Development of a simple and valid nutrition screening tool for pediatric hospitalized patients with acute illness [version 1; peer review: 2 approved, 1 approved with reservations, 1 not approved]

Hoda Atef Abdelsattar Ibrahim, Rasha Abdel-Raouf, Ahmed S. Zeid, Eman H. Elsebaie, Shaimaa Abdalaleem, Aya A. Amin, Hanna Aboulghar

1Pediatrics Department, Faculty of Medicine, Cairo University, Cairo, Egypt
2Public Health and Community Medicine, Faculty of Medicine, Cairo University, Cairo, Egypt
3Cancer Epidemiology and Biostatistics, National Cancer Institute, Cairo University, Cairo, Egypt

Abstract

**Background:** Nutritional screening, intervention and assessment in patients with undernutrition are key components of any nutritional care. The goal of any nutritional assessment is to determine the specific nutritional risk(s). Presently, there are no guidelines on any ideal screening tool to be used on admission for identification of children that are at risk of developing malnutrition during their hospital stay. The objective of the study was to develop a valid and simple nutritional screening tool which can be used on hospital admission to identify pediatric patients at risk of malnutrition.

**Methods:** This study was cross sectional analytical that enrolled children (n:161) admitted with acute illness to the general wards at Cairo University Children Hospitals (CUCH). The answers to the developed questionnaire were compared to the Subjective Global Assessment (SGA), those with high accuracy (≥80%) were used for validity with anthropometric measures.

**Results:** In the ‘less than two years of age’ group, the simple and valid nutritional screening tools were the following questions: (Is there a problem during breast-feeding?), (Is there scanty breast milk?), (Is there appetite loss?). The simple and valid nutritional screening tools during the ‘early childhood’ group were the following questions: (Is there appetite loss?), (Is there any skipping of meals?), (Are they watching TV, videotapes and/or playing computer games for more than two hours/day?). The simple and valid nutritional screening tools during the ‘late childhood’ group were the following questions: (Is there appetite loss?), (Are they watching TV, videotapes and/or playing computer games for more than two hours/day?).

Open Peer Review

**Reviewer Status**

**Invited Reviewers**

1. Andrew S Day, University of Otago, Christchurch, Christchurch, New Zealand
2. Osama El-Asheer, Assiut University, Assiut, Egypt
3. Ali El-shafie, Menoufia University, Shebin El-Koum, Egypt
4. Areej Alkhaldy, King Abdulaziz University, Jeddah, Saudi Arabia

Any reports and responses or comments on the article can be found at the end of the article.
Conclusion: The simple and valid nutritional screening tools differ according to age groups. The one which is valid in all ages is the question about the appetite loss.

Keywords
Nutritional screening tools, appetite loss, acute illness, SGA, children

This article is included in the Agriculture, Food and Nutrition gateway.
**Introduction**

Nutrition is an essential factor in the development, growth, and functioning of any child. Good nutritional status provides energy and nutrients which are essential to maintain our life and promote social, physical, emotional, and cognitive development.

Childhood malnutrition is known to be a global health concern as it is complicated with poor development and growth, as well as reduced educational outcomes of children and can have negative implications on their adulthood.

The incidence of the undernutrition among the inpatients is seeming to be more than that noticed among the community; malnourished children have a comorbid association, and are vulnerable to developing further medical complications. In addition, evidence indicates that the nutritional state of the admitted ill children deteriorates during the hospital stay. Besides, the absence of any known nutritional screening tool in these circumstances could result in an underestimation of that condition. The nutritional screening tool tries to identify the patients that are at nutritional risk, including not only the children who are undernourished, but also children who may develop any form of undernutrition during their hospital stay, and, the children whose prognosis can be improved as a result of the nutrition intervention.

The Subjective Global Nutritional Assessment (SGNA) is a systematic nutritional assessment method which had been validated. It contains items of a physical examination and nutrition-focused medical history, and it is the closest nutrition tool that is available for assessing the nutritional state in pediatrics. Although it is a systematic nutritional evaluation and screening tool, it does not give a chance for a simple and rapid pediatric nutritional screening tool owing to the time that is required for its completion. The characteristics of a nutritional screening tool are (1) sensitivity, specificity, and validity; (2) easy to use, simple, and without any need for training; (3) cheap, noninvasive and quick.

**Methods**

**Study design**

A cross-sectional analytical study. **Study population and setting:** The current study was conducted at Cairo University Children Hospitals (CUCHs) for all children admitted with acute illness in the general wards over a period of 18 months.

**Sample size and technique**

A convenient sample of all children (n =161) who were admitted to CUCHs were recruited for this study.

**Inclusion criteria:** 1-Children with acute illness, in the first two days of admission (to avoid the effect of hospitalization and possible weight loss, to prevent bias). 2- Both male and female genders. 3- Approval of the parent or legal guardian.

**Exclusion criteria:** 1- Children who have gross physical disabilities, mental retardation, and chronic illnesses. e.g., sickle cell disease and cystic fibrosis. 2- Patients admitted for more than two days.

**Data collection and study tools**

A semi-structured questionnaire form was used while interviewing the patients. The answers were compared with Pediatric Subjective Global Assessment (PSGA) validated tool. Answers with accuracy more than 80% were validated with the anthropometric measures. It covered the following items in the questionnaire: Appetite, Weight loss, Food allergies, Morbidity evidenced by recurrent hospitalizations, Enforcement to eat or not, Family eating together or not, Vitamins and minerals supplementations and Maternal deprivation, with focus on certain points in each stage as:

- **Infancy:** breast-feeding, feeding on colostrum, any problems during breast-feeding, developmental history, adverse reactions to vaccines, and feeding disorders. N.B The criteria for successful breast feeding was checked to exclude those if there were actual breastfeeding problems e.g., scanty breast milk.

