Author’s response to reviews

Title: Concurrent presentation of thyroid storm and diabetic ketoacidosis: a systematic review of previously reported cases

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The Editor
BMC Endocrine Disorders

Dear Sir / Madam,

BEND-D-19-00045

Submission of revised manuscript and replies to reviewers’ comments

Concurrent presentation of thyroid storm with diabetic ketoacidosis: a systematic review of previously reported cases

On behalf of the authors, I would like to submit our replies to the comments by reviewers along with the edited version of the manuscript. We value the comments of the two reviewers which have helped us to improve our manuscript. Comments of the reviewers were accepted and necessary alterations were made to the manuscript.

We feel that the findings described in this manuscript will be of special interest to the readers of the BMC Endocrine Disorders. All authors have read the final manuscript and have approved this submission. We do not report any conflicts of interest.
Yours Sincerely,

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Replies to reviewer’s comments

We value the comments of the two reviewers which have helped us in improving the manuscript. The replies to the comments are stated below.

Reviewer #1:

Reviewer 1 comment 1

The manuscript contains important information; however, the manuscript was too descriptive and redundant, and thus, authors should try to improve it by focusing only on the important findings, not everything they found.

Authors Response

The results and the discussion sections of the manuscript were re-written to focus only on the important findings.

Reviewer 1 comment 2

Authors should also try to discuss what could be learned from the study in discussion. The current discussion is not more than a summary of the findings.
Authors Response

Discussion section of the manuscript was re-written to focus on what could be learned from the study.

Reviewer 1 comment 3

"Japan" Burch-Wartofsky Point Scale in line 7 of page 4 should be incorrect.

Authors Response

The word “Japan” was omitted.

Reviewer 1 comment 4

It was not clear what was meant in line 9-10 of page 4.

Authors Response

The particular sentence was thought to be unnecessary and it was omitted.

Reviewer 1 comment 5

The number of case reports should be described such as N=4, but not (4). Readers may think the number in the parenthesis indicate the reference.

Authors Response

The number of case reports were mentioned as advised (e.g. n=4) and the correction was made throughout the manuscript.

Reviewer #2:

Reviewer 2 comment 1

In the abstract the results section needs to be tidied up. Most of the second half of the results paragraph is rather confusing and I would suggest they say that 'in all cases where it was measured the tests were positive'.
Authors Response

In the abstract the relevant part of the result section was re-written as “In all cases where HbA1C (7/7) and T4 (16/16) were measured, the results were elevated and where TSH (17/17) was measured the results were low”.

Reviewer 2 comment 2

In the conclusion I would suggest that maybe the emphasis needs to change and it should say that efforts should be made to maximise patient compliance to treat them, rather than predispositions due to poor compliance.

Authors Response

The conclusion was edited as “Therefore, efforts should be made to maximise patient compliance to anti-thyroid and anti-diabetic agents in treating such patients”.

Reviewer 2 comment 3

In the background section most of the first paragraph can be safely omitted in terms of what DKA is and how it occurs, because it is irrelevant to the thrust of the manuscript. The background really should be just a small paragraph on what is known, what is not known and what they have done to fill the gap.

Authors Response

The background was edited to make it concise.

Reviewer 2 comment 4

They also need to consider the grammar throughout the document

Authors Response

The grammar throughout the document was re-visited for improvement.

Reviewer 2 comment 5
Instead of reference 6 I would suggest they use the paper by Umpierrez and colleagues from Nature Reviews Endocrinology 2016;12(4):222-232. I wonder whether the authors may want to use a better reference than reference 7, such as the paper in Thyroid 2019 from Galindo and colleagues; 29(1):36-43, or from Akamizu and colleagues from Thyroid in 2012;12(7):661-679.

Authors Response


Reviewer 2 comment 6

The authors suggest that it may be the DKA which causes the thyroid storm; I would strongly argue it's the other way round, that the thyroid storm precipitates the DKA

Authors Response

We are humbled in informing that we did not intend to suggest “DKA may cause thyroid storm”. Instead, we summarized a possible explanation with the reference “Potenza M, Via MA, Yanagisawa RT. Excess thyroid hormone and carbohydrate metabolism. Endocr Pract. 2009;15(3):254–62”. The above evidence also suggest that the initial trigger is an “excessive thyroid hormone”. We could not find any other evidence for the pathophysiology of the concurrent presentation of DKA and thyroid storm.

Reviewer 2 comment 7

In the methods section the authors use reference 16, which is the old version of their reference 1 and I am unsure as to why they have used 2 different references for the same thing.

Authors Response

The authors regret for the mistake and both citations were done using the latest version “Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care. 2009;32(7):1335–43”.


Reviewer 2 comment 8

Throughout the document I am not sure why the authors have put in the single figures with the number zero prior to it, such as in the first line of the results section and in line 17, where they say 04 rather than just 4.

Authors Response

The authors regret for the mistake and appropriate corrections were done throughout the manuscript.

Reviewer 2 comment 9

It should be 112 articles and they should say the full text of the remaining 28 reports in that paragraph on the results.

