Reviewer's report

Title: Adverse drug events in hospitalized children at Ethiopian University Hospital: A prospective observational study

Version: 2  Date: 6 March 2015

Reviewer: Mio Sakuma

Reviewer's report:

Comments to the Author

General comment

This is an interesting study conducted in Ethiopia, which used the similar methodology of the published articles such as the one by Bates et al in JAMA, 1995 or the one by Takata et al in Pediatrics, 2008. The authors assessed the incidence of ADEs and their severity and preventability in pediatric patients hospitalized in a large hospital which was the only teaching and referral hospital in the southwestern part of Ethiopia. It is important to assess the local data on drug safety in other parts of the world from the western countries, i.e. Africa; however, the paper would be more interesting if the authors sought to offer clinical implications of the observation or further discussion for improving drug safety. There are some major and minor concerns with this paper. The following are my thoughts as I reviewed this paper.

Major compulsory comments

1. Methods, Study setting and design: Please explain more precisely about inclusion criteria of pediatric patients here; all patients that were hospitalized at any period between Feb 1st and May 1st were included? All patients that were hospitalized within the period between Feb 1st and May 1st? Or all patients whose admission date was included between Feb 1st and May 1st?

2. Methods, Study setting and design: The authors stated that “the study definitions used in this study…. in different clinical settings” showing several references; however, the definition of each study might not be completely identical. Thus, the authors should specify the definition of ADEs, preventable ADEs, the category of severity, and preventability (medication error) here.

3. Methods, Data collection procedure: Much more detail is needed about what the data collection tool was. Was that developed by the authors? How?

4. Methods, Data collection procedure: Much more details and organized explanation are needed about how ADEs were identified by whom. One nurse and two pharmacists data collectors also identified ADEs?

5. Methods, Data collection procedure: The authors stated in this section that the physician responsible for the care of the patient was contacted when there was a dose change and so on, that al pediatric ward staff was informed about the study and asked to submit reports of any events or potentially unsafe medication
systems, that the PI of this study made a daily visits to the ward and attend the clinical rounds and meetings, and that the pediatrics team intervened a specific medical care to prevent further damage or manage the ADEs. All of them were considered as interventions to prevent or reduce ADEs. Therefore, the results of this study would be significantly biased, and then, the incidence of ADEs and severity or preventability of ADEs would not be assessed appropriately.

6. Methods, data analysis: Please specify how to decide the covariates of the multiple logistic model; it seems that the covariates were chosen arbitrarily as well as the cutoff point of length of hospital stay (Table 3). Needs scientific reason for them. Furthermore, it is unclear what the authors assessed by the logistic models. Estimated the odds ratios of the patients’ characteristics for the risk of ADE occurrence on patients? If so, the dependent variable in the model should be patient (with ADEs or without ADEs), then, please specify it with the number of patients who were included in the final model.

7. Results, Study population characteristics: What is meant by “600 patients reflecting a total of 634 admissions”? Please specify how multiple admissions of the same patient were handled, and clarify the unit to calculated the incidence in this study: patients or admissions? It is confusing that the authors used both admissions and patients. How many patients or admissions were included in this study finally?

8. Results, Incidence, preventability and severity of ADEs: How were multiple ADEs in the same patient determined and handled?

9. Results, Incidence, preventability and severity of ADEs: What is meant by “4 of the 58 ADEs were the primary reason for initial hospitalization”? Did the study include ADEs which occurred before admission?

10. Results, Incidence, preventability and severity of ADEs: The authors classified phlebitis with swelling and redness as non preventable ADEs; however, they might be ameliorable if monitoring was appropriate. In such case, these events might be classified as preventable ADEs. Please define precisely how to define preventable ADEs and non-preventable ADEs in the method section.

11. Results, Incidence, preventability and severity of ADEs, fifth paragraph: The authors stated that children with length of stay greater than 23 days were 8 fold more likely to develop ADEs than children with less than 9 length of stay; however, this result could be interpreted that ADEs increased the length of stay rather than that longer stay cause more ADEs.

12. Results, Table1: Table1 needs to show more detailed patients’ characteristics such as age category, gender, ward category to be hospitalized, and so on, otherwise, table 1 has little value.

13. Results: There is no description or mention of figure4 within the text of result.

14. Discussion, second paragraph: The authors explained several data regarding preventable ADEs that were not shown in the results section. Please show them in the result section. Similarly, the authors stated that 9% of ADEs resulted in permanent harm/death in this study; however, this data was not clarified in the result section. Again, please show the detailed data in the results.
15. Discussion, fourth paragraph: There was no data shown that the most commonly affected organ system with ADEs was gastrointestinal in the results, and this statement was not consistent with the results shown in Figure 4.

16. Discussion, last paragraph: The statement that “any event that has occurred in patients less than 24 hours of hospital stay is not included” should be clarified precisely in the method section because this definition is critical in terms of how to identify ADEs. In the method section, the authors stated that “patients were excluded if the hospital admission was for less than 24 hrs”, but this part was for how to include the patients and were different from how to identify ADEs.

17. Discussion, last paragraph: The limitations should clarify that some ADEs may not have been noted in the charts and may thus have not been detected, which would make the incidence underestimated.

18. Discussion: Discussion seems to be relatively longer and a bit redundant because discussion focus on mostly summary of the result and mere comparison with previously published papers. I would recommend Discussion should explain novelty, value, and clinical implication of this observation more and make further discussion about strategy to improve drug safety based on this observation.

Minor essential revisions

1. Background, second paragraph: Please add the appropriate reference for the sentence “Currently, interventions designed to improve ADE reporting are recommended.”

2. Methods, Study setting and design, the last sentence: What do you mean that nurses were collecting medications for 24 hr consumption?

3. Methods, Data collection procedure, second paragraph: What is meant by medication related incidents/events? Was that the same as ADEs? Did the authors use the incidents and events in a different way? If so, please specify how.

4. Methods, Data collection procedure: What is the multidisciplinary team? Who was included? How were they disciplined? What was the exact role of that team in this study? Who interviewed the multidisciplinary team?

5. Methods, data analysis: What is meant by “the independent covariates and their relationship with ADE occurrence were analyzed ……between the dependent and covariates”? Please specify what the dependent was and what the covariates were here.

6. Results, Study population characteristics, second paragraph: How did the authors get 55.4 medication doses per patient? 35,117/600=58.5, which was not equal to the results. Was the final number of the eligible patients in this study 600?

7. Results, Study population characteristics, second paragraph, and table 1: Median might be the best measure of central tendency for all covariates here.

8. Results, Study population characteristics, second paragraph, and table 2: The number of prescriptions, 2072, in tables 2 meant the number of medication
orders? If so, please use the same word through the paper to avoid confusion.

9. Results, Incidence, preventability and severity of ADEs, first paragraph: The authors showed that 46 patients accounted for 58 ADEs and the incidence of ADEs was 9.2 per 100 admissions. Again, it is confusing to use both patients and admissions. Here, the word “patients” was used in the same meaning of “admission”?

10. Results, Incidence, preventability and severity of ADEs, third paragraph: Much more details of the classification of severity instead of showing just E, F, and G.

11. Table1: Add “n” for total patients.

12. Figure2: Add “n” for each age category in addition to percentage.

13. Figure5: Add the name of each medication class on X axis.

Discrepancy revisions
- Results, Incidence, preventability and severity of ADEs
1. Please consider adding the examples of symptoms for ADEs due to the most common medication classes such as anti infective, cardiovascular drugs and CNS drugs.
2. Consider adding a table showing the stage of errors in preventable ADEs with example case.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests.