**ADDIS ABABA UNIVERSITY**

**COLLEGE OF HEALTH SCIENCES**

**SCHOOL OF MEDICINE**

**DEPARTMENT OF ANESTHESIA**

# MAGNITUDE OF HEMODYNAMIC AND AIRWAY PRESSURE CHANGE AND FACTORS ASSOCIATED WITH INTRAOPERATIVE HYPOTENSION DURING ELECTIVE NEUROSURGERY

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**A THESIS SUBMITTED TO ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCES, SCHOOL OF MEDICINE, DEPARTMENT OF ANESTHESIA, IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF MASTER'S IN CLINICAL ANESTHESIA**

**JUNE, 2017**

**ADDI ABABA, ETHIOPIA**

**ADDIS ABABA UNIVERSITY**

**COLLEGE OF HEALTH SCIENCES**

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**A THESIS SUBMITTED TO SCHOOL OF GRADUATE STUDIES OF ADDIS ABABA UNIVERSITY, COLLEGE OF HEALTH SCIENCE IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR MASTER OF SCIENCES IN ANESTHESIA**

**June, 2017**

**Addis Ababa**

**Annex 1: Declaration**

I, the undersigned, senior clinical Anesthesia student declare that this thesis is my original work in partial fulfillment of the requirement for the degree of Masters of clinical Anesthesia.

Name: _____

Signature: _____

Place of submission: Department of Anesthesia, College of Health Sciences, School of Medicine Addis Ababa University.

Date of Submission: _____

This thesis work has been submitted for examination with my approval as university advisor.

Advisor

| Name | Signature |
| --- | --- |
| _____ | _____ |

**ASSURANCE OF INVESTIGATOR**

The undersigned agrees to accept responsibility for the scientific, ethical and technical conduct of the research project and for provision of required progress reports as pre terms and conditions of the research and publications office of the Addis Ababa University.

Name of the student: _____

Date: _____ Signature: _____

Approval of the advisor

Advisors

| Name | Signature | Date |
|---|---|---|
| 1. _____ | _____ | _____ |

**Acknowledgement**

I am deeply indebted to my advisor Adugna Aregawi (Msc IN ACA) for his support, comment, and guidance throughout research process I am going through. My sincere acknowledgement also goes to Sileshi Abiy, Nathan Desalegn, Tewoderos Shitemaw and Fekede Weldekidan for their valuable comments and inputs. I would also like to thank Addis Ababa University Department of Anesthesia of for giving me the opportunity to conduct this study.

**Abbreviations**

| | |
|---|---|
| AANS | American Association of National Neurological surgeons |
| ACDF | Anterior Cervical Discectomy and Fusion |
| AOR | Adjusted Odds Ratio |
| ASA | American Society of Anesthesiologists |
| BP | Blood Pressure |
| CPA | Cerebellopontine Angle |
| COR | Crude Odds Ratio |
| CSM | Cervical Spondylotic Myelopathy |
| ETV | Endoscopic Third Ventriculostomy |
| HIV | Human Immune Deficiency Virus |
| ICP | Intracranial Pressure |
| IOH | Intraoperative Hypotension |
| MAP | Mean Arterial Pressure |
| PAP | Peak Airway Pressure |
| SPSS | Statistical Package for Social Science |
| SBP | Systolic Blood Pressure |
| TASH | Tikur Anbessa Specialized Hospital |
| TIVA | Total Intravenous Anesthesia |
| TSS | Trans-Sphenoidal Surgery |

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**Abstract**

**Background:** Neurosurgery is a medical specialty which is concerned with the prevention, diagnosis, treatment and rehabilitation of disorders that affect the entire nervous system. Hemodynamic change is one of the complications of neurosurgery with an incidence differing with multiple factors. Positioning during neurosurgery has an impact on airway pressure. Poor anesthetic management during neurosurgery will lead to permanent injuries to the patient, which otherwise are largely preventable.

**Objective:** The aim of this study is to assess magnitude of hemodynamic and airway pressure change and factors associated with intraoperative hypotension during elective neurosurgery in Tikur Anbessa specialized hospital and Empress Zewditu memorial hospital, 2017

**Method:** Institutional based cross sectional study was used from December 20, 2016 to May 20, 2017 using pre-tested, interviewer administered questionnaire for 208 patients. Due to rarity of the procedure all eligible patients who underwent elective neurosurgery at Tikur Anbessa Specialized hospital and Empress Zewditu memorial hospital during the data collection period were included in the study. The data was entered to Epi Info version 7.2.1 and analyzed by SPSS version 20 software performing descriptive statistics, bivariate and multivariate logistic regression.

**Result:** The magnitude of intraoperative hypotension is found to 29.3% (95% CI: 22%-35%). Intraoperative Hypertension had magnitude of 1% (95%CI: 0.0%-2.4%) with bradycardia and tachycardia having 2.4% (95%CI: 0.5%-4.8%) and 1% (95%CI: 0.0%-2.9%) respectively. Blood loss of >10ml/Kg has >5 times [AOR=5.77; 95% CI: (1.97, 16.83)] more risk for developing intraoperative hypotension and Phenytoin use [AOR=6.96; 95% CI: (1.97, 24.50)] had significant association with intraoperative hypotension.

**Conclusion and recommendation:** The magnitude of intraoperative hypotension is high. Some of the identified factors were Blood loss of >10ml/Kg and Phenytoin use. Therefore early anticipation and preparation of intraoperative hypotension in patients especially taking phenytoin and risk of increased blood loss can improve patient outcome.

## Chapter one: Introduction

### 1.1 Background information

Neurosurgery is a medical specialty which is concerned with the prevention, diagnosis, treatment and rehabilitation of disorders that affect the entire nervous system. It includes surgeries done on the spinal column, spinal cord, brain and peripheral nerves. Craniotomy and Laminectomy are the most common types of neurological procedures performed which can be done under elective or emergency(1).

Craniotomy involves passing through the cranial cavity and delicate structures of the brain. It needs a constant communication between the anesthetist and surgeon since any miscommunication can cause debilitating consequences for the patient(2,3). Motor vehicle accidents, which are the leading cause of death among young people aged 15-29 are most often the cause for emergency neurosurgical procedures(4).

Although we could not find a publication regarding how many neurosurgeries are performed in Ethiopia or Africa, according to AANS (American Association of National Neurological surgeons) in 2011 neurosurgeons performed a sum total of 2.2 million surgeries in the United States alone(5).

Patients coming to neurosurgery often take medications for treatment and prophylaxis of some disease entities and most patients with meningioma and intracranial space occupying lesion are of advanced age. This advanced age also comes with limited physiologic capacity and Comorbidities(6,7).

General anesthesia is the preferred and mostly the only choice of anesthetic technique for neurosurgery. The cause is, substantial sum of neurosurgical procedures are done on the head, cervical and thoracic vertebrae which are almost impossible to use another anesthetic technique(8).

After surgical intervention considerable amount of head injury patients may need to be placed on mechanical ventilator with endotracheal tube in situ. Patients with large space occupying lesions often have depressed level of consciousness leading to possible aspiration of gastric contents because of patients' inability to control their airway(9).

