Predictors of difficult intubation in obstetric cohort of patients: an analysis of the prospective obstetric airway management registry (OBAMR) (substudy – R025/2018)

by

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SUBMITTED TO THE UNIVERSITY OF CAPE TOWN

In fulfilment of the requirements for the degree:

Master of Medicine in Anaesthesiology

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

Date of Submission: 22 February 2021

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DECLARATION

I, *Dr Adrian Burger*, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Date: 22 February 2021

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Acknowledgements

Professor Robert Dyer, without your unwavering support, guidance and encouragement this work would not have been possible.

Prof Ross Hofmeyr – you know that your never say die attitude, your boundless energy and positivity rubbed off on me – and here we are at last.

Professor Justiaan Swanevelder for your tireless enthusiasm and encouragement to help bring this project to fruition.

Prof Bruce Biccard for your immense work and unending patience with me and this dissertation. The statistics and results would not have been as clear to me were it not for you.

Dr Maretha Smit, who blazed the trail in setting up and validating this important database.

The registrars and medical officers of the maternity theatres of Mowbray Maternity, New Somerset and Groote Schuur Hospitals for supporting the OBAMR Registry and diligently completing the required data capturing.

Linda, my wife, and my family without whom none of this would have even seemed possible. I told you so.

Chapter 1: Review of the Literature

Factors contributing to difficult tracheal intubation in obstetric anaesthesia

1. Objectives

The airway of the pregnant patient presents unique challenges with regards to pre-anaesthetic assessment, as well as safe, expeditious and definitive management, which includes prevention of pulmonary aspiration, during the induction of general anaesthesia. Airway difficulty has been reported to be eight times more common in obstetric patients compared to the general surgical population[1,2] , with the incidence of difficult or failed tracheal intubation remaining at 2.6 (95% CI 2.0 to 3.2) per 1000 anaesthetics (1 in 390) for obstetric general anaesthesia[2]. Front of neck procedures for access to the airway is required in 3.4 (95% CI 0.7 to 9.9) per 100 000 general anaesthetics for caesarean delivery, which amounts to one procedure per 60 failed intubations. Maternal mortality from failed intubation is 2.3 (95% CI 0.3 to 8.2) per 100 000 of all general anaesthetics for caesarean delivery (one death per 90 failed intubations[2]), and occurs from aspiration or hypoxaemia secondary to airway obstruction or oesophageal intubation[2,3].

The establishment of safe regional anaesthesia for labour and caesarean delivery is one of the most important developments in the last 20 years in obstetric anaesthesia. Neuraxial anaesthesia offers the advantage of avoidance of airway management[4]. There remain, however, certain selected maternal conditions such as haemorrhage, hypovolaemia, severe valvular stenosis, cardiomyopathy, and pre-eclampsia with systolic hypofunction, which require general anaesthesia. In addition, there may be circumstances involving severe fetal compromise, including fetal bradycardia, such as abruptio placentae and cord prolapse, which still necessitate urgent general anaesthesia. In these patients, the risk of difficulty in establishing an airway, and concomitant maternal and fetal morbidity and mortality are significant.

2. Literature Search Strategy

All publications relevant to the subject were obtained online, from the University of Cape Town Health Sciences Library search facility. For the purposes of this narrative review, a search was performed in October 2020, using the Pubmed database, using combinations of the terms “caesarean”, “obstetric anaesthesia”, “airway management”, “difficult airway”, and “failed intubation”. Fifty-three relevant papers were identified. In addition, the bibliographies of the papers generated by the above search were analysed for further relevant articles. The search was restricted to adult patients ≥ 18 years of age. Literature not published in the English language was excluded.

3. Summary of the Literature

a. Physiological changes contributing to difficult intubation in obstetrics

Most airway catastrophes occur when airway difficulty is not anticipated prior to induction of anaesthesia[5]. Timely evaluation of the parturient's airway and adequate preparation to deal with potential complications are helpful in avoiding airway disasters[6]. Maternal, fetal, surgical and situational factors contribute to the increased incidence of failed intubation. Many physiological changes occur during pregnancy, including physical characteristics such as increased body mass index (BMI), breast enlargement, and generalised oedema[1,3]. The mucosa of the upper respiratory tract also becomes more vascular and oedematous, leading to increased risk of airway bleeding and swelling[7]. Fluid retention in head and neck tissues during pregnancy, particularly in preeclampsia, potentially narrows the upper airway and reduces compliance, making laryngoscopy more difficult[1]. The term parturient is also more susceptible to gastro-oesophageal reflux, due both to progesterone-mediated effects and anatomical changes due to the gravid uterus[6].

b. Bed side and other tests which may predict difficult intubation in Obstetrics

In an insightful editorial in 2002, Yentis points out the difficulties in establishing relevant cut-off scores for tests predicting difficult intubation, in terms of sensitivity, specificity, and positive predictive value, when the event under consideration is rare[8]. Nevertheless, he concedes that there is value in focussing on potential predictors, provided the anaesthetist understands the limitations of the tests.

There are a few simple preoperative bedside clinical tests that can be performed to evaluate the airway, including the Mallampati score, mouth opening (inter-incisor gap), thyromental distance, neck mobility (atlanto-occipital extension), and ability to protrude the mandible[5,7,9]. Further tests and measurements that have been analysed include the measurement of neck circumference[10], the ratio of neck circumference to thyromental distance[11], the ratio of patient height to thyromental distance[12], and a new screening test, the acromio-axillo-suprasternal notch index[13], but these have limited predictive value, are not often applied in in routine clinical practice.

The relationship between increased airway classification scores and relative ease or difficulty of intubation in pregnant patients undergoing caesarean delivery during general anaesthesia has been studied by Rocke *et al,* who studied 1500 pregnant women who had emergency or elective caesarean delivery under general anaesthesia[14]. A strong correlation was found between the difficulty in identifying oropharyngeal structures and difficulty with tracheal intubation. The authors found that the relative risk of encountering difficult intubation in a gravid parturient with a Mallampati class 3 airway was 7.6 times higher than in a parturient with a Mallampati class 1 airway. This relative risk increased to 11.3 in pregnant patients with a Mallampati class 4 airway[14]. Using a combination of risk factors, they showed that the presence of a class 3 or 4 airway together with protruding maxillar incisors, a short neck, and a receding mandible, increased the probability of difficult laryngoscopy to >90%.