- **Early childhood (2–8 years):** feeding disorders, eating out, skipping meals, child abuse, school achievement, functional impairment, mealtime atmosphere and watching TV or video-tapes and/or playing computer games for more than two hours per day.

- **Late childhood and early adolescence (8–12 years):** skipping meals, child abuse, school achievement, functional impairment, mealtime atmosphere and watching TV, or video-tapes and/or playing computer games for more than two hours per day.

Subjective global assessment evaluates the nutritional state which is based on the components of the history (any change in the weight, any change in the dietary intake, any gastrointestinal symptoms which had continued for more than two weeks, any change in the functional ability) in addition to the examination (subcutaneous fat loss, any wasting of muscles, edema in sacral/ankle area, and presence of ascites). Results were categorized subjectively into a global evaluation, where children had been rated into ‘well-nourished category’ (SGA A); ‘moderately malnourished category’ (SGA B); or ‘severely malnourished category’ (SGA C). The SGA is known to be the “gold standard” in comparison with the nutritional screening questions, for assessment of any malnutrition. The nutritional screening questions which had the highest accuracy, positive predictive and negative predictive values (≥80%) at predicting nutrition state (according to the comparison with SGA) were considered as the final nutrition screening tool. The Predictive Validity of our nutritional screening tool was established through comparison of the nutritional screening tool with anthropometric measures. When the tool is confirmed to be valid, it can be considered as a screening tool of the nutritional status.
Definitions of malnutrition used in the study

- **Underweight**: when the weight for age is less than the mean by two standard deviations (SD) of the World Health Organization (WHO) Child Standards for growth or less than 5th centile for age.
- **Stunting**: when the height for age is less than the mean by two standard deviations of the WHO Child Standards for growth or less than the 5th centile for age.
- **Wasting**: when the weight for the height age is less than the mean by two standard deviations of the WHO Child Standards for growth or Body Mass Index (BMI) is less than the 5th centile for age.
- **Overweight**: when the weight for the height is more than the mean by two standard deviations of the WHO Child Standards for growth or Body Mass Index (BMI) is more than 85th centile for age.
- **Obesity**: when the weight for the height is more than the mean by three standard deviations of the WHO Child Standards for growth or BMI is more than 95th centile for age.

Efforts to address and avoid potential sources of bias

1. The study was done on the admitted children in the first two days to avoid the effect of the hospital admission due to the possible weight loss owing to the possible appetite loss.

2. We excluded children with chronic illness as they may have external factors for malnutrition due to chronic disease, so we enrolled only patients with acute illnesses such as bronchiolitis, or glomerulonephritis as these diseases are acute and haven’t yet affected the nutritional state.

Data analysis

After the step of data collection, the questionnaires with their answers were revised for the completeness and the logical consistency. The pre-coded data was subsequently entered on the computer using the Program of the Microsoft Office Excel for Windows. Data were then double checked and transferred to The Statistical Package of the Social Science, Version 21 (SPSS-V21). The provided graphs were consequently constructed using SPSS Program. All the statistical analysis was done using the two tailed tests and the alpha error of 0.05. P value less than or equal to 0.05 was identified to be statistically significant. Simple descriptive statistics (arithmetic mean and standard deviation) are used for the summary of the quantitative data and frequencies are used for qualitative data. Bivariate relationship was identified and displayed in cross tabulations and a subsequent comparison of proportions was performed through the chi-square and Fisher’s exact tests.

Ethical considerations

The study was revised and approved by the scientific research committee and ethics of Cairo University, Faculty of Medicine (ethical clearance number, I-071017) and the study was done in accordance with Cairo University’s laws for human research. Written informed consent for participation and publication of the patient’s details was obtained from parent/guardians/relative of the patients. The study was done after the explanation of its importance and the objectives of the study to the participants. Only subjects who clearly agreed were enrolled and those who refused after the explanation were excluded.

Results

The present study was conducted in CUCHs on children admitted with acute illnesses in the general wards. The answers to the developed questionnaire were compared to SGA, those with high accuracy (≥80%) were used for validity with anthropometric measures. Table 1 shows the characteristics of the study participants.

### ‘Less than two years age’ group

There were (n = 66) patients in this group, 40 males, and 26 females. Comparison of the answers of the developed questionnaire to those of the SGA was done to detect the questions which have the highest sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and level of accuracy. Table 2 summarizes the comparison results. Table 3 illustrates the validity. Table 4 illustrates the tool.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of the study participants.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age group</strong></td>
</tr>
<tr>
<td>Infancy (≤ 2 years) (months)</td>
</tr>
<tr>
<td>Early childhood (2≤8 years) (years)</td>
</tr>
<tr>
<td>Late childhood (&gt;8 –12 years) (years)</td>
</tr>
</tbody>
</table>

* SD: Standard Deviation. ** The percentage is raw percentage. ***The percentage is column percentage
Table 2. Comparison between the screening questions and the subjective global assessment in the less than 2 years group.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.Problem during breast-feeding</td>
<td>70.0%</td>
<td>87.0%</td>
<td>70%</td>
<td>87%</td>
<td>81.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1.a Scanty breast milk</td>
<td>55%</td>
<td>93.5%</td>
<td>78.6%</td>
<td>82.7%</td>
<td>81.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>1.b Delayed weaning</td>
<td>15%</td>
<td>100%</td>
<td>100%</td>
<td>73%</td>
<td>74.2%</td>
<td>0.007</td>
</tr>
<tr>
<td>1.c Retracted nipple</td>
<td>0%</td>
<td>95.7%</td>
<td>0%</td>
<td>68.8%</td>
<td>66.7%</td>
<td>0.344</td>
</tr>
<tr>
<td>1.d Sore nipple</td>
<td>5%</td>
<td>100%</td>
<td>100%</td>
<td>70.8%</td>
<td>71.2%</td>
<td>0.126</td>
</tr>
<tr>
<td>1.e Thumb sucking</td>
<td>5%</td>
<td>100%</td>
<td>100%</td>
<td>70.8%</td>
<td>71.2%</td>
<td>0.126</td>
</tr>
<tr>
<td>1.f Early cessation due to pregnancy</td>
<td>0%</td>
<td>97.8%</td>
<td>0%</td>
<td>69.2%</td>
<td>68.2%</td>
<td>0.506</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td>95%</td>
<td>2.2%</td>
<td>29.7%</td>
<td>50%</td>
<td>30.3%</td>
<td>0.538</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>50%</td>
<td>95.7%</td>
<td>83.3%</td>
<td>81.5%</td>
<td>81.9%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enforcement to eat</td>
<td>40%</td>
<td>93.5%</td>
<td>72.2%</td>
<td>78.2%</td>
<td>77.3%</td>
<td>0.001</td>
</tr>
<tr>
<td>Eating together</td>
<td>55%</td>
<td>41.3%</td>
<td>28.9%</td>
<td>67.9%</td>
<td>45.5%</td>
<td>0.780</td>
</tr>
<tr>
<td>Weight loss measured</td>
<td>35%</td>
<td>95.7%</td>
<td>77.8%</td>
<td>72.2%</td>
<td>77.3%</td>
<td>0.001</td>
</tr>
<tr>
<td>Weight loss, not measured</td>
<td>15%</td>
<td>95.7%</td>
<td>60%</td>
<td>72.1%</td>
<td>72.1%</td>
<td>0.133</td>
</tr>
<tr>
<td>Significant weight loss</td>
<td>30%</td>
<td>100%</td>
<td>100%</td>
<td>76.7%</td>
<td>78.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Food allergy</td>
<td>15%</td>
<td>91.3%</td>
<td>42.9%</td>
<td>71.2%</td>
<td>68.1%</td>
<td>0.445</td>
</tr>
<tr>
<td>Morbidity like hospitalization</td>
<td>15%</td>
<td>97.3%</td>
<td>75%</td>
<td>72.6%</td>
<td>72.7%</td>
<td>0.045</td>
</tr>
<tr>
<td>Feeding disorders</td>
<td>10%</td>
<td>97.8%</td>
<td>66.7%</td>
<td>71.4%</td>
<td>71.2%</td>
<td>0.161</td>
</tr>
<tr>
<td>Developmental history delay</td>
<td>20%</td>
<td>97.8%</td>
<td>80%</td>
<td>73.8%</td>
<td>74.3%</td>
<td>0.012</td>
</tr>
<tr>
<td>Any reactions to vaccines</td>
<td>10%</td>
<td>87%</td>
<td>25%</td>
<td>69%</td>
<td>63.6%</td>
<td>0.728</td>
</tr>
<tr>
<td>Vitamins and/or, mineral supplements</td>
<td>20%</td>
<td>80.4%</td>
<td>30.8%</td>
<td>69.8%</td>
<td>62.2%</td>
<td>0.967</td>
</tr>
<tr>
<td>Feeding on colostrum</td>
<td>95%</td>
<td>2.2%</td>
<td>29.7%</td>
<td>50%</td>
<td>30.3%</td>
<td>0.538</td>
</tr>
</tbody>
</table>

Table 3. Validation with anthropometric measures of the questions which have the highest sensitivity, specificity and accuracy by the SGA.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Problem during breast feeding</td>
<td>66.7%</td>
<td>86.7%</td>
<td>70%</td>
<td>84.8%</td>
<td>80.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Scanty breast milk</td>
<td>93.3%</td>
<td>52.4%</td>
<td>78.6%</td>
<td>80.8%</td>
<td>80.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>47.6%</td>
<td>95.7%</td>
<td>83.3%</td>
<td>79.6%</td>
<td>80.4%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 4. Development of the simple and valid nutritional screening tool in the ‘less than two years age’ group.

<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there a problem during breast feeding?</td>
</tr>
<tr>
<td>Is there scanty breast milk?</td>
</tr>
<tr>
<td>Is there appetite loss?</td>
</tr>
</tbody>
</table>

'The Early Childhood' Group
There were (n = 66) patients in this group, 37 male, and 29 female. The questionnaire was answered. Then the questions were compared with SGA to detect the questions which have the highest specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and level of accuracy. Table 5 summarizes the comparison results. Table 6 illustrates the validity. Table 7 illustrates the tool.
There were \( n = 29 \) patients in this group, 13 male and 16 female. The questionnaire was answered. Then the questions were compared with SGA to detect the questions which have the highest specificity, sensitivity, positive predictive value (PPV), negative predictive value (NPV), and level of accuracy. Table 8 summarizes the comparison results. Table 9 illustrates the tool.

The nutrition screening tools for all age groups are illustrated in Table 11.