Majority of the neurosurgical procedures require the patient to undergo some sort of position change during surgery which will affect their respiration and bring about cardiovascular changes. In addition changing patients' position after endotracheal tube placement poses its own kind of challenge. Placements used include prone, head up and sitting position(10). From here on hemodynamic changes in this thesis will imply blood pressure and heart rate changes.

## 1.2 Statement of the problem

Hemodynamic change is one of the complications of neurosurgery with an incidence differing with multiple factors. Intraoperative hypotension (IOH) being the most commonly occurring hemodynamic instability has up to 65% incidence from 113 patients with traumatic head injury and had 19% in hospital mortality rate(11). The other hemodynamic instability which occurs on patients with raised intracranial pressure (ICP) is Cushing reflex which is characterized by hypertension, bradycardia and apnea(12). Hemodynamic changes occurring during surgery are associated with cardiovascular status changes and can lead to cardiac death or stroke even in postoperative period(13). Hypotension can be caused by blood loss and patient positioning(14). Hypotension has variety of complications that arise from failure of circulation to deliver oxygen and nutrients to body organs. Depending on its severity, increased fluctuation and duration the complications on the brain vary from Postoperative delirium to focal neurologic deficit and even irreversible brain damage(15,16). Bradycardia and hypotension are the primary causes of vasovagal syncope which is loss of consciousness secondary to limited blood supply to brain which can result in mortality rate of 5-10%(12). Systemic hypertension associated with emergence from anesthesia, has long been believed to contribute to postoperative hematoma resulting from intracranial hemorrhage, which is one of the major complications after intracranial surgery of devastating consequence and has an incidence of 0.8%-2.2%(17).

There are different definitions given to intraoperative hypotension and hypertension during surgery with incidences and complications varying accordingly(18–23). Although there are diverse definitions, literatures agree mean arterial pressure(MAP)<55mmHg is considered to be a risk factor for acute kidney and myocardial injury(24). Certain patient positions are associated with minor cardiovascular derangements. Prone position which is the patient is placed during posterior fossa surgery causes a decrease in cardiac index, decrease cardiac output by inferior vena-caval obstruction and decreases mean arterial pressure in low blood volume patients(25). An increase in airway pressure causes barotrauma leading to pneumothorax and pneumopericardium and ruptured alveoli(26). Peak airway pressure (PAP) of >50cmH2O and plateu pressure of <35cmH2O are considered to be a risk factor for ruptured alveoli(27). Resources for this topic are scarce and we couldn't find a published study with the same topic in Ethiopia and this continent.

### 1.3 Justification of the study

Neurosurgery is a delicate and time consuming surgery with complications that are life threatening. Any kind of vital sign derangement is associated with poor outcome. The incidence of hemodynamic change is alarming even with the highest monitoring and standards of the developed countries and can only be guessed in this country with less monitoring and without standard drug choices. An increase in airway pressure can cause a debilitating lung injury and is most commonly associated with position changes. Without proper monitoring and decreased availability of ways to minimize the effects of positioning, studying its incidence would be a wise choice.

Since the main objective of this study is to assess magnitude of hemodynamic and airway pressure change and factors associated with Intraoperative Hypotension during elective neurosurgery, the result will fill the knowledge gap of anesthesia professionals and other concerned bodies on the magnitude and associated factors of IOH. It'll have a direct impact on the satisfaction and outcome of patient which is the main content of upholding the standard of safe surgery and anesthesia that will decrease patients' hospital stay and expense. The result will have an effect on anesthetists to better consider their management protocols.

To the best of our search published researches which can be used as a reference could not be found in this country, which will make this study to be used as a baseline for further country wide study.

## Chapter Two: Literature Review

Neurosurgery is associated with various complications that can arise from the surgery itself, patient's condition, during anesthesia delivery or patients positioning. Their incidence and consequence may vary significantly depending on their severity. But the major complications are hemodynamic instability and airway pressure change.(28)

### 2.1 Hemodynamic change

During surgery hemodynamic instability may occur due to blood loss, drugs used and patient's previous cardiovascular and hydration states.(29) The highest incidence of cardiovascular disturbance during neurosurgery occurred during traumatic brain injury. A retrospective cohort study of 113 patients who were 18 years and above done by D. Sharma et.al revealed IOH being high (n=73, 65%) with duration of anesthesia labeled as independent risk factor (AOR 1.1 [95% CI: 1.01–1.30]; p=0.009). The increase in incidence might be explained by blood loss because of trauma and the sophisticating accuracy of monitoring devices.(11)

On another research done on 108 children (<13 year old) by P. Miller et al reported the incidence of IOH as 52%. It concluded that 10 mL estimated blood loss/kg (ARR 1.15 95% CI 1.08–1.22), each millimeter of computed tomography (CT) midline shift (ARR 1.04 95%CI 1.01–1.07 and CT midline shift ≥4 mm (ARR 1.67 95% CI 1.06–2.63) predicted the occurrence of IOH.(30)

The incidence of cardiovascular changes also differs with respect to type of neurosurgery. Endoscopic third ventriculostomy (ETV) is mostly associated with heart rate and rhythm disturbances. El-Dawlalty et.al concluded that serious bradycardia might occur during ETV, mostly because of mechanical factors after conducting a study on 49 pediatric patients and reporting the incidence of bradycardia as 41%. Increased incidence was seen during perforation of third ventricle (P<0.05).(31)

After studying the experience of same surgeon for 7 years on 298 patients, Ganjoo P. et.al noted the incidence of tachycardia as (57 patients, 20.1%), bradycardia (35 patients, 12.4%) and hypertension.(32)

On other research done by G. Singh et.al reported the incidence of tachycardia as 18.8%, bradycardia 11.3%, hypertension 16.1%, and IOH 16.6% after conducting retrospective analysis of 223 patients of whom 119 were pediatrics.(33)

A case report by Chowdhury et.al narrates a 47 year old patient who came for supratentorial surgery suffered cardiac rhythm fluctuation with three episodes of bradycardia (heart rate of 32, 45 and 30 respectively) then going into asystole which lasted for 20 seconds. Trigeminocardiac reflex and increased ICP were the attributable factors for the episodes of bradycardia and asystole.(34)

Different kinds of patient positioning are adopted during neurosurgery which has impact on hemodynamic parameters. K. Poon et.al who conducted a research on 20 patients scheduled for elective spinal surgery on prone position discovered significant reduction in mean blood pressure (during placement 85.6 ± 15.2 to 68.5 ± 10.0 one hour after prone) and heart rate (during placement 89.8 ± 20.4 to 80.6 ± 7.1 one hour after prone) ($p < 0.05$).(35) After conducting retrospective analysis of 601 adult and 91 pediatrics, Korkomaz et.al found out that the incidence of positioning induced hypotension was more in adults (37.6%) compared to children (18.6%, p=0.00001). They also noted the incidence of bradycardia as 63 (10.4%) and 5 (5.4%) in adults and pediatrics respectively.(36)

**2.2 Airway Pressure Change**

Different positions in neurosurgery affect the mean airway pressure and PAP. Finding from Saudi Arabia showed that prone position has significant increase in airway pressure compared to supine position. After conducting a research on 12 patients they witnessed an increased PAP (baseline 15.42 ± 2.50 to 17.75 ± 2.73 during prone p= 0.002) and Mean airway pressure (baseline 6.33 ± 0.89 to 6.67 ± 0.65 during prone p= 0.015).(37)

