## 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

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| **TITLE (PROVISIONAL)** | The Accuracy of pH Strip Testing and pH Liquid Testing Versus Standard pH Meter of Gastric Contents in Critically Ill patients: A Diagnostic Accuracy Study |
| **AUTHORS** | Phukpattanachai, Kanjanaporn; Praditseree, Nutcha; Skjolaas, Smith; Klaychaiya, Sirilux; Trongtrakul, Konlawij |

## VERSION 1 – REVIEW

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| **REVIEWER** | Taskiran, Nihal<br>Adnan Menderes University Faculty of Nursing |
| **REVIEW RETURNED** | 12-Dec-2023 |

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| **GENERAL COMMENTS** | Thank you for offering me the opportunity to review this manuscript.<br>- In the introduction section you could mention more about the results of studies investigating the effectiveness of pH tests. It is recommended to emphasize the importance of pH tests supported by literature. Thus, it will be easier for readers to understand the gaps in this field in line with the literature knowledge. For example, mortality and morbidity rates due to incorrect nasogastric tube placement can be mentioned.<br><br>- The hypotheses of the research should be written in the method section<br><br>- H2 receptor antagonist, antacid or proton pump inhibitor drugs are drugs that affect the pH of gastric fluid. Therefore, patients should stop taking these drugs at least 4 hours prior to take gastric fluid samples.<br><br>- It is reported that PPI was routinely used as a prophylactic drug for stress ulcers in the hospital where the study was conducted. This is a limitation of the research. This limitation should be mentioned in the limitations of the research section.<br><br>- In order to accurately determine the pH value of gastric fluid samples taken from the patients within the research of the inclusion criteria, the patient must stop feeding at least 1 hour before. Was this taken into consideration in your study? If so, please indicate in the inclusion criteria that the patients were fasting.<br><br>- Statistical analyses Line 50-55: “We found a strong reliability for both pHS and pHL methods, with values of ICC at 0.93 (0.90, 0.96) and 0.94 (0.90, 0.96), respectively” This sentence is a finding of this research. Therefore, the sentence should be included in the findings section. |

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| | - Results Line 19: Please, write the “SOFA” in clear terms and write the abbreviation in parentheses.<br><br>- Page 12: first sentence of the second paragraph, “ We expressed the linear function between the pHS vs. pHM and the pHL vs. pHM values as Y = aX + b and calculated the Spearman’s correlation coefficient (rho)” This information is available in the statistical analysis section. Therefore, only the findings should be given in this section, it is recommended to delete this sentence |

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| **REVIEWER** | Savarino, Vincenzo<br>University of Genoa |
| **REVIEW RETURNED** | 14-Mar-2024 |

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| **GENERAL COMMENTS** | This study was carried out to evaluate the accuracy of pH strip and pH liquid tests compared with the standard pH meter in gastric samples obtained from critically ill patients. The authors state that both pH tests are valid and comparable to the standard one, even tough the pH strip is preferable because of the better perception of colors and other practical reasons. The methodology used and the statistical analysis are strong. The limitations of the study are adequately reported and the conclusions respect the results of the study. However, several aspects need to be clarified, as it follows:<br>- It is not clear whether all patients recruited for the study were taking PPI therapy and which were the dosages of these drugs which can affect strongly the level of intragastric pH<br>- The presence of bile acids or blood in gasric juice are an important limitation to be considered because it is not easy to see clearly these substances in the aspirated material and this should be discussed more in depth<br>- The study seems to be more suitable for chemical or pharmacological than medical journals because the clinical features are scant |

## VERSION 1 – AUTHOR RESPONSE

Response to Reviewer 1 Comments
Comments to the Author:
Thank you for offering me the opportunity to review this manuscript.
1. In the introduction section you could mention more about the results of studies investigating the effectiveness of pH tests. It is recommended to emphasize the importance of pH tests supported by literature. Thus, it will be easier for readers to understand the gaps in this field in line with the literature knowledge. For example, mortality and morbidity rates due to incorrect nasogastric tube placement can be mentioned.
Response
Thank you for your consideration. We have adjusted the introduction based on the reviewer’s valuable suggstion.
Please look at page 5-7.

2. The hypotheses of the research should be written in the method section.
Response
We have relocated the hypotheses to the introductory part of the section.
Please look at page 7 at the study design and participants heading.

3. H2 receptor antagonist, antacid or proton pump inhibitor drugs are drugs that affect the pH of gastric fluid. Therefore, patients should stop taking these drugs at least 4 hours prior to take gastric fluid samples.
Response
We value your insight; however, our research primarily focuses on evaluating the precision of pH measurement techniques. Our study is designed to compare pH levels obtained through pH strip and liquid testing methods with those from a standard pH meter, utilizing identical samples at concurrent intervals. Therefore, we gathered data across various gastric environments, rather than solely at specific times, to gain a more comprehensive understanding of the accuracy of gastric pH measurements. Consequently, factors such as PPI usage, other medications to reduce gastric acid, and fasting should not impact our findings.
Furthermore, the cessation of these medications before gastric fluid collection highlights another intriguing area of study: establishing the baseline or typical pH range in critically ill patients who have ceased PPI or acid suppression medication. This aspect may warrant further investigation.

