A COMPARATIVE CROSS-SECTIONAL STUDY ON COMPARISON OF HYPERKALEMIA MEASUREMENT BETWEEN BLOOD GAS ANALYZER IN EMERGENCY DEPARTMENT AND MAIN LABORATORY BIOCHEMISTRY ANALYZER IN HOSPITAL UNIVERSITI SAINS MALAYSIA

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ABSTRAK

Pengenalan: Tahap kalium dinilai untuk pesakit yang mempunyai risiko tahap kalium yang tinggi di unit kecemasan dengan menggunakan mesin gas darah dan mesin biokimia. Kajian ini dijalankan untuk mengkaji kolerasi dan persetujuan pengukuran tahap kalium di antara mesin gas darah dan mesin biokimia.

Bahan dan metodologi: Kajian ini ialah kajian keratan rentas berdasarkan data yang diambil dari Hospital Universiti Sains Malaysia (HUSM) dari Jun 2018 sehingga Mei 2019. Sample darah diambil dengan satu suntikan daripada vein yang dihantar secara berasingan menggunakan 1 milimeter picagari dan dianalisa segera di unit kecemasan menggunakan mesin gas darah (*Radiometer, ABL800 FLEX, Denmark*) dan satu lagi daripada sampel dihantar ke pusat makmal Hospital Universiti Sains Malaysia dan dianalisa menggunakan mesin biokimia. Pesakit yang hanya mempunyai tahap kalium ≥ 5.0 mmol/L daripada mesin gas darah dikaji. Korelasi dan persetujuan dianalisa menggunakan *Passing and Bablok regression, Linear Regression* dan *Bland-Altman test.*

Keputusan: Sejumlah 173 sampel berpasangan telah direkodkan. Nilai purata tahap kalium daripada mesin gas darah dan mesin biokimia masing-masing ialah 5.77 mmol/L (SD±0.74) dan 6.05 mmol/L (SD±0.91). Tahap kolerasi di antara kedua mesin penganalisa adalah sederhana (P<0.001, r: 0.36). Tahap persetujuan di antara kedua mesin penganalisa adalah dalam julat yang diterima iaitu 0.27 mmol/L dengan had persetujuan 95% iaitu -1.21 mmol/L sehingga 1.73 mmol/L.

Kesimpulan: Keputusan pengukuran tahap kalium di antara mesin gas darah dan mesin biokimia ialah tahap kolerasi yang sederhana dan tahap persetujuan di julat yang diterima. Walaubagaimanapun, keputusan mesin gas darah cenderung kepada tahap yang lebih rendah daripada keputusan mesin biokima. Oleh itu, perawat mestilah

berhati-hati dalam menggunakan keputusan mesin gas darah sebagai panduan untuk memulakan rawatan tahap kalium yang tinggi dalam kes yang kritikal yang mana masa adalah faktor yang terpenting.

Kata kunci: kalium yang tinggi, mesin gas darah, mesin biokimia, titik penjagaan, persetujuan

ABSTRACT

Background: Potassium level is measured for patient with high risk of hyperkalemia in an emergency department (ED) using both blood gas analyser (BGA) and biochemistry analyser (BCA). The purpose of study to evaluate the correlation and agreement of hyperkalemia measurement between these two analysers.

Methods and Materials: This is a prospective cross-sectional study was conducted at Hospital Universiti Sains Malaysia (HUSM) from Jun 2018 until May 2019. The blood samples were taken by single pricked from venous blood and were sent separately using 1-ml heparinized syringe and analysed immediately in the emergency department (ED) using BGA (Radiometer, ABL800 FLEX, Denmark) and another sample was sent to the main laboratory of HUSM and analysed by BCA (Architect, C8000, USA). Only patients who had potassium level ≥ 5.0 mmol/L on blood gas results were included. The correlation and agreement were evaluated using Passing and Bablok regression, Linear Regression and Bland-Altman test.

Result: A total of 173 sample pairs were included. The mean of potassium level based on BGA and BCA were 5.77 mmol/L (SD±0.74) and 6.05 mmol/L (SD±0.91) respectively. There was moderate correlation between two measurements ($P<0.001$, r: 0.36). The agreement between two measurements showed within acceptable mean difference which was 0.27 mmol/L with 95% limit of agreement was –1.21 mmol/L to 1.73 mmol/L.