On other research from South Korea 18 patients were turned to prone for spinal surgery and the increase in PAP was significant from supine position.(38) A Prospective randomized Research done on 45 patients by A.Malhotra et.al observed that there is a significant increase in Mean airway pressure (7.86 ± 0.88 mm Hg at baseline to 8.73±1.28 mm Hg, $p < 0.05$) after prone position was endorsed.(39)

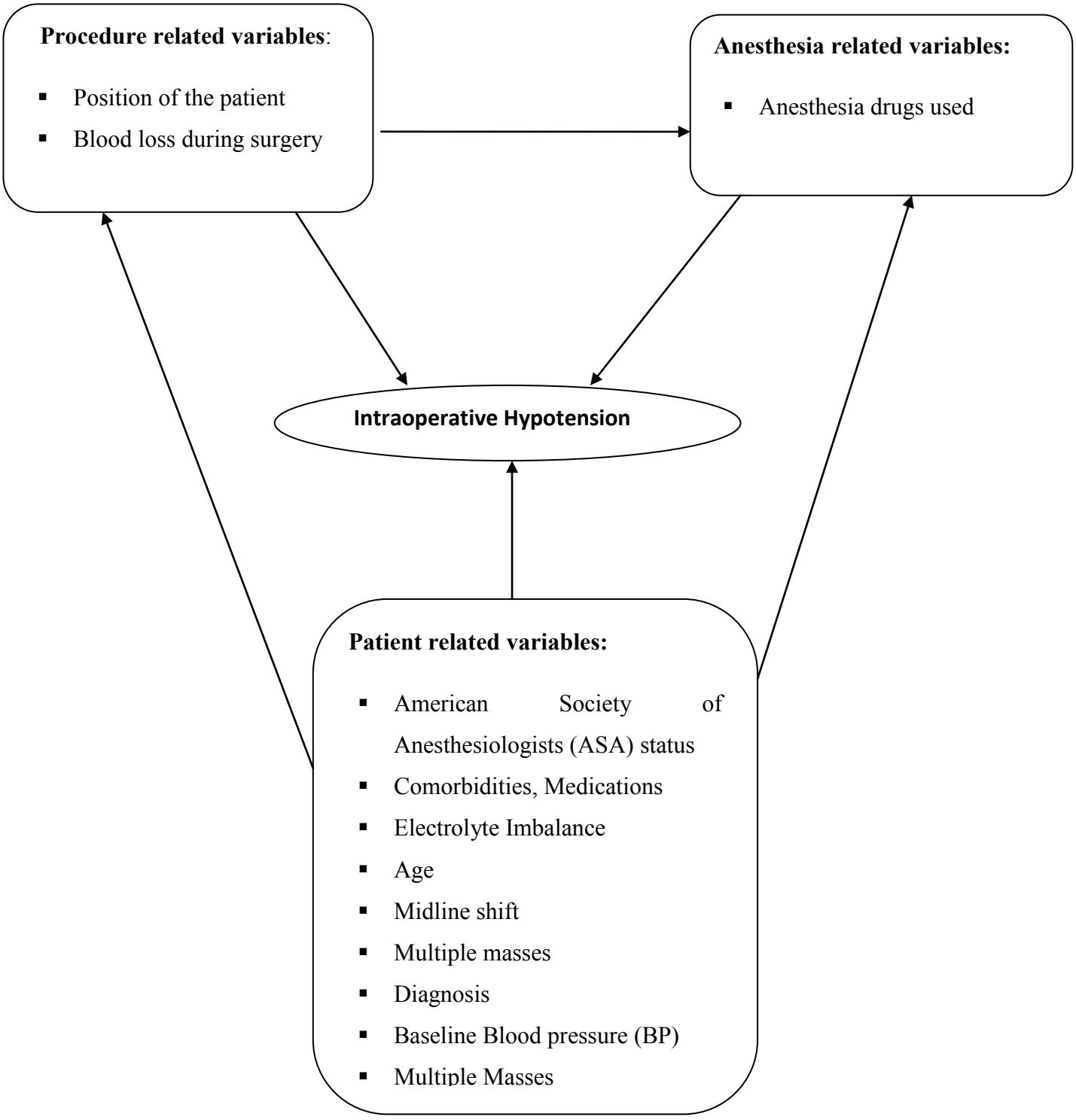


**Fig Conceptual framework for assessing the factors associated with IOH, developed after literature review**

## Chapter Three: Objectives

### 3.1 General Objective

- To assess the magnitude of hemodynamic and airway pressure change and factors associated with Intraoperative Hypotension during elective neurosurgery at Tikur Anbessa Specialized Hospital (TASH) and Empress Zewditu Memorial Hospital, 2017.

### 3.2 Specific Objectives

1. To determine the magnitude of blood pressure changes during elective neurosurgery at TASH and Empress Zewditu Memorial Hospital, 2017.
2. To determine the magnitude of heart rate changes during elective neurosurgery at TASH and Empress Zewditu Memorial Hospital, 2017.
3. To determine the magnitude of airway pressure changes during elective neurosurgery at TASH and Empress Zewditu Memorial Hospital, 2017.
4. To identify factors associated with Intraoperative Hypotension during elective neurosurgery at TASH and Empress Zewditu Memorial Hospital, 2017.

## Chapter Four: Method

### 4.1 Study Area

The study was conducted at public hospitals in Addis Ababa, the capital city of Ethiopia. With an area of 527 square kilometers and 10 sub cities, it is the largest city in the country. The city has 12 government hospitals.

Two governmental hospitals were used for this study. They are TASH and Empress Zewditu memorial hospital. The two hospitals were chosen for this study because they are the only government hospitals in Addis Ababa in which most neurosurgeries are performed. TASH, located in the nation's capital Addis Ababa, is Ethiopia's largest referral hospital. It offers diagnosis and treatment for approximately 370,000- 400,000 patients a year with nearly 8000 surgeries are performed annually with 14 operation rooms. Empress Zewditu memorial hospital is named after Empress Zewditu, predecessor on the throne Emperor Haile Selassie I. Today Empress Zewditu memorial hospital is operated by the Ministry of Health and has 4 major operating theaters. Approximately 100 neurosurgeries are performed annually.

### 4.2 Study design and Period

Institution based cross-sectional study was conducted from December 20, 2016 to May 20, 2017.

### 4.3 Source population

All patients who were admitted to undergo neurosurgery at TASH and Empress Zewditu memorial hospital

### 4.4 Study population

All eligible patients who underwent elective neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017.

### 4.5 Study Subject

Selected patients who underwent elective neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017

### 4.6 Eligibility Criteria

#### 4.6.1 Inclusion Criteria

- Elective patients of all age group who underwent elective neurosurgery

#### 4.6.2 Exclusion Criteria

- Patient who underwent repeat craniotomy

### 4.6 Sample size determination& Sampling technique

The sample size was determined based on a single population proportion using Epi info version 7 Stat Calc computer program by assuming that 50% of the patients IOH during neurosurgery (to obtain the maximum representative sample size since no similar study was found in the area) with 95% confidence interval (CI) and 5% margin of error**.** Population correction was used since the source population is <10,000. Situational analysis of neurosurgeries was done on the 3 months before the start of the study and an average of 45 procedures is done per month.

