STUDY PROTOCOL

Arm and Finger measurement for Blood Pressure Surveillance

CIRB NUMBER:
2019/2290

PROTOCOL VERSION: 1.0

PROTOCOL DATE: 10 May 2019

PRINCIPAL INVESTIGATOR:
Dr Farida Binte Ithnin, Senior Consultant, KK Women's and Children's Hospital (KKH)

*Also refer to Section F9 on the statistical analysis details.

Section A : Protocol Title & Protocol Administrators

A1.Please enter the Full Protocol Title and Protocol Number (if available) for this Study

Protocol Title : Arm and Finger measurement for Blood Pressure Surveillance

A2.You may assign Protocol Administrators for this study below

No.	Name	Institution/Organization	Department	Email
1	Tan Chin Wen	KK Women's and Children's Hospital (KKH)	Department of Women's Anaesthesiology	Tan.Chin.Wen@kkh.co m.sg
2	Teo Pei Chih Agnes	KK Women's and Children's Hospital (KKH)	Department of Women's Anaesthesiology	Agnes.Teo.PC@kkh.c om.sg

Section B : Study Sites, Study Team & Submission Board

B1. Please select the study sites

(i) SingHealth and Partner Institutions (PI listed in Section B2(i) should be from any of the selected institution(s) under "SingHealth and Partner Institutions".) KK Women's and Children's Hospital (KKH)

B2. Study Team Members

(i) Add Study Team Members

No.	Name	Study Role	Department	Institution	Designation	Involve in Informed Consent
1	Dr Ithnin Farida Binte	PI	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Senior Consultant	[x]
2	Dr Cheng Shang-Ming	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Associate Consultant	[x]
3	Dr Lim Ming Jian	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Resident	[x]
4	Dr Sng Ban Leong	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	Senior Consultant	[x]
5	Ms Kee Hwei Min	Co-I	Division of Nursing	KK Women's and Children's Hospital (KKH)	NC, APN (Anaesthesia)	[x]

B3. Submission Board and other IRB

(i) Which CIRB is this application being submitted to?

CIRB D- Anaesthesia (including acupuncture)

(ii) Has the study been submitted to another IRB? No

(iii) Has the application been previously rejected by any IRB? (Including SingHealth CIRB) No

Section C: Conflict of Interest

Does the Principal Investigator or any Study Team Member have any potential conflict of interest?The Declaration is also for the immediate family members of the PI and Team Members listed below.

Name	Study Role	Department	Institution	Yes/No
Dr Ithnin Farida Binte	PI	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	No
Dr Cheng Shang-Ming	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	No
Dr Lim Ming Jian	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	No
Dr Sng Ban Leong	Co-I	Department of Women's Anaesthesiology	KK Women's and Children's Hospital (KKH)	No
Ms Kee Hwei Min	Co-I	Division of Nursing	KK Women's and Children's Hospital (KKH)	No

Section D: Nature of Research

D1. Please select one category that best describes your research activities.

Clinical Research

D2. Is this a US FDA IND/IDE study or data is intended to be reported to FDA in support of an IND/IDE Application?

No

Section E: Study Funding Information

E1.Please give information regarding the study's funding source or sponsor information.

Grant

i. Name of Grant Agency: SingHealth

ii. Grant Name: ACP

iii. Amount: 10000

iv. Deadline of Grant Application: 31 Jan 2019

v. Has the grant been approved? Yes

File Name	Description	Version Number	Version Date
ANAES ACP Letter of Award - Dr Lim MJ.pdf	Letter of award		-
ACP Letter of Acceptance-(Arm and finger measurement) .pdf	Letter of acceptance_ LimMJ		-

vii. Grant Reference Number ANAESPRG/02

Submission Date: 05-Apr-2019

E3. Who will be responsible for the payment and compensation of injury or illness to participants arising from participation in the study?

If the patients follow the directions of the Principal Investigator of this research study and are injured due to the trial substance or research procedure given under the plan for the research study, our institution will provide them with appropriate medical treatment. Payment for management of the normally expected consequences of their treatment will not be provided by KK Women's and Children's Hospital.
The patients still have all their legal rights. Nothing said in the informed consent document on treatment or compensation in any way alters their rights to recover damages where they can prove negligence.

E4. Who will be responsible for research-related costs? For sponsored studies, please list the costs that will be borne by the sponsor.

SingHealth ACP funding

Section F: Research Methodology

F1. Please provide an abstract of your proposed research (Up to 300 words).

