PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY
AUTHORS	Bayoumi, Mohammad; van Rens, Roland; CHANDRA, PREM; Shaltout, Deena; Gad, Ashraf; Elmalik, Einas; Hammoudeh, Samer

VERSION 1 – REVIEW

REVIEWER	Tang, Bin-Zhi University of Electronic Science and Technology of China Sichuan Provincial People's Hospital
REVIEW RETURNED	10-Dec-2021

GENERAL COMMENTS	The main aim of the present study was to compare Peripherally Inserted Central Catheters (PICCs) with non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) including femoral, jugular, brachiocephalic and subclavian lines in the NICU. In large part, this is a common designed and written manuscript and there are some concerns and comments.
	1. Page 3 - In the Abstract section, I would like to point out the sample size between PICCs group and USG-CVCs group are so different (1264 vs. 69) that may cause some statistic bias or error. How did the authors solve this problem?
	2. Page 6- In the Methods part, Figure 1 shows the 3 types of PICCs available in our NICU…What are the characteristic differences among these 3 types of PICCs, which type of PICC was the most often used in the NICU and why the authors choose this type rather than the other 2 types?
	3. Page 7- In the Results part, as the author mentioned, there were such a significant difference of patients' profiles (for example gestational age and birth weight) and catheter-related parameters between PICCs group and USG-CVCs group. Therefore, were the data yield from each group comparable and the results reliable? (for example a higher success rate in PICCs group)
	4. Page 9- In Table 2, Catheter type- PICC, (%) Line 17~19. Side of the body, the sum of left (484) and right (667) was not equal the number of PICCs (1264), then where were the other 113 PICCs? And also, in Line 20~23. site of insertion, 323+829=1152, not 1264, so where were the other 112 PICCs? Similar results could also be found in Line 28~33. Reason for catheter insertion. And in Line 38~41. reasons for removal. Could the authors give us an explanation for these numbers?
	5. Page 10- Line 7~8, In the PICC group, 804 (71.1%) were removed electively after completion of therapy compared to 29 (47.5%) in the USG-CVC group. It can be easily calculated as 804/1137(Successful PICC insertion, as described in Table 1)=70.7%, not 71.1%.
	6. Page 12- Line 30~32. In another report, no statistical difference in the complication rate or efficacy between those who had PICC and those who had USG-CVC (7, 32)…. There were two references listed

| | here (7,32), so, it should not be described as in another report….. |
| | 7. I suggest the authors check all the data throughout the whole paper carefully, and the discussion should go further. |

REVIEWER	Rahman, Sajjad recommended
	Dr Sulaiman AlHabib Medical Center
REVIEW RETURNED	28-Dec-2021

GENERAL COMMENTS	Abstract: Appropriate
	Introduction: Please shorten to the introduction of PICC line and USG-CVCs, their importance in NICU and the need for comparative analysis.
	The rest of the material like complications etc. can be moved to discussion.
	Methods: Appropriate
	Results and statistical analysis: Properly analyzed and very nicely presented.
	Discussion: Appropriate
	Figures and Tables: Appropriate
	The comments and suggestions of previous reviewers have been addressed appropriately.
	Recommendation: Accept after minor changes.
	Many thanks for giving me the opportunity to review this manuscript.

VERSION 1 – AUTHOR RESPONSE

Reviewers' Comments
bmjopen-2021-058866 - "PERIPHERALLY INSERTED CENTRAL CATHETERS VERSUS NON TUNNELLED ULTRASOUND-GUIDED CENTRAL VENOUS CATHETERS IN NEWBORNS: A RETROSPECTIVE OBSERVATIONAL STUDY"
Dear Dr. Bayoumi,
Following review of your article to BMJ Open, we invite you to submit a major revision.
The review comments can be found at the end of this email, together with any comments from the Editorial Office regarding formatting changes or additional information required to meet the journal's policies at this time.
Please note that your revision may be subject to further review and that this initial decision does not guarantee acceptance.
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Please replace any other files that have been updated e.g. Images, forms.

The reviewers' comments, your response, and the previous versions of your article will be published as supplementary information alongside the final version of your article.

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Please submit your revised article by 09-Feb-2022. If you have not submitted by this date, or would like an extension, please email our Editorial Office.

Thank you for submitting your article to BMJ Open; we look forward to receiving your revision.

If you have any queries, please contact the Editorial Office at info.bmjopen@bmj.com.

Kind regards,

Victoria Lee

on behalf of

Andy McLarnon

Senior Assistant Editor

BMJ Open

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Editor(s)' Comments to Author (if any):

1. Please ensure that the Patient and public involvement statement is included as part of the Methods section rather than being included at the end of the paper.

The statement has been moved to the methods section.

2. Please include page numbers on your checklist stating where each item can be found in your manuscript.

A checklist has been added.

*****

Reviewer: 1

Dr. Bin-Zhi Tang, University of Electronic Science and Technology of China Sichuan Provincial People's Hospital

Comments to the Author:

The main aim of the present study was to compare Peripherally Inserted Central Catheters (PICCs) with non-tunnelled ultrasound-guided Central Venous Catheters (USG-CVCs) including femoral, jugular, brachiocephalic and subclavian lines in the NICU. In large part, this is a common designed and written manuscript and there are some concerns and comments.