Hemodynamic and airway pressure change (p) =50%

Confidence Level = 95%

Margin of error =5%

After obtaining sample size of n=196 and adding 10%for incomplete data total sample size of **n=206** was obtained.

Due to rarity of the surgical procedure, all eligible patients who underwent Neurosurgery between December 20, 2016 and May 20, 2017 were included in the study.

### 4.7 Variables

#### 4.7.1 Dependent variable

- Intraoperative Hypotension

#### 4.7.2 Independent variables

**Patient related variables:**

- American Society of Anesthesiologists (ASA) physical status
- Comorbidities
- Electrolyte Imbalance
- Medications
- Age
- Midline shift
- Multiple masses
- Diagnosis
- Baseline Blood pressure (BP)
- Multiple Masses

**Anesthesia related variables:**

- Anesthesia drugs used

**Procedure related variables**:

- Position of the patient
- Blood loss during surgery

## 4.8 Operational definitions

1. **American Society of Anesthesiologists (ASA) physical status classification:** developed by the ASA taskforce which classify patients according to their physical status (systemic well being)

   **ASA class I**: normal healthy patient except the surgical compliant he had

   **ASA class II**: a patient with a mild systemic disease without substantive functional limitation

   **ASA class III**: a patient with severe systemic disease with substantive functional limitation

   **ASA class IV**: a patient with severe systemic disease that is a constant threat to life

   **ASA class V**: moribund patient who is not expected to survive without the operation
2. **Baseline value:** measurement taken before induction
3. **Hypotension:** a decrease in ≥30% from baseline value or for adults SBP<80mmHg
4. **Hypertension**: an increase in ≥30% from baseline value or for adults SBP>160mmHg
5. **Tachycardia:** an increase in heart rate of ≥20% of the baseline value
6. **Bradycardia**: a decrease in ≥30% from baseline value
7. **Episode**: for hypotension or hypertension that lasts for ≥ 5 minutes or that requires therapeutic action of the attending anesthetist, such as administering fluids or a vasopressor, for bradycardia and tachycardia an episode is a single measurement.

**4.9 Data collection procedure:** After Briefing of the data collectors who are anesthetists (2nd year Msc students and Anesthesiology residents) data was collected from all eligible patients after informed consent was obtained. Medication, Comorbidity and medical history were extracted from patient records. Airway pressure was monitored by integrated airway pressure monitors on the Aeonmed Gloryplus® and Mindray® anesthesia machines. Blood pressure was monitored using automatic non invasive blood pressure monitor and invasive Arterial Blood pressure monitoring system. Pulse oximeter and electrocardiograph was used to measure pulse rate and are electronically collected data. Midline shift was taken from official reports from attending Radiologists. Episodes of hemodynamic changes were recorded including the time they occurred. Total blood loss, Anesthesia time and amount of fluid given were recorded from anesthesia chart.

**4.10 Data quality assurance**: Briefing and explanation was given for data collectors on the data collection tool. Collected data were checked once a week for its completeness, clarity, consistency and accuracy by the principal investigator. In case of missed measurement electronic data store of the machines were recalled and back traced data was filled.

**4.11 Data analysis:** Data was coded, entered, cleaned and edited using Epi Info version 7 and exported to Statistical package for Social Sciences (SPSS) software version 20.0. Using SPSS basic descriptive statistics like frequency of preoperative and intraoperative factors, socio demographic variables and prevalence of Hemodynamic and airway pressure changes was done. Multivariable logistic regression analyses were carried out to examine the predictors of the outcome variable. On binary logistic regression analysis, a P-value of $\leq 0.2$ was used as a candidate for multivariable logistic regression analysis. For both Crude Odds Ratio (COR) and Adjusted Odds Ratio (AOR), P value of $<0.05$ reflects significance.

**4.12 Ethical considerations:** permission was obtained from Addis Ababa university ethical committee before the start of the research. The hospital administrators received letters containing objective and purpose of the research. Data collectors took informed consent orally from each patient to collect data. During the data collection process. Norms, values and morals of patients were respected by data collectors.

## 5. Results

### 5.1 Preoperative characteristics of patients

During the study period data was collected from 216 patients. A total number of 208 patients were included in the analysis after 8(3.7%) patients were removed due to incomplete data. The median age of patients was 42 ±24. Most of the patients were ASA II and had Midline shift of 0-5 mm. With regard to Comorbidities 3(1.4%) patients had Asthma, 1 (0.5%) patient had retroviral infection, 1(0.5%) was with Diabetes Mellitus and 7 (3.4%) had Hypertension.

**Table 1: Pre operative characteristics of patients who underwent elective Neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017**

| | Category | Frequency |
|---|---|---|
| **Sex (n=208)** | Male | 110 (52.9%) |
| | Female | 98 (47.1%) |
| **ASA status (n=208)** | 1 | 82 (39.4%) |
| | 2 | 126 (60.6%) |
| **Diagnosis (n=208)** | CPA Mass | 28 (13.5%) |
| | CSM | 37 (17.8%) |
| | Intracranial Mass | 26 (12.5%) |
| | Lumbar Radiculopathy | 25 (12.0%) |
| | Meningioma | 39 (18.8%) |
| | Obstructive Hydrocephalus | 14 (6.7%) |
| | Pitutary Macroadenoma | 12 (5.8%) |
| | Posterior Fossa Tumor | 27 (13.0%) |
| **Midline shift (n=48)** | ≤ 5 mm | 195 (93.7%) |
| | ≥ 6 mm | 13 (6.3%) |

| | | |
|---|---|---|
| **Medication History (n=52)** | Calcium Channel Blockers | 6(11.5%) |
| | Hydrocortisone | 1(1.9%) |
| | Insulin | 1(1.9%) |
| | Phenytoin | 44(84.7%) |

**CPA Mass**= Cerebellopontine Angle mass; **CSM**= Cervical Spondylotic Myelopathy

### 5.2 Intraoperative characteristics

All of the 208(100%) patients underwent their surgeries under General Anesthesia with Endotracheal intubation. Intraoperative anesthesia was maintained with volatile anesthesia (≤1minimum alveolar concentration). Intermittent boluses of fentanyl (30-100mcg) were used for Intraoperative pain control for 189(90.9%) patients), 4(1.9%) patients were given a combination of Fentanyl and Tramadol and Tramadol only was used for 23(11.1%) patients.