Accurate blood pressure (BP) measurement plays an important role in peripartum care as it is essential in detecting hypertensive disorders in pregnancy and medical decision making during the pregnancy. The cuff and bladder size have been highlighted as an important factor affecting the accuracy of BP measurement. Current international BP measurement recommendations are based on mid-arm circumference (MAC) assuming the arm is cylindrical in shape. However, evidence have shown a mismatch between these sizes, leading to BP overestimation or underestimation in obese patients. This is because the shape of the arm is a truncated cone instead of a cylinder, and the cuff will expand irregularly during inflation thus yielding inaccurate BP measurements. This is especially evident in Asian pregnant patients whereby no available guideline can recommend a suitable cuff for parturients with different MAC. Nexfin is a finger cuff device that can be a suitable alternative BP measurement device for such patients. In this study we will recruit 300 parturients in third trimester and undergoing nonemergent caesarean section in our institution. We will measure their arm and finger sizes, and collect their user experience on current practices on BP measurement. The arm measurements will help us identify the proportion of women that may require non-standard cuff sizes for BP measurement. It also allows us to derive a conicity index and determine whether the MAC, finger measurement or body mass index (BMI) is the best clinical predictor. The finger measurements will also help us determine the proportion of women that may require non-standard cuff sizes on the Nexfin device for BP measurement. The knowledge gathered in this pilot study will be used to design future studies in which we will compare the accuracy of Nexfin with standard BP measurement, which in turn will improve BP detection, subsequent patient monitoring and satisfaction.

F2. What are the specific aims and hypothesis of this study?

The primary hypothesis of this proposed study is the right Mid-Arm Circumference (MAC) is correlated with the right arm conicity index (r = 0.4). The specific aims of the study are as below:

i) In this cohort, to determine the arm conicity index and the association with MAC;

ii) To obtain arm measurements of parturients of third trimester (>=32wks gestation) to determine the proportion of women requiring non- standard BP arm cuff based on their right and left MAC;

iii) To obtain finger measurements of parturients of third trimester to determine the proportion of women requiring non- standard BP finger cuff based on the circumference measured at the middle phalanx of the right and left middle finger;

iv) To gain user feedback on the experience of current practice of BP measurement according to a three-point rating scale.

F3. Please briefly describe the background to the current study proposal. Critically evaluate the existing knowledge and specifically identify the gap that the proposed study is intended to fill.

Accurate measurement of blood pressure is an important part of peripartum care as it is essential in detecting hypertensive disorders in pregnancy and medical decision making during the pregnancy. According to the recommendations by the European Society of Hypertension, the cuff and bladder of BP device has been highlighted as an important factor in the accuracy of BP measurement. [1] Most guidelines recommend a bladder width and length of 40% and 80% of arm circumference respectively [1-3], however this may not apply in obese patients. Palatini et al. showed that a mismatch between the arm size and the bladder might lead to overestimation or underestimation of up to 30mmHg in obese patients [4] and that this overestimation was more significant when standard cuff was used instead of a larger cuff [5]. The increase in arm circumference may also contribute to the BP overestimation [5].

Another problem with the above recommendation is that it is impractical and costly to manufacture a large variety of cuff and bladder sizes for an ideal fit. Several approaches have been suggested, such as application of correction factors, having a range of cuffs and having a variety of cuff bladders, but none of them is ideal. [1] The recommendation also does not take into consideration the shape of the arm and assume it is in a cylindrical form. However, Bonso et al. observed that the arm becomes cone-shaped when the circumference of the upper arm is greater than that of the lower arm [6], resulting in a gap between the rectangular blood pressure cuff and the surface of the distal part of the arm. [4] When this difference becomes too large, a cylindrical cuff will expand irregularly during inflation and yield inaccurate BP measurements. This is proven by Palatini et al. in which rectangular cuffs could overestimate BP in non-pregnant patients with large conical arms with difference in systolic BP up to 9.7mmHg and diastolic BP up to 7.8mmHg. [7]