Pilkington et al demonstrated that airway oedema may increase during the course of pregnancy and result in an increased Mallampati score[15]. Kodali et al observed airway changes during labour and delivery[16]. There was a significant increase in airway class from the pre-labour period to after labour. The airway increased by one grade in 20/61 patients (33%), and by 2 grades in 3 women (5%). At the end of labour there were 8 patients with a class 4-, and 30 women with a class 3 or 4 airway ($p < 0.001$). Oral volume and pharyngeal area and volume also decreased significantly after labour. In a further case-control study, changes in Mallampati grade were compared in healthy women and those with preeclampsia. In addition, sonographic measurements were made of tongue thickness, anterior neck soft tissue, thyromental distance and neck circumference. Mallampati score was found to increase from the pre-labour period in both groups. In addition, there was a significant between group difference in tissue thickness at the hyoid level before and after labour and postpartum ($p = 0.035$, 0.05, and 0.05 respectively[17]. Various difficult airway algorithms exist as memory and training aids to mitigate this risk once a difficult airway is encountered[18,19].

In a recent study which focussed on patients who had an anticipated difficult airway in obstetric general anaesthesia, previous difficulty with airway management was noted in 14/158 patients[19]. However, unfortunately such records are often unavailable. An airway assessment was only reported in 102/158 cases. The Mallampati grade was given in 82 of these women, of whom 7 had were grade 1, 17 grade 2, 33 grade 3, and 30 grade 4. All of the women with grade 1 and 2 airways had other predictors of difficulty. Other features or tests were neck movement in 75 cases, mouth opening in 68, thyromental distance in 36, and jaw protrusion or micrognathia in 24 patients. In one patient the neck was assessed for front of neck access, and in 2 cases there was obstructive sleep apnoea. No studies described the use of a combined score. In the presence of specific airway pathology, respiratory investigations were performed, including CT imaging. In 15/158 patients awake laryngoscopy or nasal endoscopy was performed to guide the choice of anaesthesia technique. Fifty two women required awake intubation using flexible bronchoscopy, of whom 3 had this procedure after an initial poor direct laryngoscopic view, and 5 after failed regional anaesthesia. Most of the women had congenital abnormalities, but other indications were morbid obesity, goitre, mediastinal mass, HELLP syndrome, a swollen tongue in a woman with eclampsia, and reduced mouth opening.

c. Hypoxaemia as a composite indicator of anatomical and physiological difficulty during intubation

Historically, studies assessing difficulty of intubation in obstetrics have focussed primarily on the physical and anatomical challenges associated with insertion of an endotracheal tube. However, there is increasing recognition of the concept of a physiologically or pathophysiologically difficult airway (when patients rapidly become hypoxaemic during airway management), which uses hypoxaemia as a composite indicator of both anatomical and physiological difficulty. There are a limited number of studies in the literature exploring this concept. Smit et al compared the prevalence and risk factors for hypoxaemia ($SpO_2 < 90\%$) during induction of general anaesthesia in parturients with and without hypertensive disorders of pregnancy[20]. They hypothesised that hypertensive disorders of pregnancy are associated with desaturation during tracheal intubation. In a cohort of

402 cases, hypoxaemia occurred in 19% with and 9% without hypertension (estimated risk difference, 10%; 95% CI 2% to 17%; $p = 0.005$). Quantile regression demonstrated a lower SpO_2 nadir associated with hypertensive disorders of pregnancy as body mass index increased. Room-air oxygen saturation, Mallampati grade, and number of intubation attempts were associated with the relationship. In a multicentre study, Bonnet et al[21] studied the incidence and risk factors for maternal hypoxaemia during tracheal intubation for non-elective caesarean delivery. Hypoxaemia occurred in 172/895 women (19%, 95% CI 17 to 22%). Multivariate analysis showed that risk factors associated with hypoxaemia were difficult or failed intubation (adjusted odds ratio [aOR] 19.1 [8.6-42.7], $p < 0.0001$), and BMI> 35 kg/m^2, (aOR = 0.53 [0.28 to 0.998], $p = 0.0495$). Intubation was found to be difficult in 40 patients (4.5%, 95% CI 3.3 to 6%), and 5 women had failed intubation (0.56%, 95% CI 0.1 to 1%). Propofol was found to associated with a significantly lower risk of failed intubation. In a further recent publication from South Africa, the authors performed a prospective, observational, dual-centre cohort study, aiming to establish the incidence of hypoxaemia, defined as SpO2 < 90%, during induction of general anaesthesia for caesarean delivery[27]. Factors investigated as potential predictors of hypoxaemia were body mass index, the level of experience of the operator, predicted difficult airway, Cormack-Lehane grading, and the absence of planned mask ventilation. They also reported on complications related to tracheal intubation. The incidence of hypoxaemia was found to be 61/363 (16.8%, 95% CI 13.29 to 21.02). BMI > 30 kg/m^2 and Cormack-Lehane grade 4 predicted hypoxaemia. The failed intubation rate was 1.4% (95% CI 0.57 to 3.28), and the regurgitation rate 0.8% (95% CI 0.27 to 2.54). No patients experienced pulmonary aspiration or required surgical intervention to secure the airway.

d. The role of an airway management registry in improving safety of tracheal intubation in obstetric anaesthesia

The Obstetric Airway Management Registry (ObAMR), recently validated by Smit et al[53], was established at the University of Cape Town in 2018, with a view to collecting data on every tracheal intubation in Obstetrics, with the purpose of improving the safety of the procedure. The aim of the present retrospective analysis of the data from >1000 patients from this registry, is to identify certain routine and common clinical pre-induction measurements, tests and risk factors that might help to predict a difficult airway in our Obstetric Anaesthesia practice, allowing time for the anaesthetist to prepare adequately, and thereby reduce morbidity and mortality. In this study, hypoxaemia will be used as the composite indicator of difficult intubation. Using this concept, a predictive tool could be developed to aid in the identification of a difficult airway in obstetrics. This could also guide the choice of anaesthesia for urgent caesarean delivery in women with anticipated difficult tracheal intubation, including the use of simple decision analysis[5].

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Chapter 2: Manuscript

Title Page

Predictors of difficult intubation in obstetric cohort of patients: an analysis of the prospective obstetric airway management registry (OBAMR) (substudy – R025/2018)

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Conflicts of interest:

The authors have no conflicts of interest to declare.