Conclusion: There is moderate correlation and acceptable agreement in hyperkalemia measurement between BGA to BCA. However, the BGA results tend to be lowered compared to BCA results. Therefore, the clinicians should use the BGA result with caution in certain clinical situation where time-is-of-the-essence to initiate treatment for hyperkalemia.

Keywords: hyperkalemia, blood gas analyzer, biochemistry analyzer, point-of-care, agreement

CHAPTER 1: INTRODUCTION

Hyperkalemia is a life-threatening electrolyte disorder that may cause cardiac arrest if not treated early. It is commonly seen in patients who present with acute kidney injury and chronic kidney injury in emergency department (ED) (Budak et al., 2012). The lethal toxicity of hyperkalemia is known due to it reduces myocardial conduction velocity and accelerates the repolarization phase, producing well-described changes on surface electrocardiogram(ECG), including narrow, symmetrical T wave, prolonged PR interval, diminished P-wave amplitude, QRS widening and ultimately sinusoidal QRST that terminates in asystole or ventricular fibrillation (Freeman et al., 2008).

Even though hyperkalemia may be fatal condition, but it can be reversible if immediately diagnosed and treated promptly by physicians. Therefore, immediate measurement of serum potassium become clinical importance as it change treatment approach in hyperkalemic patients, even during cardiac arrest (Acikgoz et al., 2016). Blood gas analyzer (BGA) is frequently used as point-of-care test and used to measure potassium level while waiting for definitive result of biochemistry analyzer (Acikgoz et al., 2016). BCA is usually located in the main laboratory and is considered as primary reference and assignment of reference values which is accredited by respective organizations (Reed, 2017). However, the results from BCA are always delay due to its distance, therefore lead to the difference between the time at which a test is ordered, the sample is received and the time at which the result is released. Delay in getting the results may compromise the treatment in critically ill patients, thus affecting their outcome (Budak et al., 2012).

There are two methods used to measure potassium level using electrolyte assay either direct or indirect which both employing ion-sensing electrodes (ISEs). (Budak et al., 2012, Gupta et al., 2016). Direct measurement does not require diluent solution for sample to interact with ISE membrane which apply to devices are typical of point of care testing analyzers such as BGA (Gupta et al., 2016). The indirect technique on the other hand need pre-analytical dilution with fixed volume diluent which take about 20-30 minutes for centrifuge process which is always employed in high-throughput central hospital laboratories running automated analyzers (Budak et al., 2012).

Bedside point-of-care is becoming important test in ED, intensive care unit and operation theatre (Budak et al., 2012, Leino and Kurvinen, 2011, Zhang et al., 2015, Jain et al., 2009, Morimatsu et al., 2003). Blood gas test is one of the test that many physicians rely on to measure electrolytes but still an additional sample is required to be sent to the central laboratory (Budak et al., 2012). Hence, the reliability and validity of using BGA should be comparatively accepted with the use of BCA as known to be gold standard for potassium measurement. According to United State of Clinical Laboratory Improvement Act (USCLIA), the acceptance bias of BGA measurement of potassium level is ±0.5 mmol/L (Sharon, 1990).

There were many previous studies had been done to determine the correlation and agreement between BGA and BCA. Unfortunately, there are no consensus on its correlation and agreement of the result between these two analyzers. The controversy probably is due to diversity in types of analyzer (Alanazi et al., 2015). Previous studies had compared variety of BGA and BCA such as Radiometer ABL505 versus Hitachi 717, Seimens Rapid Point 500 versus Abott C8000 Architect, GEM 3000 ABG analyzer versus Olympus AU2700 discrete chemistry analyzer, ABL825 FLEX analyzer versus AU2700 Autoanalyzer, Bayer Rapidlab 865 versus Olympus AU640,

Radiometer ABL800 versus AU640, Radiometer ABL90 FLEX versus Vy-5600 automatic biochemical analyzer and other different types of analyzers (Campbell, 2000, Yilmaz et al., 2016, Allardet-Servent et al., 2017, Chacko et al., 2011, Auvet et al., 2016, Jose and Preller, 2008, Banerjee and Mehrotra, 2018, Zhang et al., 2015). In Malaysia, we believe that majority of laboratories in Malaysia are using Radiometer models such as ABL800 FLEX, ABL90 FLEX and ABL80 FLEX. In our institution, we use BGA of Radiometer ABL800 in ED and BCA of Architech C8000 in central biochemistry laboratory. To the best of our knowledge, there is no previous study worldwide comparing these two analyzers that we used in our study. Objective of this study is to evaluate the correlation and agreement of potassium measurement between BGA and BCA.