The Australasian Society for the Study of Hypertension in Pregnancy has recommended that a standard cuff should be used for parturients with arm circumference of £ 33cm, while the large cuff (15x33cm bladder) should be used in arm circumference of > 33cm. [8] However, a study by Kho et al. has shown that the 33 cm 'cut-off' is an arbitrary one, and that hypertension was diagnosed more often with a standard cuff in women with an arm circumference < 33cm, as well as in women with arm circumference ≥ 33cm regardless of cuff size. [9] Our overseas collaborator, Eley et al. has shown that some parturients (n=58/450 or 12.9%) might require a large cuff based on their right MAC, and a further six patients (1.3%) would need a thigh cuff instead, and that this right MAC is correlated with BMI (r=0.45). This suggested that finger cuff may be more suitable for this group of patients, however we have little evidence on whether these data are applicable to the Asian parturient population too. [10] Wang et al. did observe that there was no MAC difference in adult female when comparing whites and Asians, yet no further data was available on comparing the parturients in both groups, and the correlation between BMI and conicity index in Asian parturients remains unknown. [11]

Finger cuff devices such as the Nexfin monitor (BMEYE B.V., Holland) are commonly used for BP measurement nowadays. These devices apply the volume-clamp method described by Penaz [12] to provide a continuous non-invasive blood pressure reading that avoid the problems of poorly-fitting arm cuffs, and hence offer an alternative in women with large or conical arms. However, these patients may have peripheral edema and vasodilatation in pregnancy which may lead to poorly fitting finger cuffs and inaccuracies in BP measurement.

With the above background information, we intend to examine the arm and finger sizes of pregnant women in our local population in Singapore. These will help us derive a conicity index which will be compared to the arm and finger sizes, and BMI to determine which the best clinical predictor is. The finger sizes will also provide insights into the proportion of women who require non-standard finger cuffs on the Nexfin monitors to determine the suitability of the device for use in our population. Through the knowledge gained from this study, we hope to improve the accuracy of BP measurement, change current practices to improve detection of hypertensive disorders in pregnancy for early intervention, subsequent patient monitoring and improve patient experience during BP measurement.

F4. Please provide a list of relevant references.

1. O'Brien, E., et al., European Society of Hypertension recommendations for conventional, ambulatory and home blood pressuremeasurement. J Hypertens, 2003. 21(5): p. 821-48.

2. Pickering, T.G., et al., Recommendations for blood pressure measurement in humans and experimental animals: part 1: bloodpressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. Circulation, 2005. 111(5): p. 697-716.

3. Perloff, D., et al., Human blood pressure determination by sphygmomanometry. Circulation, 1993. 88(5 Pt 1): p. 2460-70.

4. Palatini, P. and G. Parati, Blood pressure measurement in very obese patients: a challenging problem. J Hypertens, 2011. 29(3): p.425-9.

5. Fonseca-Reyes, S., et al., Effect of standard cuff on blood pressure readings in patients with obese arms. How frequent are arms of a'large circumference'? Blood Press Monit, 2003. 8(3): p. 101-6.

6. Bonso, E., et al., Accuracy of a single rigid conical cuff with standard-size bladder coupled to an automatic oscillometric device over awide range of arm circumferences. Hypertens Res, 2010. 33(11): p. 1186-91.

7. Palatini, P., et al., Rectangular cuffs may overestimate blood pressure in individuals with large conical arms. J Hypertens, 2012. 30(3): p. 530-6.

8. Brown, M.A., et al., The Classification and Diagnosis of the Hypertensive Disorders of Pregnancy: Statement from the InternationalSociety for the Study of Hypertension in Pregnancy (ISSHP). Hypertension in Pregnancy, 2001. 20(1): p. ix-xiv.

9. Kho, C.L., et al., Blood pressure measurement in pregnancy: the effect of arm circumference and sphygmomanometer cuff size.Obstet Med, 2009. 2(3): p. 116-20.

10. Eley, V.A., et al., Arm and finger measurements in the third trimester: Implications for blood pressure measurement. PregnancyHypertens, 2018. 14: p. 105-109.

11. Wang, J., et al., Asians have lower body mass index (BMI) but higher percent body fat than do whites: comparisons of anthropometricmeasurements. Am J Clin Nutr, 1994. 60(1): p. 23-8.

12. Penaz, J., Criteria for set point estimation in the volume clamp method of blood pressure measurement. Physiol Res, 1992. 41(1): p.5-10.

F5. Please attach at least two relevant publications that support the conduct of the study.

File Name	Description	Version Number	Version Date
PregHTN Arms and fingers.pdf	Ref 10. Eley et al.		-
palatini2012.pdf	Ref 7. Palatini et al.		-

F6. Please provide an account of the Principal Investigator's preliminary studies and progress reports (if any) pertinent to this application.

Not available.

F7. Please state concisely the importance of the research described in this application by relating the specific aims to the long term objectives.