Number of words in Abstract: 381

Number of words in Introduction: 454

Number of words in Discussion: 2046

Abbreviated Title (running head): Predictors of difficult obstetric airway

Abstract

Background: Hypoxaemia during tracheal intubation in obstetrics remains a life-threatening complication. This study aimed to identify common clinical pre-induction predictors of difficult intubation.

Methods: A retrospective analysis was performed of data pertaining to tracheal intubation in patients requiring general anaesthesia for caesarean delivery, with a gestational age from 20 weeks, and until 7 days post-delivery, obtained from an obstetric airway management registry (ObAMR) at the University of Cape Town. Data was entered anonymously into a secure UCT REDCap database. Data categories were: patient and pregnancy characteristics, airway characteristics, details of management, and operator experience. The primary aim of the study was to identify anatomical and physiological risk factors for hypoxaemia. The primary outcome was defined as arterial desaturation to <90% during obstetric airway management. For this purpose, multivariable binary logistic regression was performed. Hypoxaemia was thus used as a composite indicator of anatomical and physiological difficulty.

Results: Data was collected for 1095 general anaesthetics in the ObAMR. Overall, 143/1091 of patients (13.1%, 95%CI 11.1 to 15.4%) experienced peripheral oxygen saturation below 90%. Univariate analysis showed that 91/142 (64.1%) of patients who desaturated were obese (body mass index [BMI] >30 kg/m^2), compared with 347/915 (37.9%) who were obese and did not experience desaturation (p <.001). A receiver operating curve (ROC) was constructed *post hoc*, which showed a cut-point for BMI of 29.76, and a sensitivity of 0.66, and specificity 0.62 for the prediction of hypoxaemia. Desaturation occurred in 17.0% of patients with hypertensive disorders of pregnancy, versus 11.0 % without (p=0.005). Increasing Mallampati class was associated with an increased incidence of hypoxaemia. The incidence of hypoxaemia was 25.8% for interns, compared with 8.0 % for consultant anaesthesiologists (p=0.005). In the multivariate analysis of factors associated with hypoxaemia, body mass index (p<0.001), room air saturation prior to preoxygenation (p=0.008), and the presence of airway oedema (p=0.027), were independently associated with hypoxaemia.

Conclusions: In this study, both anatomical and physiological predictors of hypoxaemia were identified. Using this concept, a predictive tool could be developed to aid in the identification of a difficult airway in obstetrics. Simple interventions such as face mask ventilation and the use of high flow nasal oxygenation, could be introduced to protect the parturient from the consequences of life-threatening hypoxaemia.

Keywords: caesarean delivery, general anaesthesia, hypoxaemia, obstetric anaesthesia, airway management

Introduction

The airway of the pregnant patient presents unique challenges as regards pre-anaesthetic assessment, as well as safe, expeditious and definitive management. This includes prevention of hypoxaemia and/or pulmonary aspiration during the induction of general anaesthesia. Airway difficulty has been reported to be eight times more common in obstetrics patients compared to the general surgical population[1,2], with the incidence of difficult or failed tracheal intubation remaining at 2.6 per 1000 anaesthetics (95% CI 2.0 to 3.2; 1 in 390) for obstetric general anaesthesia[2]. Maternal mortality from failed intubation is 2.3 per 100 000 (95% CI 0.3 to 8.2) of all general anaesthetics for caesarean delivery (one death per 90 failed intubations)[2], and occurs from hypoxaemia secondary to airway obstruction or oesophageal intubation, and/or pulmonary aspiration[2,3]. This has resulted in a significant reduction in the use of general anaesthesia for caesarean delivery, and a corresponding increased application of neuraxial techniques, thus avoiding airway management by the anaesthesiologist in a large proportion of patients.

There remain, however, certain selected maternal conditions such as significant haemorrhage, hypovolaemia, severe valvular stenosis, cardiomyopathy, and preeclampsia with systolic hypofunction, which require general anaesthesia. In addition, there may be circumstances involving severe fetal compromise (including fetal bradycardia) such as abruptio placentae and cord prolapse, which still necessitate rapid surgery most swiftly facilitated by urgent general anaesthesia. In these patients, the risk of difficulty in establishing an airway (with concomitant maternal and fetal morbidity and mortality) are significant. Various difficult airway algorithms exist as memory and training aids to mitigate this difficulty once a challenging airway is encountered[3,4].

In 2018, the Department of Anaesthesia and Perioperative Medicine of the University of Cape Town (UCT) established an obstetric airway management registry (ObAMR), in order to improve clinical governance and monitor and assess airway management during general anaesthesia in this critically vulnerable group of patients. At all obstetrics facilities under auspices of the Department, standard clinical airway assessment and measurements forms an integral part of the pre-anaesthetic examination, whether a neuraxial or general anaesthetic technique is employed. These are validated tools in the non-obstetric population, but their performance has not been formally assessed in our parturient population. The aim of this retrospective analysis of registry data is to identify certain common, clinical pre-induction predictors of a difficult airway, allowing time for the anaesthesiologist to prepare adequately, and thereby reduce morbidity and mortality. Historically, studies assessing difficulty of intubation in obstetrics have focussed primarily on the physical and anatomical challenges associated with insertion of an endotracheal tube. However, increasing recognition of the concept of a physiologically difficult airway (when patients rapidly become hypoxaemic during airway management), prompted the present analysis, which uses hypoxaemia as a composite indicator of both anatomical and physiological difficulty during intubation.

Methods

This study was a retrospective observational study of data pertaining to tracheal intubation, obtained from the ObAMR. The registry was approved by the Human Research Ethics Committee of the Faculty of Health Sciences of UCT (HREC R025/2018). Data is collected at all sites performing obstetric anaesthesia under the supervision of the UCT Department of Anaesthesia and Perioperative Medicine, namely Groote Schuur Hospital (Maternity Centre), New Somerset Hospital and Mowbray Maternity Hospital, in Cape Town, South Africa. The registry contains data from all pregnant patients requiring general anaesthesia for caesarean delivery, with a gestational age from 20 weeks until 7 days after delivery, undergoing both elective and emergency surgery. Data is entered by the anaesthesiologist involved in the particular case into a secure UCT REDCap (Research Electronic Data Capture) database. Clinicians obtain simple verbal consent from patients prior to the induction of anaesthesia, as approved by the HREC when establishing the registry. They are then able to enter the de-linked anonymous patient data via their mobile devices using a designated uniform resource locator (URL) or quick reaction (QR) code displayed in the obstetric theatres. All data collected for the study purposes had been documented as part of the routine anaesthesia management. Anonymity is maintained, since access to the entire database is restricted to the investigators, and password protected. The registry has been validated and the findings published[1].