### Table 5. Comparison between the screening questions and the subjective global assessment in the early childhood group.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetite loss</td>
<td>88.6%</td>
<td>100.0%</td>
<td>100.0</td>
<td>88.6%</td>
<td>94%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skipping meals</td>
<td>88.6%</td>
<td>90.3%</td>
<td>91.2%</td>
<td>87.5%</td>
<td>89.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Watching TV, video-tapes and/or computer games for more than two hours/day</td>
<td>77.1%</td>
<td>90.3%</td>
<td>90.0%</td>
<td>77.8%</td>
<td>83.3%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Child abuse</td>
<td>60.0%</td>
<td>77.4%</td>
<td>63.2%</td>
<td>75%</td>
<td>68.2%</td>
<td>0.002</td>
</tr>
<tr>
<td>Enforcement to eat</td>
<td>45.7%</td>
<td>96.8%</td>
<td>94.1%</td>
<td>61.2%</td>
<td>69.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>weight loss, not measured</td>
<td>31.4%</td>
<td>90.3%</td>
<td>78.6%</td>
<td>53.8%</td>
<td>59.1%</td>
<td>0.031</td>
</tr>
<tr>
<td>Eating together</td>
<td>82.9%</td>
<td>3.2%</td>
<td>49.2%</td>
<td>14.3%</td>
<td>45.4%</td>
<td>0.067</td>
</tr>
<tr>
<td>Maternal deprivation</td>
<td>2.9%</td>
<td>100.0%</td>
<td>100.0</td>
<td>47.7%</td>
<td>48.5%</td>
<td>0.343</td>
</tr>
<tr>
<td>Feeding disorders</td>
<td>22.9%</td>
<td>96.8%</td>
<td>88.9%</td>
<td>52.6%</td>
<td>57.6%</td>
<td>0.020</td>
</tr>
<tr>
<td>Eating out</td>
<td>45.7%</td>
<td>71.0%</td>
<td>64%</td>
<td>53.7%</td>
<td>57.5%</td>
<td>0.163</td>
</tr>
<tr>
<td>School achievement</td>
<td>40.0%</td>
<td>38.7%</td>
<td>42.4%</td>
<td>36.4%</td>
<td>39.4%</td>
<td>0.084</td>
</tr>
<tr>
<td>Functional impairment</td>
<td>31.4%</td>
<td>83.9%</td>
<td>68.8%</td>
<td>52%</td>
<td>56.1%</td>
<td>0.148</td>
</tr>
<tr>
<td>Vitamin and/or mineral supplements</td>
<td>2.9%</td>
<td>90.3%</td>
<td>25%</td>
<td>45.2%</td>
<td>43.9%</td>
<td>0.246</td>
</tr>
<tr>
<td>Morbidity like hospitalization</td>
<td>20.0%</td>
<td>96.8%</td>
<td>87.5%</td>
<td>51.7%</td>
<td>56.1%</td>
<td>0.037</td>
</tr>
<tr>
<td>Food allergy</td>
<td>11.4%</td>
<td>80.6%</td>
<td>40%</td>
<td>44.6%</td>
<td>44%</td>
<td>0.370</td>
</tr>
<tr>
<td>Significant weight loss(based on measurement)</td>
<td>8.6%</td>
<td>100.0%</td>
<td>100.0</td>
<td>49.2%</td>
<td>51.5%</td>
<td>0.095</td>
</tr>
<tr>
<td>Weight loss, measured</td>
<td>8.6%</td>
<td>100.0%</td>
<td>100.0</td>
<td>49.2%</td>
<td>51.5%</td>
<td>0.095</td>
</tr>
<tr>
<td>Fair mealtime atmosphere</td>
<td>25.7%</td>
<td>0.0%</td>
<td>0%</td>
<td>22.5%</td>
<td>13.6%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 6. Validation with anthropometric measures of the questions which have highest sensitivity, specificity and accuracy with the SGA.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetite loss</td>
<td>88.6%</td>
<td>100.0%</td>
<td>100.0</td>
<td>88.6%</td>
<td>94%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skipping meals</td>
<td>88.6%</td>
<td>90.3%</td>
<td>91.2%</td>
<td>87.5%</td>
<td>89.4%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Watching TV, video-tapes and/or computer games for more than two hours/day</td>
<td>77.1%</td>
<td>90.3%</td>
<td>90.0%</td>
<td>77.8%</td>
<td>83.3%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 7. Development of the valid and simple nutritional screening tool during the early childhood group.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetite loss</td>
<td>88.6%</td>
<td>100.0%</td>
<td>100.0</td>
<td>88.6%</td>
<td>94%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skipping meals</td>
<td>88.6%</td>
<td>90.3%</td>
<td>91.2%</td>
<td>87.5%</td>
<td>89.4%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 8. Summary of the comparison results.