1. To identify the most suitable cuff size for BP measurement for parturients of different arm and cuff sizes. These data may be presented to hospital administrators for guideline review, which in turn improves the BP detection and the subsequent better patient monitoring and satisfaction.

2. To prepare for future cluster and national level grants that will look into broader applications during the postpartum period for early identification of those at high risk of hypertension, and thereby the appropriate intervention and treatment at earlier time.

F8. Discuss in detail the experimental design and procedures to be used to accomplish the specific aims of the study. If this study involves a retrospective medical record review,

This research is a single-centre pilot study by which a number of 300 parturients will be recruited from antenatal clinics in KKH. Caesarean delivery constitutes about 30% total delivery in our institution, contributing to 3000-4000 cases annually. There are 9 months for clinical trial recruitment. We will aim to recruit at least 34 cases per month (worst case scenario of 13.6% of available patient caseload). We have engaged anaesthetists and nursing division that worked on the previous ACP project (EPOC, ANAESPRG18/02) working on the same patient population with a more complex protocol and have managed to recruit 200 patients within 9 months. Hence, the study is feasible. Written informed consent will be obtained. Baseline demographic and obstetric characteristics will be obtained from patient medical records during the admission of labour and delivery. Body mass index (BMI) will be calculated from patient's height and weight measured on the day of recruitment. We will collect the below measurements using a measuring tape on both arms:

Measurement	Description
Arm length	The distance between the tip of the acromion process to the tip of the olecranon process on the pos terior aspect of the arm, with the elbow in the flexed position.
MAC	The circumference of the arm at the mid-point of the arm length as measured above, with the arm h anging by the side.
Proximal arm circumference	Arm circumference of the arm measured at the axilla, with the arm hanging by the side.
Distal arm circumference	The circumference at the elbow above the elbow crease, with the arm hanging by the side.
Finger circumference	The circumference of the mid-point of the middle phalanx of the middle finger will be measured with the hands placed flat on a table. This site is also the recommended site for the Nexfin finger cuff.
Conicity index	The conicity index of the arms will be calculated according to Bonso et al. [6] as 100 (proximal arm diameter – distal arm diameter)/arm length.

Appropriate arm cuff size as determined by MAC and finger cuff size as determined by finger circumference matched to the manufacturer's recommendations will be determined by investigators in each subject, and the selection will be documented accordingly. Ideally, the upper arm cuff should have an inflatable bladder with a length of 80% and a width of at least 40% of the circumference of the upper arm. [2] Participants will also respond to a three-point rating scale (Never, sometimes, always) about their experience of the procedures for previous BP measurement during the current pregnancy, with questions such as the length of time taken to obtain a reading, the need to change a cuff when taking BP, the need to take BP on the leg and whether the arm felt uncomfortable when taking BP.

F9. Please provide details on sample size and power calculation and the means by which data will be analyzed and interpreted (If applicable).

Sample size calculation: Sample of 300 patients will be adequate to estimate a correlation coefficient of 0.4 with 95% confidence interval width as 0.2 i.e. a sample size of 300 produces a two-sided 95% confidence interval with a width equal to 0.200 when the estimate of Pearson's product-moment correlation is 0.400. This is based on the correlation results found by investigators at the Royal Brisbane and Women's Hospital in Caucasian population [10].

Statistical analysis: For primary hypothesis, we will calculate pearson's correlation between MAC and coincity index with 95% confidence interval for right arm. We will also fit univariate and multivariable linear regression between conicity index (outcome variable = Y) and MAC along with BMI and weight. Association between coincity index and other variables will be expressed as estimate with its 95%CI. We will also estimate arm and finger measurements of women requiring non-standard BP arm cuff with 95%CI based on right and left arm MAC respectively. We will also compare difference between right and left arm measurements using paired t – tests. We will also estimate finger measurements of women requiring nonstandard BP cuff with 95%CI based on right and left middle finger respectively. We will also compare difference between right and left finger measurements using paired t – tests. Patient's experience on BP measurement will be expressed as frequency with proportion. Categorical data will be presented using frequency (percent). Continuous variables will be expressed as mean (standard deviation (SD)) or median (interquartile range (IQR), range) whichever appropriate. A statistical significant will be set at < 0.05. All the analysis will be done using SAS 9.4 software.

F10. List all activities that are carried out as part of research in this study. Please state/list all procedures involved in this research study and attach the data collection form (if any) which will be used for CIRB review.