CHAPTER 2: STUDY PROTOCOL

2.0 Introduction

Hyperkalemia is a life-threatening electrolyte disorder that may cause cardiac arrest if not treated early. It is commonly seen in patients who present with acute kidney injury and chronic kidney injury in emergency department (ED) (Budak et al., 2012). The lethal toxicity of hyperkalemia was known due to it reduces myocardial conduction velocity and accelerates the repolarization phase, producing well-described changes on surface electrocardiogram(ECG), including narrow, symmetrical T wave, prolonged PR interval, diminished P-wave amplitude, QRS widening and ultimately sinusoidal QRST that terminates in asystole or ventricular fibrillation (Freeman et al., 2008).

Even though hyperkalemia may be fatal condition, but it can be reversible if immediately diagnosed and treated by physicians in the event of cardiac arrest. Therefore, immediate measurement of serum potassium become clinical importance as it may change treatment approach in hyperkalemic cardiac arrest (Acikgoz et al., 2016). Blood gas analyzer is frequently used in patient with acute kidney injury while waiting for result of biochemistry analyzer to officially come out in ED (Acikgoz et al., 2016). The use of central laboratory testing in a hospital cause long delay, between the time at which a test is ordered and the time at which the result is received, this delay may compromise the treatment critically ill patient. If some processing steps taken to analyze the potassium level are eliminated, results are received immediately, patient is timely managed and outcome is improved (Budak et al., 2012).

There are two methods used to measure potassium level using electrolyte assay either direct or indirect which both employing ion-sensing electrodes (ISEs) that currently used in most hospitals (Budak et al., 2012, Gupta et al., 2016). Direct

measurement does not require diluent solution for sample to interact with ISE membrane which apply to devices are typical of point of care testing analyzers such as blood gas analyzers (Gupta et al., 2016). The indirect technique on the other hand need pre-analytical dilution with fixed volume diluent which take about 20-30 minutes for centrifuge process which is always employed in high-throughput central hospital laboratories running automated analyzers (Budak et al., 2012).

Bedside point-of-care is becoming important test in ED, intensive care unit and operation theatre (Budak et al., 2012, Leino and Kurvinen, 2011, Zhang et al., 2015, Jain et al., 2009, Morimatsu et al., 2003). Blood gas test is one of the test that many physicians rely on to measure electrolytes but still an additional sample is required to be sent to the central laboratory (Budak et al., 2012). Hence, the reliability and validity of using blood analyzer should be comparatively accepted with the use of biochemistry analyzer as known to be gold standard measurement of serum potassium. A study should be conducted on this subject so that the use between blood gas analyzer and central biochemistry analyzer in measurement of serum potassium can be clinically relied on in interchangeable manner.

2.1 Literature review

There are several studies done worldwide to assess the correlation and agreement of measurement of potassium between blood gas analyzer and biochemistry analyzer (Acikgoz et al., 2016, Alanazi et al., 2015, Jain et al., 2009, Zhang et al., 2015, Budak et al., 2012, Gupta et al., 2016). Unfortunately, there are no consensus between these results, probably due to different types of analyzers. According to United State Clinical Laboratory Improvement Amendments (CLIA) stated that

acceptable analytical performance of blood gas analyzer used for measurement of potassium should not exceed ±0.5 mmol/L (Zhang et al., 2015, Sharon, 1990).

A study done by (Jain et al., 2009) stated that there is no significant difference between the potassium values measured by the blood gas machine and main laboratory analyzer. There is a mean difference of 0.46 mmo/L, p value is 0.2679 with mean of potassium (blood gas) is 3.7mmol/L (SD±1.9) from the blood gas analyzer compare to 3.9 mmol/L (SD±1.8) from the main laboratory. Furthermore, another study done by (Zhang et al., 2015) stated that there are statistical differences and acceptable biases between ABG and Laboratory-measured potassium and sodium but the biases do not exceed USCLIA-determined limits and therefore, blood gas analyzer is reliable for measurement. In addition, a prospective study revealed that there is significant correlation between measurement of sodium, potassium and calcium by blood gas and serum biochemistry analyzer and therefore, the critical decision can be made by trusting the values obtained through both ABG and serum levels (Alanazi et al., 2015).