### Table 9. Illustration of the tool.

### Table 10. Illustration of the tool.

### Table 11. Illustration of the tool.
### Table 8. Comparison between the screening questions and the subjective global assessment in the late childhood group.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetite loss</td>
<td>75.0%</td>
<td>92.3%</td>
<td>92.3%</td>
<td>75.0%</td>
<td>82.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Watching TV, video-tapes and/or computer games for more than two hours/day</td>
<td>93.8%</td>
<td>69.2%</td>
<td>78.9%</td>
<td>90.0%</td>
<td>82.7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight loss, measured</td>
<td>25.0%</td>
<td>92.3%</td>
<td>80.0%</td>
<td>50.0%</td>
<td>55.2%</td>
<td>0.220</td>
</tr>
<tr>
<td>Weight loss, not measured</td>
<td>18.8%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>50.0%</td>
<td>55.1%</td>
<td>0.099</td>
</tr>
<tr>
<td>Significant weight loss</td>
<td>25.0%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>52.0%</td>
<td>58.6%</td>
<td>0.052</td>
</tr>
<tr>
<td>Morbidity like hospitalization</td>
<td>6.3%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>46.4%</td>
<td>48.2%</td>
<td>0.359</td>
</tr>
<tr>
<td>Enforcement to eat</td>
<td>56.3%</td>
<td>69.2%</td>
<td>69.2%</td>
<td>56.3%</td>
<td>62.0%</td>
<td>0.170</td>
</tr>
<tr>
<td>Eating together</td>
<td>75.0%</td>
<td>0.0%</td>
<td>48.0%</td>
<td>0.0%</td>
<td>41.4%</td>
<td>0.052</td>
</tr>
<tr>
<td>Maternal deprivation</td>
<td>6.3%</td>
<td>100.0%</td>
<td>100.0%</td>
<td>46.4%</td>
<td>48.2%</td>
<td>0.359</td>
</tr>
<tr>
<td>Eating out</td>
<td>37.5%</td>
<td>61.5%</td>
<td>54.5%</td>
<td>44.4%</td>
<td>48.3%</td>
<td>0.958</td>
</tr>
<tr>
<td>Skipping meals</td>
<td>43.8%</td>
<td>92.3%</td>
<td>87.5%</td>
<td>57.1%</td>
<td>65.5%</td>
<td>0.031</td>
</tr>
<tr>
<td>Child abuse</td>
<td>43.8%</td>
<td>76.9%</td>
<td>70.0%</td>
<td>52.6%</td>
<td>58.6%</td>
<td>0.244</td>
</tr>
<tr>
<td>School achievement satisfaction</td>
<td>75.0%</td>
<td>23.1%</td>
<td>54.5%</td>
<td>42.9%</td>
<td>51.7%</td>
<td>0.904</td>
</tr>
<tr>
<td>Functional impairment</td>
<td>25.0%</td>
<td>76.9%</td>
<td>57.1%</td>
<td>45.5%</td>
<td>48.3%</td>
<td>0.904</td>
</tr>
<tr>
<td>Fair mealtime atmosphere</td>
<td>25.0%</td>
<td>7.7%</td>
<td>25.0%</td>
<td>7.7%</td>
<td>17.2%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 9. Validation with anthropometric measures of the questions which have highest sensitivity and specificity and accuracy with the SGA.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appetite loss</td>
<td>66.7%</td>
<td>90.9%</td>
<td>92.3%</td>
<td>62.5%</td>
<td>75.9%</td>
<td>0.002</td>
</tr>
<tr>
<td>Watching TV, video-tapes and/or computer games for more than two hours/day</td>
<td>94.4%</td>
<td>81.8%</td>
<td>89.5%</td>
<td>90.0%</td>
<td>89.6%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Table 10. Development of the valid and simple nutritional screening tool during the late childhood group.

<table>
<thead>
<tr>
<th>Question</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there appetite loss?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Are they watching TV, video-tapes and/or computer games for more than two hours/day</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Discussion
The nutritional state of any child is a determinant of the body composition and the functional state. Deficient states badly affect the patient’s outcomes, mortality, morbidity, hospital stay, and re-admission rates. Thus, screening for risk factors which are known to be present with the deficiencies should be part of the evaluation of any child on admission.9,10.

The hospitalized children have high risks to develop severe malnutrition. The nutritional risk screening is an essential tool to maintain the nutritional status in any hospitalized patient owing to different reasons. For example, the energy need is increased and the subsequent decreased appetite is problematic.11

It is important to know the inpatients children who are with nutrition risks so that the appropriate timely nutritional intervention and the planned treatment can be performed and the nutritional deterioration prevented to improve the health outcomes12.

Hartman et al. recommended that “a valid and a simple nutritional screening tool appeared highly needed to improve the early cost effective identification of pediatrics who will get benefits later from the nutrition intervention”9,10.

There are many nutritional screening tools which are currently being used in hospitals and the community, but most of them are difficult and sophisticated. In this work, we aimed to develop an ideal nutritional pediatric screening tool which can be easily and rapidly implemented, and with a high level of sensitivity, specificity and good accuracy in the identification of the nutritional risks together with the nutrition-related outcomes.

Unfortunately, there is no previous study that has used the Pediatric Subjective Global Assessment as a gold standard method to compare the screening tools on hospital admission of pediatric patients to detect the tools which have the highest sensitivity, specificity, and accuracy. There is a lot of debate among doctors and professionals on the way to validate the nutritional screening tools, especially if they have higher accuracy, which can predict the present nutritional status. Some hospitals have validated their nutritional screening tools using a full nutrition evaluation. Nevertheless, it is questionable if this is the standard tool, especially as not all countries have sufficient dieticians and their role might be different depending on the country14. In this study, SGA was used as the gold standard to identify the nutritional screening tools with the highest accuracy in order to be validated with anthropometric measures. The Pediatric Subjective Global Assessment consists of both objective and subjective items in a physical examination and detailed questionnaire; then each child is categorized into (1) well-nourished category, (2) moderately malnourished category, or (3) severely malnourished category.15

Our study resulted in a simple, valid and effective nutritional pediatric screening tool for the early identification of at-risk admitted children who require thorough nutritional assessment and subsequent individualized nutritional intervention. In this study, we tried to detect the ability of the tool to pick up those children who have malnutrition.

In all age groups, the screening tool question about lost appetite was one of the most sensitive, specific, and accurate questions in prediction of the nutritional risk.

