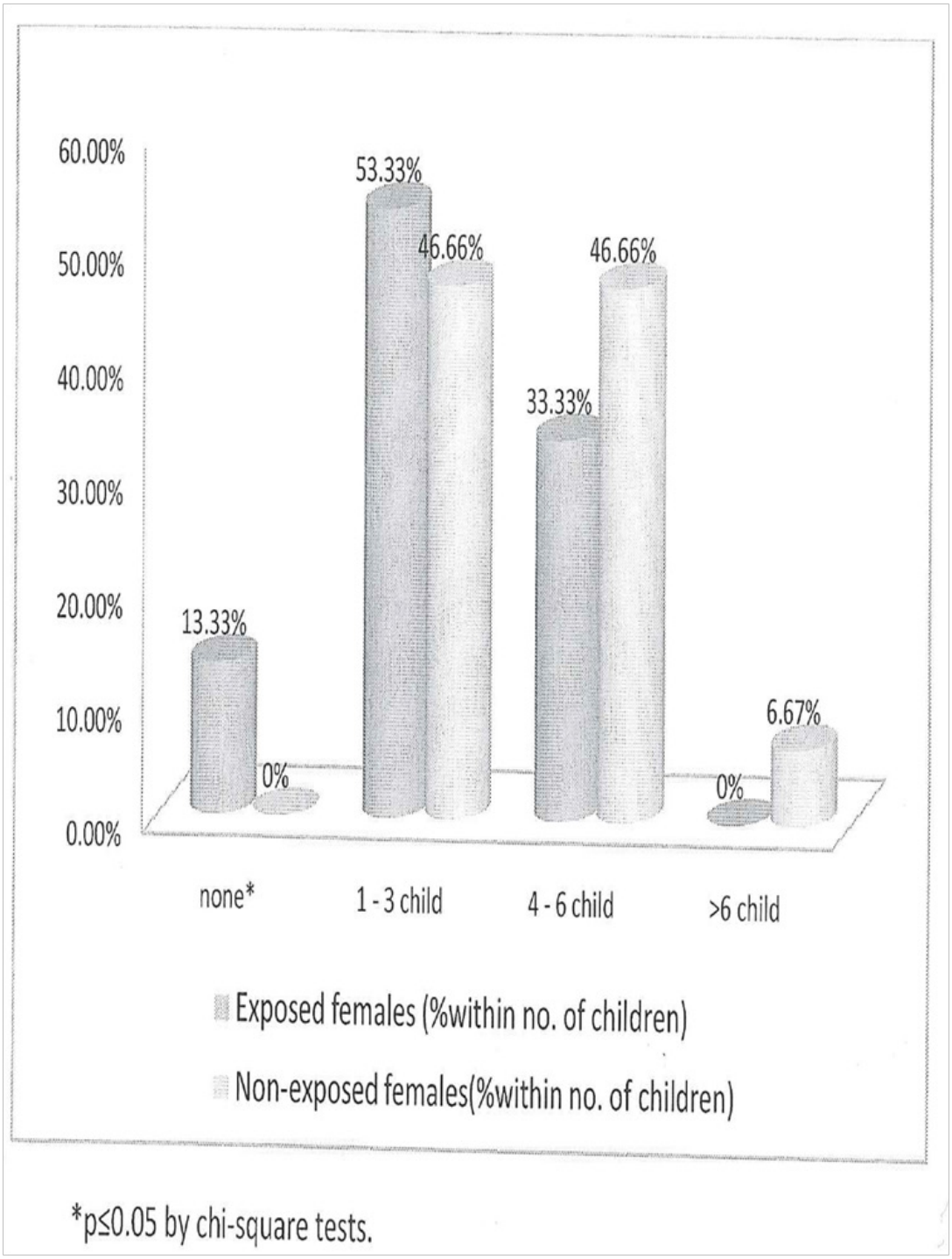


Figure 9: Comparison between number of outcomes female health workers exposed and non-exposed to WAGs.

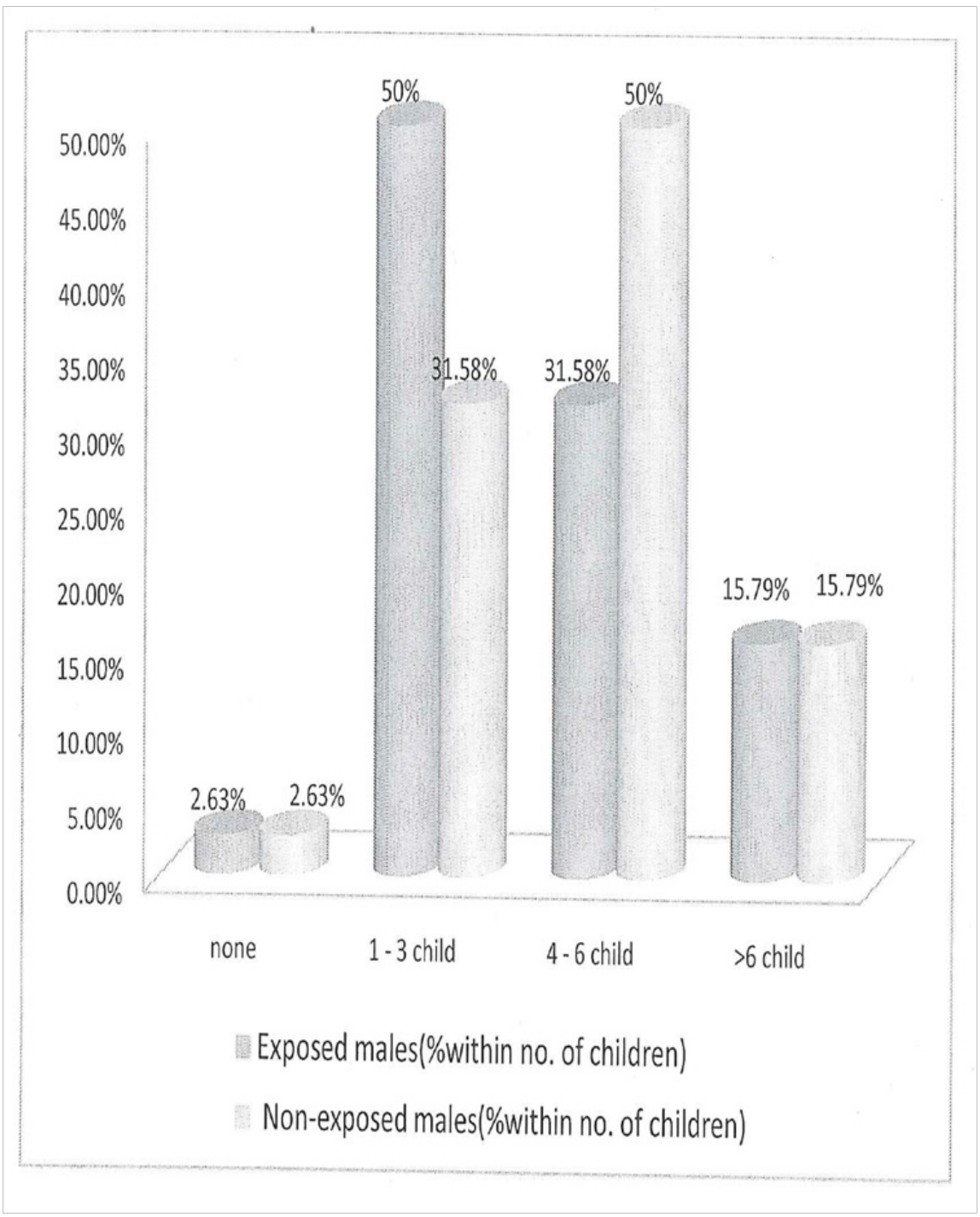


Figure 10: Comparison between number of outcomes male health workers exposed and non-exposed to WAGs.

Table 7: The different job groups involved in the study.

Job group	Frequency	Percent
Anesthesia	25	18.40%
Surgery	12	8.80%
OR nurse	31	22.80%
Medicine	13	9.60%
Technologists	15	11.00%
Ward nurse	40	29.40%
Total	136	100.00%

OR: Operating Room

Table 8: The incidence of negative reproductive effects in healthcare personnel exposed and non-exposed to WAGs in three hospitals in Khartoum State.

