A COMPARATIVE STUDY ON THE EFFECTS OF DRY ELECTROLYTE BALANCED HEPARIN VERSUS LIQUID HEPARIN ON ARTERIAL BLOOD GAS PARAMETERS IN CRITICALLY ILL PATIENTS.

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A DISSERTATION SUBMITTED IN PART-FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE IN ANAESTHESIA AT THE UNIVERSITY OF NAIROBI.

DECLARATION

I, **Dr. Emma Ngarama,** do hereby declare that this proposal is my original work, and it has not been presented before either in whole or part to this institution or any other institution elsewhere for academic qualification.

I further declare that all material cited in this report which are not my own have been duly acknowledged.

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DEDICATION

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ABBREVIATIONS

ABG	Arterial Blood Gas
ASA	American Society of Anaesthesiologists
BGA	Blood Gas Analysis
CCU	Critical Care Unit
DBH	Dry Electrolyte Balanced Heparin
G.A	General Anaesthesia
HCO_3^-	Bicarbonate.
IFCC	International Federation of Clinical Chemistry
iCa^{2+}	Ionized Calcium.
ICU	Intensive Care Unit
IPC	Infection and Prevention Control
K^+	Potassium
K.N.H	Kenyatta National Hospital
LH	Liquid Heparin
Mg^{2+}	Magnesium
Na^+	Sodium
pCO_2	Partial Pressure of Carbon dioxide
pO_2	Partial Pressure of Oxygen.
pH	Potential of Hydrogen.
PICU	Paediatric Intensive Care Unit
STATA	Software for Statistics and Data Science
TEa	Total Allowable Error
WHO	World Health Organization

ABSTRACT

Background: Arterial Blood gas (ABG) analysis is an important investigation and diagnostic tool done on patients admitted in Critical Care Units (CCUs). ABG analysis is used to monitor acid base balance and effectiveness of gas exchange. It is also important in evaluating response to therapeutic and diagnostic interventions, electrolyte and metabolite imbalances and even monitoring progress and severity of diseases. This information enables clinicians in effective diagnosis and management of life-threatening pathophysiological processes in critically ill patients, which greatly improves their prognosis and outcomes**.** Multiple errors are encountered during the ABG analysis process. ABG samples require artificial anticoagulation with heparin to prevent in-vitro clotting.

Objective: To evaluate the effects of Dry electrolyte balanced heparin compared to Liquid heparin on arterial blood gas parameters.

Design: A comparative cross-sectional study involving 46 patients admitted at the Kenyatta National Hospital (KNH) Main CCU.

Methodology: Patients aged 18 years and above admitted to the KNH Main CCU were enrolled consecutively upon admission to the CCU. Two ABG samples were collected from the same patient concurrently, one in a dry electrolyte balanced heparin syringe and the second in a syringe coated with liquid heparin. They were analyzed using the *ABL800 FLEX* blood gas analyzer and the LH ABG parameters compared to DBH ABG parameters.

Data Analysis: Patients' demographic and clinical characteristics were analyzed and presented as frequencies and proportions. The paired samples t-tests method was used to elucidate the strength of association between the two sets of ABG parameters upon the use of LH and DBH. The statistical significance level was set at $\alpha=0.05$. Comparative data analysis was conducted using the Bland Altman methodology

Results: This study established clinically equivalent results for pH, pO_2, pCO_2, HCO_3, K^+ and Hemoglobin between the LH and DBH group. However, the differences in Na^+ and Cl^- between the two groups were statistically significant. The additives in LH upregulated the two parameters.

Conclusion: There was no significant advantage of using DBH over LH for ABG anticoagulation of pH, pO_2, pCO_2, HCO_3 and haemoglobin. When the LH has been flushed out completely, the LH and DBH syringes could be used interchangeably for these parameters. Liquid Sodium Heparin affected Na and CL electrolytes, even in very small amounts. DBH would be the preferred anticoagulant when assessing these two electrolytes.

1.0 CHAPTER ONE: INTRODUCTION

The use of point of care arterial blood gas analysis (ABG) is an important investigation and diagnostic tool for patients admitted in Critical Care Units(1). ABG analysis is done by collecting an arterial blood sample in a heparinized syringe from a patient and subjecting it for analysis via a blood gas analyzer. The blood gas analyzer then gives results in form of ABG parameters (2).

ABG analysis is used to monitor acid base balance and effectiveness of gas exchange(3). It is also important in evaluating response to therapeutic and diagnostic interventions, electrolyte and metabolite imbalances and even monitoring progress and severity of a disease(4). This enables clinicians in effective diagnosis and management of life-threatening pathophysiological processes in critically ill patients (5) which in turn improves patient prognosis and outcomes(1)

Heparin is the only recommended anticoagulant for use in ABG analysis(11) and is available in two forms; Liquid heparin (LH) and Dry Electrolyte balanced heparin (DBH)(12). LH (sodium, lithium) is associated with dilutional, binding and chemical properties that effect ABG parameters, resulting in erroneous ABG parameters(13). The Clinical and Laboratory Standards Institute guidelines approve the use of the recommended standard DBH, but due to costs factors, most institutions in poor resource countries still use LH (14). DBH has been specially formulated to eliminate the erroneous effects associated with the use of LH on ABG parameters (15).

In the absence of DBH, the IFCC guidelines recommend the use of minimal amounts of LH to exterminate these errors(16). It has not been established whether the ABG parameters after using minimal amounts of LH matchup to DBH parameters. The aim of this study was to compare the effects of DBH to LH on arterial blood gas parameters.

2.0 CHAPTER TWO: LITERATURE REVIEW

2.1. Background

The first Blood gas analysis was performed in 1957, when John Severinghaus developed the first blood gas analyzer that measured pH, pCO_2, and pO_2. In 1985, the first combined blood gas and electrolyte analyzer was introduced, and it was able to measure pH, pCO_2, pO_2, Na^+, K^+, $iCa^+$and hematocrit. Blood gas analysis has evolved over time, and the current point of care machines can measure more parameters like iMg, metabolites (glucose, lactate, urea and creatinine), oxygen saturations and co- oximetry within minutes(17).

A blood gas sample can be obtained anywhere within the circulatory system i.e. artery, vein or capillary (18). Using arterial blood samples in blood gas analysis is accepted as the gold standard (19). Arterial blood gas sampling is purely blood taken from an artery via arterial puncture or an indwelling arterial catheter, and is the first choice specimen for BGA for acid base balance , oxygenation and ventilation status(20). It is uniform in composition, and is independent of changes in local and chemical composition. The radial artery is the commonest site for arterial blood sampling by arterial puncture (20).

Aspiration of a homogenous arterial blood gas sample into a blood analyzer requires an artificially anticoagulated sample to prevent in vitro clotting. Clots in the sample can cause unreliable results and also block the analyzer(21).

Since inception of BGA, heparin has been the anticoagulant of choice. The syringes are prepared by inspiration of a small volume of liquid of heparin, which is then expelled out leaving a small coating on the walls of the syringe. This has been found to be sufficient to anticoagulate the collected blood sample(12). Heparin is still the only recommended anticoagulant for use in ABG(11). It is available in two forms, the first is liquid (sodium, Lithium) heparin, which is older and cheaper. The second is the newer preweighed dry electrolyte balanced heparin(12)**.** The pre-heparinized dry electrolyte balanced heparin is the recommended standard for anticoagulation of ABG syringes (14). It is widely used in well-resourced hospitals(12). However, there is risk of incomplete anticoagulation as it less easily mixes with blood and this can also introduce errors to ABG analysis. It is also expensive(11).

Liquid heparin (sodium, lithium) is still being used in most institutions in the world. This is due to the shortage of dry electrolyte balanced heparin and its high cost(16). Liquid heparin is associated with dilutional, binding and chemical properties effects that result in erroneous measured parameters(13). Multiple parameters are lowered by dilution effect of liquid heparin, with pCO2 being the most affected (22)(23)(24).These errors occurring in the preanalytical phase lead to incorrect diagnosis and improper treatment of patients (9). Misdiagnosis can result in a cascade of life-threatening outcomes including worsening of the underlying

pathological process(s) and/or development of new conditions. There will result in poor utilization of resources, increased hospital stay, more expenses on patients and stress to the patients and their next of kin(25).

Its dilution effects are due to its liquid nature and not chemical properties. It has a strong negative charge that binds to positively charged electrolytes in blood resulting in lower electrolyte values after ABG analysis (5). Liquid heparin is an acidic solution when equilibrated with air, with an approximate pH of 6.5, pO_2 of 160mmHg (21kpa) and pCO_2 of 7.5mmHg (1kpa) (11). Liquid sodium heparin is also associated with falsely high sodium levels(20). Sampling from indwelling arterial lines, that are continuously heparinized has also been recognized as one of the most common sources of laboratory errors(7).

2.2 Arterial Blood Gas Analysis Procedure

2.2.1 Sample Collection Procedures

Safe blood gas sample collection is recommended to obtain high quality results, by following set guidelines(13). The Procedure should be performed only by a health worker for whom the procedure is in their scope of practice(26). Patient assessment and identification, indication for ABG, pathology request form for ABG and informed consent from patient should be ascertained. This ensures that the process follows the defined ethical procedures and medical safety measures(20). Intensive hand hygiene should be maintained during the procedure, and use of personal protective equipment to ensure maximum safety and sanitation of the healthcare provider and the patient(26). The artery is located using appropriate landmarks and palpation and the site is disinfected with 70% alcohol, which is allowed to dry to prevent hemolysis(26).

The arterial site is then punctured and the needle gently advanced until free flowing bright red blood is encountered. A sufficient sample is collected into a heparinized syringe. Pre-heparinized syringes should be used in the procedure, with correct heparin concentration to reduce the risk of clots, which can have adverse negative effects on the ABG parameters(27). The use of a correct quantity of heparin is vital since excessive heparin can lead to bias on patient results while not enough will lead to inadequate anticoagulation(13).

A clean dry gauze/cotton wool should then be placed over the site of puncture and some pressure applied until bleeding stops(26). The air bubbles are safely removed and the syringe's vent closed with the tip cap to avoid contact with patients' blood(13) .The mixing of blood in the syringe is gently done by rotating the syringe between palms to ensure mixing of blood with heparin for 10 seconds(27). Correct labelling of the patient sample with a unique patient ID before leaving the patient and entering of the ID should be done in the analyzer before analysis to avoid patient sample mix-ups (13) .The final step is safe disposal of the sharp equipment and PPE, and hand hygiene(26).