**Table 2: Intraoperative Characteristics of patients who underwent elective Neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017**

| | **Category** | **Frequency** |
|---|---|---|
| **Procedure name (n=208)** | ACDF | 27 (13.0%) |
| | Craniotomy | 120 (57.7%) |
| | ETV | 14 (6.7%) |
| | Laminectomy | 35 (16.8%) |
| | TSS | 12 (5.8%) |
| **Position of Patients (n=208)** | Prone | 107 (51.4%) |
| | Supine | 101 (48.6%) |
| **Anesthesia induction Agent** | Propofol | 83 (39.9%) |
| | Thiopentone | 125 (60.1%) |

| | | |
|---|---|---|
| **Anesthesia Maintainance Agent** | Isoflurane | 191 (91.8%) |
| | Halothane | 17 (8.2%) |

**ACDF**= Anterior Cervical Discectomy and Fusion; **TSS**= Transsphenoidal Surgery; **ETV**-=endoscopic Third Ventriculostomy

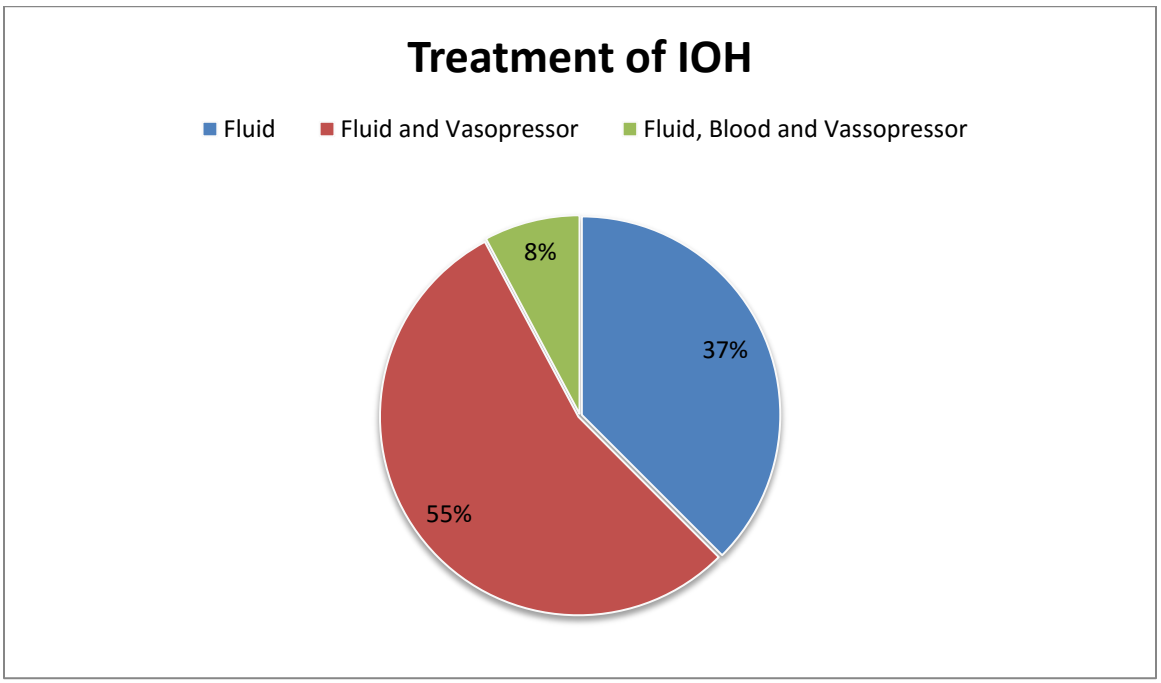


**Figure 1: Treatment of intraoperative hypotension for patients who underwent elective Neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017**

Mannitol 0.5-1g/kg was given 120 (57.7%) patients who underwent craniotomy. Invasive monitoring with arterial catheter was used on 39(18.8%) patients. Treatment of intraoperative hypotension is at the accord of the attending anesthetist or anesthesiologist. Adrenaline was used on 10(4.8%) and Phenylephrine was used on 7(3.4%) patients for treatment of hypotension.

**Table 3: Intraoperative Characteristics of patients who underwent elective Neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017**

| **Variable** | Median ± IQR |
|---|---|
| **Fluid Given (L) (n=208)** | 3 ± 2.3 |
| **Urine Output (L) (n=208)** | 1.4 ± 1.2 |
| **Blood loss (L) (n=208)** | 0.5 ± 0.7 |
| **Fluid Balance (L)(n=208)** | 0.44 ± 1.11 |
| **Blood Given (mL) (n=208)** | 161.06 ± 370 |
| **Anethesia Duration (min) (n=208)** | 260± 165 |
| **Baseline BP (mmHg) (n=208)** | 123.5 ± 15.75 |

**L**= Liter; **Min**= Minutes; **mL**= Milliliter

### 5.3 Magnitude of airway pressure and Hemodynamic change

IOH occurred in 61(29.3%) with lowest intraoperative systolic blood pressure median value of 74± 19. Frequencies and percentages of Magnitude of airway pressure and Hemodynamic change are presented on tables below.

**Table 4: Magnitude of Hemodynamic change of patients who underwent elective Neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017**

| Variable | Frequency | Percent |
|---|---|---|
| **Hypertension (n=208)** | 2 | 1% |
| **Hypotension (n=208)** | 61 | 29.3% |
| **Tachycardia (n=208)** | 2 | 1% |
| **Bradycardia (n=208)** | 5 | 2.4% |

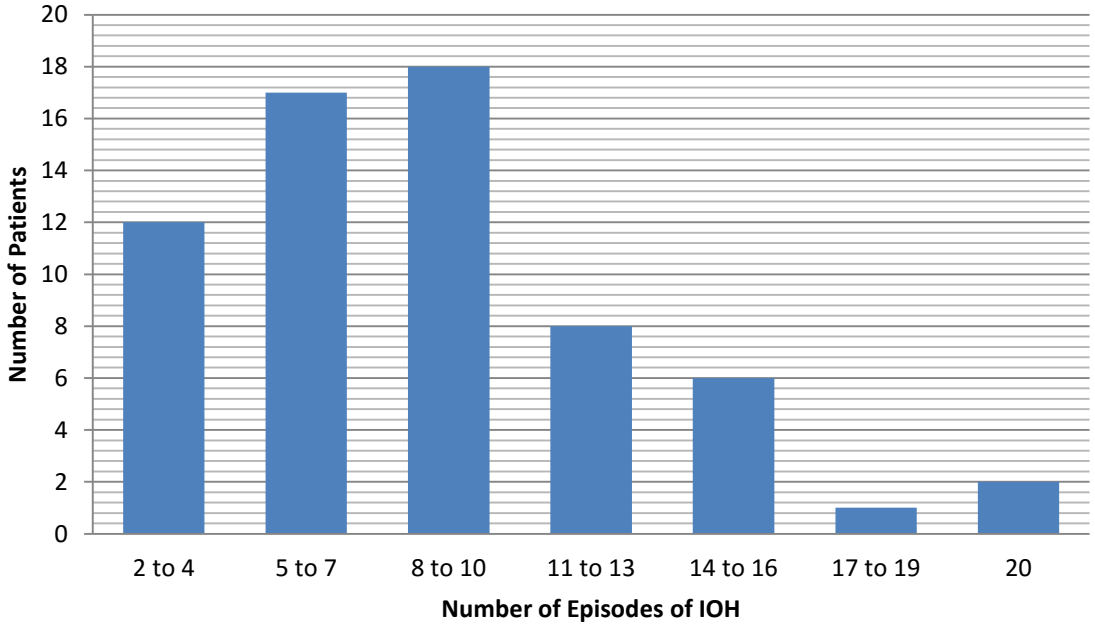


**Figure 2: Number of episodes of IOH during Neurosurgery**

Prone position was adopted for 107(51.4%) of patients after they are intubated. The patients PAP and mean airway pressure showed increase from baseline immediately after patients are turned to prone.