In contrary to above study, a study done by (Budak et al., 2012) revealed that mean potassium level result yielded 3.5 mmol/L by blood gas analyzer and 3.7 mmol/L by auto analyzer, with biases ranging of 0.15-0.352, inter-analyzer agreement is not acceptable and the results cannot be used interchangeably in clinical practice, however, they use P value < 0.001. The potassium level included in this study ranging between 3.79-5.60 mmol/L which is in physiologic range. Another study assessed the agreement of blood gas analyzer and central biochemistry laboratory analyzer in measurement of electrolyte that reported no significant difference within physiologic range however, in higher concentration of potassium which more than 5 mmol/L showed significant difference (Quinn et al., 2013). As far as we concern, there is only study done by (Acikgoz et al., 2016) focused on higher concentration of potassium

level ranging between 6.0 mmol/L and 9.3 mmol/L which showed no agreement between measurement by blood gas analyzer and biochemistry analyzer with mean difference between these analyzers is 0.62 mmol/L. There is vast controversy in the results of different laboratories due to use of divergent model of devices used in different hospitals (Alanazi et al., 2015). Ideally, a study should be done in every hospital to assess reliability measurement of Blood gas analyzer before it operates. It is due to different hospital use different machine and different calibration method (Budak et al., 2012).

In spite of there are still no previous statistical data available among the most frequently used blood gas analyzers in Malaysia, we believe that majority of laboratories in Malaysia are using Radiometer models such as ABL800 FLEX, ABL90 FLEX and ABL80 FLEX. But there are still few models of blood gas analyzers available in markets such as Gastat, Nova, Siemens, Roche and Istat which are less frequently used.

2.2 Problem statement and study justification

1. Prompt diagnosis of hyperkalemia is paramount importance as it is one of the reversible cause of fatal condition that need bedside point-out care investigation for diagnosis and prompt treatment. Blood gas analyzer is frequently and routinely used as an immediate guide for potassium level of patient in ED.
2. Even though biochemistry analyzer is gold standard test for measurement of serum potassium, however, its limitation in term of delay for official result is an issue for diagnosis. Key performance index of our central biochemistry analyzer Hospital Universiti Sains Malaysia (HUSM) for non-urgent test result

to come out will take about 4 hours and for urgent (upon request) test result is 1 hour. Any abnormal results will be notified by laboratory staff to physician within 30 minutes.

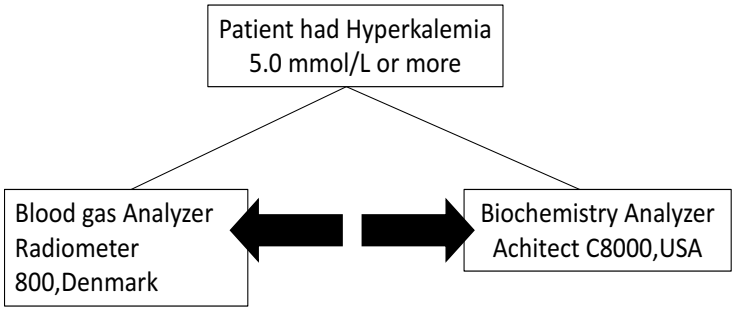
3. Due to the above limitations and inconsistent data from the previous studies, a study should be conducted to assess the reliability of blood gas analyzer in mini laboratory ED which is ABL800 FLEX Radiometer compare to Architech C8000 biochemistry analyzer in the central laboratory.
4. Based on previous literatures, there are lacking of studies comparing abnormal potassium level between blood gas analyzer and main laboratory. Therefore, this study is going to focus on patients who presents to ED with abnormal potassium level that is more than 5.0 mmol/L based on blood gas analyzer.
5. To the best of our knowledge, there is no previous study worldwide comparing two analyzers that we use in this study which are blood gas analyzer (Radiometer ABL800 FLEX) and biochemistry analyzer (Architech C8000).

2.3 Benefit of study

1. The result of this study will change the approach of physician either to rely on or not to blood gas analyzer as a guide for point-of-care bedside investigation for immediate diagnosis of hyperkalemia and treatment.
2. The result of this study can make improvement in term reliability of measurement of blood gas analyzer in ED comparably to gold standard biochemistry analyzer in central laboratory, HUSM by improving the quality control and assurance of blood gas analyzer according to National Institute of Standards and Technology (NIST) recommendation.