2.2.2 Sample Storage Temperature and Time

After sample collection, cellular metabolism continues and is dependent on factors like storage temperature, time taken to analysis and patient factors(13). The sample is transported by hand in recommended syringes, without sudden vigorous movements as hemolysis and air contamination tends to occur with shaking(20). The sample should be sent to the laboratory immediately, and analyzed promptly. If this is not possible, it should be then stored in ice – water slurry for a maximum of 30 minutes to reduce cellular metabolism. If stored for too long, plastic syringes are partially permeable to gas, and this permeability increases with lower temperatures(27).

There is also an increased risk of hemolysis with lower temperatures. Glass syringes if available are recommended for use in ice slurry water(20). The ABG analysis within 30 minutes has been shown to give reliable results, except in patients with high leukocyte and platelet count when it should be analyzed within 5 minutes. High leukocyte and platelet count is associated with pseudo hypoxemia(20). If the time interval between sample collection and analysis exceeds 30 minutes, non-conformity should be recorded and a fresh sample collected(20). In such samples, pO_2, pH, and glucose have been shown to decrease while pCO_2 and lactate increase due to metabolism(13).

2.2.3 Sample Analysis and Quality Control

The first step in analysis is the comparison of the details on the sample to those on the pathology request form(20). Sample collection time should be noted and if one is not able to analyze immediately the specimens are stored appropriately for the recommended time(20).The special instructions on the pathology request form should be checked to ensure actions on emergency issues are addressed; for example the high leukocyte count for immediate analysis(20) . Sample integrity should be determined, especially for clots, air bubbles, insufficient volume and any other non-conformities, which should warrant recollection(20).

The following is the procedure for the analysis of the blood gas analyzer:

- Step 1: Enter patient details to the analyzer before analysis(20).
- Step 2: Introduce sample to the analyzer by aspiration from syringe(20).

The automated blood gas analyzers are commonly used to analyze the blood samples and results are produced immediately. They directly or indirectly (calculate) measure specific parameters of the ABG samples(28). The analyzer calibration, maintenance, quality checks and quality control measures are done as per the laboratory protocols and the manufacturer's recommendations(20).

2.3 Anticoagulation Using Heparin

Heparin is a naturally occurring anticoagulant in mammalian species, synthesized in mast cells and basophils and stored in their secretory granules. It was first isolated from liver tissue in 1916. Commercial preparations are mainly derived from mucosal intima of porcine intestines(11). Heparin is a complex carbohydrate, glycosaminoglycan, with a molecular weight that ranges from 3kDa to 30kDA. It has a unique highly sulphated pentasaccharide sequence, present in 30% of heparin molecules, which accounts for its anticoagulant effect(11). This pentasaccharide sequence binds avidly to antithrombin III and activates it more than 1000-fold. Antithrombin III is a plasma protein that inhibits blood clotting by binding and inhibiting enzymatic actions of activated clotting factors IIa, IXa, Xa, and XIa. This prevents fibrin formation. Heparin anticoagulation effect occurs both in vivo and in vitro. Its concentration is defined in International Units by the World Health Organization(11).

2.4 Recommended Guidelines on Liquid Heparin

To avoid potential dilutional errors, IFCC recommends that the volume of liquid heparin should be less than 10% and preferably equal to or less than 5% of the total sample volume (11) The liquid heparin should be flushed out completely. The volume left should only be sufficient to wet the walls of the syringe and fill the dead space of the syringe hub(29). In addition, use of low heparin concentration (1000IU/ml) is recommended compared to high concentration (5000IU/ml) as it results in a lower final heparin concentration. The volume of blood collected should then be 20 times the dead space(27).

For a standard 2ml syringe, the dead space is around 0.1ml. A dilution with 0.1ml of liquid heparin (1000IU/ml) in 2.0 ml of blood, which is 20 times the dead space, results in a dilution of 5% (0.1 ml of heparin in 2ml of blood) and heparin concentration of 50IU/ml(27).

2.5 Recommended Guidelines on Dry Electrolyte Balanced Heparin

DBH is formulated in powder form. It is a mixture of lithium and sodium heparinates to which electrolytes have been added. The final individual electrolyte concentration in DBH is the midpoint of the normal electrolyte concentration range. This novel heparin concentration eliminates the effect of electrolyte binding(11).

WHO recommends the use of DBH syringes that give a final heparin concentration of 40 – 60IU/ml after sample collection. For a standard 2ml syringe with a total DBH concentration of 80IU, collection of a 2ml blood sample will give a final concentration of 40IU/ml. This concentration has been shown to adequately anticoagulate ABG samples(30).

2.6 Studies Done on Effects of Liquid Heparin on ABG Parameters

Savas et al., conducted a study on 100 patients comparing dry lithium heparin to liquid sodium heparin in two different BGA samples on each patient. 2mls of blood were collected in two syringes. The first syringe contained 72IU of dry lithium heparin and the second was pre-washed with liquid sodium heparin 25000IU/5ml that was then flushed out completely. The interclass correlation of pH, pCO_2, pO_2, HCO_3, Base Excess, Hb, Hct, SaO2, Na^+ and K^+ parameters from blood gas analysis results obtained with liquid heparin and dry electrolyte heparin was found to be positively high, between 0.879 and 0.995. The study found no significant advantage of using the dry lithium heparin over liquid heparin, as pH, pCO_2, pO_2, HCO_3, Base Excess, Hb, Hct, SaO2, Na^+ and K^+ correlated with each other. However, the interclass correlation of Ca+ levels between liquid heparin and dry lithium heparin was significantly poor at 0.099. This means Ca^+ was significantly lower in the liquid heparin sample and DBH was a better ABG anticoagulant when measuring Ca^+ (19).

Sandler et al. conducted a study on 54 patients where they compared ABG parameters from 4 samples. Each had 1ml of arterial blood but with different forms of heparin, from the same patient. The first sample was in a dry electrolyte balanced heparin syringe, the second was in a spray coated lithium heparin syringe, the third was self-prepared with 1000IU/ml sodium LH and the fourth was self-prepared with 5000IU/ml of sodium LH. They then compared results from the three samples with the recommended dry electrolyte balanced heparin syringe. For both liquid heparin cohorts i.e. 1000 IU/ml and 5000 IU/ml, pCO_2, Na^+, K^+, iCa^+ and Hb had greater than 20% of the differences falling outside the TEa. This was found to be statistically significant. In the spray coated lithium heparin syringe, pH, pCO_2 and iCa + had greater than 50% of the differences falling outside the TEa, which was statistically significant. The study concluded that for the parameters with majority of the results falling beyond the TEa, the concerned methods of anticoagulation could not be used interchangeably with DBH as the errors were not medically acceptable.(14).

Pallavi et al. compared 35 paired samples of BGA. The first sample was collected in commercially prepared DBH and the second sample was collected in a syringe coated with 1000IU/ml of liquid heparin. They found a poor agreement between DBH and LH in pCO_2, $p0_2$, HCO_3, K, Na^+, Cl^- . These parameters had 23%– 77% of their differences falling outside the TEa. This was statistically significant. Thus LH was not comparable to DBH as the errors were not medically acceptable(31).

2.7 Study Justification

Anticoagulation of ABG with LH causes multiple pre-analytical errors on ABG parameters compared to anticoagulation with DBH (31). These erroneous ABG parameters will not reflect

the correct patient diagnosis (9). Misdiagnosis can lead to inaccurate treatment and interventions; a cascade of life-threatening outcomes including worsening of the underlying pathological process(s) and/or development of new conditions. This will result in poor utilization of resources, increased hospital stay, more expenses on patients and stress to the patients and their next of kin (25) .

Authors have reported varying findings after comparing ABG parameters following anticoagulation with LH and DBH. The majority have reported most of the differences between the two methods as medically unacceptable as most differences were falling outside the TEa (31), (14). This was found to be statistically significant, thus DBH was not comparable to LH. LH use for ABG anticoagulation is the standard practice in KNH. This necessitated us to carry out this study in our setting. The results of this study were expected to reveal the differences and or similarities in ABG analysis by comparing ABG parameters anticoagulated with the recommended standard DBH to those anticoagulated with LH.

2.8 Study Question

What were the effects of Dry electrolyte heparin compared to liquid heparin on arterial blood gas analysis parameters in critically ill patients admitted at the Kenyatta National Hospital Main Critical Care Unit?

2.9 Objectives

2.9.1 Broad Objective

To determine the effects of dry electrolyte balanced heparin compared to liquid heparin on arterial blood gas analysis parameters in critically ill patients admitted at the Main Critical Care Unit in Kenyatta National Hospital.

2.9.2 Specific Objectives

- To determine the effects of dry electrolyte balanced heparin compared to liquid heparin on arterial blood parameters-pH, pO_2, pCO_2, HCO_3.
- To investigate the effects of dry electrolyte balanced heparin compared to liquid heparin on arterial blood electrolytes- Na, K, CL
- To determine the effects of dry electrolyte balanced heparin compared to liquid heparin on arterial blood Hemoglobin.

3.0 CHAPTER THREE: METHODOLOGY

3.1 Study Design

This was a comparative cross-sectional study.

3.2 Study Area and Site Description

The study was carried out at the Main Critical Care unit of the Kenyatta National Hospital (KNH).

KNH is a public, tertiary hospital in Kenya, with a total bed capacity of 1800, offering specialized medical, surgical, research and rehabilitative health care services to patients referred from within the country, Eastern, Southern and Central African region; It is also the teaching hospital for the University of Nairobi, College of Health Sciences(32).

KNH has a total of 8 critical care units: Main CCU (21 bed-capacity); Pediatric CCU (6 bed capacity) ; Obstetrics and Gynecology CCU(5 bed capacity); Neuro-oncology CCU (5 bed capacity); Medical CCU (13 bed-capacity); Cardiothoracic CCU (5 bed capacity); the private wing CCU (10 bed capacity).

The Main CCU attends to acute trauma and surgical patients of all age groups who need critical care. Due to its larger capacity, any type of critically-ill patient may be admitted and managed in the main CCU whenever other suitable CCUs are full. Main CCU is equipped with many facilities including: Invasive and non-invasive mechanical ventilation equipment; Oxygen supply; Supplemental Oxygen delivery equipment; Physiotherapy facility; Vital signs monitoring equipment; Resuscitation equipment; Blood vessel cannulation equipment; Drug and fluid delivery equipment; Emergency and non-emergency drugs; Nursing facilities; BGA laboratory. The CCU staff include consultant anesthesiologists, medical officers, nurses, nutritionists, physiotherapists, counsellors and support staff.

3.3 Study Population Description

The study participants were critically ill patients admitted at the Main Critical Care Unit during the period of the study.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

- The critically ill patients of age 18 years and older admitted at the Kenyatta National Hospital Main Critical Care Unit. The 4mls of ABG sample required for the study was safely collected from this age group's blood volume without causing complications like anemia. Also, to facilitate ease of sample collection a large artery was found in this age group, this helped avoid multiple pricks which might have interfered and introduced errors to the samples.
- The critically ill patients who gave consent or whose next kin gave consent (for those with impaired state of consciousness) to participate in the study

3.4.2 Exclusion Criteria

- The critically ill patients of age 18 years and older who were admitted at the Kenyatta National Hospital Main Critical Care Unit, whose blood sample for ABG was obtained from an indwelling arterial catheter. These catheters are continually heparinized with LH, which would introduce errors to our ABG samples.
- The critically ill patients of age 18 years and older admitted at the Kenyatta National Hospital Main Critical Care Unit with a known coagulopathy. The study procedure involved puncturing the patient twice, consequently increasing the risk of bleeding in these patients with deranged hemostasis.
- The critically ill patients of age 18 years and older admitted at the Kenyatta National Hospital Main Critical Care Unit whose identity was not established by virtue of challenges in obtaining informed consent.

3.5 Sample Size Determination

The study sample size was calculated using Altman Nomogram formula (33). ABG analysis includes multiple parameters. Sample size was calculated for pCO_2 measurements as previous studies had shown pCO2 as the parameter most sensitive to dilution (22)(23)(24)**.**

Altman Nomogram Formula

$$n = \left[\frac{2}{d^2}\right] \times \mathbf{C}_{p,power}$$

n= desired sample size

d= Standardized difference

Cp,power= Constant defined by values chosen for the p value and the power.(33)

Substitution

- Assumed P value of 0.05
- Assumed Power of 0.9 i.e. 90%
- Required difference of 5.7% (total allowable error for pCO_2) (34)
- Assumed SD of differences of pCO_2 in paired samples of 5 mm Hg
- Standardized difference will be (5.7 – 5)= 0.7
- Cp,power- With p value of 0.05 and power of 90% the Cp,power =10.5 (33)

$$n = \left[\frac{2}{0.7^2} \right] \times 10.5$$

n = 43

From the above calculation, a convenient sample size of 46 paired samples was targeted for this study.

3.6 Sampling Method and Procedure

The consecutive sampling method was used in this study. At admission to the main critical care unit, all patients meeting the eligibility criteria were included until the desired sample size of 46 participants was achieved.

3.7 Study Procedure and Recruitment

A total of 46 participants who met the study inclusion criteria were enrolled into the study via consecutive sampling. Informed consent to participate was sought from the patients or their next of kin for the critically ill in impaired state of consciousness. The study procedure including the harms, benefits and process of final results dissemination was explained to the patients or their next of kin. Consent to participate in the study was then obtained by the principal investigator (PI) or research assistant (RA) in either Swahili or English. Each participant was engaged in the study only once.

The PI or RA drew two arterial blood samples (2mls each) from each participant concurrently after aseptic preparation of the puncture site with alcohol-soaked cotton swabs; one using the *BD Discardit* II 2 milliliters syringe containing the Liquid Heparin and another using the commercially prepared *Set blood gas syringes* 2milliliter syringe containing 80 IU of dry electrolyte balanced Heparin. The *BD Discardit* II syringe was self-prepared by first filling the barrel with liquid heparin (sodium heparin solution 1000IU/ml) until the 2ml mark, which was then flushed out completely so that no visible heparin was left in the barrel syringe or hub. After sample collection, the syringes were capped, air bubbles were expelled and samples mixed by gently rotating the syringe between palms for 10 seconds to ensure homogenous sample. They were labeled with unique IDs. Dry clean gauze was applied on the puncture site immediately and hemostasis achieved before leaving the patient.

The two blood samples from each patient were then transported by hand to the laboratory and subjected to analysis within 10 minutes of collection. Sample collection time and sample analysis time were noted. The two blood samples were inspected for errors such as insufficient sample volume, air bubbles, micro-clots, time taken for analysis and any other non-conformities before analysis. Erroneous samples were discarded. The samples were analyzed using the *ABL800 FLEX* blood gas analyzer by the laboratory technologist. The sample unique IDs were entered in the analyzer before analysis and the sample introduced to the analyzer by aspiration from the two syringes concurrently. The analyzer subsequently recorded the results of the ABG analysis in the report forms. The laboratory technologist then submitted the results to the principal investigator or the research assistant. The sharps, blood samples and PPE were safely disposed after sample analysis. The survey CTO tool was used to capture the findings from the laboratory reports electronically. Correct hand hygiene and proper utilization of personal protective equipment was adhered to by the PI, RA and Laboratory technologist during the entire procedure.

The following table summarizes the demographic data that was collected in the study:

Table 1: Demographic Data

Variable	Variable Description	Data Type
Age Group	Age group in years categorization	Categorical
Sex	Male or female genders	Categorical
Diagnosis	The illness causing the patient to be critically ill.	String-Open-ended response.
Time of sample collection	The time the blood sample is drawn from the patient	Continuous
Time of Blood gas analysis	The time the blood samples are analysed in the analysis tool.	Continuous

3.8 Consenting Procedures

The informed consent form was administered to eligible patients or their next of kin at admission by the PI or RA in a language that they understood (Swahili or English). The study purpose, study procedure, benefits and the possible risks of the project were fully explained to the patients or next of kin. The consenting personnel made any clarifications and the patient was then enrolled into the study. Voluntary participation in the study was emphasized.

3.9 Role of the Research Assistant, Laboratory Technologist, and the Principal Investigator

The principal investigator was in charge of sample collection following the appropriate guidelines. The laboratory technologist was in charge of the blood gas analysis procedure in the laboratory. The research assistant assisted in data collection after completion of blood gas analysis of the two samples. They entered the data accurately in the Survey CTO tool and later shared the data with a statistician for data analysis. Quality control checks on the data were done by the statistician and the principal investigator to ensure that all the protocols in data collection and dissemination were strictly followed; this was done tentatively before embarking on data analysis and interpretation.

3.10 Quality Assurance Procedures

All data collection activities followed the set guidelines that protect the rights of patients at the Kenyatta National Hospital. KNH safety guidelines protocols were adhered to throughout the study to prioritize patients' wellbeing and care. Data protection was enhanced to maximize confidentiality; hence ensuring that the ethical guidelines for protecting human participants in the study were effected. Heparin, ABG syringes and needles were stored in locked steel cupboards at room temperature, and were only accessible to the principal investigator. The blood gas analyzer underwent hourly automatic calibrations, quality checks twice a day with control solutions and monthly electrode exchange. External quality assessment with control solutions was done monthly. The principal investigator closely monitored the progress of the study. A pilot study was conducted on 30% of the required sample size to give the general insights and expectations of the main study.

3.11 Ethical Considerations

Approval was sought from the Kenyatta National Hospital - University of Nairobi Ethics and Research Committee. Permission was also sought from KNH administration before commencement of the data collection. Written informed consent administration played a major role in the enrolment of patients in the study. The consent forms were administered in both English and Swahili. The patients were briefed about the arterial puncture procedure which is a painful procedure. There was no repetition of the procedure after an unsuccessful first attempt to avoid further side effects such as bleeding, reddening and swelling after several procedures. COVID-19 protocols and guidelines were strictly followed to avoid risking the patients' health during the period. The principal investigator, research assistant and laboratory technician donned their personal protective equipment i.e. surgical face masks, face shield, exam gloves and disposable fluid resistant aprons during collection and handling of the ABG samples. Proper hand hygiene before donning and after doffing PPE use was observed. The PPE was correctly doffed and safely disposed after handling each patient and a new set donned for a new patient. Social distance of 6 feet was observed among the personnel in the CCU and those in the ABG laboratory.

Anonymization of the patient data was done to ensure patient confidentiality and data safety. Only the authorized staff were allowed access to the data since the data was password protected. The study did not pose any dangers to the patients' health since all the guidelines in the protocol aimed at improving the patient care. No additional cost was incurred and there were no any added benefits or allowance to participate in the study. This was clearly explained when administering the consent forms to the patients. The participants had the right to opt out of the study at any stage with no any expected consequences since the participation was voluntary. Standard patient care was maintained for all.

3.12 Data Storage and Security

The data was collected using the blood gas analysis report forms and immediately captured in the survey CTO tool in preparation for data cleaning and analysis. The physical laboratory reports were collected by the principal investigator and research assistant upon the analysis of samples, and were later filed in folders. These report forms were used in case some of the information was missing from the system in the analysis stage. The report forms were stored in locked steel cupboards to ensure privacy and confidentiality of the patient information.

These cupboards were located in the CCU data storage room and are provided to the residents by KNH. They were only be accessed by the principal investigator and the research assistant.

Tablets were used for data capture after reviewing the laboratory report forms. These tablets were password protected to ensure that the data is only accessible to the designated study staff. Participant anonymization was done and the identifier information removed to ensure that confidentiality of the participants was maintained. The data was backed up in password-protected hard disks to ensure the availability of data in case of data loss in the laptops due to technical constraints.

3.13 Data Analysis Plan

Upon the completion of the data collection exercises, consistency checks were done on the data to ensure quality. The data quality aspects that were checked included missing values, duplicates and outliers. The data corresponding to the missing cases were further collected and checked to ensure completeness and accuracy of the records. The Stata 15 software and Microsoft excel were used for the statistical analysis.

The Shapiro Wilk normality test was conducted to ascertain whether the measurements of the ABG parameters were normally distributed. Descriptive data analysis was conducted for the two sets of data using mean and standard deviations for normally distributed data, and median with interquartile ranges for skewed data. Paired sample T-test was used to display the statistical significance of the differences in mean of the two ABG parameters.

Comparative data analysis was conducted using the Bland Altman methodology. For each participant, we calculated an average ABG parameter, e.g. Average of pH on DBH and on LH. We then calculated a difference between the two ABG parameters for each patient e.g. pH on DBH minus pH on LH. These data were presented on a Bland Altman plot, where the average data was plotted on the x- axis against the difference data on the y-axis. The mean bias, which is the mean difference was established by adding up all the differences and diving this by the total number of participants. It was plotted using a line graph on the Bland Atman plot. The mean bias indicated that DBH parameters differed from LH parameters by that particular mean bias value. 95% limits of agreement were calculated i.e. ± 1.96 standard deviations from the mean bias, to elucidate the level of agreement between the two sets of data and plotted on Bland Altman Plot as well. The wider the difference between the 95% limits of agreement, the poor the agreement between the two methods of anticoagulation. The closer the difference between the 95% limits of agreement, the stronger the agreement between the two methods of anticoagulation. The limits of agreement of the ABG parameters were then compared with specifications of total allowable error (TEa). Total allowable error is that error can be tolerated between the two sets of data without invalidating the medical usefulness of the results. The proportion of samples with differences beyond TEa % was calculated. Two methods are considered to give clinically equivalent results if results measured on the same specimen do

not differ by more than the specified TEa for that analyte. This determined whether the differences between the two methods of anticoagulation were medically acceptable. The specifications of TEa that were for this analysis were compiled by Ricos *et al* from data within subject and between subject biologic variations (34), with updated figures available online (35)(36).