**Table 5: Magnitude of Airway pressure change for prone position on patients who underwent elective Neurosurgery at TASH and Empress Zewditu memorial hospital from December 20, 2016 to May 20, 2017 (n=107)**

| Variable | After securing the airway (Before position change) (Median ± IQR) | Immediately after position Change (Median ± IQR) | 30 mins after position Change (Median ± IQR) |
|---|---|---|---|
| **PAP** | 15±5 | 17±5 | 17±4 |
| **Mean Airway Pressure** | 6±2 | 7±2 | 7±1 |

***PAP**- Peak Airway Pressure

### 5.4 Factors associated with Intraoperative hypotension

#### 5.4.1 Result of Bivariate analysis

Binary logistic regression analysis was conducted for factors that could possibly affect the presence of IOH. The result of the bivariate analysis presented in a table below showed significance preoperative and intraoperative factors such as ASA classification of patients and Midline shift.

**Table 6: Preoperative and intraoperative factors associated with IOH in TASH and Zewditu Memorial Hospital**

| Variables | Hypotension | | COR (95% CI) | P-value |
|---|---|---|---|---|
| | Yes | No | | |
| | n(%) | n(%) | | |
| **Age** | | | | |
| <20 | 3(17.6%) | 14(82.4%) | 1.00 | |
| 20-59 | 54(30.9%) | 121(69.1%) | 2.08(0.57-7.54) | 0.264 |
| >60 | 3(18.8%) | 13(81.2%) | 1.07(0.18-6.31) | 0.93 |
| **Sex** | | | | |
| Female | 28(28.6%) | 70(71.4%) | 1.00 | |
| Male | 33(30%) | 77(70%) | 1.07 (0.58-1.95) | 0.821 |
| **ASA class** | | | | |
| 1 | 7(8.5%) | 75(91.5%) | 1.00 | |
| 2 | 54(42.9%) | 72(57.1%) | 8.03(3.43-18.82)** | **0.0001** |
| **Diagnosis** | | | | |
| CSM | 1(8.1%) | 34(91.9%) | 1.00 | |
| CPA Mass | 14(50%) | 14(50%) | 11.33(2.81-45.66)** | **0.001** |
| Intracranial Mass | 5(19.2%) | 21(80.8%) | 2.69(0.58-12.47) | 0.204 |
| Lumbar Radiculopathy | 1(4%) | 24(96%) | 0.47(0.04-4.81) | 0.527 |
| Meningioma | 21(53.8%) | 18(46.2%) | 13.22(3.47-50.38)** | **0.0001** |
| Obstructive Hydrocephalus | 1(7.1%) | 13(92.9%) | 0.87(0.08-9.15) | 0.909 |
| Pitutary Macroadenoma | 1(8.3%) | 11(91.7%) | 1.03(0.09-10.94) | 0.980 |
| Posterior Fossa Tumor | 15(55.6%) | 12(44.4%) | 14.16(3.48-57.64)** | **0.0001** |
| **Midline Shift** | | | | |
| ≤ 5 mm | 52(26.7%) | 143(73.3%) | 1.00 | |
| ≥ 6 mm | 9(69.2%) | 4(30.8%) | 6.18(1.82-20.95)** | **0.003** |
| **Mannitol** | 55(45.8%) | 65(54.2%) | 0.846(0.09-10.54) | 0.362 |

| | | | | |
|---|---|---|---|---|
| **Position of Patient** | | | | |
| Supine | 20(19.8%) | 81(80.2%) | 1.00 | |
| Prone | 40(37.4%) | 67(62.6%) | 2.51(1.34-4.70)** | **0.004** |
| **Induction Agent** | | | | |
| Thipentone | 35(28%) | 90(72%) | 1.00 | |
| Propofol | 26(31.3%) | 57(68.7%) | 1.17(0.64-2.15) | 0.606 |
| **Maintainance Agent** | | | | |
| Isoflurane | 60(31.4%) | 131(68.6%) | 1.00 | |
| Halothane | 1(5.9%) | 16(94.1%) | 0.13(0.01-1.05)** | **0.056** |
| **Baseline BP** | | | | |
| ≤139 | 50(27.3%) | 133(72.7%) | 1.00 | |
| ≥140 | 11(44%) | 14(56%) | 2.09(0.89-4.90)** | **0.091** |
| **Medication Taking** | | | | |
| No medication | 31(19.9%) | 125(80.1%) | 1.00 | |
| Phenytoin | 27(61.4%) | 17(38.6%) | 6.40(3.10-13.19)** | **0.0001** |
| Others | 3(37.5%) | 5(62.5%) | 2.41(0.54-10.67) | 0.223 |
| **Multiple Mass** | | | | |
| No | 47(25%) | 141(75%) | 1.00 | |
| Yes | 14(70%) | 6(30%) | 7(2.54-19.25)** | **0.0001** |
| **Total Blood loss** | | | | |
| <10 ml/Kg | 15(11.8%) | 112(88.2%) | 1.00 | |
| >10ml/Kg | 46(56.8%) | 35(43.2%) | 9.81(4.89-19.67)** | **0.0001** |

**** statistically significant**

### 5.4.2 Result of Multivariable Analysis

After excluding variables which doesn't fit for the model using P-value >0.2 in Likelihood ratio test, multivariable analysis was performed. The result showed Patients taking phenytoin as a medication for epilepsy or prophylaxis seizure and patients with blood loss of >10ml/kg have a higher risk to develop IOH.

**Table 7: Preoperative and intraoperative factors associated with IOH in TASH and Zewditu Memorial Hospital**

| Variables | Hypotension | | COR (95% CI) | AOR (95% CI) | P-value |
|---|---|---|---|---|---|
| | Yes | No | | | |
| | n(%) | n | | | |
| **ASA class** | | | | | |
| 1 | 7(8.5%) | 75 | 1.00 | 1.00 | |
| 2 | 54(42.9%) | 72 | 8.03(3.43-18.82) | 0.858(0.17-4.12) | 0.848 |
| **Diagnosis** | | | | | |
| CSM | 1(8.1%) | 34 | 1.00 | 1.00 | |
| CPA Mass | 14(50%) | 14 | 11.33(2.81-45.66) | 0.44(0.03-5.06) | 0.512 |
| Intracranial Mass | 5(19.2%) | 21 | 2.69(0.58-12.47) | 0.28(0.02-2.98) | 0.297 |
| Lumbar Radiculopathy | 1(4%) | 24 | 0.47(0.04-4.81) | 0.23(0.01-2.98) | 0.267 |
| Meningioma | 21(53.8%) | 18 | 13.22(3.47-50.38) | 2.71(0.35-16.08) | 0.375 |
| Obstructive HCP | 1(7.1%) | 13 | 0.87(0.08-9.15) | 1.53(0.12-18.42) | 0.738 |
| Pitutary Macroadenoma | 1(8.3%) | 11 | 1.03(0.09-10.94) | 1.04(0.077-14.09) | 0.974 |
| Posterior Fossa Tumor | 15(55.6%) | 12 | 14.16(3.48-57.64) | 2.82(0.33-23.82) | 0.340 |
| **Midline Shift** | | | | | |
| ≤ 5 mm | 52(26.7%) | 143 | 1.00 | 1.00 | |
| ≥ 6 mm | 9(69.2%) | 4 | 6.18(1.82-20.95) | 1.52(0.27-8.48) | 0.628 |
| **Position of Patient** | | | | | |
| Supine | 20(19.8%) | 81 | 1.00 | | |
| Prone | 40(37.4%) | 67 | 2.51(1.34-4.70) | 2.42(0.64-9.06) | 0.188 |