4. It is reported that PPI was routinely used as a prophylactic drug for stress ulcers in the hospital where the study was conducted. This is a limitation of the research. This limitation should be mentioned in the limitations of the research section.
Response
We appreciate your valuable input. As previously noted, our research is centered on assessing the accuracy of pH measurement techniques, particularly in comparison with standard pH meter measurements, which inherently encompass a diverse range of gastric pH levels. Hence, we do not perceive PPI usage as a limiting factor in our study.
Nonetherless, we addressed this issue at the discussion as follows:
“Finally, stress ulcer prophylaxis may affect the precision of pH testing in determining the position of NG tube, especially when gastric pH levels exceed 5.00. However, the use of PPIs was not considered to compromise the accuracy of the pH testing in our study. It was essential to consider gastric sampling from a wide range of pH levels to effectively demonstrate the accuracy of the pH testing methods.”
Please look at the last line of last paragraph of page 17 and at the beginning of page 18.

5. In order to accurately determine the pH value of gastric fluid samples taken from the patients within the research of the inclusion criteria, the patient must stop feeding at least 1 hour before. Was this taken into consideration in your study? If so, please indicate in the inclusion criteria that the patients were fasting.
Response
Your suggestion is greatly appreciated. It seems we inadvertently omitted this information in the manuscript. Nonetheless, the samples collected were from patients who had genuinely refrained from consuming food for a minimum of two hours. Therefore, we incorporated the inclusion criterion of “Gastric content was retrieved following a minimum two-hour fasting period.”.
Please look at line number 2-3 of page 8.

6. Statistical analyses Line 50-55: “We found a strong reliability for both pHS and pHL methods, with values of ICC at 0.93 (0.90, 0.96) and 0.94 (0.90, 0.96), respectively” This sentence is a finding of this research. Therefore, the sentence should be included in the findings section.
Response
Thank you for your suggestion. We have moved this sentence to the results section.

7. Results Line 19: Please, write the “SOFA” in clear terms and write the abbreviation in parentheses.
Response
Thank you for your consideration. We have provided a full annotation for the first SOFA score in the Data Collection subsection.

Please look at page 9, data collection subsection.

8. Page 12: first sentence of the second paragraph, “We expressed the linear function between the pHS vs. pHM and the pHL vs. pHM values as Y = aX + b and calculated the Spearman’s correlation coefficient (rho)” This information is available in the statistical analysis section. Therefore, only the findings should be given in this section, it is recommended to delete this sentence
Response
Thank you for your consideration. We have deleted these sentences as the reviewer’s suggestion.

Response to Reviewer 2 Comments
Prof. Vincenzo Savarino, University of Genoa
Comments to the Author:
This study was carried out to evaluate the accuracy of pH strip and pH liquid tests compared with the standard pH meter in gastric samples obtained from critically ill patients. The authors state that both pH tests are valid and comparable to the standard one, even though the pH strip is preferable because of the better perception of colors and other practical reasons. The methodology used and the statistical analysis are strong. The limitations of the study are adequately reported, and the conclusions respect the results of the study. However, several aspects need to be clarified, as follows:
1. It is not clear whether all patients recruited for the study were taking PPI therapy and which were the dosages of these drugs which can affect strongly the level of intragastric pH

Response
We value your insight. However, our research primarily focuses on evaluating the precision of pH measurement techniques. Our study is designed to compare pH levels obtained through pH strip and liquid testing with those from a standard pH meter, utilizing identical samples at concurrent intervals. Therefore, we gathered data across various gastric environments, rather than solely at specific times, to gain a more comprehensive understanding of the accuracy of the gastric pH measurement. Consequently, factors such as PPI usage, other medications to reduce gastric acid, and fasting should not impact our findings.

2. The presence of bile acids or blood in gastric juice are an important limitation to be considered because it is not easy to see clearly these substances in the aspirated material and this should be discussed more in depth.
Response
We appreciate your valuable perspective. It is indeed noteworthy that the presence of blood and bile acid may impact the accuracy of pH testing readings. Consequently, we have incorporated this crucial information into the manuscript as outlined below:
“Relying solely on pHS or pHL tests for measuring gastric pH in the presence of bile acids or blood poses challenges. These substances introduce complexities that can hinder accurate visual interpretation of the pH test due to varaitions in color shades. Indeed, it is advisable to exercise caution in using both pHS and pHL when blood is present. In situations where the presence of blood or bile acid is not clearly discernible, additional intricate tests may be required such as pH meters or a combination of pH testing methods offering varied color interpretations.”
Please look at the first paragraph of page 17.

3. The study seems to be more suitable for chemical or pharmacological than medical journals because the clinical features are scant.
Response
Thank you for your consideration. The research team has made efforts to compare the performance of the pH testing methods with standard pH meters, providing data that can be applied in clinical settings. This information should be useful for healthcare professionals in determining the most

appropriate pH testing method. Therefore, it may be more beneficial to consider a broader range of publications beyond solely chemical or pharmacological journals.

## VERSION 2 – REVIEW

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| **REVIEWER** | Taskiran, Nihal<br>Adnan Menderes University Faculty of Nursing |
| **REVIEW RETURNED** | 04-Jun-2024 |

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| **GENERAL COMMENTS** | Dear Authors;<br>Thank you for taking my suggestions into consideration. After the corrections you have made, I think that your article is publishable in its final form. Thank you for your contribution to the field with this study. I wish you success.<br>Best regardes. |