Our present study is in line with a study done on a simple nutritional screening tool for hospitalized pediatric children after checking the accuracy of a new, rapid, and simple pediatric nutritional screening method. The question (Has child been feeding less during the last weeks?) was one of the most sensitive and specific questions in detection of the patients with nutrition risks. On the other hand, it disagrees with the rest of questions screening tool as they were (Has the child lost weight unintentionally?), and (Has the child had poor or unsatisfied weight gain during the last months?). This difference may be due to the accuracy in weight detection objectively by the mothers16.

<table>
<thead>
<tr>
<th>Table 11. The nutrition screening tool.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>The nutrition screening tool</strong></td>
</tr>
<tr>
<td><strong>Less than two years</strong></td>
</tr>
<tr>
<td>Is there problem during breast feeding?</td>
</tr>
<tr>
<td>Is there scanty breast milk?</td>
</tr>
<tr>
<td>Is there appetite loss?</td>
</tr>
<tr>
<td><strong>The early childhood</strong></td>
</tr>
<tr>
<td>Is there appetite loss?</td>
</tr>
<tr>
<td>Is there any skipping of meals?</td>
</tr>
<tr>
<td>Are they watching TV, video-tapes and/or computer games for more than two hours/day?</td>
</tr>
<tr>
<td><strong>The late childhood</strong></td>
</tr>
<tr>
<td>Is there appetite loss?</td>
</tr>
<tr>
<td>Are they watching TV, video-tapes and/or computer games for more than two hours?</td>
</tr>
</tbody>
</table>
In this study, we found that one of the nutritional screening tools was about the appetite loss. There was a study that used STAMP (Screening Tool Assessment of Malnutrition in Pediatrics) for the determination of the malnutrition and malnutrition risks in the pediatric primary health care setting. One of the items of this screening tool was (what is the nutritional intake of the child) which may be related to his appetite. However, it incorporated weight and height (anthropometric measures) in this screening tool unlike the case in our study. That is because we aimed to find a quick screening tool. Thus, we didn’t consider the anthropometric measures in the tool13.

This study agrees with a previous study that found that one of the nutritional screening tools among the adult hospitalized patients was (Have you had poor eating because of the presence of a decreased appetite?), but disagrees with that the other tools were (Have you lost weight unintentionally?), (If yes, how much weight have you actually lost?). This difference may be due to the age group difference18.

This study is very near to a previous study that was worked on the evaluation of the screening tool for further assessment of malnutrition in children. Significant predictors of the nutritional risks were decreased dietary intakes which was due to a recent poor appetite. Other predictors found were reported19.

This study agrees with a study that was done to detect the nutritional screening tool. One of the main principles of nutritional screening was about reduced intake due to a poor appetite. It disagrees with it that the other principle was about the severity of the disease whether acute or chronic. This disagreement may be due to that in our present study we intentionally removed the effect of the chronic element on the disease which may affect the nutritional status. That is why we enrolled admitted patients with acute illnesses only20.

In the ‘less than two years age’ group, it was found that the presence of any problems during breast-feeding or scanty breast milk were predictors of nutritional risks. They affect the nutritional status as seen in the underweight and the stunted groups. There was a significant association (P-value <0.001) between the presence of any problems or scanty breast milk and the prediction of any nutritional risk.

This study agrees with a study in which a relationship was observed between the presence of any problems or scanty breast milk were predictors of nutritional risks. They affect the nutritional status as seen in the underweight and the stunted groups. There was a significant association (P-value <0.001) between the presence of any problems or scanty breast milk and the prediction of any nutritional risk.

This study agrees with a study in which a relationship was observed between the presence of any problems or scanty breast milk were predictors of nutritional risks. They affect the nutritional status as seen in the underweight and the stunted groups. There was a significant association (P-value <0.001) between the presence of any problems or scanty breast milk and the prediction of any nutritional risk.

This disagrees with a previous study in that they aimed to detect a score to be used on hospital admission to pick up patients who are at risk of acute malnutrition during the hospital stay27. The nutritional risk was evaluated within 48 hours of admission. The nutritional predictor score consisted of history of weight loss, decreased food intake, disease severity divided into Grades 1, 2 and 3 and pain. This disagreement may be owed to the fact that the present study didn’t use a scoring system in the questionnaire.

The current study found that, in the early childhood group, one of the predictors of nutritional risks was the question about skipping meals

This study agrees with a previous one which found that more subjects of the non- breakfast skippers were found to have BMI in the normal range than breakfast skippers. Unlike our study, they found that more of the breakfast skippers were overweight than the non-breakfast skippers. This may be a result of more consumption of junk food, i.e., high in saturated fat, by the breakfast skippers23.

This study is similar to a previous one which found that there is an association between meal skipping and malnutrition. Among the skippers, 12.1% of children were in the underweight category and 10.3% of the children were overweight. The malnutrition is represented in the underweight and the overweight groups24.

In the present study it was found that in the early and late childhood groups, there is a significant association between watching TV, video-tapes, and/or playing computer games for more than two hours per day and the presence of a nutritional risk with (P-value <0.001).

This agrees with a study which found that the older age of the child, the presence of multiple televisions at home, having her or his own television and number of hours spent inside watching television at the weekend were essentially associated with increased risk of childhood obesity25.

The current study also agrees with a previous study that was done on an Egyptian cross-sectional survey on children aged between 6 and 17 years in Manshit El Gamal region of Fayoum Governorate. Increasing age and not eating breakfast were associated risks for stunting, whereas the incidence of obesity was higher in the children who eat while watching TV26.

In the present study, no significant association was found between history of weight loss and the nutritional status of the child.