3. To indirectly educate dedicated staffs especially houseman, medical officers and specialists as well to improve techniques using heparinized syringes to measure potassium by blood gas analyzer to minimize bias.

2.4 Conceptual framework



2.5 Research question

1. Can we rely on potassium level measured by blood gas analyzer and be used interchangeably with potassium level measured by biochemistry analyzer?
2. What are demographic data and the common causes of hyperkalemia among patients in ED, HUSM?

2.6 Objectives

2.6.1 General objective

To compare the potassium level measured by blood gas analyzer in ED and main laboratory biochemistry analyzer among hyperkalemic patients in HUSM.

2.6.2 Specific objectives

1. To determine the demographic data and common causes of hyperkalemia among patients in ED HUSM.
2. To determine the correlation between measurement of potassium level between two analyzers.
3. To determine the agreement between measurement of potassium level between two analyzers.

2.7 Hypothesis

2.7.1 Null hypothesis

There is no difference between measurement of the hyperkalemia by blood gas analyzer in ED and main laboratory biochemistry analyzer in HUSM

2.7.2 Alternative hypothesis

There is difference between measurement of the hyperkalemia by blood gas analyzer in ED and main laboratory biochemistry analyzer in HUSM

2.8 Methodology

2.8.1 Study Design

This is a comparative cross-sectional study involves hyperkalemic patients who presented to ED, HUSM.

2.8.2 Study area

Emergency Department, Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan.

2.8.3 Study Population

Reference population: All patients with potassium level of 5.0 mmol/L or more based on blood gas analyzer in ED.

Source population: All patients with potassium level of 5.0 mmol/L or more based on blood gas analyzer in ED

Study participants: All patients with potassium level of 5.0 mmol/L or more based on blood gas analyzer in ED during study period and fulfilled the inclusion and exclusion criteria.

2.8.4 Inclusion criteria

- Age 18 years old and above.
- All patients whose venous blood gas (VBG) results show potassium level of 5.0 mmol/l or more from blood gas analyzer in ED

2.8.5 Exclusion criteria

- Blood sample sent for VBG and biochemistry analyses are taken separately based on the documentation in patient's folder.
- Both of the blood samples or either one of the samples are taken after definitive treatment or supportive treatment of hyperkalemia initiated.
- Result of potassium measured by blood gas analyzer is faulty or machine error.

2.8.6 Sampling method

Universal sampling method will be applied in this study in which all patients who fulfill the inclusion and exclusion criteria will be recruited in this study. According to data from Pathology department in 2015, approximately about 5000 patients annually who had been diagnosed mild to severe hyperkalemia in ED, HUSM by using

biochemistry analyzer. Unfortunately, there is no available data of hyperkalemic patients diagnosed by using blood gas analyzer.

2.8.7 Operational Definition

Hyperkalemia is defined as serum potassium more than 5.5 mmol/L. The severity of hyperkalemia is classified as follows (Ooi et al., 2015):

I. Mild: The potassium level less than 6.0 mmol/L
II. Moderate: The potassium level between 6.0 mmol/L and 7.0 mmol/L
III. Severe: The potassium level more than 7.0 mmol/L

However, for this study, the chosen level of hyperkalemia patient is 5.0 mmol/l as only ± of 0.5 mmol/l is allowed.

2.8.8 Methods and Reseach Tools

All patients are older than 18 years, with hyperkalemia between Jun 2018 until May 2019 will be enrolled in the study. Any patients who are indicated by the managing team for potassium level investigation using the blood gas analyzer in ED will be analysed. If the result of venous potassium is 5.0mmol/L or more, the results will be compared with the main laboratory results. It is a standard practice that blood samples are taken from a single prick and put in separate containers for investigations. It is also a standard practice that the blood that is sent for VBG investigation in ED is the same with the blood sample that is sent for biochemistry analyzer in the main lab. For this study, the VBG results and biochemistry results from the main lab are considered from the same source of blood taking, unless specifically mention in the patients' folder. The duration of this study will take about 10 minutes which is the time taken for blood taking process. There are no attempts to interfere with the standard of care by the

managing team. Since this study is part of the quality control of the department and the implement is approved by head of department, the notice about the study will be pasted at the waiting area as well as at three zone area which are red, yellow and green zone. All patients will be informed about the study and their results are being used if they fulfilled our criteria. All the blood results are confidential and anonymous. All blood gas samples will be discarded after being analysed and will not be used for future study. All data will be recorded in ED HUSM Hyperkalaemia patient checklist form.

