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OPEN PEER REVIEW

# The Prevalence and Incidence of Endocrine Disorders After Traumatic Brain Injury in Hamadan City, Iran

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## About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

More about open peer review: brieflands.com/knowledgebase/opr

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## 1 Original submission

5 comments · 1 Mar 2026 – 10 May 2026

### Referee 1 Reviewer

MAJOR REVISION 1 Mar 2026

Dear AE,
Thank you for inviting me to review this manuscript. Below are some comments that should be addressed by the authors:
1. The study design is described as a retrospective review, but it is not explicitly labeled as cross-sectional.
2. The abstract does not provide detailed eligibility criteria or methods of participant selection.
3. Data were sourced from hospital databases, but specific measurement methods are not detailed in the methods section.
4. The abstract does not mention any efforts to address potential sources of bias.
5. The methods section does not explain how the study size was determined.
6. The methods section does not provide details on the handling of quantitative variables.
7. Statistical methods are mentioned, with data analyzed using SPSS software, but specific methods to control for confounding are not detailed.
8. The abstract does not report the number of individuals at each stage of the study.
Kind regards

### Referee 2 Reviewer

MAJOR REVISION 10 May 2026

Dear Authors,

We have reviewed your manuscript and provide below the additional scientific reviewer comments that have not already been addressed during the editorial-screening stage. The major comments focus on substantive scientific and reporting issues, while the minor comments address editorial clarity, presentation quality, and language.

The manuscript reports a retrospective database-based study estimating the prevalence and incidence of hormonal disorders after traumatic brain injury in Hamadan, Iran, from 2020 to 2024. The study uses hospital database records to compare TBI patients with and without hormonal disorders and evaluates differences by sex, age, calendar year, and time from TBI to hormonal disorder diagnosis.

The topic is clinically important because endocrine dysfunction after TBI can be delayed, underdiagnosed, and relevant to long-term follow-up planning. The manuscript also has potential local value because it attempts to provide epidemiological evidence from Hamadan over a five-year period.

Major Comments:

1. Clarify the source population, database coverage, and case ascertainment (STROBE: setting, participants, and data sources):

> *The manuscript states that the study reviewed the database of Besat Hospital, Hamadan, while the abstract and title refer more broadly to hospitals or patients of Hamadan city (source: Abstract; Materials and methods, Study design). This creates uncertainty about whether the data represent one hospital, multiple hospitals, or the entire city population, which directly affects the validity of prevalence and incidence estimates.*
> *Author to-do list:*

** Specify whether the dataset came from Besat Hospital only or from all relevant hospitals in Hamadan city (source: Materials and methods, Study design).*
** Define the source population used as the denominator for prevalence and incidence calculations (source: Materials and methods; Results, Table 1).*
** Explain whether the hospital database captures all TBI cases in Hamadan or only hospital-presenting cases (source: Materials and methods, Study design).*
** Revise the title, abstract, and conclusions so that the geographic claim matches the actual database coverage (source: Title; Abstract; Conclusion).*

2. Define hormonal disorders and diagnostic criteria in sufficient clinical detail (STROBE: variables and measurement):

*The manuscript refers to "hormonal disorders," "endocrine disorders," "endocrinopathies," and "hypopituitarism," but it does not specify which diagnoses were included, which ICD codes or laboratory criteria were used, or how new post-TBI hormonal disorders were distinguished from pre-existing disorders (source: Abstract; Introduction; Materials and methods, Study design). Without clear diagnostic definitions, the outcome is not reproducible and may combine clinically heterogeneous conditions.*
*Author to-do list:*

** List the exact endocrine diagnoses included under "hormonal disorders" (source: Materials and methods, Study design).*
** Provide the ICD codes, clinical criteria, or laboratory thresholds used to identify each endocrine outcome (source: Materials and methods, Study design).*
** Clarify how pre-existing endocrine disorders were excluded or distinguished from post-TBI disorders (source: Materials and methods, Study design).*
** Use one consistent term for the outcome throughout the manuscript, such as "post-TBI endocrine disorders" or "post-TBI hormonal disorders" (source: Abstract; Introduction; Results).*

3. Correct and fully report the contingency-table groups and epidemiological formulas (STROBE: statistical methods):

*The methods state that patients were divided into four groups, but groups C and D are both labeled as TBI–, H-, even though group C is described as patients with a hormonal disorder without TBI (source: Materials and methods, Data analysis). In addition, the prevalence and incidence formulas are introduced but not displayed, making it impossible to verify how the reported rates were calculated.*
*Author to-do list:*