- Patient recruitment with informed consent obtained
- Demographic data collection
- Measurement of arms and fingers
- Cuff Fitting
- Questions on previous BP measurement experiences

Data Collection Form:

File Name	Description	Version Number	Version Date
DATA COLLECTION FORM_Armfin SBL.docx	data collection form		-

F11. Please describe the participant's visits (frequency and procedures involved). For studies with multiple visits, please attach study schedule.

One time visit. Once the informed consent is obtained, the arm and finger measurements as well as data collection will be done in the same visit.

F12. Discuss the potential difficulties and limitations of the proposed procedures and alternative approaches to achieve the aims.

Having used a different definition of arm length to calculate conicity, it is not possible to directly compare our conicity results with those of Bonso and Palatini [6,7]. This study has not measured the accuracy of blood pressure measurements as this may require a longer observation period and therefore add on to patients' inconvenience. Subsequently we are unable to provide an arm conicity cut-off, above which finger cuffs may be more suitable. However we have reported the frequency of aberrant cuff placement as a surrogate measure of blood pressure measurement difficulty.

F13. What are the potential risks to participants?

The potential risks to participants related to the measuring tape and the cuff are that patients may be inconvenienced from moving around due to the tape, and also the possible discomfort or poor blood circulation if the cuff is used on the same position for an extended period of time.

NOTES:
It is not appropriate to provide a nil response as all research procedures have some risks or side effects. For retrospective medical records review or questionnaires study, although the risks are expected to be minimal, there may be a potential risk from the breach of confidentiality.

F14. What are the potential benefits (direct as well as indirect) to participants? Indirect benefit may refer to the medical knowledge gained in the future, from the research.

There is no direct benefit to the participants. Their participation may contribute to the medical knowledge about the effect of arm conicity on the accuracy of BP measurements in obese pregnant women and explore the accuracy of alternative devices.

F15. What is the estimated timeline for this study?

(i) Estimated start date 01-May-2019

(ii) Estimated end date 30-Apr-2021

F16. Does this study have a Study Protocol?

No

NOTES:
Investigators conducting Clinical Trials must submit a Study Protocol for CIRB review. You may refer to the CIRB website for the Protocol template (Clinical Trial) and Protocol Template (Clinical Research).

http://research.singhealth.com.sg/pages/centralisedinstitutionalreviewboard.aspx

F17. The Principal Investigator is responsible for ensuring that all study participants give informed consent before enrolling into the study.

Please select the applicable consent scenarios. Please select "Waiver of Informed Consent" if consent has been obtained for research purposes.

Informed Consent will be taken for all study subjects.

Section H: Recruitment Details

H1. How will potential participants be identified? Please tick all the applicable boxes.

[x] Referral by attending healthcare professional
[ ] Patients of study team
[ ] Databases
[x] Other methods of participant identification
Investigators and the clinical research coordinators in the study team will approach patients in the antenatal clinics while they are waiting for their visits. Brochures will also be placed in the clinics so that patients can contact the research team should they express interest to join the study.

H2. Who will make the first contact with participant?

Investigators and the clinical research coordinators in the study team will make the first contact with participant.

H3. How will the participant be contacted?

This study will be advertised with study brochures. These will be posted and distributed through KKH, and given to all patients who meet the inclusion/exclusion criteria during antenatal period. Potential study patients may be invited to participate by study team members in the antenatal clinics at KKH, whereby the research team will provide information about the study. The investigators and study team will be available to

Section I: Study Sites & Recruitment Targets

I1. Please state the target number of research participants to be recruited for each site in Singapore.If exact numbers are not available, please give a number range in the recruitment target.

No.	Study Site	Total Target	Adults (Male)	Adults (Female)	Children
1	KKH	300	0	300	0

I2. Is this study part of an international study?

No

Section K: Research Participant Characteristics

K1. Please list the inclusion criteria for research participants in this study.

- American Society of Anaesthesiologists physical status 1 or 2 (ASA 1 or 2) parturients at >=32 weeks of gestation
- Multiparous or nulliparous;
- Age 21-50 years old;
- Undergoing Caesarean section in KKH.

K2. Please list the exclusion criteria for research participants in this study.

Lower Age limit 21

Upper Age limit 50

NOTES:

Persons below the age of 21 and are unmarried are considered minors in Singapore and will require parental consent prior to participation.

K4. Are there any recruitment restrictions based on the gender of the research participants (e.g. only males will be included in this study)?

Yes

Only women undergoing cesarean delivery in KKH will be recruited.

K5. Are there any recruitment restrictions based on the race of the research participants (e.g. only Chinese participants will be included in this study)?

No

K6. Do the potential research participants have a dependent relationship with the study team (e.g. doctor-patient, employee-employer, head-subordinate, student-teacher, departmental staff relationship)?

No

NOTES:

If you have selected that participants are 'Patients of study team' in Section H1, then the answer should be 'Yes'.

K7. Does the study involve any vulnerable research participants? Please select 'Yes' to view the options and select the applicable population(s). Yes

[x] If Pregnant Women, Foetuses and Neonates is selected, please respond to Section L.
[ ] If Children is selected, please respond to Section M.
[ ] If Prisoners is selected, please respond to Section N.
[ ] If a Cognitively Impaired Persons is selected, please respond to Section O.
[ ] Others

K8. Does the study involve any of the following?

[x] Inpatients.
[ ] Outpatients.
[ ] Healthy Volunteers.
[ ] Not applicable.

Section L: Research Participants – Pregnant Women, Foetuses & Neonates

L1. Please indicate if your research involves:

[x] Pregnant Women and Foetuses.
[ ] Neonates of Uncertain Viability and/or Nonviable neonates.
[ ] Nonviable neonates.

NOTES:

Please ensure that your research does not involve maintaining the vital functions of the neonate artificially or terminating the heartbeat or respiration of the neonate.

L2. Describe if appropriate preclinical studies, including studies on pregnant animals and clinical studies including studies on non-pregnant women, have been conducted and data is available to assess risks to pregnant women and foetus.

Our collaborator from Royal Brisbane Women's Hospital/The University of Queensland (Victoria Eley) has performed similar studies on pregnant women and reported no adverse events in the studies, despite the fact that the recruited patients were from a high-risk tertiary obstetric population.

L3. Describe if the risk to the foetus is the least possible in order to achieve the research objectives.

The arm and finger measurements are of minimal risks to the mothers and pose no risk to the foetus.

L4. Describe the additional safeguards that will be provided to protect the rights, safety and welfare of these vulnerable participants.

The informed consent process will be conducted during recruitment at the antenatal clinic/wards before their cesarean delivery. it will take place in a single private room. They will be given time and space to make an informed decision with their partner or husband present at all times. They will be given verbal as well as written information. With the activation of HBRA, informed consent will be obtained in the presence of a prescribed witness.

L5. Special Informed Consent Requirements (Check all that apply).

[x] I will obtain consent from the pregnant women because:

[x] Research holds out the prospect of direct benefits to the pregnant women.

[ ] Research holds out the prospect of direct benefits to both the pregnant women and the foetus.

[x] Risk to the foetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

[ ] I will also obtain consent from the father because the research holds out the prospect of direct benefit solely to the foetus.

[ ] The Informed Consent document(s) will provide information regarding the reasonably foreseeable impact of the research on the foetus or neonate.

L6. Assurances by Principal Investigator.

- There will be no inducements, monetary or otherwise, offered to terminate a pregnancy.
- Individuals engaged in the research will not have any part in any decisions as to the timing, method, or procedures used to terminate a pregnancy.
- Individuals engaged in the research will not have any part in determining the viability of a neonate.

I agree with the above statements. Kindly select response "Yes" or "No". Yes

Section P: Consent Process – Consent Required

P1. Describe when the consent process will take place with the potential participant.

Participants should be approached prior to the initiation of any study procedures and should not be approached in a situation where they may feel compromised (e.g. while in labour, just prior to a surgical procedure or under sedation).

With effect from 1 November 2017, for studies regulated under HBRA, please include a statement that informed consent will be taken in the presence of a witness (applicable to restricted human biomedical research and research that are interventional or invasive).

This study will be advertised on study brochures placed in the antenatal clinics. They will be given to all parturients who meet the inclusion criteria during the antenatal period. All patients who choose to enrol in the study will be counselled by the investigators about the study protocol, both verbally and with the patient information sheet. Adequate time will be given for discussion and with the investigators to clarify any doubts. The risks and benefits in joining this study will be clarified at recruitment prior to written consent. With the activation of HBRA, informed consent will be obtained in the presence of a prescribed witness.

P2. Where will the consent process take place with the potential participant (e.g. in room ward, outpatient clinic etc.)? Please justify why the place chosen for the consent process is suitable.

Informed consent will be taken place in the antenatal clinics in a private manner.

P3. Please describe the consent process as follows:

i. Explain if adequate time will be given to the participant to consider their participation.