Reproductive Effect	Incidence in Exposed (% of Exposed)	Incidence in Non-Exposed (% of Exposed)	RR	AR	CI
Infertility	7.35%	1.47%	4.93	0.8	0.6-41.7
Abortion	39.71%	39.71%	1	*	0.66-1.51
Perterm delivery	8.82%	13.23%	0.67	-0.5	0.25-1.77
Congenital anomaly	1.47%	1.47%	1	*	0.96-1.04

RR: Relative Risk; AR: Attributable Risk; CI: Confidence interval, 95%.

* cannot be calculated

Table 9: Percentage of childless personnel according to duration of years they have been working.

	Exposed Personnel		Non-Exposed Personnel	
Working Years	Frequency	Percentage	Frequency	Percentage
5-10 years	1	4.30%	1	7.70%
11-15 years	1	14.30%	0	0%
16-20 years	2	15.40%	0	0%
≥20 years	1	4%	0	0%
Total	5	7.40%	1	7.70%

p value = 0.002 by chi-square tests

Table 10: Comparison between causes of abortion in female and male health workers exposed and non-exposed to waste anesthetic gases.

Abortion	Exposed	Non-Exposed
cause unknown and not investigated*	92.60%	62.96%
Obstetrical	3.70%	18.52%
Non-obstetrical	3.70%	18.52%
Total % within total abortions	100.00%	100.00%

*Incidence of abortion in exposed 67.57 and 11.76 in non-exposed Relative Risk RR=5.75 (95% confidence interval 0.12 to 0.25) Attributable Risk AR=o.83.

Table 11: Incidence of abortion in each of the three hospitals in Khartoum State.

Hospital	Incidence in Exposed	Incidence in Non-Exposed	RR	CI
OMH	26.09%	47.83%	0.55	0.03-0.23
OTH	40.00%	30.00%	1.33	0.08-0.32
BTH	52.00%	40.00%	1.3	0.32- 0.72

OMH: Omdurman Military Hospital, OTH: Omdurman Teaching Hospital, BTH: Bahri Teaching Hospital; RR: Relative Risk; CI: 95%, Confidence Interval.

Chapter 5

Discussion

Research on the effects of WAG exposure started appearing in the literature in 1967, as Smith has concluded that the reproductive effect of long-term exposure was infertility, spontaneous abortion, premature birth and congenital abnormalities [29]. Infertility or childlessness is the inability of a couple to obtain a clinically recognizable pregnancy after twelve months of unprotected intercourse [30]. "The WHO has stated the global prevalence rates of infertility are difficult to determine due to presence of both male and female factors which complicates any estimate [31]. A study found the prevalence rate of infertility in France was 14.1% [32]. An international study showed a 9% prevalence rate of infertility [33].

Starek et al. [34] found from epidemiological studies that nitrous oxide exerts multiple deleterious effects on human organisms especially fertility and pregnancy [34]. In this study, there was a high risk of having no children in the personnel exposed to waste anesthetic gases compared to the non exposed, it was statistically insignificant, relative risk was 5 (95% confidence interval 0.6 to 41.7), this insignificance could have been due to studying both sexes. When studying only female workers who had no children, there was significant difference in exposed and non-exposed groups (p50.05 iy chi-square tests). A study on female dental assistants showed a significant relationship between high exposures to nitrous oxide and a decrease in fertility [1,2].

In this study, personnel working for more than 15 years in the OR, 22.1% had no children, which was significantly higher than non-exposed personnel 7.7% (p=0.002) suggesting that chronic exposure had an effect on fertility. In addition, long-term exposure may cause subfertility; in the study, it was noticed that no female worker had more than six children, while 53.3% had up to three kids, and only 33% had four to six kids. When comparing this to the non-exposed female workers, they all had children, the number of children was the same (47%) and 7% had more than six kids.