This disagrees with a previous study in that they aimed to detect a score to be used on hospital admission to pick up patients who are at risk of acute malnutrition during the hospital stay27. The nutritional risk was evaluated within 48 hours of admission. The nutritional predictor score consisted of history of weight loss, decreased food intake, disease severity divided into Grades 1, 2 and 3 and pain. This disagreement may be owed to the fact that the present study didn’t use a scoring system in the questionnaire.
Limitations
Some limitations to our study should be mentioned which, may in turn lead to the limitation of its generalizability to the total population. For example, the study sample was limited to Cairo University Children Hospitals; a broader geographic sample may lead to different results. Furthermore, this study has used a cross sectional design, thus a rather prospective one can help in making other predictions through follow up. One limitation of the Subjective Global Assessment to be mentioned is the limitations of attempts to only categorize undernutrition. Obese patients are effectively categorized as normal.

Conclusion
This study has established the validity of a simple nutrition screening tool that can be implemented on infants and children at the time of admission to hospital. In the ‘less than two years of age’ group: the simple and valid nutritional screening tools were: (Is there a problem during breast-feeding?), (Is there scanty breast milk?), (Is there appetite loss?). In the ‘early childhood group’: the simple and valid nutritional screening tools were: (Is there appetite loss?), (Is there any skipping of meals?), (Are they watching TV, video-tapes and/or playing computer games for more than two hours/day?). The ‘late childhood group’: the simple and valid nutritional screening tools were: (Is there appetite loss?), (Are they watching TV, video-tapes and/or playing computer games for more than two hours/day?).

Data availability
Underlying data
Open Science Framework: Development of a simple and valid nutrition screening tool for pediatric hospitalized patients with acute illness, https://doi.org/10.17605/OSF.IO/6YTMN28

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).

Acknowledgements
The Pediatric Department and the Pediatric Clinical Nutrition Department, Faculty of Medicine, Cairo University.

References


Areej Alkhaldy
Clinical Nutrition Department, Faculty of Applied Medical Sciences, King Abdulaziz University, Jeddah, Saudi Arabia

It has been a great honour to review the article entitled “Development of a simple and valid nutrition screening tool for pediatric hospitalized patients with acute illness.” The paper aims to develop a valid and simple nutritional screening tool which can be used on hospital admission to identify pediatric patients at risk of malnutrition. The paper is interesting; however, there are some comments that need to be addressed to improve it.

Abstract:
○ The age, sex, and groups need to be indicated in the abstract.

○ The results need to be improved and expanded along with numbers.

○ The conclusion needs to be rewritten. What is the main message regarding the use of these screening tools?

Introduction:
○ The introduction was written in a consistent manner, yet you need to add more information including recent research in the area of SGA and pediatrics. There is a need to focus more on the nutrition screening tool for pediatric patients than general ones for adults.

○ At the end of the last paragraph, the objectives need to be expressed in a clear manner and include the rational of conducting the study.

Methods:
○ You need to include more information in the sample size section. How was the sample size calculated in terms of population size, source of the data, and references of the equation or website, or program you used to calculate the sample size?

○ Explain the validation process in more detail.
Briefly explain the questionnaire (for example: sections and numbers of questions)

Define abbreviations at first mention; the abbreviation should always be used in the rest of the manuscript instead of the complete term. All group abbreviations need to be indicated and explained in the methods.

Results:
○ Table 2, 5, and 8 could be combined and compared
○ Footnotes need to be added to all tables (example PPV and NPV)

Discussion:
○ You need to discuss your findings in the context of the other studies in the same area.
○ The manuscript requires minor language editing throughout.

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
I cannot comment. A qualified statistician is required.

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Clinical Nutrition

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 22 April 2021

https://doi.org/10.5256/f1000research.54320.r83395
Thank you for your kind invitation to be a reviewer for this study.

The study investigated a nutritional screening tool for pediatrics. The researchers tried to reveal the sensitivity, specificity and validity of this tool. Although the results of the study are intriguing, few flaws remain in the paper.

Title: It would be better that more specific term would have been chosen for the title of study. I suggest you describe the tool as it is rapid. In addition, I suggest you describe those pediatrics as having acute malnutrition as this way of description is more specified. Thus, the title would be (Development of a rapid and valid nutritional screening tool for pediatric hospitalized patients with acute malnutrition).

Abstract: The first sentence would have been removed as the paper didn't incorporate any methods for nutritional intervention.

Introduction: The subjective global assessment is needed to be further explained. In addition, the basis of choosing the questionnaire for each group and previous studies that used similar questionnaires would have been better introduced.

Method: The logic for calculating the sample size is missed in this study. The calculation of sample size or a power analysis is better to be added. The acute illnesses would have been prescribed and correlations between them and types of malnutrition would have been addressed. Regarding the SGA, its method is better to be mentioned clearly.

Results: I noticed that there are no graphs to explain the groups of malnutrition revealed in the study. I think it was better to add these graphs. Concerning the applied questionnaire, what is meant by "weight loss measured", it would have been better explained. Furthermore, the question of "food allergy" is not clear as symptoms of food allergy that you asked should be associated with the questionnaire.

Discussion: The first four paragraphs could be removed as they are repeated. The aim of the study should have been mentioned at the end of the Introduction part instead of at the beginning of the Discussion one.