For this study we conducted a retrospective analysis of this registry, extracting data recorded from 1095 obstetric general anaesthetics during the period 2018 – 2020, into an Excel spreadsheet. The details of the recorded data were as follows:

1 Patient and pregnancy characteristics (age, height, weight, body mass index [BMI], gestational age, hypertensive disorders of pregnancy, indication for general anaesthesia).
2 Airway characteristics (Mallampati score, thyromental distance, mouth opening, mandibular protrusion).
3 Details of management (number of attempts at tracheal intubation, use of bougie, video laryngoscope used).
4 Operator experience (level of qualification, years of experience).
The primary aim of the study was to identify anatomical and physiological risk factors for hypoxaemia. The primary outcome was defined as arterial desaturation to <90% during obstetric airway management. For this purpose, multivariable binary logistic regression was performed.

Data Analysis

Patient details and pregnancy characteristics were reported as mean (standard deviation [SD]), if variables were normally distributed, median (interquartile range [IQR]) if not normally distributed, and count (%) for categorical variables. Normally distributed data were compared using Student's t-test, and for data not normally distributed using the Wilcoxon-Mann-Whitney U test. Categorical data was analysed using the chi square test. In a recent study analysing data from the first 402 patients in the registry, the overall incidence of hypoxaemia during tracheal intubation in obstetrics was 12.3%. Assuming a similar incidence in the present study of the total number of approximately 1000 patients recorded in our registry, and allowing for 10 events per predictor of hypoxaemia, 10 variables could be included in a multivariate logistic regression. For all data analysed, statistical significance was defined by a p value of 0.05, and 80% was accepted as adequate statistical power.

For multivariate binary logistic regression, variables were defined as follows: "In labour" was defined as being in the first to fourth stages of labour, whereas "Not in labour" was defined as prior to onset of labour or after delivery. Mallampati classes were subdivided into class I and II (easy) versus class III and IV (difficult). Mandibular protrusion was allocated to class A (easy) versus classes B and C (difficult). Number of attempts was subdivided into single or multiple (two or more). Experience in terms of years of training was allocated as up to five years versus more than five years. Room air oxygen saturation was dichotomised to abnormal (<94 %) and within normal range (94-100%). Hypertensive disorders of pregnancy (HDP) were classified as per our previous work, whereby patients with no hypertension or chronic hypertension alone were classified as non-HDP, and patients developing gestational hypertension, preeclampsia, preeclampsia superimposed upon chronic hypertension, and eclampsia were defined as having HDP[1].

Data analysis and summary statistics were performed with MedCalc (MedCalc® Statistical Software version 19.6, MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2020, and logistic pregression was performed in SPSS. We conducted a *post hoc* receiver operating characteristic (ROC) curve to determine the optimal cut point for BMI associated with desaturation to less than 90%.

Results

The data for 1095 obstetric general anaesthetics from the registry was examined. Patient characteristics are reported in Table 1.

Table 1: Patient characteristics

	N	Min	Max	Mean	SD	95% CI	Median	IQR	Normal Distribution
Age (years)	1093	13	46	29,1	6,7	28,7 to 29,5	-	-	<0,0001
Height (cm)	1070	117	220	162,2	6,9	161,8 to 162,6	-	-	<0,0001
Weight (kg)	1070	28	195	78,3	210,1	77,1 to 79,6	-	-	<0,0001
BMI (kg/m^2)	1063	9,7	72,6	29,6	8,0	29,2 to 30,1	-	-	<0,0001
Gravidity	1085	1	11	-	-	-	2	1 to 3	<0,0001
Parity	1083	0	10	-	-	-	1	0 to 2	<0,0001
Gestational age (weeks)	1016	20	44	35,9	4,2	35,7 to 36,2	37	34 to 39	<0,0001
SpO_2_RA	889*	9	100	97,1	5,0	96,7 to 97,4	98	97 to 99	<0,0001
SpO_2_Max	891*	50	100	99,2	2,9	99,0 to 99,4	100	99 to 100	<0,0001
SpO_2_nadir	1091	7	100	94,6	9,0	94,1 to 95,2	98	95 to 99	<0,0001

*Normality was tested using the D'Agostino-Pearson test. Data on starting room-air saturation and maximum saturation attained after preoxygenation were only recorded after the first 200 cases in the registry.
IQR interquartile range; SpO_2_RA = peripheral oxygen saturation breathing room air; SpO_2_Max = maximum peripheral oxygen saturation after preoxygenation; SpO_2_nadir = lowest peripheral oxygen saturation after tracheal intubation.

Patients in the registry ranged from 13 to 46 years of age, with a mean (SD) of 29.1 (6.6) years. Mean (SD) height, weight and BMI were 162 (6.9) cm, 78.3 (21.0) kg and 29.6 (8.0) $kg.m^{-2}$ respectively. Median (IQR) gravidity and parity were 2 (1-6) and 1 (0-5) respectively. Gestational age of patients entered into the registry ranged from 20 to 44 weeks with a mean (SD) of 35.9 (4.2) weeks.

Data for the primary outcome (peripheral oxygenation desaturation below 90%) was available for 1091 patients. Overall, 143/1091 (13.1%, 95%CI 11.1 to 15.4%) of patients suffered a peri-induction hypoxaemic event.
Of the cases analysed, 99.5 % were undertaken in maternity theatres at the three contributing hospitals, with the remaining 5 patients receiving their operations in the main theatre complex for specific logistic reasons. The overall rate of desaturation at

GSH and NSH was 15.8 and 15.5% respectively, and 8.6% at MMH (p=0.01). The incidence of hypoxaemia was 25.8% for interns performing airway management during obstetric general anaesthesia, compared with 8.0 % for consultant anaesthesiologists (p=0.005). The incidence of hypoxaemia for medical officers and registrars was 13.4 and 13.0% respectively. The incidence of hypoxaemia was not significantly associated with the number of years of experience.

There was no difference in the incidence of hypoxaemia related to gravidity, parity, stage of labour, primary anaesthesia strategy (GA versus neuraxial), or the presence of partial dentition.