Bland-Altman Plot

The Bland-Altman analysis plots were used to visually showcase the nature of the relationship between the two sets of parameters. The correlation analysis method was used to indicate the strength of association between the two ABG parameters. The paired samples T-tests were also used to display the significant differences in means of the ABG parameters for the LH and DBH case (7)-(31). The statistical significance levels of the tests were all set at $\alpha=0.05$.

3.14 Data Presentation

The frequency tables were used to illustrate the patient demographic characteristics such as the Age Group and Gender. These frequency tables were also used to indicate the clinical diagnosis among the critically ill patients. The Bland Altman plots were used to ascertain the mean bias, 95% limits of agreement and the total allowable error between arterial blood gas parameters. The paired samples T-tests were represented in tabular format.

3.15 Study Results Dissemination Plan

The study results will be disseminated and presented to the department of Anaesthesia, University of Nairobi, KNH Anaesthesia Department and KNH BGA laboratory. The dissemination will entail a detailed report of the study, study dissertation, and a scientific publication. The study results will also be shared with collaborators and health stakeholders in Kenya to form a basis in formulation of policies aimed towards recovery and improved outcomes of critically ill patients.

4.0 CHAPTER FOUR: RESULTS

4.1 Patient Demographic Characteristics

A total of 46 critically ill patients were recruited to participate in the study. The majority of the patients were male (67.4%, n=31) and the age ranged between 18-70 years old, with a mean age of 42.7 years (standard deviation=17.6). Patients in the 30-59 years age group comprised the majority (56.5%) of the total study participants. The average analysis time was 6 minutes 36 seconds, with the majority (82.6%) of the samples being analyzed between 5 and 9 minutes. Majority of the study participants (45.7%) had traumatic brain injury, followed by polytrauma (17.4%), as shown in the Table 4.1 below.

Table 4. 1:Patient demographic characteristics

Variable	Description	Frequency (%) N= 46	Mean(SD)
Sex			
	Male	31(67.4)	
	Female	15(32.6)	
Age-group			42.7(17.6)
	< 30 years	12(26.1)	
	30-59 years	26(56.5)	
	>60 years	8(17.4)	
Sample analysis time			6.36(8.40)
	5-9minutes	38(82.6)	
	<5 minutes	8(17.4)	
Diagnosis			
	Traumatic Brain Injury	21(45.7)	
	Polytrauma	9(19.6)	
	Tumor Lesions	8(17.4)	
	Haemorrhagic Cerebrovascular Accident	5(10.9)	
	Brain Abscess	1(2.1)	
	Congestive Cardiac Failure	1(2.1)	
	Spine Injury	1(2.1)	

4.2 Analysis of The Effects of DBH Compared to LH On Arterial Blood Gas Parameters

A T-test analysis of the DBH and LH arterial blood gas samples showed no statistically significant difference in the results of the measured parameters, with the exception of the measured sodium (p value= 0.000, <0.05).

Table 4. 2:ABG Analysis – Mean (SD)/ Median and T-test

	LH	**DBH**	**(T-test Analysis)**
Analyte	**Mean(SD)**	**Mean (SD)**	**P- value**
pH	7.4(8.7)	7.4(9.6)	0.179
PCO2 (mmHg)	4.7(9.8)	5.1(1.0)	0.947
PO2 (mmHg)	12(17.8)	14.0(6.3)	0.712
Bicarbonate (mmol/L)	22.8(3.4)	23.2(3.8)	0.990
Sodium (mmol/L)	141.6(6.6)	137.9(7.0)	0.000
Potassium (mmol/L)	4.0(6.7)	4.1(12.4)	0.872
Chloride (mmol/L)	108.4(8.9)	107.7(10.3)	0.166
Hemoglobin (g/dl)	10.8(2.3)	10.9(2.3)	0.960

The Bland Altman Analysis demonstrated a narrow difference between the DBH and LH group for pH, pCO2, Bicarbonate, K and Hemoglobin parameters. This was expressed by the close 95% limits of agreement. Furthermore, none of these parameters were beyond the TEa. pO2 revealed a big difference between the two groups with widespread 95% limits of agreement. TEa is not applicable for this parameter.

However, Na and Cl parameters exhibited a wide difference between the two groups, with broad 95% limits of agreement. In addition, Na and Cl had 89.13% and Cl 32.61% of their parameters beyond the TEa respectively.

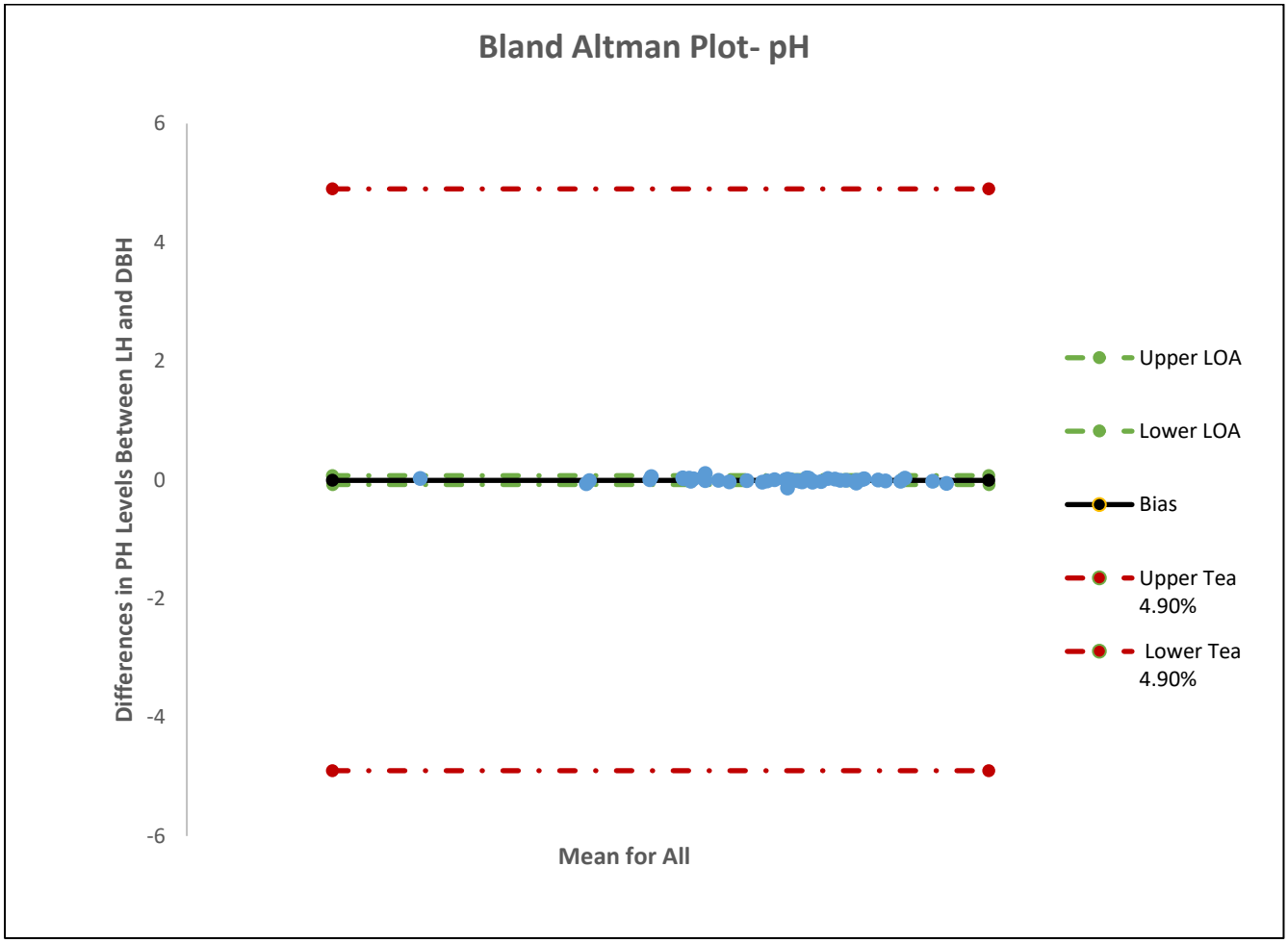
Table 4. 3:Bland Altman analysis

Analyte	Standard Deviation	Mean Bias	Lower 95% LOA	Upper 95% LOA	Total Allowable Error	Proportion Beyond Tea (%)
pH	0.04	-0.01	-0.08	0.07	4.90%	0
PCO2 (mmHg)	0.66	0.16	-1.13	1.46	5.70%	0
PO2 (mmHg)	5.80	0.48	-10.89	11.86	N/A	-
Bicarbonate (mmol/L)	1.21	0.44	-1.17	2.82	4.90%	0
Sodium (mmol/L)	3.69	-3.74	-10.97	3.49	0.90%	41 (89.13%)
Potassium (mmol/L)	0.30	0.05	-0.55	0.65	5.61%	0
Chloride (mmol/L)	4.91	-0.72	-10.34	8.91	1.50%	15(32.61%)
Hemoglobin (g/dl)	0.26	0.07	-0.44	0.58	4.19%	0