** Correct the four contingency-table group definitions so that each TBI/hormonal-disorder category is distinct (source: Materials and methods, Data analysis).*
** Display the exact prevalence formula and define every numerator and denominator (source: Materials and methods, Data analysis).*
** Display the exact incidence formula and define whether the denominator is person-time, population at risk, or another denominator (source: Materials and methods, Data analysis).*
** Ensure that Table 1 labels match the corrected contingency-table definitions (source: Table 1).*

4. Strengthen statistical analysis beyond descriptive comparisons (STROBE: statistical methods and main results):

*The manuscript reports sex and age differences in prevalence, incidence, and time gap, but it does not report statistical tests, confidence intervals, regression models, or adjustment for potential confounders such as age, sex, calendar year, TBI severity, skull fracture, or hospitalization factors (source: Materials and methods, Data analysis; Results). The*

*current analysis therefore cannot distinguish descriptive differences from statistically supported associations.*
*Author to-do list:*

** Report statistical tests used to compare prevalence or incidence across sex and age groups (source: Materials and methods, Data analysis; Results).*
** Provide confidence intervals for prevalence and incidence estimates (source: Results; Tables 1–2; Figures 1–2).*
** Consider multivariable regression or stratified analysis to assess whether sex and age differences persist after adjustment (source: Results; Discussion).*
** Clearly distinguish descriptive findings from inferential conclusions (source: Results; Discussion; Conclusion).*

5. Define and analyze the time gap from TBI to hormonal disorder diagnosis more rigorously (STROBE: variables and outcome data):

*The manuscript reports that the mean time gap between TBI onset and hormonal disorder diagnosis was shorter in women than in men, but it does not explain how the TBI onset date and endocrine diagnosis date were extracted, whether follow-up time differed by patient, or whether delayed diagnosis could reflect healthcare access rather than biological onset (source: Results, Figure 3; Discussion). This limits interpretation of the conclusion that onset is earlier in women.*
*Author to-do list:*

** Define "time gap" operationally and specify the exact dates used for calculation (source: Results, Figure 3).*
** Report the sample size used for the time-gap analysis by sex (source: Results, Figure 3).*
** Provide a statistical comparison and confidence intervals for the sex-specific time-gap estimates (source: Results, Figure 3).*
** Reframe "earlier onset" as "shorter time to recorded diagnosis" unless true biological onset was measured (source: Results; Discussion; Conclusion).*

Minor Comments:

1. Tables and figures:

*The manuscript contains two tables and three figures. Table 1 and Table 2 are cited in the Results; Figure 1, Figure 2, and Figure 3 are also cited in the Results, so all tables and figures appear to be cited in the main text (source: Results; Tables 1–2; Figures 1–3). Please improve table formatting, define all abbreviations in table footnotes, and ensure that figure captions include enough information to be understood without returning to the main text.*

2. Early-stage editorial and language red flags:

*Several wording problems should be corrected during revision. "TBI is one of the common cause of death" should be revised to "TBI is one of the common causes of death" (source: Introduction). "During five years (2020-2024), 39709 patients were suffered from TBI" should be revised to "During the five-year period from 2020 to 2024, 39,709 patients experienced TBI" (source: Results). "The prevalence and incidence for endocrine dysfunction after TBI calculated" should be revised to "The prevalence and incidence of endocrine dysfunction after TBI were calculated" (source: Materials and methods, Data analysis). "B) TBI with without following hormonal disorder" should be revised to "TBI without subsequent hormonal disorder" (source: Materials and methods, Data analysis).*

3. Terminology consistency:

*The manuscript alternates between "hormonal disorders," "endocrine disorders," "endocrine dysfunction," "endocrinopathies," and "hormonal disturbance" (source: Abstract; Materials and methods; Results; Discussion). Please select one main term and use it consistently, defining any narrower terms such as hypopituitarism separately.*

4. Title and keyword consistency:

> *The manuscript title uses "hormonal disorders," while the keywords include "Trauma" and "Damage," which are too broad and less informative than standard indexing terms (source: Title; Keywords). Please revise the keywords to include more specific terms such as "Traumatic brain injury," "Endocrine dysfunction," "Hypopituitarism," "Incidence," and "Prevalence."*

5. Reference currency:

> *Several references were published before 2010 and should be reviewed for replacement with newer and more directly relevant sources where appropriate, while retaining seminal references only when necessary. These include older references from 1959, 1977, 2002, 2005, 2006, and 2009 (source: References 4, 11, 12, 15, 16, 17). Please also review whether older mechanistic references are essential to the argument or can be replaced by recent reviews.*

6. Reference-list cleanup:

> *The reference list appears to contain a duplicate or near-duplicate pair for the Arizona pediatric TBI study, listed as both Ref 6 and Ref 8 (source: References 6 and 8). Please remove duplicate entries, renumber citations if needed, and ensure that each reference is cited only once in the final reference list.*

Please revise the manuscript carefully in response to the points above.