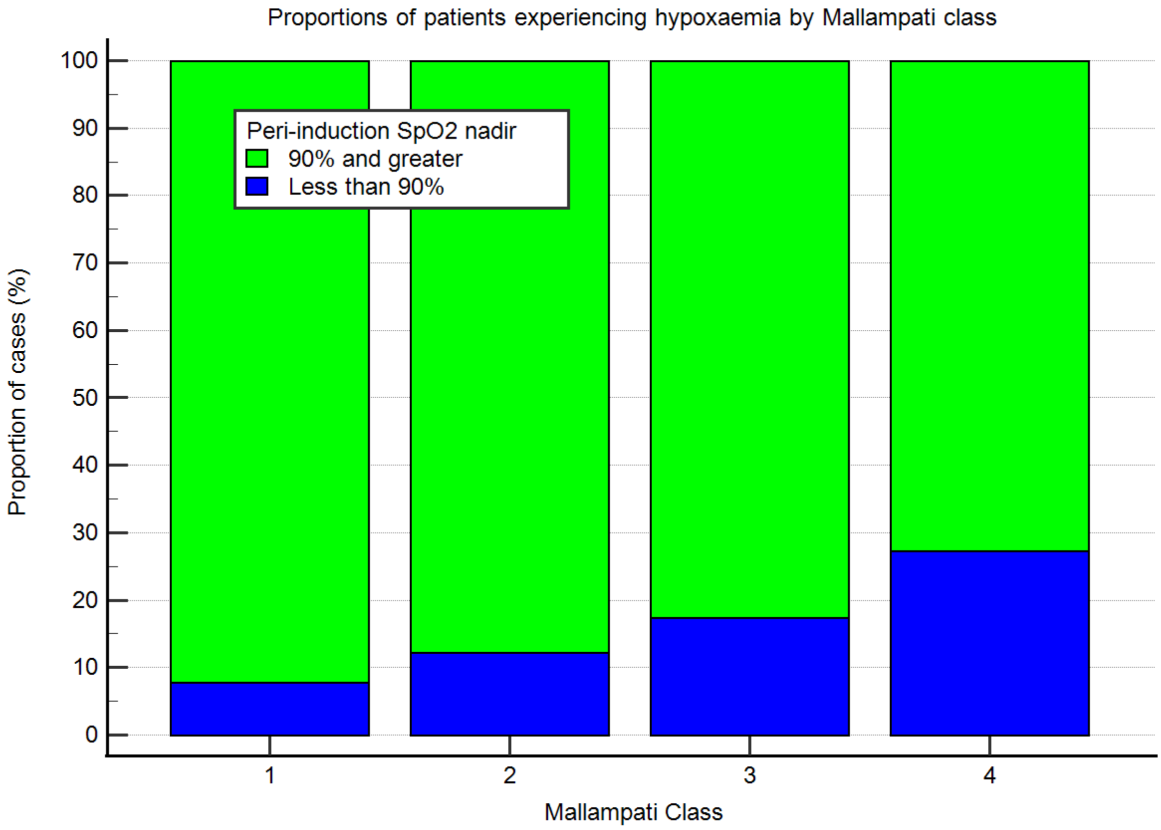
Univariate analysis showed that 91/143 (63.6%) of patients who desaturated were obese, compared with 347/915 (37.9%) who were obese and did not experience desaturation (p <.001).

Overall, 31.4% of patients had preeclampsia or eclampsia. Desaturation occurred in 17.0% of patients with HDP, versus 11.0 % without (p=0.005). The highest rates of hypoxaemia occurred in those with preeclampsia superimposed on chronic hypertension, and with imminent and established eclampsia (25.0 and 28.2%). Patients with chronic hypertension desaturated more frequently than those with pregnancy induced hypertension (19.5 versus 12.8% respectively).

Data describing indication for general anaesthesia showed no significant association with airway difficulty or hypoxaemia with respect to abnormal placentation, cardiac disease, coagulopathy, fetal distress, failed spinal anaesthesia or prolonged surgery, or postpartum haemorrhage. However, 33.3% of patients undergoing general anaesthesia because of decreased level of consciousness experienced hypoxaemia, compared to 12.5% for those with normal level of consciousness (p<0.001).

The Mallampati class was assessed in 1056 patients (96.8%). Classes 3 and 4 comprised 17.8 and 4.6% respectively There was a significant progression in incidence of hypoxaemia with increasing Mallampati class. The mean incidences for classes 1 and 2 were 8.1 % and 12.9%, and 17.5% and 26.0% for classes 3 and 4 respectively (p=0.002). This is illustrated in Figure 1.

Figure 1:



A thyromental distance of less than 6.5 cm (or four fingers) was associated with an increased incidence of difficulty (21.2 versus 13.2%, p=0.028). Mandibular protrusion was assessed in 539/1089 (49.5%) of cases. Limited protrusion (Class B or C) was associated with increased difficulty (24.0 or 25.0%, compared to 10.7% in cases in whom protrusion was normal, p = 0.013). Limited mouth opening was described in 65/1090 patients. Desaturation occurred in 21.5% of these cases, compared to 12.25% in those with mouth opening of at least 5 cm. Ten patients had limited neck mobility, of whom 3 experienced hypoxaemia.

In this study, video laryngoscopy (VL) was available in 97% (1058/1091) of patients. VL use was highly associated with peri-induction hypoxaemia (21.0 versus 9.0%, p<0.001). Later in the study, we introduced a question documenting whether the VL was used as the primary strategy, or was introduced as a rescue strategy after failed direct laryngoscopy. Where VL was used on the first attempt, there was no association with desaturation/hypoxaemia (p=0.25). Similarly, the use of an introducer was highly associated with difficulty (p <0.001), however later data documenting whether the introducer was used on the first attempt showed no association with difficulty (p=0.65).

The Cormack-Lehane (CL) grading was designed for assessment of laryngoscopy in obstetric patients. Our data showed an increase in difficulty associated with increasing Cormack-Lehane grade. Grade 1 views showed an incidence of hypoxaemia below the overall rate (11.2 vs 13.1%), Grade IIa 15.1%, Grade IIb 25.9% Grade III 26.7%, and Grade IV 50% (1 of 2 patients), *p*=0.003.