| | | | | | |
|---|---|---|---|---|---|
| **Maintainance Agent** | | | | | |
| Isoflurane | 60(31.4%) | 131 | 1.00 | | |
| Halothane | 1(5.9%) | 16 | 0.13(0.01-1.05) | 0.71(0.06-7.90) | 0.708 |
| **Baseline BP** | | | | | |
| ≤139 | 50(27.3%) | 133 | 1.00 | | |
| ≥140 | 11(44%) | 14 | 2.09(0.89-4.90) | 2.23(0.58-8.51) | 0.785 |
| **Medication Taking** | | | | | |
| No medication | 31(19.9%) | 125 | 1.00 | 1.00 | |
| Phenytoin | 27(61.4%) | 17 | 6.40(3.10-13.19) | 6.96(1.97-24.50)** | **0.002** |
| Others | 3(37.5%) | 5 | 2.41(0.54-10.67) | 4.05(0.51-31.89) | 0.184 |
| **Multiple Mass** | | | | | |
| No | 47(25%) | 141 | 1.00 | 1.00 | |
| Yes | 14(70%) | 6 | 7(2.54-19.25) | 1.86(0.52-6.60) | 0.332 |
| **Total Blood loss** | | | | | |
| <10 ml/Kg | 15(11.8%) | 112 | 1.00 | | |
| >10ml/Kg of TBV | 46(56.8%) | 35 | 8.18(4.13-16.18) | 5.77(1.97-16.83)** | **0.001** |

**** Statistically significant**

## 6. Discussion

The magnitude of IOH was found to be 29.3% (95% CI: 22%-35%). This magnitude is lower than a study done by D.Sharma et al where 65% (n=73) of the patients had at least one episode of hypotension.(11) But it is close to the result of a research conducted by G.Singh et.al in which the magnitude of hypotension is reported as 16.6% and with Korkomaz et.al who stated an IOH incidence of 18.6% in pediatrics and 37.6% in adults.(33,36) The higher incidence of hypotension on the study conducted by D. Sharma et al may be attributed to the frequent use of intra-arterial invasive monitoring which have better detection ability of IOH . The increased IOH incidence during neurosurgery can be associated to ongoing surgery, fluid shifts and exposure to anesthetic agents which have hypotensive effects.(40,41) Another basis for its incidence can be surgical intervention with dural opening causing decompression hypotension which is thought to result from sudden loss of the Cushing's response.(42,43) Turning the patient prone from the supine position increases intra-abdominal pressure, decreases venous return to the heart, and increases systemic and pulmonary vascular resistance with pooling of venous blood in the lower part of the body occurs ultimately decreasing venous return and causing hypotension.(44,45)

Intraoperative Hypertension is found to be at magnitude of 1% (95%CI: 0.0%-2.4%), which is lower than a study done by G.Singh et.al in which 16.1% of the patients had hypertension.(33) The difference in magnitude might be credited to a change of socio-demographic characteristic where the study used 119 pediatric patients out of the total 223 studied. Hypertension during neuro surgery can be precipitated by an acutely raised ICP.

With regard to bradycardia and tachycardia this study found a magnitude of 2.4% (95%CI: 0.5%-4.8%) and 1% (95%CI: 0.0%-2.9%) respectively, much lower than El-dawlalty et al study which reported bradycardia incidence of 41%.(31) It is also lower than in studies done by G.Singh et al and Ganjoo et al with bradycardia incidences of 11.3% and 12% respectively. Their incidence of tachycardia is also higher than this study with a result of 18.8% and 20% respectively.(11,32) The change in incidence can be caused by the fact that all three studies used data from ETV, a procedure associated with higher incidence of heart rhythm disturbance. These responses in heart rate can be caused due to acute rises in ICP secondary to continuous use of high-speed irrigation or obstruction to the outflow of fluid leading to impairment of cerebral perfusion.(46–48)

Korkomaz et al also noted a tachycardia and bradycardia incidence of 8.8% in adults and 13.1% in pediatrics.(36) The increase in incidence might be associated to a difference in operational definitions with the above research defining bradycardia as heart rate of <50 and tachycardia as heart rate of >90.

The PAP after the patients are turned to prone rose to median of 17±5 from a measurement of 15±5 at the supine position. E.M Mana et al also reported an increase in PAP from 15.42 ± 2.50 to 17.75 ± 2.73 when patients are turned to prone. E, M Manna et al and A.Malhotra et al concluded that there is an increment in mean airway pressure the only difference being the percentage. This research obtained a 21% increase whereas E, M Manna et al and A.Malhotra et al found an increase in mean airway pressure of 5.3% and 0.6% respectively.(37,39) This change might be caused by the formers smaller sample size of 12, difference at measurement times and different setup of Operation Theater.

Significant association is found between blood loss of greater than 10ml/Kg and IOH. Patients with blood loss of >10ml/Kg are observed to have >5 fold risk [AOR=5.77; 95% CI :( 1.97, 16.83)] of developing hypotension. This result is supported by a study made by P. Miller.(30) The reason for this result might be associated the appearance of IOH with hypovolemia that follows blood loss.

There is significant risk of IOH on patients who are taking Phenytoin as a treatment or prophylaxis for seizure. There was about 7 times risk [AOR=6.96; 95% CI: (1.97-24.50)] to develop hypotension in reference to patients taking no medication. Even though similar studies couldn't be found for comparison, the result is supported by American Food and Drug Association. Hypotension caused by Phenytoin arises by depression of myocardial contractility and decreased peripheral vascular resistance (49)

We did not find any association among anesthesia induction and maintainance agents with IOH. Since total intravenous anesthesia was not used for patients in this study, we cannot make a comment on the relative effect of inhalational versus intravenous anesthetic agents on IOH.

## 7. Conclusion and Recommendations

### 7.1 Conclusion

The findings of this study have shown that overall magnitude of IOH was 29.3% in patients who underwent elective neurosurgery at TASH and Zewditu Memorial Hospital. Hypertension, Bradycardia and tachycardia had magnitudes of 1%, 2.4% and 1% respectively.

There is also a 28.9% and 21% increment in PAP and MAP respectively when patients are turned to prone.

Factors that have association with IOH were Phenytoin use and blood loss of >10ml/Kg.

### 7.2 Recommendations

Based on the findings of the present study, the following recommendations are forwarded:-

- ✓ **For Anesthetists**
  - Precaution for estimated>10ml/kg in Intra-op blood loss.
  - Early preparation for Patients who are taking Phenytoin.