Best regards,
Scientific Reviewer

**Referee 3** Reviewer

MAJOR REVISION 10 May 2026

Dear Authors,

Thank you for submitting your manuscript to the journal. Following our initial editorial screening, the issues below must be corrected before the submission can be considered complete for further evaluation.

Please note that references are very important for publication, and all cited sources must include DOI/PMID information when supplied, be cited appropriately in the manuscript text, and be suitable for the journal.

2-1- Ethical approval and consent status are not acceptable as currently reported:

* What the author wrote: The manuscript states that data were collected and analyzed and that there is no need for an ethical code, and it does not report informed consent or a formal waiver of consent. (source: Metadata ethical approval field; Materials and methods)
* Why correction is required: This must be corrected because the manuscript is not compliant with basic editorial requirements regarding ethical oversight for retrospective research using patient records. (source: Metadata ethical approval field; Materials and methods)
* To do: Provide the ethics committee approval code, or provide an official exemption or waiver statement from the relevant institutional review board, and clarify the consent or consent-waiver status. (source: Metadata ethical approval field; Materials and methods)

2-2- Source population and database coverage are unclear:

* What the author wrote: The manuscript refers to hospitals in Hamadan and patients in Hamadan city, but the methods state that the database of Besat Hospital, Hamadan, was reviewed. (source: Abstract; Materials and methods, Study design)
* Why correction is required: This must be corrected because internal inconsistency currently prevents reliable assessment of whether the prevalence and incidence estimates represent one hospital, multiple hospitals, or the city population. (source: Abstract; Materials and methods; Results)
* To do: Reconcile the setting description and clearly state whether the data came from Besat Hospital only,

multiple hospitals, or a population-level registry for Hamadan city. (source: Abstract; Materials and methods; Results)

2-3- Diagnostic definitions for hormonal disorders are incomplete:

* What the author wrote: The manuscript reports endocrine disorders, hormonal disorders, endocrinopathies, and hormonal disturbance after TBI but does not define the included diagnoses, ICD codes, laboratory thresholds, or diagnostic criteria. (source: Abstract; Materials and methods)
* Why correction is required: This must be corrected because the manuscript is not fully evaluable without reproducible outcome definitions and clear diagnostic criteria. (source: Materials and methods)
* To do: Define all included endocrine or hormonal disorders, provide the codes or clinical/laboratory criteria used for diagnosis, and use one consistent outcome term throughout the manuscript. (source: Materials and methods; Results)

2-4- Contingency-table categories and epidemiological formulas require correction:

* What the author wrote: The manuscript contains four patient groups, but group C and group D are both labeled as TBI–, H-, and the prevalence and incidence equations are introduced but not displayed. (source: Materials and methods, Data analysis)
* Why correction is required: This must be corrected because internal inconsistency currently prevents reliable assessment of the prevalence and incidence calculations. (source: Materials and methods, Data analysis; Table 1)
* To do: Correct the four TBI/hormonal-disorder categories, display the exact prevalence and incidence formulas, and define each numerator and denominator used in the calculations. (source: Materials and methods, Data analysis; Table 1)

2-5- Statistical analysis is insufficient for the stated comparisons:

* What the author wrote: The manuscript reports differences by sex, age, year, and time gap, but does not report statistical tests, confidence intervals, adjusted models, or control for confounding factors. (source: Materials and methods, Data analysis; Results)
* Why correction is required: This must be corrected because the manuscript is not fully evaluable without statistical evidence supporting the reported group differences and trend interpretations. (source: Results; Discussion)
* To do: Add appropriate statistical comparisons, confidence intervals, and, where possible, adjusted analyses for sex, age, year, and relevant clinical covariates. (source: Materials and methods; Results)

2-6- Data availability and supplementary material are not addressed:

* What the author wrote: The manuscript does not include a data availability statement and does not state whether supplementary files, coding lists, extraction forms, or statistical outputs are available. (source: Metadata; Full manuscript)
* Why correction is required: This must be corrected because the manuscript is not fully verifiable without information on data availability and supporting materials. (source: Metadata; Materials and methods)
* To do: Add a data availability statement and clarify whether supplementary materials, diagnostic code lists, database extraction details, or analysis outputs are submitted. (source: Metadata; Materials and methods)