All venous blood samplings are performed by trained staffs either houseman or medical officers in sterile environment. They are collected in 1 ml blood-gas syringes which are flushed with heparin (1:1000) beforehand and syringed out completely to prevent clotting and dilution that affect the results. They also have to make sure there is no bubble inside blood sample taken to minimize pre-analytical error. Then, all venous blood samples are not stored in ice but are analyzed immediately after collection. We use two models of blood gas analyzer ABL800 FLEX Radiometer from Denmark which are operating 24-hour in our mini laboratory situated in ED, HUSM. Our mini Laboratory is operated by two dedicated laboratory staffs who monitor and maintain the function of these analyzers. The maintenance of machine follows manufacturer's recommendation which is based on standard of National Institute of Standards and Technology (NIST). Automated internal Quality Control is done daily with regular two points calibration every two hours to make sure analyzer is performing correctly and minimizing errors. For minimizing bias or measurement error from sampling method of blood gas, short presentation on how to optimize on sampling method of blood gas will be conducted during weekly department Continuing Medical Education (CME) for master students or medical

officers, housemen and all staffs and keep reminding on regular basis during daily morning pass-over meeting.

Meanwhile, same venous blood samples for biochemistry analyses are collected and sent to central laboratory of HUSM. Model of biochemistry analyzer is used in this study is Architect C8000 from USA which operates under Pathology Department and located at different place with Blood Gas Analyzer used in this study. It is considered as gold standard of test for measurement of potassium level and is under regular maintenance by pathology department. Quality control and assurance done regularly to ascertain reliability of test based on manufacturer recommendation and International guideline (NIST).

There are several differences between blood gas analyzer and biochemistry analyzer which are as following:

Blood Gas Analyzer	Biochemistry Analyzer
Analyze whole blood	Analyze serum
Arterial sample used conventionally	Venous sample used conventionally
Use direct ion selective electrode	Use indirect ion-selective electrode
Use heparin-diluted sample	Serum sample diluted with fixed volume diluent
Processing time short	Processing time long
no effect of protein levels in blood	Affected by protein level in blood

(Jain et al., 2009)

In theory, the expert explained the reasons for different result between blood gas analyzer and biochemistry analyzer which are(Jain et al., 2009):

1. Dilution with heparin raises the volume of the sample, thereby lowering the value of the measured electrolytes on the blood gas.
2. High volume of heparin itself binds the electrolytes, thereby lowering the value of measured electrolytes on blood gas.

Due to this evidence, we estimate that potassium level measured by blood gas analyzer may be lower than biochemistry analyzer. According to United State of Clinical Laboratory Improvement Amendment, potassium bias should be limited ±0.5 mmol/L (Zhang et al., 2015). This is the reason we enroll patients with venous blood gas of potassium measuring 5.0 mmol/L and above in our study

2.8.9 Sample size calculation

For first specific objective: To study demographic data and common causes of hyperkalemia.

No calculation for sample size for descriptive analysis

For second and third specific objective: To access correlation and agreement between measurement of potassium level between two analyzers

Based on previous literature, we calculate sample size using MedCalc v17.8 Software (Trial Version). We use Bland-Altman plot to calculate sample size between two measurement method. According to (Budak et al., 2012) that showed mean differences between two measurement (Blood gas analyzer and biochemistry analyzer) for potassium level was 0.62 mmol/L, with Standard Deviation difference was 0.43 mmo/L. Maximal allowed difference between two measurement which based on USCLIA is 0.5 mmol/L. $P < 0.05$ is significant and the power of study is 80%. The method of calculation as followed

Sample size: Bland-Altman plot

Options

Type I error (Alpha, Significance)	0.05
Type II error (Beta, 1-Power)	0.20

Data

Expected mean of differences	0.62
Expected Standard Deviation of differences	0.43
Maximum allowed difference between methods	1.62

Result

Minimum required number of pairs	177

Table

		Type I Error - Alpha			
		0.20	0.10	0.05	0.01
Type II Error - Beta	0.20	130	149	**177**	261
	0.10	181	210	241	332
	0.05	221	257	290	397
	0.01	291	352	409	534

The sample size of this study is 177 pairs. We estimate approximately 10% of drop-out samples, so the total of sample size will be 195 samples.