4.2.1 Effects of DBH Compared To LH On Arterial Blood Parameters-Ph, Po_2, Pco_2, HCO_3

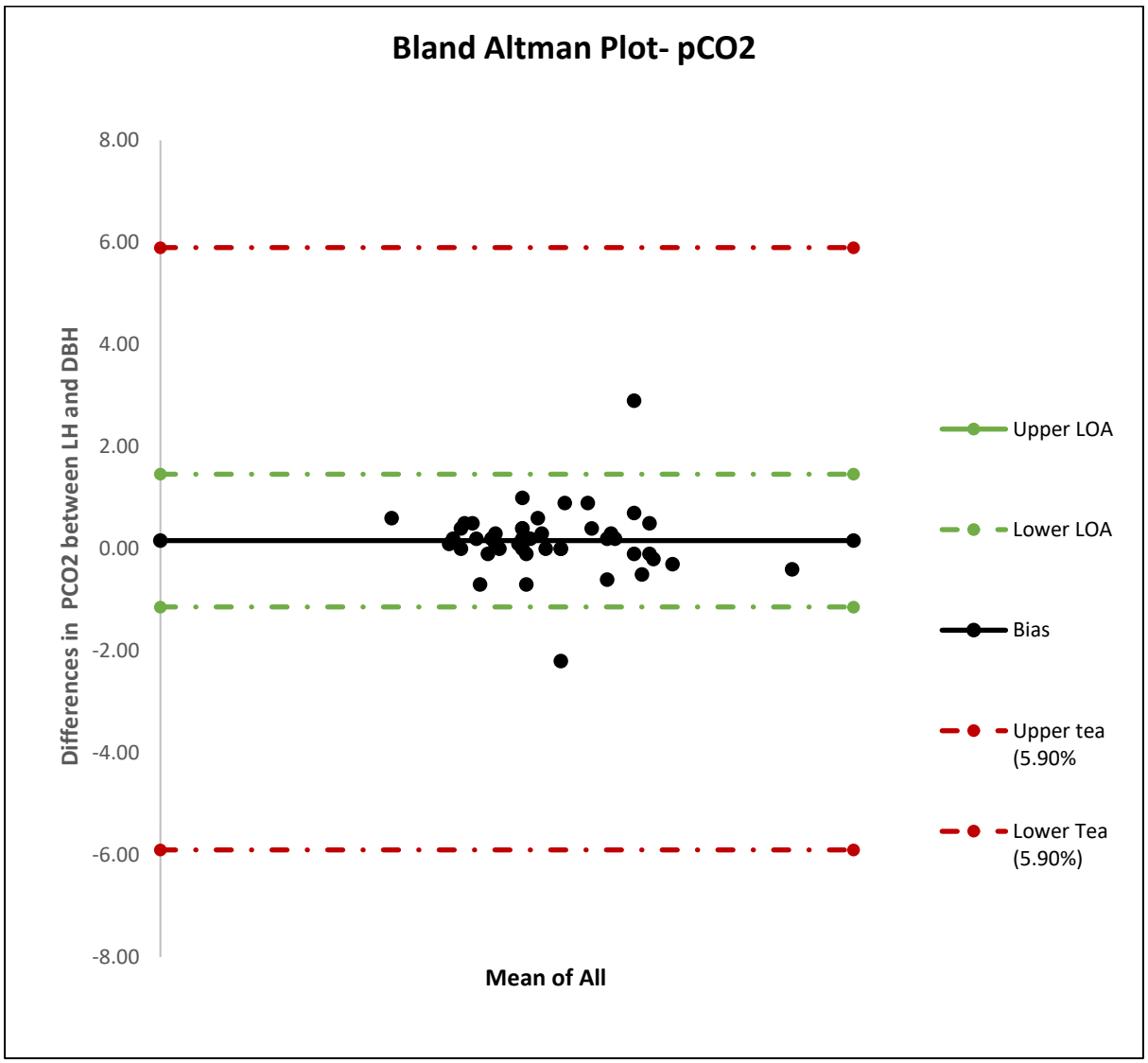
Figure 4.1 to Figure 4.8 illustrates the individual bland Altman graphs for each ABG parameter.

Figure 4. 1:Bland-Altman Plot for PH



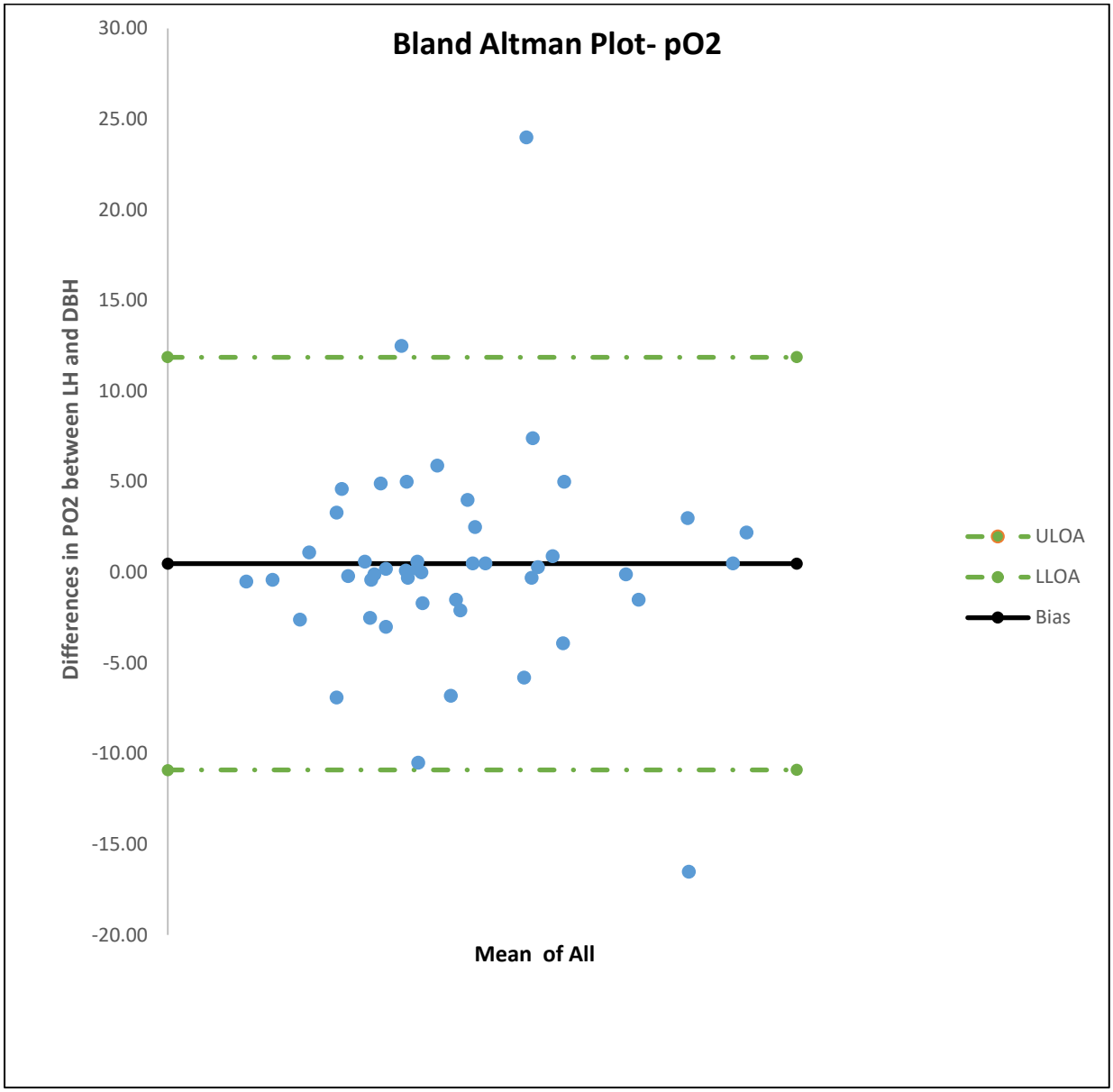
pH had a mean bias of -0.01. The differences between the two groups were very narrow, with the 95% limits of agreement between -0.08 to 0.07. With a TEa of 4.90%, none of the proportions were beyond the TEa.

Figure 4. 2:Bland-Altman Plot for PCO2



PCO2 had a mean bias of 0.16. The differences between the two groups were narrow, with the 95% limits of agreement between -1.13 to 1.46. The TEa was 5.70%, and none of the proportions were beyond the TEa.

Figure 4. 3:Bland-Altman Plot for PO2



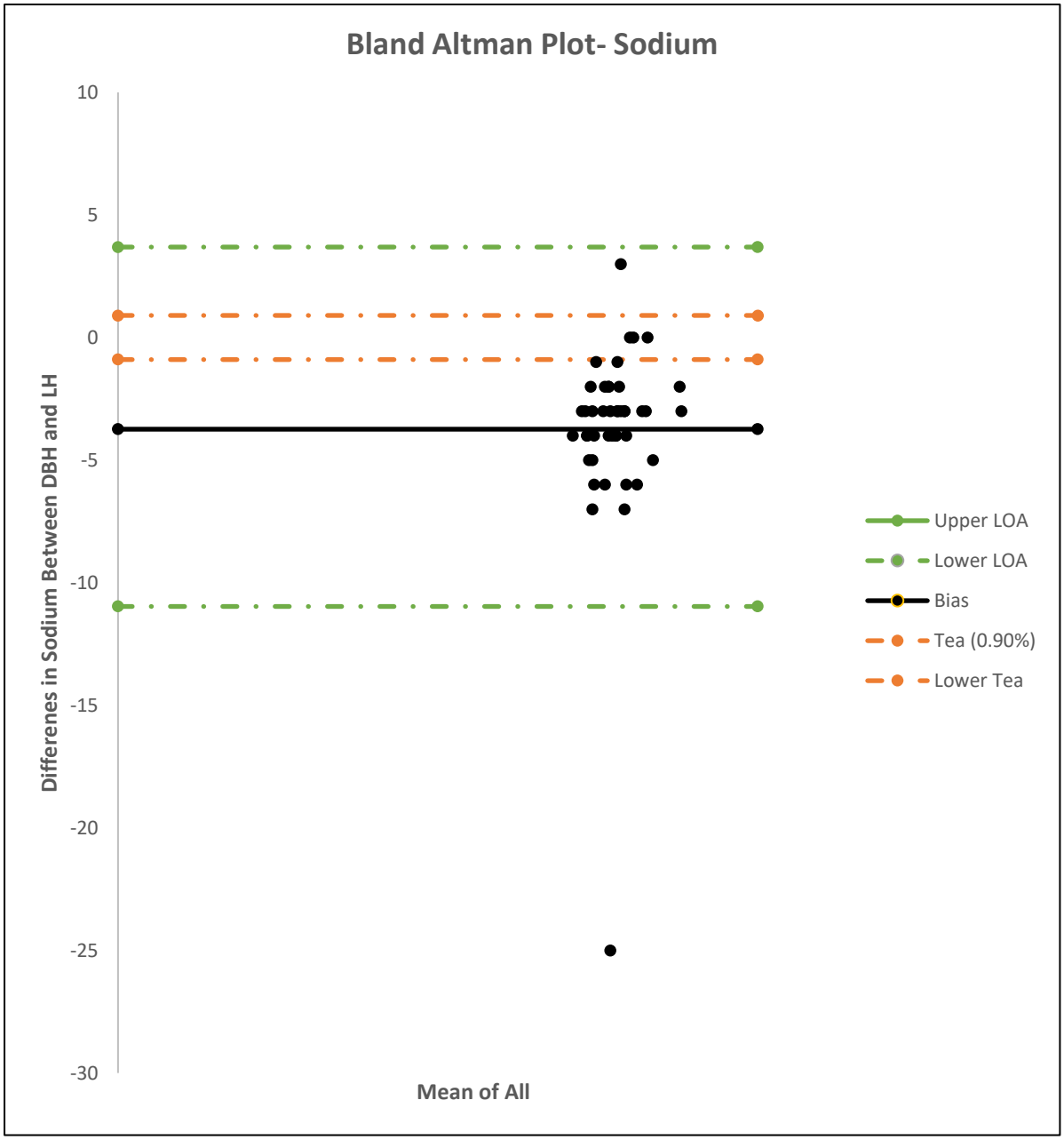
PO2 had a mean bias of 0.48. The differences between the two groups were wide, with the 95% limits of agreement between -10.89 to 11.86.