Is the work clearly and accurately presented and does it cite the current literature?  
Yes

Is the study design appropriate and is the work technically sound?  
Yes
Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 22 March 2021
https://doi.org/10.5256/f1000research.54320.r80755

© 2021 El-Asheer O. This is an open access peer review report distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Osama El-Asheer
Paediatric Department, Assiut University, Assiut, Egypt

I have reviewed the document from my Egyptian colleagues with great interest. This paper is well written and addresses an important topic which is the development of a simple and valid nutrition screening tool in pediatric hospitalized patients with acute illness. The article is clear and of relevance also because there is a need for this important tool to improve the prognosis and outcomes of pediatric diseases. Furthermore, the tool respects the age groups and also respects the time as it is rapid (unlike the subjective global assessment and the anthropometric measures) and applicable.

Although the reliability of this tool was not achieved, there are several important conclusions from this article. For example, appetite loss is the most consistent tool in all age groups. However, a scoring system for this appetite loss would have been done to improve the quality of this tool. Very important: watching television and computer games for more than 2 hours per day could represent a major nutritional risk for older children. Besides, respecting the meal time and the avoidance of skipping meals can greatly keep children away from malnutrition. Problems in breastfeeding can negatively affect the growth of infant and have earlier implications on the nutritional parameters. Correctly the authors exclude the chronic diseases to exclude bias as the chronic course could cause organic failure to thrive.
To improve paper readability, I suggest the following:

- **Abstract**: Detailed questionnaire should be removed from Results.
- Please clarify the method of getting the sample size.
- Please clarify why you did not compare with other screening tools like STAMP or STRONG Kids scoring in addition to SGNA.
- Please clarify the base of age classification 2-8 and 8-12.
- **Results**: tables are so much and should be summarized into 4-5 tables.
- The discussion should be shorter and more focused to the point. It should be more aimed more than this. You can remove the first six paragraphs in the discussion as you mentioned similar ones in the introduction.
- I suggest also to update the references.
- As a further question: Did the authors observe the nutritional lab assessment?

**Is the work clearly and accurately presented and does it cite the current literature?**
Yes

**Is the study design appropriate and is the work technically sound?**
Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**
Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**
I cannot comment. A qualified statistician is required.

**Are all the source data underlying the results available to ensure full reproducibility?**
Yes

**Are the conclusions drawn adequately supported by the results?**
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Professor Of Pediatrics - Assiut University & Head of clinical nutrition unite - Assiut University children hospital

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Hoda Atef, Faculty of Medicine, Cairo University, Cairo, Egypt

Dear Professor, DR: Osama El-Asheer

Thank you for your valuable comments

1. Regarding the results: we added the detailed questionnaire to collectively gather the ways for the aimed tool
2. Regarding the sample size: it depended on the time of study and all patients who fulfilled the inclusion criteria were enrolled in the study
3. Regarding the comparison with other tools like STAMP or STRONG Kids scoring, we didn't use them as this wasn't our aim of the study. Our aim was to find a simple and a valid tool. The process of validity required high sensitivity and specificity which needed a comparison with any valid tool such as SGA
4. Regarding the base of age classification. WHO (World Health Organization) defines the early childhood group from 0-8 years. I further categorized the first two years as a separate group as they have different feeding (e.g. breast feeding) and its problems are present during this period which is a distinctive period in the childhood
5. Regarding the tables, our aim was to explain in details. However, they could be further shortened
6. Regarding the discussion, we intended to introduce our work before comparing it with the similar articles in the discussion. However, it could be further shortened.
7. Regarding the references, we tried to update them till 2020
8. Regarding the lab comments, they weren't observed as this wasn't the aim. The aim of the study was to develop a rapid and simple tool. The labs would take time.

Competing Interests: No competing interests were disclosed
2. There was no depiction of the current nutritional state, of the underlying medical issues, the length of stay or the change in weight during the stay. NRS are focused on identifying those at risk of nutritional compromise during admission - this doesn't include that focus.

3. The METHODS should describe how the study was done. The number of subjects is a result and should be moved accordingly.

4. There are a large number of tables - are these all required? Some could be supplementary instead and some deleted.

5. The DISCUSSION should be shortened and more focused. When using et al, the reference number must follow directly afterwards. Some sentences are awkward and could be improved with revision.

**Is the work clearly and accurately presented and does it cite the current literature?**
Partly

**Is the study design appropriate and is the work technically sound?**
Partly

**Are sufficient details of methods and analysis provided to allow replication by others?**
Yes

**If applicable, is the statistical analysis and its interpretation appropriate?**
Yes

**Are all the source data underlying the results available to ensure full reproducibility?**
No source data required

**Are the conclusions drawn adequately supported by the results?**
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** paediatric gastroenterology and nutrition

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 19 Mar 2021

Hoda Atef, Faculty of Medicine, Cairo University, Cairo, Egypt

Dear : Andrew S Day
Thank you for your valuable comments

1. Regarding the point number 1: the sample size was dependent on the time of the study. In addition, we excluded patients with chronic illnesses to exclude bias as the chronic nature could cause malnutrition. These could be the causes of a smaller sample size as the inclusion criteria were very precise.
   Of course, further studies are needed to validate the tool and our study may be the point of the start for these further researches.

2. Regarding the point number 2: There was a depiction for the current nutritional status. You can get it in the supplementary files. For example, there were underweight, wasted and short status groups. Regarding the length of hospital stay, it wasn't our aim as the study aim is to find a tool on hospital admission. Further studies are required to apply it on the hospital length stay.

3. Regarding the point number 3, please explain more, what do you mean?

4. Regarding the point number 4, our aim was to explain all data but the tables could be further summarized

5. Regarding the point number 5, we tried to comment on the results as much as possible and compare them with the relevant articles. However, the discussion could be further shortened.

Thank you so much
Sincerely
Hoda Atef

**Competing Interests:** No competing interest were disclosed
The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com