Authors Response

The two sentences were re-written as “Following the exclusion of duplicates, 152 articles underwent title and abstract screening out of which 112 articles were excluded due to irrelevance to the review objective” and “The full-texts of the remaining 28 reports were studied, and 7 were excluded due to mismatch with the selection criteria (absence of thyroid storm -4, absence of DKA - 3)”.

Reviewer 2 comment 10

In the clinical presentation section, I would say what are the defining features of thyroid storms.

Authors Response

The defining features of thyroid storms were included to the clinical presentation section including the results for the Burch-Wartofsky point scale.

Reviewer 2 comment 11

The tables are extremely confusing and most of them are unnecessary because there is a large degree of overlap between the tables and the text. Certainly table 2 is extremely confusing in this respect and certainly I spent a long time trying to make sense of them, such as the section on central nervous system disturbance; mild 42%, moderate 42%, severe 11% and absent 5%, and yet they then say 19, which equals 66% so do they say that anybody who had central nervous
disturbance 66% of them had something. This is very unusually and confusingly written and I would strongly urge the authors to revise their document.

Authors Response

Table 2 was omitted as there was a large degree of overlap between the table and the text.

Reviewer 2 comment 12

In table 4, when they say the range of pH was 7.4 and a bicarbonate was up to 19, these cases were clearly not then diabetic ketoacidosis, using whichever definition they use, either the ADA or the UK guideline which states that pH must be less than 7.3. Even with the mild DKA definition using the ADA guideline it should say a bicarbonate of 18 or less and therefore with a bicarbonate of 19 this could not have been DKA, therefore I am very suspicious of the data that the authors are using.

Authors Response

The authors regret for the error. Cases with a pH > 7.3 or a bicarbonate > 18 were excluded from the review. The results section was re-written accordingly.

Reviewer 2 comment 13

Table 5 is completely unnecessary.

Authors Response

The table 5 was omitted.

Reviewer 2 comment 14

Table 6, I am not sure how the authors have defined compliance and certainly how they define poor compliance; they need to talk about papers that define these.

Authors Response

Poor compliance was reported in accordance with the findings by the relevant authors of the case reports selected for the review.
Reviewer 2 comment 15

Also, the authors talk about current diabetic type and I would strongly urge the authors to avoid the term 'diabetic' in all circumstances. A person should never be described by the condition that they have and therefore it should be current diabetes type. This also then begs the question as to whether this is a pre or post presentation.

Authors Response

The column title was changed as “Post presentation diabetes type”.

Reviewer 2 comment 16

In the paragraph saying the examination findings, the authors say the respiratory rate was present in 10 patients. I am surprised because presumably all the patients were alive, therefore they were all breathing. I wonder whether the authors meant respiratory rate was recorded in 10 patients.

Authors Response

The authors regret for the error. The sentence was changed as “Respiratory rate was reported in 9 patients”.

Reviewer 2 comment 17

This reviewer wonders why thyroglobulin would ever be measured in people with thyrotoxicosis. All it is a measure of is the presence of thyroid tissue and is really only used to monitor thyroid cancer progression once somebody has had surgery or/ and radiotherapy.

Authors Response

Details on thyroglobulin was omitted from the results section.

Reviewer 2 comment 18

In the same paragraph the authors say that the reported ECG findings, which 80% reported tachycardia, but earlier on they mention that 100% of all patients had tachycardia, so this is surprising that there is a 20 % discrepancy.

Authors Response
The authors regret for the error. Among patients having their heart rate reported via ECG, all had tachycardia. Details on ECG and other investigation findings were summarized only in Additional file.1.

Reviewer 2 comment 19

I wonder what the relevance is of the autopsy reports and certainly also the chest x-ray, and how this can be relevant other than if it showed the presence of heart failure due to high output heart failure due to tachycardia.

Authors Response

Details on chest x-ray and other investigation findings were summarized only in Additional file.1.

Reviewer 2 comment 20

Similarly, table 9 is completely unnecessary and adds nothing to the manuscript.

Authors Response

The table 9 was omitted.

Reviewer 2 comment 21

In the treatment modality section they said 28 cases out of the 29 and similarly in the second paragraph they said 12 patients were reported to be discharged from hospital. Once again this is a matter of language and I am sure all of the patients were discharged from hospital, other than those that died, and therefore this is a strange sentence.

Authors Response

The authors regret for the error. Both the sentences were omitted.

Reviewer 2 comment 22

The discussion reads very unusually. The discussion should start by stating what the findings of the study were within one or two sentences. Otherwise it is currently very rambling as it is currently written and really doesn't add very much.
Authors Response

Discussion section of the manuscript was re-written according to the reviewer comments to focus on what could be learned from the study.

Reviewer 2 comment 23

In summary I do not think this paper is suitable for publication. There also seems to be an omission with this reviewer doing at least one further search and finding a further paper by Mercer and colleagues in the Journal of Diabetes and its Complications 2011;25:208-210.

Authors Response

The authors excluded the above-mentioned study at title and abstract screening as the patient was not reported to have a thyroid storm. The authors are grateful for the reviewer’s comments and hope that the revised manuscript is suitable for publication.