Figure 4. 4:Bland-Altman Plot for Bicarbonate

Bicarbonate had a mean bias of 0.44. The differences between the two groups were narrow, with the 95% limits of agreement between -1.17 to 2.82. The TEa was 4.90%, and none of the proportions were beyond the TEa.

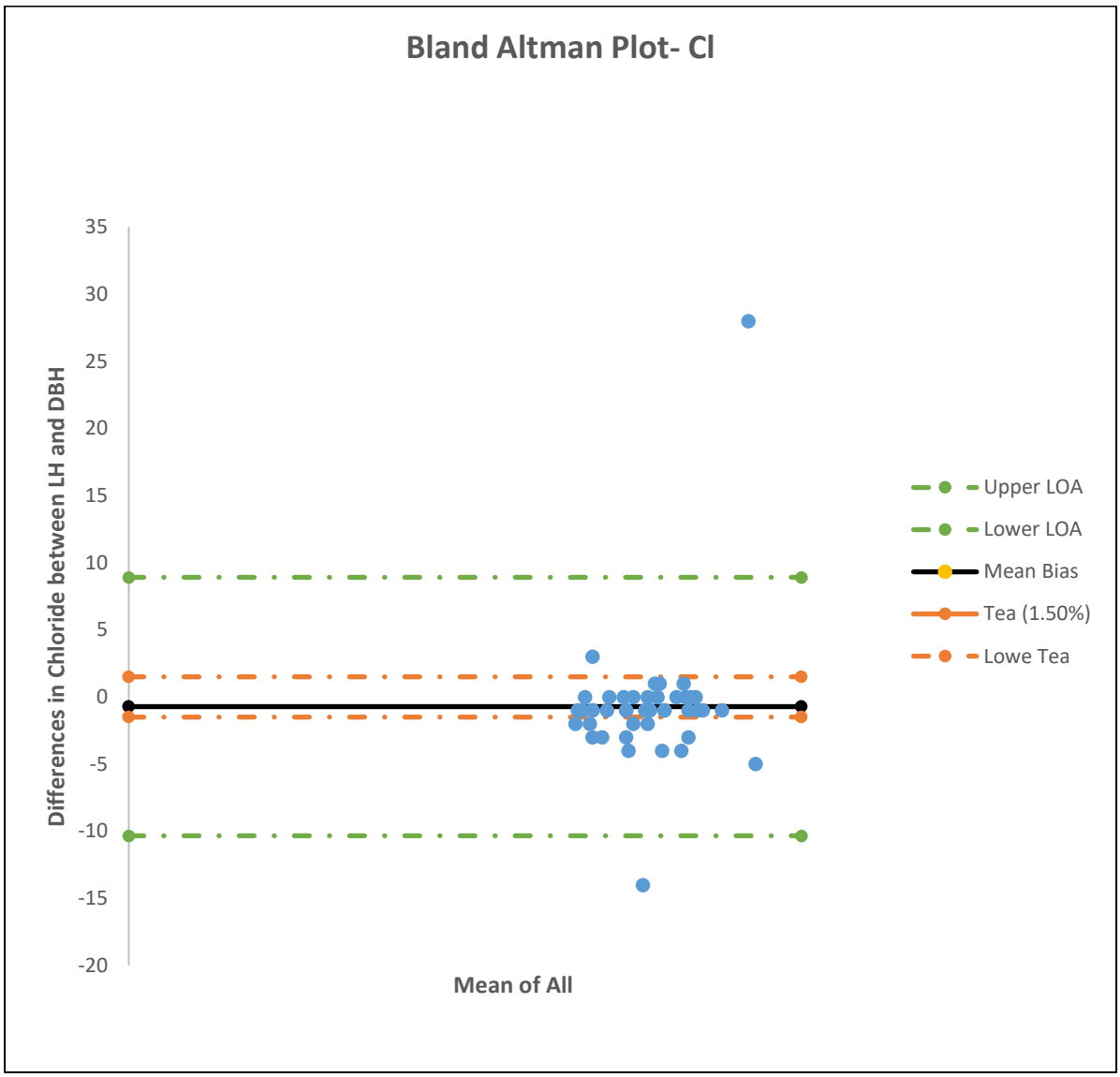
4.2.2 Effects of Dry Electrolyte Balanced Heparin Compared To Liquid Heparin On Arterial Blood Parameters-Na, CL, K

Figure 4. 5: Bland-Altman Plots for Sodium



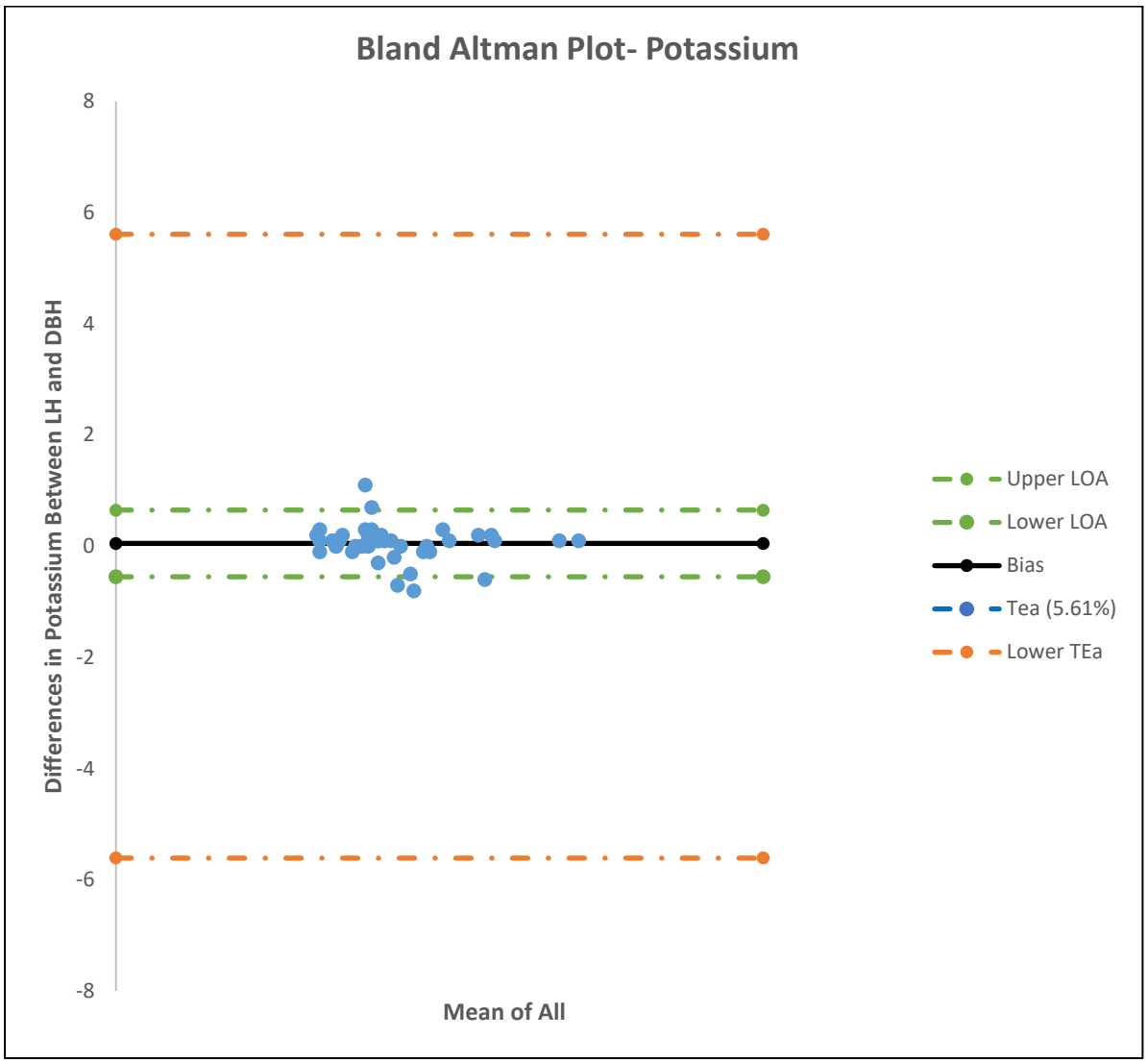
Sodium had a mean bias of -3.74. The differences between the two groups were wide, with the 95% limits of agreement between -10.97 to 3.49. The TEa was 0.90%, with 41 (89.13) proportions beyond the TEa.

Figure 4. 6:Bland-Altman Plots for Chloride



Chloride had a mean bias of -0.72. The differences between the two groups were wide, with 95% limits of agreement between -10.34 to 8.91. The TEa was 1.50%, with 15 (32.61%) of the proportions beyond the TEa.

Figure 4. 7:Bland-Altman Plots for Potassium



Potassium had a mean bias of 0.05. The differences between the two groups were narrow, with the 95% limits of agreement between -0.55 to 0.65. The TEa was 5.61%, with none of the proportions beyond the TEa

4.2.3. Effects Of Dry Electrolyte Balanced Heparin Compared to Liquid Heparin On Arterial Blood Parameters-Hb

Figure 4.8: Bland-Altman Plot for Hemoglobin

Haemoglobin had a mean bias of 0.07. The differences between the two groups were narrow, with the 95% limits of agreement between -0.44 to 0.58. The TEa was 4.19%, and none of the proportions were beyond the TEa.