2.9 Ethical consideration

During this study, all the data collected in confidential manner and only can be accessible by investigator team. We would like to declare no conflict of interest with regard of this study. We uphold patient's right and their safety will not be jeopardized and become our priority in this study. The blood samples which are included in this study will be discarded immediately after used and will not be used for other study. Furthermore, there will be an assumption that it may needs additional cost to patients and specific allocation budgets. So, we would like to clear that we don't need any additional budget to conduct our study and we only enroll patients who are indicated for blood taking based on their clinical justification by the managing team or attending doctors.

2.10 Data collection

Data will be collected by the investigator or any attending doctor from enrolled patients or patient relatives by using the data collection form in Appendix 1 (EDHUSM Hyperkalemia checklist). The enrollment of sample is based on inclusion and exclusion criteria stated above and are consented to enter into this study. Specific study ID will be assigned to all patients to maintain their confidentiality. Any data collection process will undergo without jeopardizing patient's priority to receive immediate treatment.

2.10.1 Data entry

Data will be entered and analyzed using Statistical Package for Social Science (SPSS) for Macintosh, version 23.0

2.10.2 Statistical Analysis

For first specific objective, we will use descriptive analysis. Meanwhile, for second specific objective, Pearson correlation analysis will be used to calculate the correlation of these two measurements. For third specific objective, we will use Bland-Altman plot to analyze the agreement between two measurement method blood gas analyzer and biochemistry analyzer. We will construct a line graphic to show correlation and level of agreement of blood gas and biochemistry analysis. Statistical significance is defined as P value <0.05.

2.10.3 Dummy table

Table 1: Demographic data and common causes of hyperkalemia among patient in HUSM

Patients		**N**	**Percentage(%)**
Gender	Male		
	Female		
Age (years)	18-40		
	41-60		
	>60		
Race	Malay		
	Indian		
	Chinese		
	Others		
Initial triage	Red		
	Yellow		
	Green		
Causes of Hyperkalemia	Acute kidney failure		
	Chronic kidney failure		
	Drug-related		
	Hyperglycemia		
	Others		

Table 1, continued

Prognosis	General ward
	ICU/CCU/HDW
	Death

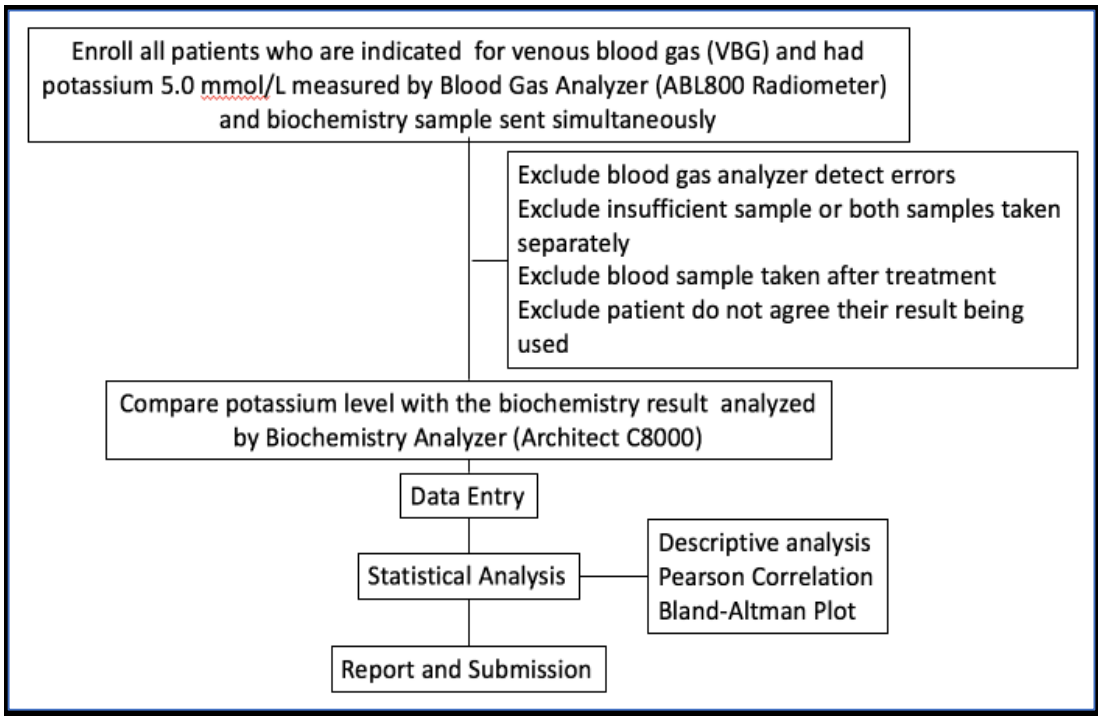
Table 2: correlation statistics between blood gas analyzer (ABL800 FLEX Radiometer) and Biochemistry analyzer (Architect C8000)