Where patients in our study were graded on the basis of a practitioner's impression of the degree of airway oedema (absent, mild or severe) the presence of any airway oedema was associated with difficulty/hypoxaemia (*p*<0.001). Of patients assessed to have severe oedema, 47% (8/17) had hypoxaemia.

Patients who required multiple attempts at intubation had a higher incidence of hypoxaemia (p<0.0001). When intubation was accomplished on the first attempt, the incidence of hypoxaemia was 9.7%. If multiple attempts are required, desaturation ranged from 46% (two attempts) to 60% (three attempts). No patient required more than three attempts at intubation. In our registry, there were four cases of rescue using a supraglottic airway (SGA), and none required emergency front of neck access. Two of four patients requiring supraglottic rescue had hypoxaemia. In the other 2, an SGA was used before (and avoiding) hypoxaemia.

In the multivariate logistic regression, only high BMI, low room air oxygen saturation and presence of airway oedema as assessed by the anaesthesiologist, reached statistical significance (Table 2). Risk (95% CI) for hypoxaemia with low starting saturations was 3.98 (1.43-11.16), 3.02 (1.87 – 4.89) for obesity, and 1.86 (1.07-3.22) for airway oedema.

Table 2: Multivariate analysis of factors associated with hypoxaemia

Binary variable	**OR**	**95% CI**	***p* value**
Training years (<5 vs 5 or more)	1.36	0.78 – 2.35	0.28
Presence or absence of labour	0.98	0.62 – 1.56	0.94
Hypertensive disorders of pregnancy	0.89	0.54 – 1.47	0.65
Mallampati grade (1/2 vs 3/4)	1.33	0.78 – 2.26	0.29
Mouth opening (limited or normal)	1.25	0.46 – 3.39	0.66
Neck mobility (limited or normal)	0.88	0.15 – 5.18	0.88
Body mass index (<30 or ≥30 kg/m^2)	3.02	1.87 – 4.89	<0.001
Room air peripheral saturation (<94% or ≥94%)	3.98	1.43 – 11.13	0.008
Presence of airway oedema	1.86	1.07 – 3.22	0.027

A receiver operating curve (ROC) was constructed *post hoc*, which showed a cut-point for BMI of 29.76, and a sensitivity of 0.66, and specificity 0.62 for the prediction of hypoxaemia.

Discussion

In this analysis of general anaesthesia in over 1000 parturients whose data was entered into the ObAMR, there was an overall incidence of 13.1% of hypoxaemia during tracheal intubation. Obesity, room air peripheral saturation <94% prior to preoxygenation, and the presence of airway oedema were found to be independent predictors of hypoxaemia during airway management before commencement of maintenance anaesthesia. These findings serve as an alert to anaesthesiologists managing this challenging and vulnerable group of patients and could assist in the generation of a difficult intubation score.

Most airway catastrophes occur when airway difficulty is not anticipated prior to induction of anaesthesia[2]. Timely evaluation of the parturient's airway and adequate preparation to deal with potential complications are helpful in avoiding airway disasters[5]. Maternal, fetal, surgical and situational factors contribute to the increased incidence of failed intubation. Many physiological changes occur during pregnancy, including physical characteristics such as increased body mass index (BMI), breast enlargement, and generalised oedema[6,7]. The mucosa of the upper respiratory tract also becomes more vascular and oedematous, leading to increased risk of airway bleeding and swelling[8]. Fluid retention in head and neck tissues during pregnancy, particularly in preeclampsia, potentially narrows the upper airway and reduces compliance, making laryngoscopy more difficult[6]. The term parturient is also more susceptible to gastro-oesophageal reflux, due both to progesterone-mediated effects and anatomical changes due to the gravid uterus[5].

Our obstetric airway management registry (ObAMR), recently validated by Smit et al[1], was established at the University of Cape Town in 2018, with a view to collecting data on every tracheal intubation in Obstetrics, with the purpose of improving the safety of the procedure. The aim of the present retrospective analysis of the data from >1000 patients from this registry, was to identify certain routine and common clinical pre-induction measurements, tests and risk factors that might aid in the prediction of a difficult airway in our Obstetric Anaesthesia practice, allowing time for the anaesthesiologist to prepare adequately and introduce focussed precautions and interventions, thereby potentially reducing morbidity and mortality.

There are a few simple preoperative bedside clinical tests that can be performed to evaluate the airway, including the Mallampati score, mouth opening (inter-incisor gap), thyromental distance, neck mobility (atlanto-occipital extension), and ability to protrude the mandible[2,8,9]. Further tests and measurements that have been analysed include the measurement of neck circumference[10], the ratio of neck circumference to thyromental distance[11], the ratio of patient height to thyromental distance[12] and a new screening test, the acromio-axillo-suprasternal notch index[13], but these have limited predictive value and are not often applied in routine clinical practice.

The relationship between increased airway classification scores and relative ease or difficulty of intubation in pregnant patients undergoing caesarean delivery during general anaesthesia has been studied by Rocke et al*,* who studied 1500 pregnant women who had emergency or elective caesarean delivery under general anaesthesia[14]. A strong correlation was found between the difficulty in identifying oropharyngeal structures and difficulty with tracheal intubation. The authors found that the relative risk of encountering difficult intubation in a gravid parturient with a Mallampati class 3 airway was 7.6 times higher than in a parturient with a Mallampati class 1 airway. This relative risk increased to 11.3 in pregnant patients with a Mallampati class 4 airway[14]. Using a combination of risk factors, they showed that the presence of a class 3 or 4 airway together with protruding maxillar incisors, a short neck, and a receding mandible, increased the probability of difficult laryngoscopy to >90%. Our study showed that there was a significant progression in incidence of hypoxaemia with increasing Mallampati class.

Pilkington et al demonstrated that airway oedema may increase during the course of pregnancy and result in an increased Mallampati score[15]. Kodali et al observed airway changes during labour and delivery[16]. There was a significant increase in airway class from the pre-labour period to after labour. The airway increased by one grade in 20/61 patients (33%), and by 2 grades in 3 women (5%). At the end of labour there were 8 patients with a class 4-, and 30 women with a class 3 or 4 airway ($p < 0.001$). Oral volume and pharyngeal area and volume also decreased significantly after labour. In a further case-control study, changes in Mallampati grade were compared in healthy women and those with preeclampsia. In addition, sonographic measurements were made of tongue thickness, anterior neck soft tissue, thyromental distance and neck circumference. Mallampati score was found to increase from the pre-labour period in both groups. In addition, there was a significant between group difference in tissue thickness at the hyoid level before and after labour and postpartum[17].

Predictably, in our study patients who required multiple attempts at intubation suffered a much higher incidence of hypoxaemia. Where intubation was accomplished on the first attempt, incidence of hypoxaemia was only 9.7%. (This in itself is clinically significant, showing that one in 10 patients who can be intubated with a single attempt will still experience hypoxaemia). However, where multiple attempts are required, desaturation was common, ranging from 46% (two attempts) to 60% (three attempts). It is heartening to note that no patient in our cohort of over a thousand underwent more than three attempts at intubation, in keeping with modern difficult airway management guidelines. In our registry, there were four cases of rescue using a supraglottic airway and none using emergency front of neck access. Of note, although 50% (two of four) cases of supraglottic rescue underwent profound desaturation, in the other two patients an SGA was used before (and avoiding) hypoxaemia. This may indicate increasing acceptance of the role of supraglottic airways in error rescue, and the increasing emphasis placed upon oxygenation rather than intubation as an airway management goal. Various difficult airway algorithms exist as memory and training aids to mitigate risk once a difficult airway is encountered[3,4]. The present study included patients before, during and after labour.

In a recent study which focussed on patients who had an anticipated difficult airway in obstetric general anaesthesia, previous difficulty with airway management was noted in 14/158 patients[4]. However, unfortunately such records are often unavailable, as was the case in the present study. In the study by Mushambi et al, an airway assessment was only reported in 102/158 cases. The Mallampati grade was given in 82 of these women, of whom 7 had were grade 1, 17 grade 2, 33 grade 3, and 30 grade 4. All of the women with grade 1 and 2 airways had other predictors of difficulty. Other features or tests were neck movement in 75 cases, mouth opening in 68, thyromental distance in 36, and jaw protrusion or micrognathia in 24 patients. In one patient the neck was assessed for front of neck access, and in 2 cases there was obstructive sleep apnoea. No studies described the use of a combined score. In the presence of specific airway pathology, respiratory investigations were performed, including CT imaging. In 15/158 patients awake laryngoscopy or nasal endoscopy was performed to guide the choice of anaesthesia technique. Fifty- two women required awake intubation using flexible bronchoscopy, of whom 3 had this procedure after an initial poor direct laryngoscopic view, and 5 after failed regional anaesthesia. Most of the women had congenital abnormalities, but other indications were morbid obesity, goitre, mediastinal mass, HELLP syndrome, a swollen tongue in a woman with eclampsia, and reduced mouth opening. A strength of the present study was that the Mallampati class was assessed in 97% of 1056 patients.

Historically, as indicated above, studies assessing difficulty of intubation in obstetrics have focussed primarily on the physical and anatomical challenges associated with insertion of an endotracheal tube. However, there is increasing recognition of the concept of a physiologically or pathophysiologically difficult airway (when patients rapidly become hypoxaemic during airway management), which uses hypoxaemia as a composite indicator of both anatomical and physiological difficulty. There are a limited number of studies in the literature exploring this concept. Smit et al compared the prevalence and risk factors for hypoxaemia ($SpO_2 < 90\%$) during induction of general anaesthesia in parturients with and without hypertensive disorders of pregnancy[18]. They hypothesised that hypertensive disorders of pregnancy are associated with desaturation during tracheal intubation. In a cohort of 402 cases, hypoxaemia occurred in 19% with and 9% without hypertension, $p = 0.005$. Quantile regression demonstrated a lower SpO_2 nadir associated with hypertensive disorders of pregnancy as body mass index increased. Room-air oxygen saturation, Mallampati grade, and number of intubation attempts were associated with the relationship. In the present study, involving a much larger sample size from the ObAMR, the significantly higher rate of desaturation demonstrated by Smit et al[18] in patients with HDP than in those without the condition, was again shown in univariate analysis. This did not prove to be an independent predictor of hypoxaemia, due to the greater risk of hypoxaemia shown to be associated with obesity.

In a multicentre study, Bonnet et al[19] studied the incidence and risk factors for maternal hypoxaemia during tracheal intubation for non-elective caesarean delivery. Hypoxaemia occurred in 172/895 women (19%). Multivariate analysis showed that risk factors associated with hypoxaemia were difficult or failed intubation, and BMI> 35 kg/m^2. Intubation was found to be difficult in 40 patients (4.5%), and 5 women (0.56%) had failed intubation. Propofol was found to associated with a significantly lower risk of failed intubation. In a further recent publication from South Africa, the authors performed a prospective, observational, dual-centre cohort study, aiming to establish the incidence of hypoxaemia, defined as $SpO_2 < 90\%$, during induction of general anaesthesia for caesarean delivery[20]. Factors investigated as potential predictors of hypoxaemia were body mass index, the level of experience of the operator, predicted difficult airway, Cormack-Lehane grading, and the absence of planned mask ventilation. They also reported on complications related to tracheal intubation. The incidence of hypoxaemia was found to be 61/363 (16.8%). BMI > 30 kg/m^2 and Cormack-Lehane grade 4 predicted hypoxaemia. The failed intubation rate was 1.4%, and the regurgitation rate 0.8%. No patients experienced pulmonary aspiration or required surgical intervention to secure the airway.

Limitations of our study include possible reporting bias based upon the perception of the anaesthesiologist that tracheal intubation might be difficult, but we believe that this was unlikely. The body mass captured in the notes may have been transcribed from notes made earlier in pregnancy, so that the recorded BMI may have been an underestimate of the true BMI. Furthermore, the data capture rate was 80% or less, and there may have been errors in some entries, as well as some degree of interobserver variability. Some aspects of the airway assessment were not completed by all anaesthesiologists. For example, mandibular protrusion was only fully assessed in 50% of cases.

Further strengths of the study included the use of a previously validated airway registry specifically focussed on Obstetric Anaesthesia, and the considerable sample size. The study also provided valuable data on the use of VL in obstetric anaesthesia and provides a basis for focussed future studies in this area. A pragmatic interpretation of our data is that VL is frequently used as a rescue strategy where difficult intubation has already been encountered, explaining the early high incidence of desaturation associated with VL use. However, where VL is selected as the primary strategy, despite anticipated airway difficulty, desaturation is not a significant occurrence. Similarly, whilst the use of an introducer was highly associated with difficulty, later data documenting whether the introducer was used on the first attempt shows no such association. A pragmatic interpretation of these data is that an introducer is often used when difficulty is encountered, but when it is used from the outset, peri-induction hypoxaemia can be prevented.