2-7- Reference integrity and recency require correction:

* What the author wrote: The manuscript contains 20 references; all references contain DOI and/or PMID information, but 7 references were published in 2011 or earlier, one local citation entry contains an implausible PubMed ID format, and one duplicate or near-duplicate reference pair is present. (source: References)
* Why correction is required: This must be corrected because the manuscript is not fully verifiable without a

current, nonduplicated, and internally consistent reference list. (source: References)
* To do: Correct the affected reference entries, remove duplicate or near-duplicate entries, and replace older references with newer sources unless a strong justification exists for retaining them. (source: References)
* References with DOI/PMID: Ref 1 - Izzy et al., Ref 2 - Emelifeonwu et al., Ref 3 - Lauzier et al., Ref 4 - Cohan et al., Ref 5 - Mele et al., Ref 6 - Ortiz et al., Ref 7 - Maleki et al., Ref 8 - Ortiz et al., Ref 9 - Oruganti et al., Ref 10 - Aljboor et al., Ref 11 - Labrie et al., Ref 12 - Daniel et al., Ref 13 - Yang et al., Ref 14 - Wagner et al., Ref 15 - Berry et al., Ref 16 - Hoffman et al., Ref 17 - Feldman et al., Ref 18 - Zhong et al., Ref 19 - Mahajan et al., Ref 20 - Tanriverdi et al. (source: References)
* References requiring further review:

* Ref 4 - Cohan et al. — published in 2005; contains an implausible PubMed ID format in the manuscript reference list; correct the citation details and replace with a newer study unless a strong justification exists for retaining it. (source: References 4)
* Ref 6 - Ortiz et al. — duplicate or near-duplicate of Ref 8; correct the duplication and retain only one complete reference entry. (source: References 6 and 8)
* Ref 8 - Ortiz et al. — duplicate or near-duplicate of Ref 6; correct the duplication and retain only one complete reference entry. (source: References 6 and 8)
* Ref 11 - Labrie et al. — published in 1977; replace with a newer study unless a strong justification exists for retaining it. (source: References 11)
* Ref 12 - Daniel et al. — published in 1959; replace with a newer study unless a strong justification exists for retaining it. (source: References 12)
* Ref 14 - Wagner et al. — published in 2011; replace with a newer study unless a strong justification exists for retaining it. (source: References 14)
* Ref 15 - Berry et al. — published in 2009; replace with a newer study unless a strong justification exists for retaining it. (source: References 15)
* Ref 16 - Hoffman et al. — published in 2006; replace with a newer study unless a strong justification exists for retaining it. (source: References 16)
* Ref 17 - Feldman et al. — published in 2002; replace with a newer study unless a strong justification exists for retaining it. (source: References 17)

Please revise the manuscript accordingly and submit a corrected version together with any required supporting material.

Kind regards,
Screening Reviewer

## Associate Editor

MAJOR REVISION 10 May 2026

Dear Authors,

I have assessed your Research Article, which examines the prevalence and incidence of hormonal disorders after traumatic brain injury in Hamadan, Iran. The manuscript addresses an important biomedical and epidemiological topic, but its current form has substantial methodological, ethical, and reporting limitations that prevent reliable editorial evaluation.

The strongest aspect of the manuscript is its focus on post-TBI endocrine dysfunction, a clinically important complication that may require long-term surveillance and follow-up. The five-year dataset and the attempt to describe sex-, age-, and time-related patterns could provide useful regional evidence if the source population, diagnostic criteria, and analytical methods are clarified.

The scientific review indicates that the manuscript requires substantial revision before it can be considered further. The most important concerns involve unclear database coverage, insufficient diagnostic definitions for hormonal disorders, incomplete epidemiological formulas, inadequate statistical testing, and overinterpretation of descriptive findings. The editorial screening also identified major compliance and reporting issues, particularly the inadequate ethics statement, missing consent or waiver information, absent data availability statement, and reference-list problems.

Title and abstract: 6/10
Introduction and rationale: 6/10
Methods rigor: 4/10
Results presentation: 5/10
Discussion and interpretation: 5/10
Reporting quality: 4/10
Language and structure: 5/10
Clinical relevance or scholarly value: 7/10
Overall quality: 5/10

Overall, the manuscript may be reconsidered only after major revision. The authors should substantially revise the methods, ethics/compliance statements, statistical analysis, reference list, and language, and should ensure that all conclusions are supported by clearly defined denominators, diagnostic criteria, and appropriate statistical evidence.