Analyte	**Range**	**Biochemistry Analyzer(x) vs Blood gas analyzer(y)**				
		Slope (95% CI)	Intercept (95% CI)	Mean Diff.	r	Range Transformed
Potassium	5.0-6.0					
	6.1-7.0					
	>7.0					

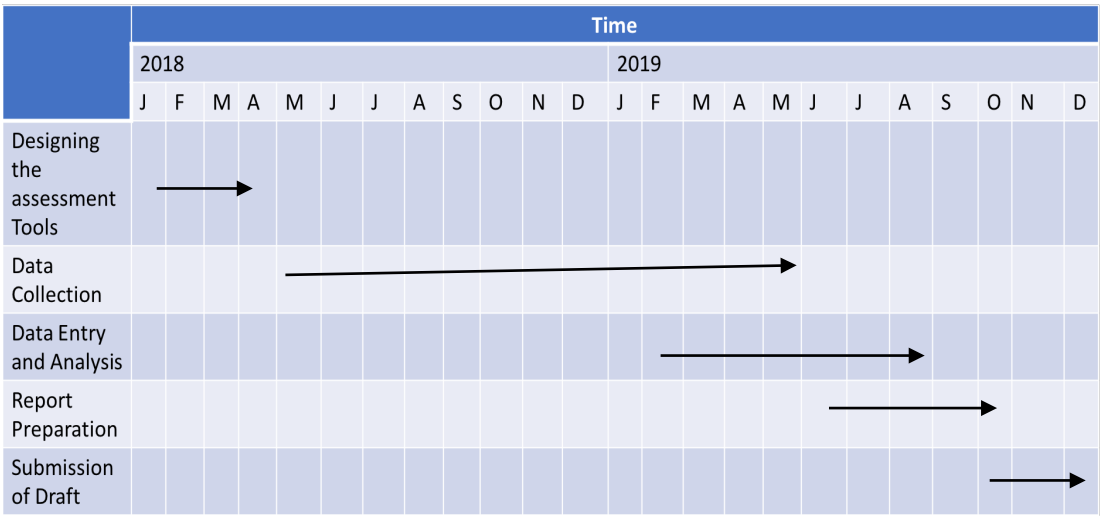
Table 3: Bland and Altman plot statistics between Potassium measured by Blood gas analyzer and biochemistry analyzer

Group Mmol/L	**Mean difference mmol/L**	**SD difference mmol/L**	**Max. difference mmol/L**	**Min difference mmol/L**	**P value**
5.0-6.0					
6.1-7.0					
>7.0					

2.11 Flow chart



2.12 Gannt chart and milestones



Milestone:

1. Designing the assessment tools is expected to be completed by the end of March 2018.
2. Data collection is expected to be completed by the end of April 2019.
3. Data entry and data analysis are expected to be completed by the end of June 2019.
4. Report preparation is expected to be completed by the end of September 2019.
5. Submission of draft is expected to be done by December 2019

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APPENDICES

ED HUSM Hyperkalaemia Checklist

1. ID/RN				
2. Gender	Male ☐		Female ☐	
3. Age				
4. Nationality				
5. Race	Malay ☐		Chinese ☐	
	Indian ☐		Other ☐	
6. Initial Triage	Red ☐	Yellow ☐	Green ☐	
7. Serum Potassium level (mmol/L)	VBG		Biochemistry Analyzer	
8. Causes of Hyperkalemia	• Acute renal failure ☐ • Chronic renal failure ☐ • Drug-related ☐ • Hyperglycemia Emergencies ☐ • Others: _____			
9. Initiation of treatment is based on	• VBG ☐ • Biochemistry Analyzer ☐			
10. Disposition/Prognosis	• Ward ☐ • Intensive Care Unit ☐ • Death ☐			

Filled By:
Doctor's Name:
Designation: