Written Informed Consent Form for Enrollment into PSBI Study 2

This consent form will be administered to the parent/ accompanying guardian of a young infant (i.e. aged 0-59 days) after the hospital physician/nurse have completed screening and hospitalized the infant for treatment with relatively higher-mortality risk signs of clinical severe infection (not feeding well, movement only on stimulation, low body temperature < 35.5°C, two or more of the six signs of clinical severe infection). Further, hospital physician/nurse assess the infant again on day 3 (i.e. 48-72 hours) after treatment initiation and find the young infant to be eligible for enrollment into Study 2, based on pre-specified inclusion and exclusion criteria laid out in the study protocol.

Study Title: Optimizing place of treatment and antibiotic regimens for young infants presenting with two or more signs of clinical severe infection or any single high-mortality-risk sign of clinical severe infection
Overall Principal Investigator (UP): Dr. Vishwajeet Kumar, Community Empowerment Lab (CEL) **Site Principal Investigator:** Prof (Dr) Yashwant Kumar Rao, Head of the Pediatrics Department, GSVM Medical College, Kanpur
Organization: GSVM Medical College, Kanpur
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Part I: Invitation for Participation

Namaskar! My name is_____, and I represent the GSVM Medical College, Kanpur and Community Empowerment Lab (CEL), Lucknow. We are supporting the government and medical and scientific communities in developing evidence-based solutions to improve the health of children. We are conducting a research study in collaboration with the World Health Organization (WHO) and National Health Mission, Uttar Pradesh (NHM-UP) in Kanpur Nagar district. This research study is implemented such that some infants aged < 2 months who are admitted to the hospital with two or more signs of clinical severe infection or any single high-mortality-risk sign of clinical severe infection, but are clinically well with negative laboratory investigation for infection 48-72 hours of hospital treatment, receive inpatient treatment, while others are receiving outpatient treatment at home. The purpose of this study is to find out which of these two approaches is better. I am working as a study team member associated with this research study. Your infant has been screened to be eligible to participate in this study and I would like to give you complete information about this study, and seek your consent to allow your child to participate in it.

Before you decide, you can talk to anyone you feel comfortable with. If there is any information that you do not understand well, please tell me and I will take time to explain in detail. If you have questions later at any time during the course of treatment and follow-up, you can ask them of the treating physician/nurse, study staff or me.

Purpose of the Study

It is currently recommended that all infants less than 2 months of age with clinical severe infection should be treated in the hospital. The treatment usually includes injectable antibiotics for 7-10 days. However, it has been observed that for young infants admitted to hospital with clinical severe infection, the first 2 days are the most critical. That is, if their condition worsens, it usually happens within the first 2 days. On the other hand, most infants who are clinically well and have negative laboratory test for infection after 48 hours of treatment in the hospital do reasonably well and recover completely in 2 weeks. Therefore, while the current guideline in

such a case is to continue to treat the child in the hospital for the entire duration of 7-10 days, we find that discharging infants who are clinically well and have negative laboratory test for infection after 48 hours of treatment, and subsequently continuing the treatment at home while continuing to monitor them may not pose significant additional risk to the infant. We are doing this study to compare and find which of these 2 options is better – i.e. continuation of treatment of these infants in the hospital or at home. If we find that home treatment is safer than hospital treatment for such infants, we will update the clinical guideline for all such cases.

Procedure

This study will compare hospital vs. outpatient treatment for young infants less than 2 months old who presented with two or more signs of clinical severe infection or any single high-risk sign of clinical severe infection, after clinical and laboratory evidence of improvement (in terms of no remaining signs of possible serious bacterial infection) with 2 days of treatment in the hospital. These 2 plans of treatment are as follows:

- **Treatment Plan 1:** Continued hospital admission with two injectable antibiotics - one injection (called ampicillin) will be given four times a day and the other injection (called gentamicin) will be given once daily, to complete 5 additional days of treatment (i.e. total of 7 days of hospital-based treatment). This is the current global guideline for treating such cases, and is the standard way that infants with your child's conditions are treated.
- **Treatment Plan 2:** Discharge from hospital and continuation of treatment at home with a single oral antibiotic (called amoxicillin) to be given twice daily for 5 days. Based on our assessment of available evidence, we believe that this treatment plan does not pose significant additional risk to babies, provided that they are monitored regularly. We have taken special permission to test and compare this treatment plan against the standard Treatment plan 1.

If you agree for your baby to participate in this study, then

- A sealed envelope will be opened in front of you. A paper inside the sealed envelope will have either 'Treatment Plan 1' or 'Treatment Plan 2' written on it. No one in my team knows what is written inside the envelope. This is somewhat like a lottery – we want to do this to ensure that this process is fair. By agreeing to participate, you are agreeing to accept and follow the treatment option written inside the sealed envelope for your baby – regardless of whether it is #1 or #2. We will not be able to change the treatment option after the envelope is opened. So please consider this very carefully before agreeing to consent.
- If assigned to Treatment Plan 1, i.e., standard hospital treatment, your child will be remain admitted in the hospital, and will receive two types of injectable antibiotics for 5 more days. This is our normal procedure and the entire treatment (admission charges, medicines, and consumables) is free of cost. Even if you choose to not participate in this study, this is the treatment that your child will receive, as it is currently the standard treatment.
- If assigned to Treatment Plan 2, i.e., home treatment, your child will be discharged home on oral antibiotic, to be given twice daily for 5 days. We will teach you how to administer the oral antibiotic and monitor the baby yourself at home.
- During the treatment, if anytime you feel that your child's condition is not well (such as appearance of fever, chest in-drawing, fast breathing, poor feeding, reduced movement or hypothermia), or they develop any danger signs (such as not feeding at all or no movement at all or convulsions) about which

you will be advised, please immediately bring your child back to this hospital (in case of Treatment Plan 2) or immediately consult physician/nurse (in case of Treatment Plan 1), and they will be provided prompt treatment and support. If your infant is being treated at home under Treatment Plan 2, you can call us at the number provided on the infant's treatment card, and we will facilitate the arrangement of transport.

- A study staff will visit you in the hospital or home on day 4 and 8 after initiation of treatment to collect information on the current treatment being received by your infant.
- Another study staff will visit your child (either in the hospital or at home) on day 8 and day 15 of treatment. The study staff will ask you questions about your child's condition and assess your child in detail on day 8. The study staff will record a video or make a video call to a supervising clinician to cross-verify the assessment findings. The supervising clinician will see your child on the video call which will help in ascertaining the assessment findings. This video call will not be recorded. If you do not want your child to participate in video call, you can let us know. On day 15, he/she will visit again and confirm with you how the child is doing.

Voluntary Participation

Your participation in this research is completely voluntary. You have the right to choose whether or not to allow your child to participate in this study. You can also withdraw your child from the study any time even after you have agreed for it. However, we would request you to please ask us for any clarifications and consider all the aspects into your decision-making before consenting, to the extent possible. A copy of this informed consent form will be provided to you. You will not have to pay any payment or penalty for not participating in this study. If you choose not to participate in this study, you will receive the standard treatment from hospital and your medical care or rights will not be affected in any way.

Confidentiality

Any information collected from this study will be used solely for this research study. Only authorized research staff members will have access to documents and data related to the research. If you consent for the video/ video call, it will be stored securely for quality purposes, and will never be shared with anyone other than the supervising clinician and the principal investigator/ co-principal investigator. We may publish a summary of findings from this research study but we will not publish any information that may identify you. All the information shared by you during this study will be kept strictly confidential and will be stored securely and anonymously on a digital platform.

Risks and Discomforts

Your infant was hospitalized with signs of clinical severe infection, but has been assessed to be doing well based on clinical examination and lab test. They have a good chance of improvement provided they complete their prescribed treatment as per the treatment plan.

The medicines being used in this study are used in young infants throughout the world and are generally known to be safe, but they can rarely cause diarrhea, stomach ache or a skin rash. If you see your child has skin rash, diarrhea, or any other problem irrespective of the treatment plan, please let us know immediately and we will revise the treatment plan, if needed. Contact the study staff or the person listed below if you have any questions about the drugs. As mentioned, all information, videos, etc., will be kept strictly confidential.

Based on our assessment of available evidence, we believe that outpatient treatment of infants who were found to be clinically well after 48 hours of treatment does not pose any significant additional risk to them as compared to inpatient care in the hospital if they are provided the prescribed treatment and monitored regularly. If your child is assigned Treatment Plan 2 and in the rare case of the child's condition deteriorating at home, you should immediately call us on the number provided on the child's treatment card. We will arrange to bring the child back to the hospital immediately and provide them prompt treatment and support. We will provide you detailed counseling on administering oral antibiotics at home and recognizing danger signs, so you may recognize these in time and seek prompt care. Infants assigned to Treatment Plan 1 will be monitored on a daily basis by our team of doctors and nurses, but we still advise you to be observant and let us know if you observe any deterioration in the child's condition while admitted in the hospital, and we will immediately provide the necessary care and support.

Benefits/ incentive for the participation

There is no financial or other in-kind incentive to participate in this study. Treatment for the infant will be free of cost, regardless of whether or not you consent to participate in the study. There may not be a direct benefit for your child at this stage, but their participation will bring benefit for improving care of infants in the near future. If the finding of this study shows benefits of Treatment Plan 2 (home treatment) over Treatment Plan 1 (standard hospital treatment), you will have contributed to change global recommendations on care for all young infants with a multiple low-risk sign or single high-risk sign of clinical severe infection.

Whom do I call if I have questions or problems?

This study has been reviewed and approved by the members of an ethical committee. The task of this committee is to make sure that research participants are protected from harm. If you have any questions about the study, please contact

Dr. Yashwant Rao
Site PI/ Head of Department, Pediatrics
GSVM Medical College,
Kanpur – 208002, Uttar Pradesh
Phone – +91-9415080807
Email id: ykraoneo@yahoo.co.in

Dr. Vishwajeet Kumar
Principal Investigator
Community Empowerment Lab
26/11 Wazir Hasan Road
Lucknow – 226001, Uttar Pradesh
Phone – 0522-4973444
Email id: vkumar@celworld.org

If you have any questions or concerns about the ethical conduct of the trial, you may contact the Ethics Committee of the study.

Ethics Committee GSVM medical College,
Opp. CRS Complex, GSVM Medical College, Kanpur – 208002, Uttar Pradesh
Phone – +91-9454581649
Email id: ec.gsvmmedicalcollege@gmail.com

Part II: Certificate of Consent

A. Parent/ guardian of child:

I confirm that I have read/heard this consent form and understood the purpose, procedures, possible benefits and risks of this research study. I have had the opportunity to ask questions and have got satisfactory answers to all my questions and queries.

- I understand that by consenting to participate in this study, I accept that my infant may be assigned to either hospital or home-based treatment based on a sealed envelope, and I agree to follow the assigned treatment plan.
- I am aware that if I choose not to participate in this study, my infant will be admitted and provided standard care in the hospital.
- I understand that my participation is completely voluntary and I am free to withdraw my child from this study at any time without giving any reason and without my medical care or rights being affected.
- I have agreed to cooperate/contact with the nurse/physician and the research staff and inform them or contact immediately if my child experiences any unexpected or unusual symptoms.
- I am aware that I will be given a copy of this consent form for my own records.
- My child's participation in this study will be kept strictly confidential.
- I don't need to pay and neither will I receive any payment or incentive for my child's participation in this study

I voluntarily agree to enroll my child in the study 2.

Yes ☐ No ☐

_____ _____

Name and Signature/Thumb impression of participant Date (dd/mmm/yyyy)

B. Witness to the Consent (if parent is illiterate):

[If the mother/father is illiterate and is not able to sign her/his name, a literate witness other than the member of the study team needs to sign that they confirm that the participant has agreed to allow her/his child to be the part of the study.]

I have witnessed the accurate reading of the consent form to the mother/father of the child, who has had the opportunity to ask questions. I confirm that the parent has given his/her consent freely.

_____ _____ _____

Name of Witness to the Consent Signature Date (dd/mmm/yyyy)

C. Study Team Member Obtaining Consent

I have accurately read the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm the consent was given freely.

_____ _____ _____

Name of Research Team Member Signature Date (dd/mmm/yyyy)