This study will be advertised on study brochures placed in the antenatal clinics. They will be given to all parturients who meet the inclusion criteria during the antenatal period. Investigators or Clinical Research Coordinators will explain to the patients about the study

and patients will be given ample time to read the informed consent form about the study before obtaining their consent.

ii. Please explain if the place where consent will be taken is suitable. This place should allow the participants to be comfortable and have the right frame of mind to consider participation. Participants will be approached in the antenatal clinics. The discussion will be conducted in private manner with the patient.

iii. Please explain how the person taking consent would minimise the possibility of coercion or undue influence.

Participants will receive a patient information sheet. This will be discussed with them in private manner in the antenatal clinics. The subjects are able to withdraw from the study at any point. The contact details of the Principal Investigator will be provided in the information sheet. Patients are free to withdraw the study at any time (including timing after their delivery), should they decide not to participate.

P4. Does your study involve potential vulnerable participants whereby obtaining informed consent from the participant is not possible and informed consent is required from a Legal Representative (LR)?

No

**P5. Please describe the provisions to protect the "privacy interest" of the participants (e.g.
consent will be obtained in a separate room, free from intrusion and participants are comfortable with the proposed settings).**

Research personnel will conduct all the discussions about the study and answer any question in private manner.

P6. Will consent be documented in the form of a written and signed Research Participant Information Sheet and Consent Form?

Yes

File Name	Description	Version Number	Version Date
ArmFin PIS - Ver 1 edit Clean.docx	ArmFin PIS Clean Ver 1		-
ArmFin PIS - Ver 1 edit.docx	Arm Fin tracked change ver 1		-

P7. Will research participants receive any monetary payments (including transportation allowances) or gifts for their participation in the study?

Yes

The participants will be reimbursed $10 for their time of participation.

P8. Besides the Informed Consent Form, will any other materials or documents be used to explain the study to potential Research Participants (e.g. scripts, hand outs, brochures, videos, logs etc.)?

No

P9. Will the study enrol non-English speaking participants?

No

P10. Will the study be recruiting participants under emergency situations, when prior consent of the participant is not possible, and the consent of the participant's legal representative, if present, should be requested?

No

P11. Do you have any additional comments regarding the Informed Consent process?

No

Section R: Research Data Confidentiality

R1. Will coded/anonymous research data be sent to the study sponsor (e.g. pharmaceutical sponsored studies)?

No, the study team would store all research data within the institution.

i. Please state where the research data (soft copy and/or hardcopy) will be stored and indicate if the location storage is secured (i.e Password Protected PC or Laptop, data stored in physical location with lock and key access.)

The soft copy of research data will be stored in a password protected PC. Hard copies of data collection forms are kept by the Principal Investigator under lock and key. The data is accessible only by Investigators for analysis purposes only.

ii. Who will have access to the research data, and how will access to the research data be controlled and monitored? (Please state the personnel who will have access to the study data eg.
Principal Investigator, Co-Investigator, study coordinator.)

Password protected accounts will be created for relevant study personnel and the degree of database access granted to the each relevant study personnel (Principal Investigator, Co-Investigator and Clinical Research Coordinator) account will correspond to their trial responsibilities. The research data will be locked and soft copy will be under the computer security of Singhealth.

iii. Are there any other measures in place to protect the confidentiality of the research data? No names or identification number that will identify subjects will be ensured. The subjects are only identified by study number.

iv. Are there any research data sharing agreements with individuals or entities outside the Institution, to release and share research data collected?

No

v. Describe what will happen to the research data when the study is completed.

The research data will be kept under lock and key and using computer security of Singhealth. The data will be destroyed after keeping for 7 years upon completion of the study.

R2. Will any part of the study procedures be recorded on audiotape, film/video, or other electronic medium?

No

Section S: Biological Materials Usage & Storage

S1. Will any biological materials (such as blood or tissue) be used in the study? This includes both prospectively collected and existing biological material.

No

Section T: Data & Safety Monitoring

T1. The purpose of the Data and Safety Monitoring Plan is to ensure the safety and well-being of participants, and the integrity of the data collected for the study. Depending on the type and risk level of the study, this may include the Principal Investigator, experts within the department or institution, independent consultants or a combination of the said persons.

Who will perform the data and safety monitoring?

The data is kept by the principal investigator under lock and key and using computer security of SingHealth.

The data is accessible only by the investigators for analysis purposes only. The plan for adverse effect monitoring would include reporting to CIRB.