- ✓ **For researchers**
  - Considering this study as a baseline a further long term multicenter cohort study is recommended.

## 8. Strengths and Limitations of the study

### 8.1 Strengths of the study

- It used electronically collected data.
- It assessed magnitude of multiple variables.

### 7.2 Limitation of the study

- It did not study complications and long term outcome of patients.
- Some secondary data was included in the study.

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**Annexes**

**Annex 2: Information Sheet (English version)**

**Addis Ababa University College of Health Sciences**

**School of medicine**

**Department of Anesthesia**

**Consent form**

Hello, my name is _____ and I am a data collector for research aimed at assessing the incidence of hemodynamic and airway pressure change and factors associated with Intraoperative hypotension during elective neurosurgery. Since the study is not linked with any financial aid there is no direct incentives paid as a result of you taking part in the study. However, your legitimate participation in filling the questionnaire with real information is very important and highly appreciated.

I would like to assure you, that your name will not be written on this form and all the information gathered will be kept strictly confidential.

You can decide whether you want to take part in the questionnaire or not. I would like to assure you that there is no negative impacts you face because of not taking part in the study. Please feel free to ask any questions data collector nearby.

You can also contact principal investigator with address below:

1. gyonas0@gmail.com +251912239281

We appreciate your response to us and thank you for giving us your time.

**Annex 3: Information Sheet (Amharic version)**

የአዲስአበባ ዮኒቨርስቲ

የህክምና እና ጤፍ ሳይንስ ኮሌጅ

የአንስቴሽያ ት/ክፍል

ጤፍ ይስጥልን እኔ_____እባላለሁ፡ በአእምሮ እና የጀርባ አጥንት ቀዶ ጥገና ላይ የሚሰቱ የሞትንፈሻ፣ የደም ግፊት እና የልብ ምት ለውጦች ላይ የሚደራ ጥናት ሚጃ ሰብሰቢ ነኝ:: ጥናቱ ለእርሶ ምንም አይነት የገንዘብ ጥቅም አያስገኝም ነገርግን የጥናቱ ውጠጌ በህክምና ዘርፍ ላይ ያሉትን ችግሮች ለመቅረፍ እና የታካሚዎችን ደህንነት የሚደረጋግጡ ህጎች እንዲስተካከሉ እና ሥራ ላይ እንዲውሉ የበኩሎን አስተዋፅዖ ያበረክታሉ፡፡ ስምም በዚህ ጥናት ላይ አይፃፍም፡ ስለዚህም የእርሶ ምላሽ ሚስጥራዊነቱ የተጠበቀ ነው፡:በዚህ ማስይቅ ላይ ለመሳተፍ መቀመጭም ሆነ አለመቀመጭ ይችላሉ፡፡ ባለመቀመጮ ምንም የሚዱት ነገር የለም፡

ምንም አይነት ጥያቄ ካለዎት ቀጥሎ በተፃፈው አድራሻ ተሙሚወዳ ማገኘት ይችላሉ፡፡

1. ግሩም ዮናስ (ዋና ተሙሚ)

ኢሜይል -gyonas0@gmail.com ስልክ +251912239281

2. አዳኛ አረጋዊ (አዲስ አበባ ዩኒቨርሲቲ ማሞር እና የጥናቱ አማክሪ)

በማስይቁ በመቀመጮ ከልብ አመሰግናለሁ::

የሚጃ ሰብሰቢ ስም ፊርማ

ስም_____ፊርማ_____ቀን_____

**Annex 4: Questionnaire**

**A QUESTIONNAIRE FOR A RESEARCH ON MAGNITUDE OF HEMODYNAMIC AND AIRWAY PRESSURE CHANGE AND FACTORS ASSOCIATED WITH HEMODYNAMIC CHANGES DURING ELECTIVE NEUROSURGERY AT BLACK LION AND EMPRESS ZEWDITU MEMORIAL HOSPITAL FROM DECEMBER 20, 2016 TO MAY 20, 2017.**

**1. Socio-demographic Data**

Age _____ Sex _____ Weight _____

**2. Associated Factors**

1. ASA _____
2. Diagnosis _____
3. Name of Procedure _____
4. Position of the patient Supine ☐ Prone ☐ Sitting ☐ Lateral ☐

| No. | Question | Answer | If "No" skip to question |
|---|---|---|---|
| 5. | Does the patient have co-morbidity? | | 7 |
| 6. | What is the disease? | | |
| 7. | Is the patient taking any medication? | | 9 |
| 8. | What is the drug/s? | | |
| 9. | Is there electrolyte imbalance? | | 11 |
| 10. | What is the electrolyte imbalance? | | |

11. Amount of preloading fluid given _____ml

12. Premedication drugs given _____

13. BP Monitoring Invasive ☐ Non-invasive ☐

14. Drugs -Induction Ketamine _____mg Thiopentone _____mg Propofol _____mg

-Relaxant Sux ☐ Atracurium ☐ Vecuronium ☐ Pancuronium ☐

-Maintainance Halothane ____MAC Isoflurane ____MAC -Other _____mg

- Opioid_____ mg - Other Analgesic _____ mg

15. Ventilation Controlled ☐ Spontaneous ☐

16. Tidal volume _____ ml

17. Midline shift Yes ☐ No ☐ _____mm

18. Multiple Masses Yes ☐ No ☐

**3. Vital sign**

| **Vital sign** | **Baseline** | **Post induction** | **1st hr** | **2nd hr** | **3rd hr** | **4th hr** | **5th hr** | **6th hr** | **7th hr** |
|---|---|---|---|---|---|---|---|---|---|
| MAP | | | | | | | | | |
| BP | | | | | | | | | |
| PR | | | | | | | | | |
| Blood loss | | | | | | | | | |
| Fluids given | | | | | | | | | |
| Urine output | | | | | | | | | |

**4. Airway pressure**

| Parameter | Baseline | Immediately after securing the airway | Immediately after Position change | 30 minutes after position change |
|---|---|---|---|---|
| Peak airway pressure | | | | |
| Mean airway pressure | | | | |
| MAP | | | | |
| BP | | | | |

**5. Incidence**

**I. Hypotension**

- Number of episodes: _____
- Blood pressure values:_____ _____

_____

- Duration of each episode: _____
- Intervention done: _____

**II. Hypertension**

- Number of episodes: _____
- Blood pressure values:_____ _____

  _____
- Duration of each episode: _____
- Intervention done: _____

**III. Bradycardia**

- Number of episodes: _____
- Heart rate values:_____ _____

  _____
- Duration of each episode: _____
- Intervention done: _____

**IV. Tachycardia**

- Number of episodes: _____
- Heart rate values:_____ _____

  _____
- Duration of each episode: _____
- Intervention done: _____

12. Duration of the Anesthesia _____ minutes and surgery _____minutes.
13. Total amount of intravenous fluids given in intra op period _____ml
14. Total urine output _____ ml
15. Total blood loss _____ml
16. Total amount of blood given _____ml
17. Mannitol _____gram

Name of Data collector_____ Sign _____

Name of Supervisor_____ Sign_____