1. Page 3 - In the Abstract section, I would like to point out the sample size between PICCs group and USG-CVCs group are so different (1264 vs. 69) that may cause some statistic bias or error. How did the authors solve this problem?

Thank you for your comments and feedback.

The possible reasons for unequal numbers and having much fewer cases presented in the USG-CVCs group was particularly due to much less frequent uses of USG-CVC over PICC in subsequent years due to various clinical reasons and other potential indications.

However, multivariate logistic regression analyses (as an exploratory statistical analysis) were carried out to address the issues and role of possible potential predictors and confounders on catheter types (USG-CVC and PICC) and catheter insertion success rates.

Please note that because of the current study design i.e., retrospective-observational-descriptive study, all comparative analysis was performed mainly as an 'Exploratory statistical analysis' rather than 'Confirmatory statistical analysis' approach which might limit the generalizability and conclusive inferences derived from this current study which essentially requires further prospective and well-designed clinical trial study with adequate statistical power and sample size needed in each group. This was clearly stated within the manuscript as one of the main limitations in our current study (stated as follows):

"The limitation of this study is being retrospective with potential risks of bias and confounding factors

especially when single centre studies. The imbalance in numbers between the two groups suggest that the inferences may not be robust".

2. Page 6- In the Methods part, Figure 1 shows the 3 types of PICCs available in our NICU…What are the characteristic differences among these 3 types of PICCs, which type of PICC was the most often used in the NICU and why the authors choose this type rather than the other 2 types?

The following sentences have been added to the methods section:

PremiStar 1 Fr; Vygon is an antimicrobial impregnated catheter that is used in our unit for babies born less than 28 weeks gestation or when sepsis is suspected. We use NutriLine 2 Fr; Vygon, when a double lumen PICC or a long line is needed in big babies as its length is 30 cm. PremiCath 1 Fr; Vygon is used for the rest of our NICU babies who need PICC insertion.

3. Page 7- In the Results part, as the author mentioned, there were such a significant difference of patients' profiles (for example gestational age and birth weight) and catheter-related parameters between PICCs group and USG-CVCs group. Therefore, were the data yield from each group comparable and the results reliable? (for example a higher success rate in PICCs group)

Thank you for your valuable comments. Please see our response provided above. Furthermore, multivariate logistic regression analyses (as an exploratory statistical analysis) were applied to examine and assess the effect of potential factors associated with catheter types (USG-CVC and PICC) and catheter insertion success rates adjusting possible potential predictors and confounders.

4. Page 9- In Table 2, Catheter type- PICC, (%) Line 17~19. Side of the body, the sum of left (484) and right (667) was not equal the number of PICCs (1264), then where were the other 113 PICCs? And also, in Line 20~23. site of insertion, 323+829=1152, not 1264, so where were the other 112 PICCs? Similar results could also be found in Line 28~33. Reason for catheter insertion. And in Line 38~41. reasons for removal. Could the authors give us an explanation for these numbers?

Thank you for your observations.

Please note that regarding the discrepancy in n-value, we therefore already had placed a footnote beneath the table as:

"This is a retrospective study design and for some parameters, the data values were incomplete due to the unavailability of the information in the patients' record files. All percentage (%) was computed using non-missing data values".

just to clarify that some of the variables had incomplete information and hence corresponding percentage (%) values were computed using non-missing data. Being retrospective data review study, such discrepancies could happen and quite obvious particularly due to incomplete documentation/information available in some cases.

5. Page 10- Line 7~8, In the PICC group, 804 (71.1%) were removed electively after completion of therapy compared to 29 (47.5%) in the USG-CVC group. It can be easily calculated as 804/1137(Successful PICC insertion, as described in Table 1)=70.7%, not 71.1%.

Thank you. As mentioned above please note that all respective percentage (%) values were computed using non-missing data. Information on reasons for catheter removal in the PICC group was available only in 1131 cases and therefore the percentage was computed based on 804/1131=71.1%.

6. Page 12- Line 30~32. In another report, no statistical difference in the complication rate or efficacy between those who had PICC and those who had USG-CVC (7, 32)…. There were two references listed here (7,32), so, it should not be described as in another report…..

The sentence has been edited to be as follows:

Another 2 studies reported no statistical difference in the complication rate or efficacy between those who had PICC and those who had USG-CVC (4, 29).

7. I suggest the authors check all the data throughout the whole paper carefully, and the discussion should go further.

The study data and the discussion have been checked thoroughly.

Reviewer: 2

Dr. Sajjad Rahman, Dr Sulaiman AlHabib Medical Center

Comments to the Author:

****See attached file****

Abstract: Appropriate

Introduction: Please shorten to the introduction of PICC line and USG-CVCs, their importance in NICU and the need for comparative analysis.

Two paragraphs have been removed from the introduction.

The following sentence has been added.

There is a limited number of studies comparing PICCs with USG-CVCs in neonates that necessitated

further research and comparative analysis.

The rest of the material like complications etc. can be moved to discussion.

It has been moved to the discussion.

Methods: Appropriate

Results and statistical analysis: Properly analyzed and very nicely presented.

Discussion: Appropriate

Figures and Tables: Appropriate

The comments and suggestions of previous reviewers have been addressed appropriately.

Recommendation: Accept after minor changes.

Many thanks for giving me the opportunity to review this manuscript.