If the DSMB/DMC is an external committee, please include information/details of the composition of the external DSMB/ DMC. Kindly attach relevant file(s).

T2. Please describe the frequency of review (e.g. daily, weekly, quarterly) and what data (e.g. adverse events/serious adverse events) will be monitored for safety.

Safety data is monitored at all times by the investigators. There will be monthly meeting to review the study.
Adverse events and serious adverse events will be reported to CIRB accordingly.

T3. How is data integrity monitored to ensure that study data is authentic, accurate and complete, and if the data correlates with the case report forms?

Data is extracted from data collection forms and random audits will be performed to make sure it is authentic, accurate and complete.

T4. Please describe the stopping criteria for the research study based on efficacy, futility and safety criteria.

The stopping criteria for the research study will be based on safety criteria. The review of serious adverse effects will be performed.

T5. Please state the route of dissemination of any data and safety information to the study sites, as well as the person/team responsible for doing so.

Face-to-face communication and email correspondence.

Other Attachments

Note: Please attach only documents that are not relevant to the above sections.

File Name	Description	Version Number	Version Date
ArmFin PDPA.pdf	Armfin PDPA		-

Section U: Declaration of Principal Investigator

Declaration of Principal Investigator

This is the Principal Investigator's Declaration.

I will not initiate this study until I receive approval notification from CIRB and regulatory authority approval (if applicable).

I will not initiate any change in the protocol without prior written approval from CIRB, except when it is necessary to reduce or eliminate any immediate risks to the Study Participant. Thereafter, I will submit the proposed amendment to the CIRB and other relevant authority for approval.

I will promptly report any unexpected or serious adverse events, unanticipated problems or incidents that occur in the course of this study.

I will maintain all relevant documents and recognize that the CIRB staff and regulatory authorities may inspect these records.

I understand that failure to comply with all applicable regulations, institutional and CIRB policies and requirements may result in the suspension or termination of this study.

I declare that there are no existing or potential conflicts of interest for any of the study team members participating in this research study and their immediate family members. If there are, I have declared them in the relevant section of this application form.

Site	Principal Investigator	Study Role	Email	Declaration	Date
KK Women's and Children's Hospital (KKH)	Dr Ithnin Farida Binte	PI	Farida.ithnin@kkh.com.sg	Yes	28-Mar-2019

Endorsements Page

KK Women's and Children's Hospital (KKH)

Stage	Name	Role	Endorsement Status	Date
Department	A/Prof Ong Chiou Li	DR	Endorsed	29-Mar-2019

Department Representative Endorsement

1. Significance:

Does the study address an important problem? Will the study affect concepts and methods that drive the field?
Yes

2. Approach:

Is the conceptual framework adequately developed? Are the design, methods and analyses adequately developed and appropriate? Yes

3. Innovation:

Does the study challenge existing paradigms? Does it employ novel concepts, approaches and methods?
No

4. Principal Investigator:

Is the Principal Investigator appropriately trained to conduct this study? Does the Principal Investigator have evidence of commitment (e.g. previous track record)? Yes

5. Environment:

Is the Principal Investigator's environment suited to conduct the study? Is there an adequate patient pool and are there adequate resources? Yes

6. Budget:

Are the projected costs appropriate (i.e. accurate)? Is the overall budget reasonable for the significance of the study? Yes

7. Time:

Does the Principal Investigator have adequate resources and time to conduct and complete the study? Yes

Comments:

Important study to obtain data for Asian patients.

[x] I acknowledge that this research is in keeping with standards set by the Principal Investigator's Department.

Date: **29-Mar-2019**

Full Name: **A/Prof Ong Chiou Li**

Department: **Division of Clinical Support Services**

Institution: **KK Women's and Children's Hospital (KKH)**

Endorsement Status : Endorsed

Stage	Name	Role	Endorsement Status	Date
Institution	Dr Chan Wei Shih Derrick	IR	Endorsed	29-Mar-2019

Institution Representative Endorsement

The Institution Representative has been determined by your institution as the authority that declares whether your research is in keeping with the institution's research objectives, reputation and standards. The role of the Institution Representative is not to evaluate the scientific or ethical aspects of your study, although they may offer their comments.

Comments:

[x] I acknowledge that this research is in keeping with standards set by my Institution.

Date: **29-Mar-2019**

Full Name: **Dr Chan Wei Shih Derrick**

Department: **Department of Paediatrics**

Institution: **KK Women's and Children's Hospital (KKH)**

Endorsement Status : Endorsed