This study showed no significant difference between the sexes of the offspring, in both exposed and non-exposed health-care personnel. Spontaneous miscarriage is the termination of pregnancy before the 24th week of pregnancy and accounts for up to 20% of all pregnancies. (35P277). Boivin [22] had concluded from his meta-analysis the increased risk of spontaneous abortion in non-scavenged theatres. In this study, the incidence of abortion was the same in exposed and non-exposed personnel (40%), which is double the incidence in the general population. But exposed personnel in the first ten years of exposure (age of reproduction) had a significantly higher incidence of abortion than non-exposed personnel, the relative risk was 2 (95% confidence interval 0.04 to 0.52). Askrog et al. [24] found that frequency of abortion was significantly higher during employment than before, for both females and wives of anesthesiologists. Vaisman also noted that anesthesiologists with abnormal pregnancies had exposures of 25 hours per week while those with normal pregnancies did not exceed 15 hours per week [23]. Shirangi et al. [36] showed a significant increased risk of abortion in Australian women exposed to unscavenged gases for >1 hour a week [36].

When known causes of spontaneous abortion in this study was excluded, there was a significantly high risk of spontaneous abortion in exposed personnel to WAGs; relative risk was 5.8 (95% confidence interval=0.12 to 0.25). The incidence was approximately 68% in exposed personnel while 12% in non exposed workers. When comparing to the general population, the incidence is three times higher. Premature birth is delivery before completion of the 3 6 t h week of gestation, it occurs in about 6% of pregnancies. (35° 71). In Shirangi's study, he found that long working hours and in unscavenged eras were important risk factors for preterm birth in female veterinarians [37]. But in this study, incidence of preterm birth was higher in the non-exposed group 13% than the exposed group 9%, and overall they were both higher than the general population, possibly due to the stressful nature of work they are all exposed to while providing health care.

The incidence of congenital abnormalities has been estimated at 25-30/1000 births and this figure has remained relatively constant in England since 1920. (3513129). A Canadian study on female veterinary staff exposed to inhaled anesthetics and radiation did not seem to be at increased risk for major malformations above baseline risk [38]. This study showed the same incidence of congenital abnormalities in both exposed and non-exposed personnel to WAGs (1.5%), but greatly higher than the general population, showing the great risk health care providers are exposed to. In each hospital in the study, risks of each reproductive effect was different, which may be due to the different direct environment; the levels and types of anesthetic gases the personnel are exposed to, as well as length of exposure and room ventilation in relation to room sizes. Unfortunately, all ORs are not equipped with scavenging systems and depend mainly on ventilation for reducing WAGs. NIOSH suggests that operation theatre team are at risk of anesthesia exposure even when operating theatre are provided with scavenging equipment, this matched Khalil et al. [39] findings. Hazard of anesthetic gas inhalation was reduced by 90% after installing efficient ventilation system and scavenging equipments with proper maintenance [39]. In poorly ventilated rooms, exposure of health personnel may exceed recommended levels [40]. Exposure to WAGs has not been shown to cause adverse health effects to personnel working in operating rooms in which scavenger systems are being used [28].

Chapter 6

Conclusion and Recommendations

Conclusion

There is a reproductive health risk from exposure to WAGs. Long duration of exposure to anesthetic gases, more than 15 years, have greater risks of infertility than non-exposed personnel. Female health care workers exposed to anesthetic gases have a high risk of infertility than non-exposed females, as well as a degree of subfertility. Incidence of abortion in health care personnel is two-fold higher than the general population. Risk of spontaneous abortion in the reproductive period of work; i.e.; the first ten years, is high in exposed personnel to WAGs. There is a great risk for abortion due to unknown cause in exposed individuals to WAGs. Incidence of preterm delivery and congenital anomalies is the same in both exposed and non-exposed personnel while higher than in the general population.

Recommendations

Limit exposure of OR personnel to WAGs by continuous training and maintaining good work practices and regular anesthetic machine checking for leaks. Special consideration for female workers by limiting exposure when planning to conceive and during pregnancy, especially in the first trimester. Adequate hazard control can be achieved by equipping theatre rooms with effective ventilation and scavenging systems. Developing a control program for gas monitoring and exposure limits. More studies on this topic are needed with gas level measurement.

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