In this study, which contributes to the limited literature on the use of hypoxaemia as a composite indicator of difficult intubation in obstetrics, both anatomical and physiological predictors of hypoxaemia were identified. Using this concept, a predictive tool could be developed to aid in the identification of a difficult airway in obstetrics. This could also guide the choice of anaesthesia for urgent caesarean delivery in women with anticipated difficult tracheal intubation, including the use of simple decision analysis[8]. Simple interventions such as face mask ventilation and the use of high flow nasal oxygenation, could be introduced to protect the parturient from the consequences of life-threatening hypoxaemia.

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Chapter 3

Appendix 1 – HREC Approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room G50-46 Old Main Building
Groote Schuur Hospital
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09 January 2020

HREC REF:839/2019

Prof R Hofmeyr
Department of Anaesthesia & Perioperative Medicine
D-23
NGSH

Dear Prof Hofmeyr

PROJECT TITLE: PREDICTORS OF DIFFICULT INTUBATION IN OBSTETRIC COHORT OF PATIENTS: AN ANALYSIS OF THE PROSPECTIVE OBSTETRIC AIRWAY MANAGEMENT REGISTRY (OBAMR) (SUB-STUDY - R025/2018) (MMED DEGREE - DR ADRIAN BURGER)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 January 2021.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Adrian Burger will also be involved in this study.

Please quote the HREC REF in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

HREC 839/2019sa

Appendix 2 - Instruction to authors, SAJAA

Available online from www.sajaa.co.za/index.php/sajaa/about/submissions

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

- This manuscript has currently only been submitted to SAJAA and has not been published previously.
- This work is original and all third party contributions (images, ideas and results) have been duly attributed to the originator(s).
- Permission to publish licensed material (tables, figures, graphs) has been obtained and the letter of approval and proof of payment for royalties have been submitted as supplementary files.
- The submitting/corresponding author is duly authorised to herewith assign copyright to the South African Society of Anaesthesiologists (SASA).
- All co-authors have made significant contributions to the manuscript to qualify as co-authors.
- Ethics committee approval has been obtained for original studies and is clearly stated in the methodology as well as provided as a supplementary file.
- A conflict of interest statement has been included where appropriate.
- The submission adheres to the instructions to authors in terms of all technical aspects of the manuscript.
- Plagiarism: The submitting author acknowledges that the Editorial Board reserves the right to use plagiarism detection software on any submitted material.

Author Guidelines

Submitted manuscripts that are not in the correct format and without the required supporting documentation specified in these guidelines will be returned to the author(s) for correction and will delay publication.

AUTHORSHIP

Named authors must consent to publication **by signing a covering letter** which should be submitted as a supplementary file. Authorship should be based on substantial contribution to:

(i) conception, design, analysis and interpretation of data;

(ii) drafting or critical revision for important intellectual content; and

(iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to **www.icmje.org**); and

(iv) exact contribution of each author must be stated.

DECLARATION OF CONFLICT OF INTEREST

Authors must declare all sources of support for the research and any association with a product or subject that may constitute a conflict of interest. If there is no conflict of interest to declare please include the following statement: The authors declare no conflict of interest.

FUNDING SOURCE

All sources of funding should be declared. Also define the involvement of study sponsors in the study design, collection, analysis and interpretation of data; the writing of the manuscript; the decision to submit the manuscript for publication. If the study sponsors had no such involvement, this should be stated as follows: No funding source to be declared.

RESEARCH ETHICS COMMITTEE APPROVAL

The submitting author must provide written confirmation of Research Ethics Committee approval for all studies including case reports. The ethics committee as well as the approval number should be included.

STATISTICAL ANALYSIS

Authors are advised to involve medical statisticians at the protocol stage of their research project: to plan sample size, and the selection of appropriate statistical tests for analysis and presentation.

PROTECTION OF PATIENT'S RIGHTS TO PRIVACY

Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published. Refer to **www.icmje.org**.

ETHNIC CLASSIFICATION

The rationale for analysis based on racio-ethnic-cultural categorisation should be indicated.

CATEGORIES OF SUBMISSIONS

Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences.

Original articles

Original articles on research relevant to anaesthesia and analgesia should not exceed 3 200 words, no more than 30 references, with up to 6 tables or figures. A structured abstract under the following headings, Background, Methods, Results, and Conclusions is a requirement and should not exceed 300 words.

Clinical Review articles

Review articles relevant to anaesthesia and analgesia should not exceed 2 400 words, with a maximum of 20 references and no more than 6 tables or figures. A summary of 300 words or less is required.

Case reports

Case reports should not exceed 1 800 words with no more than 10 references. Figures are limited to 2 figures and may include images or photographs. The case report should have three headings: Summary (not exceeding 100 words), Case report (with no introduction) and Discussion. Case reports will be published online only. The summary and the URL will appear in the printed version.

Scientific Letters

Scientific Letters should not exceed 2 400 words with a maximum of 10 references. Only one table or illustration is permissible. A structured abstract under the following headings, Background, Methods, Results, and Conclusions, is a requirement and should not exceed 250 words.

Letters to the editor

Letters to the editor should be 800 words or less with only one image or table.

MANUSCRIPT PREPARATION

Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements' - **www.icmje.org**. Manuscripts must be provided in **UK English**.

Qualification, affiliation and contact details

This information must be provided for ALL authors and must be submitted as a supplementary file.

Email addresses of all author must be provided.

ORCID number of **ALL** authors must be provided – if authors do not have ORCID, please register at https://orcid.org/

Abbreviations

All abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

Scientific measurements

Scientific measurements must be expressed in SI units except blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres). Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and 40 years of age) should also be preceded by a space e.g. > 20 years. No spaces should precede ± and °, i.e. '35±6' and '19°C'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160...

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Disclaimers should follow the Conclusion and it should be in the following order: Acknowledgements, Declaration conflict of interest, Funding source, Ethics declaration and ORCID.

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If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

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Internet references: World Health Organization. The World Health Report 2002 - Reducing Risks, Promoting Healthy Life. Geneva: World Health Organization, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

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