5.0 CHAPTER FIVE: DISCUSSION, CONCLUSION AND RECOMMENDATIONS

5.1 Discussion

There was no statistically significant difference in pH, pCO2 and HCO3 between the LH and DBH group. Furthermore, pH, pCO2 and HCO3 demonstrated a strong agreement between the two groups. The differences between the two groups were within the total allowable error, demonstrating clinically equivalent results. pO2 on the other hand established a low agreement between the two groups, however the differences were statistically insignificant. This study did not therefore find an advantage of using DBH over LH when analysing these parameters. The dilutional effects of LH were not experienced in these parameters. This could be explained by the minimal amount and concentration of LH used for anticoagulation. The LH in this study was flushed out of the syringe completely so that no visible heparin was left in the syringe barrel or hub. This is in comparison to a study done by Savas et al. who conducted a study on 100 patients comparing DBH to LH in two different BGA samples on each patient. They found a highly positive correlation in pH, pCO_2, pO_2 and HCO_3 between the two groups with no significant advantage of using the DBH over LH.

This study found a rich agreement in K^+ between the LH and DBH group. Additionally, the differences between the two groups were statistically insignificant. All the differences in potassium between the two groups were within the TEa, thus giving clinically equivalent results. There was therefore no benefit of using DBH over LH when analysing K on ABG. This is also in line with the study carried out by Savas et al. The level of agreement of Na and Cl between the LH and DBH group was poor, demonstrated by a wide difference between their 95% limits of agreement. Moreover, they had parameters outside the TEa, Na at 89.13% and Cl at 32.61 %. The two methods of anticoagulation ie LH and DBH did not therefore indicate clinically equivalent results, and cannot be used interchangeably in the analysis of these two parameters. This is similar to a study done by Pallavi et al who compared ABG parameters after anticoagulation with DBH and LH parameters, the Na & CL had 77% and 54% of their parameters outside the TEa respectively. In Pallavi et al study, these parameters were lower in the LH group due to dilution effects .In this study the LH parameters were higher than the DBH parameters. This could be because we used liquid sodium heparin, in which 0.9% sodium chloride is an additive. These electrolytes are not balanced in LH. DBH is thus the preferred anticoagulant when analysing these parameters.

The binding effects of LH were not experienced in this study possibly because of the low heparin concentration and the small amount of LH used for anticoagulation as it was flushed out completely so that no visible heparin was left in the syringe barrel or hub.

There was no statistical difference in the measured haemoglobin between the LH and DBH group. There was also a strong agreement between the two groups. All the differences between the two groups were within the total allowable error, demonstrating clinically equivalent results. This study did not therefore find an upper hand of using DBH over LH when analysing these parameters. These findings are also in line with the study conducted by Savas et al. The dilutional effects of LH were not experienced here probably due to the minimal amount of LH used.

5.2 Conclusion

There is no significant advantage of DBH over LH for ABG anticoagulation of pH, pO_2, pCO_2, HCO_3, K and Haemoglobin. When the LH has been flushed out completely, the syringes can be used interchangeably. Liquid Sodium Heparin affects the electrolytes even in very small amounts; DBH is the preferred anticoagulant when assessing electrolytes especially Na and CL. Self-prepared LH syringes, in which LH flushed out completely so that no visible heparin is left in the barrel syringe or hub provide sufficient heparin to anticoagulate an arterial sample.

5.3 Recommendations

Standard operating procedures and continuous education to health care providers on how to prepare LH syringes. Investment in DBH syringes, as they are ready to use, have a standard amount of heparin and are electrolyte balanced. This is especially so when Na and Cl are the parameters of interest.

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APPENDICES

Appendix I: Consent Form: English

Study title: A Comparative study on the effects of Dry electrolyte balanced heparin versus liquid heparin on arterial blood gas parameters in critically ill patients.

Principal investigator: Dr Emma Ngarama.

Introduction:

I Dr. Emma Ngarama, a postgraduate student at the Department of Anaesthesia and Critical care, University of Nairobi, am conducting a study on '**A Comparative study on the effects of Dry electrolyte balanced heparin versus liquid heparin on arterial blood gas parameters in critically ill patients'.** You are hereby requested to participate in the study.

This information will help you make a decision on whether to participate in the study or not. You may ask any questions about the purpose of the study, what happens if you participate, the possible risks and benefits, your rights as a volunteer and anything in this form that is not clear.

Purpose of the study:

Blood gas analysis is an important investigation and diagnostic tool done on patients admitted in Critical Care Units. Blood gas analysis parameters enhance effective management of the critically ill patients. Heparin is the only anticoagulant recommended for use in ABG. The aim of the study is to compare the effects of dry electrolyte balanced heparin versus liquid heparin on arterial blood gas parameters. The results will influence change from current practice to the correct type of heparin for ABG anticoagulation. The correct form of heparin ensures reliable results that will aid in improving patient outcomes.

Possible risks:

This study will be slightly invasive as a small amount of blood (4mls) will be drawn from your vein for testing in the lab. Slight pain will be experienced during the process. There might also be slight swelling and or bleeding at the puncture site. To minimize these risks however a small gauge needle which is less painful will be used and pressure will be applied at the puncture site using a clean gauze till haemostasis is achieved. In case of failure at the first attempt the procedure will not be repeated.

There will be no added risks to your standard care as that accorded to other participants.

Benefits:

The study will help come up with recommendations on the correct type of heparin for ABG anticoagulation. This will influence change of current practice which will ensure accurate ABG results. Consequently, patient prognosis and outcomes will be improved. This will provide customer satisfaction and guarantee proper utilization of resources.

Voluntarism:

This is a voluntary exercise and you can withdraw at any point during the study with no repercussions. The management you receive at the hospital will be standard and not influenced by your decision.

Costs and compensation:

The costs incurred in performance of the additional blood tests will be catered for by the researcher and no compensation will be offered for participation in the study.

Procedure:

As a study participant, the researcher and research assistant will obtain some information from your medical records and conduct a short interview with you and your responses filled in a questionnaire. Two samples of blood, approximately 2mls in each syringe will be drawn for testing in the lab

- This will be a cross-sectional study targeting 45 patients from the KNH Main Critical Care Unit.
- Critically ill patients will voluntarily join the study if they fit the inclusion criteria and have consented to participate in the research.
- The procedure will involve collection of two arterial blood gas samples 2mls each, one in a syringe with liquid Heparin, and the other in a syringe with dry electrolyte balanced Heparin.
- The procedure will involve arterial puncture which will be painful.
- These samples will then be analysed to identify the changes/ similarities or differences between the two blood gas parameters from the same patient.
- Data collected and recording from the patients will be totally confidential and will only be accessed by authorized project staff.
- Each participant will engage in the study only once.

Confidentiality:

Total confidentiality will be maintained to ensure that the data does not get into the wrong hands. No identifier information will be used in the data collection, analysis and results presentation. All the participants and the corresponding blood samples will be labelled uniquely using anonymous IDs throughout the study.

Contact information:

If you have any questions regarding the study you may contact Dr. Emma Ngarama who is the principal investigator. You may also contact KNH/UON ERC committee. Their contacts are provided below.

Principal investigator:

Dr. Emma Ngarama
Tel: 0723378679
Email: emangarama@gmail.com

Supervisors contact:

Dr. Timothy Mwiti
Tel: 0721366294
Email: tmwiti@uonbi.ac.ke

Dr. Kaiser Fitzwanga
Tel: +254722530992
Email: kfitzwanga@yahoo.co.uk

Dr. Kevin Arunga
Tel: 0722883057
Email: kevinarunga@yahoo.com

KNH/UON ERC Secretary Contacts:

Tel: 2726300 ext 44102,
Email: uonknh_erc@uonbi.ac.ke

Your participation in the study will be highly appreciated.

Consent:

I_____ having read this consent form or having had the information read to me and having had my questions answered in a language that I understand do hereby voluntarily consent to participate in the study. I acknowledge that a thorough explanation of the nature of the study has been given to me by Dr./Mr./Mrs._____. I clearly understand that my participation is completely voluntary.

Signature of Participant _____ Date _____

Signature of Next of kin Date

Investigator's Declaration:

I have intensively explained to the patient the need for this study and the gaps existing in the research field in Kenya. I have also answered their questions satisfactorily.

Signature of Researcher/ Assistant _____ Date _____

Appendix II: Consent: Swahili

Kichwa cha Utafiti: "A Comparative Study on the Effects of Dry Electrolyte balanced heparin versus Liquid Heparin on Arterial Blood Gas Parameters in Critically Ill Patients.

Mtafiti Mkuu: Dkt. Emma W Ngarama

Utangulizi:

Mimi ni Dkt Emma Ngarama mwanafunzi wa uzamili wa ganzi katika chuo kikuu cha Nairobi/Hospitali ya Kitaifa ya Kenyatta. Mimi ndiye mpelelezi mkuu wa utafiti huu, ambao unakusudia kuboresha maisha ya wagonjwa katika Hospitali ya Kitaifa ya Kenyatta kupitia utaftaji wa fomu inayofaa zaidi ya Heparin inayotumiwa kama dawa za kuzuia maradhi katika visa vya dharura. Ushiriki wako katika utafiti huu ni muhimu sana katika kuboresha utunzaji wa wagonjwa kwa sasa na katika siku zijazo. Mnakaribishwa sana kushiriki katika utafiti huu. Maelezo haya yatakusaidia kufanya uamuzi juu ya kushiriki katika utafiti huu. Unaweza kuuliza swali lolote kuhusu utafiti au chochote katika fomu hii kukuwezesha kuelewa zaidi.

Kusudi la utafiti:

Matumizi ya Heparin katika mipangilio ya matibabu yana athari tofauti kwa matokeo ya jumla ya wagonjwa, haswa kwa wagonjwa wanaoibuka ambao wanahitaji utunzaji mkubwa. Utambulisho wa aina inayofaa zaidi ya Heparin, ikiwa LH au DBH ni muhimu katika kuamua viwango vya viwango vya gesi na makadirio ambayo yanahusishwa na kupona na kuishi kwa mgonjwa. Mahitaji ya aina anuwai ya Heparin inaweza kuwa tofauti kulingana na mpangilio. Kufanya utafiti kama huo katika KNH, moja wapo ya hospitali kuu za rufaa nchini Kenya zitajulisha kufanana au tofauti katika aina anuwai za Heparin, huku ikielezea matokeo ya jumla. Mapendekezo ya utafiti yatakuwa muhimu sana kwa KNH na taasisi zingine za afya kwani utafiti unakusudia kutambua matumizi bora ya Heparin, kwa nia ya kuboresha utoaji na huduma ya mgonjwa.

Hatari zinazowezekana:

Utafiti huu utahitaji kutolewa damu milita 4 kwa ukaguzi katika maabara ya hospitali yetu Huenda ukahisi uchungu kiasi mahali ambapo damu itatolewa. Kunaweza pia kuwa na uvimbe au kuvuja kwa damu mahali ambapo damu itatolewa. Ili kupunguza uwezekano huo sindano ya geji ndogo itatumiwa kupunguza uchungu na shinikizo la pamba kutumiwa kuzuia uvujaji wa damu na utaratibu wa mkusanyiko wa sampuli utafanywa mara moja pekee, hautarudiwa kama jaribio la kwanza limeshindwa.

Hakutakuwa na hatari zaidi ya huduma ya kawaida kama ile iliyopewa wagonjwa wengine.

Faida:

Utafiti huu utasaidia kutoa mapendekezo kuhusu aina sahihi ya heparini inayostahili kuzuia mgando wa damu inayotolewa kwenye ateri za wagonjwa. Hii itasaidia kubadili mazoea ya sasa, ili kupata matokeo sahihi baada ya uchambuzi wa damu za ateri. Hii itahakikisha kuridhika kwa wateja na utumizi bora wa rasilimali.

Hiari:

Hili ni zoezi la hiari na unaweza kujiondoa wakati wowote wakati wa utafiti bila lawama. Usimamizi unaopokea kwenye hospitali utakuwa wa kawaida na hautaathiriwa na uamuzi wako.Kwa hiyo ubashiri na matokea ya wagonjwa mahututi utaboreshwa.

Fidia:

Hakuna fidia itatolewa kwa kushiriki katika utafiti huu na hakuna malipo utakayotozwa kulipia kipimo cha damu.

Taratibu Na Itifaki za Utafiti

- Hii itakuwa uchunguzi unaotarajiwa; utafiti unaolenga wagonjwa 45 kutoka kitengo kikuu cha wagonjwa mahututi wa KNH.
- Wagonjwa wa utunzaji mkubwa watahitajika kujiunga na utafiti ikiwa wanakidhi vigezo vya kujumuishwa na wamekubali kushiriki katika utafiti.
- Utaratibu kuu katika utafiti huu ni kuchukua sampuli mbili kutoka kwa mgonjwa, moja kwenye sindano na Heparin ya kioevu, na nyingine kwenye sindano na Heparin iliyokaushwa ya elektroliti.
- Utaratibu utahusisha kuchomwa kwa ateri ambayo ni chungu kidogo.
- Sampuli hizi zitachambuliwa kubaini mabadiliko / kufanana au tofauti katika gesi za damu kwa wagonjwa hao hao.
- Takwimu zilizokusanywa na kurekodiwa kutoka kwa wagonjwa zitakuwa za siri kabisa na zitafikiwa tu na wafanyikazi wa mradi walioidhinishwa.
- Mhusika atashiriki kwenye utafiti mara moja.

Usiri:

Taarifa kutoka kwako na kutoka kwa kumbukumbu za matibabu zitakuwa siri. Hakuna majina wala maelezo yoyote ya kukutambulisha yatakayonukuliwa kwenye ripoti ya utafiti huu.

Maelezo ya mawasiliano:

Ukiwa na swali lolote kuhusu utafiti huu, unaweza kuwasiliana na Dkt. Emma Ngarama amabaye ni mchunguzi mkuu. Unawez pia kuwasiliana na KNH/UON ERC Commitee. Anwani zao zimetolewa hapa chini.

Mchunguzi mkuu:

Dr. Emma Ngarama
Nambari ya Simu: 0723378679
Barua pepe: emangarama@gamil.com

Mawasiliano ya Wasimamizi:

Dr. Timothy Mwiti
Nambari ya simu: 0721366294
Barua Pepe: tmwiti@uonbi.ac.ke

Dr. Kaiser Fitwanga
Nambari ya simu: +254722530992
Barua Pepe: kfitzwanga@yahoo.

Dr. Kevin Arunga
Nambari ya simu : 0722883057
Barua Pepe: kevinarunga@yahoo.com

KNH/UON ERC Katibu:

Nambari ya Simu: 2726300 ext 44102,
Barua pepe: uonknh_erc@uonbi.ac.ke

Tutakushukuru sana kwa ushiriki wako katika utafiti huu.

Idhini:

Mimi_____ baada ya kusoma maelekezo haya ama kusomewa na kuyaelewa na baada ya maswali yangu kujibiwa kwa lugha ninayoilewa nimeamua kwa hiari yangu mwenyewe kushiriki katika utafiti huu baada ya maelezo ya kina kutoka kwa Dkt. / Bwana / Bi._____. Ninaelewa wazi kwamba ushiriki wangu ni kwa hiari.

Sahihi ya Mshiriki _____ Tarehe _____

Jamaa wa karibu Tarehe

Azimio la Mchunguzi:

Nimefafanua kwa upana kwa mgonjwa kuhusu umuhimi wa hili somo na upungufu uliopo katika uwanja wa utafiti nchini Kenya. Nimejibu pia maswali yao kwa kuridhisha.

Saini ya Mtafiti / Msaidizi _____ Tarehe _____

Appendix III: Data Collection Tool: English Version

A Questionnaire to Investigate the Comparative Effects of Liquid Heparin versus Dry Electrolyte Balanced Heparin on Arterial Blood Gas Parameters in Critically Ill Patients.

DATE: **SERIAL NO:**

Part A: Patient Demographic Information. (Tick where appropriate)

1. Please indicate the patient's Age: ☐
2. Sex:
   i. Male ☐
   ii. Female ☐
3. Diagnosis:

Part B: Arterial Blood Gas Analysis Results.

4. Sample Collection time: ☐
5. Sample analysis time: ☐
6. Blood gas analysis parameter estimates:

	Liquid Heparin	**Dry Electrolyte Balanced Heparin**
Ph		
PCO2 (mmHg)		
PO2 (mmHg)		
Bicarbonate (mmol/L)		
Sodium (mmol/L)		
Potassium (mmol/L)		
Chloride (mmol/L)		
Hemoglobin (g/dl)		

Appendix IV: Eligibility Criteria

The study participants must meet all inclusion criteria. They must not meet any of the exclusion criterion.

Inclusion Criteria	**Exclusion criteria**
The critically ill patients of age 18 years and older admitted at the Kenyatta National Hospital Main Critical Care Unit. □YES □NO	The critically ill patients of age 18 years and older admitted at the Kenyatta National Hospital Main Critical Care Unit, whose blood sample for ABG is obtained from an indwelling arterial catheter. □YES □NO
The critically ill patients who have consented to participate in the study. □YES □NO	The critically ill patients of age 18 years and older admitted at the Kenyatta National Hospital Main Critical Care Unit with a known coagulopathy. □YES □NO
	The critically ill patients of age 18 years and above admitted at the Kenyatta National Hospital Main Critical Care Unit whose identity is not established. □YES □NO

Appendix IV: Certificate of Good Clinical Practice

NIDA Clinical Trials Network

Certificate of Completion

is hereby granted to

EMMA NGARAMA

to certify your completion of the six-hour required course on:

GOOD CLINICAL PRACTICE

MODULE:	STATUS:
Introduction	N/A
Institutional Review Boards	Passed
Informed Consent	Passed
Confidentiality & Privacy	Passed
Participant Safety & Adverse Events	Passed
Quality Assurance	Passed
The Research Protocol	Passed
Documentation & Record-Keeping	Passed
Research Misconduct	Passed
Roles & Responsibilities	Passed
Recruitment & Retention	Passed
Investigational New Drugs	Passed

Course Completion Date: 19 July 2022

CTN Expiration Date: 19 July 2025

Eve Jelstrom

Eve Jelstrom, Principal Investigator
NDAT CTN Clinical Coordinating Center

Good Clinical Practice, Version 5, effective 03-Mar-2017

This training has been funded in whole or in part with Federal funds from the National Institute on Drug Abuse, National Institutes of Health, Department of Health and Human Services, under Contract No. HHSN27201201000024C.

Appendix V: KNH/UoN-ERC Letter of Approval

UNIVERSITY OF NAIROBI
FACULTY OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/228

16th June, 2022

Dr. Emma Ngarama
Reg. No. H58/34294/2019
Dept. of Anaesthesia
Faculty of Health Sciences
University of Nairobi

KENYATTA NATIONAL HOSPITAL APPROVED 16 JUN 2022 KNH/UoN-ERC P.O. Box 20723 - 00202, NAIROBI

Dear Dr. Ngarama,

RESEARCH PROPOSAL: A COMPARATIVE STUDY ON THE EFFECTS OF DRY ELECTROLYTE BALANCED HEPARIN VERSUS LIQUID HEPARIN ON ARTERIAL BLOOD GAS PARAMETERS IN CRITICALLY ILL PATIENTS (P62/02/2022)

This is to inform you that KNH-UoN ERC has reviewed and approved your above research proposal. Your application approval number is **P62/02/2022.** The approval period is 16th June 2022 – 15th June 2023.

This approval is subject to compliance with the following requirements;

i. Only approved documents including (informed consents, study instruments, MTA) will be used.
ii. All changes including (amendments, deviations, and violations) are submitted for review and approval by KNH-UoN ERC.
iii. Death and life threatening problems and serious adverse events or unexpected adverse events whether related or unrelated to the study must be reported to KNH-UoN ERC 72 hours of notification.
iv. Any changes, anticipated or otherwise that may increase the risks or affected safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH-UoN ERC within 72 hours.
v. Clearance for export of biological specimens must be obtained from relevant institutions.
vi. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. Attach a comprehensive progress report to support the renewal.
vii. Submission of an executive summary report within 90 days upon completion of the study to KNH-UoN ERC.

Prior to commencing your study, you will be expected to obtain a research license from National Commission for Science, Technology and Innovation (NACOSTI) https://research-portal.nacosti.go.ke and also obtain other clearances needed.

Yours sincerely,

DR. BEATRICE K.M. AMUGUNE
SECRETARY, KNH-UoN ERC

c.c. The Dean, Faculty of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept., KNH
The Chair, Dept. of Anaesthesia, UoN
Supervisors: Dr. Timothy Mwiti, Dept of Anaesthesia, UoN
Dr. Kaiser Fitzwanga, Consultant Paediatrician, EMR/EPR Program-WHO Regional Office for Africa
Dr. Kevin Arunga, Consultant Anaesthesiologist, KNH

Appendix VI: Certificate of Plagiarism

A Comparative Study On The Effects Of Dry Electrolyte Balanced Heparin Versus Liquid Heparin On Arterial Blood Gas Parameters In Critically Ill Patients.

ORIGINALITY REPORT

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6	Nuri Dyah Indrasari, Jessica Purwanti Wonohutomo, Ninik Sukartini. "Comparison of point-of-care and central laboratory analyzers for blood gas and lactate measurements", Journal of Clinical Laboratory Analysis, 2019 Publication	<1%

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