Kind Regards,
Associate Editor

**Editor-in-Chief** MAJOR REVISION 10 May 2026

Dear Authors,

Thank you for submitting your manuscript to the journal. After editorial assessment and scientific review, the manuscript is considered relevant to the journal's scope and addresses a clinically important biomedical topic; however, it cannot be accepted in its current form.

The manuscript requires major revision before it can be reconsidered. The revised submission must address the major methodological, ethical, and reporting concerns raised during review, particularly the ethics approval or formal exemption status, source population and database coverage, diagnostic definitions for hormonal disorders, epidemiological formulas, statistical analysis, data availability, reference integrity, and overall language clarity.

Please submit a revised manuscript together with a clear response explaining how each reviewer and editorial comment has been addressed.

Kind Regards,
Editor-in-Chief

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# Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

**Dear Chief Editor**

Thank you very much for your e-mail having the referee's comments about our article entitled "The prevalence and incidence of hormonal disorders after traumatic brain injury in Hamadan city-Iran". I apologize for the delay in submitting the article. Unfortunately, due to the problems after the recent war, I was unable to submit the refereed article within the stipulated time. In response to the comments and suggestions in your letter, I would like to thank you and the referees for your valuable point of views and suggestions. Our changes in the text in response to respected referee are highlighted. Q is the question or suggestion raised by each of the respected referee and *Answer* is our explanation in response to the respected referee's suggestion.

**Response to respected reviewer** #1:

***Q1. 1. Clarify the source population, database coverage, and case ascertainment (STROBE: setting, participants, and data sources):***

***The manuscript states that the study reviewed the database of Besat Hospital, Hamadan, while the abstract and title refer more broadly to hospitals or patients of Hamadan city (source: Abstract; Materials and methods, Study design). This creates uncertainty about whether the data represent one hospital, multiple hospitals, or the entire city population, which directly affects the validity of prevalence and incidence estimates.***

***Author to-do list:***

***Specify whether the dataset came from Besat Hospital only or from all relevant hospitals in Hamadan city (source: Materials and methods, Study design).***

*Answer: Thank you for this important comment. We used all hospital databases of Hamadan city, Iran and we referred this in abstract and title of manuscript and highlighted by red color.*

***Define the source population used as the denominator for prevalence and incidence calculations (source: Materials and methods; Results, Table 1).***

*Answer: The source population was defined in materials and methods section of MS.*

***Explain whether the hospital database captures all TBI cases in Hamadan or only hospital-presenting cases (source: Materials and methods, Study design).***

*Answer: We used all hospital databases of Hamadan city and we referred this in abstract and title of manuscript and highlighted by red color.*

***Revise the title, abstract, and conclusions so that the geographic claim matches the actual database coverage (source: Title; Abstract; Conclusion).***

*Answer: We revised the title, abstract and conclusion accordingly.*

***Q2. Define hormonal disorders and diagnostic criteria in sufficient clinical detail (STROBE: variables and measurement):***

***The manuscript refers to "hormonal disorders," "endocrine disorders," "endocrinopathies," and "hypopituitarism," but it does not specify which diagnoses were included, which ICD codes or laboratory criteria were used, or how new post-TBI hormonal disorders were distinguished from pre-existing disorders (source: Abstract; Introduction; Materials and methods, Study design). Without clear diagnostic definitions, the outcome is not reproducible and may combine clinically heterogeneous conditions.***

***Author to-do list:***

***List the exact endocrine diagnoses included under "hormonal disorders" (source: Materials and methods, Study design).***

*Answer: The exact endocrine diagnoses included in study design section of MS and We added a table for this.*

***Provide the ICD codes, clinical criteria, or laboratory thresholds used to identify each endocrine outcome (source: Materials and methods, Study design).***

*Answer: The ICD codes, clinical criteria, or laboratory thresholds used to identify each endocrine outcome were added in study design section of MS and highlighted by red color.*

***Clarify how pre-existing endocrine disorders were excluded or distinguished from post-TBI disorders (source: Materials and methods, Study design).***

*Answer: To distinguish pre-existing from post-TBI endocrine disorders, we required that (a) the first endocrine diagnosis date be after the TBI admission date, (b) there be no mention of the same endocrine condition in any pre-TBI outpatient or inpatient records during the 2 years preceding the TBI, and (c) there be no history of pituitary surgery, radiation, or medications known to cause hormonal abnormalities (e.g., glucocorticoids, antipsychotics, opioids) prior to TBI.*

***Use one consistent term for the outcome throughout the manuscript, such as "post-TBI endocrine disorders" or "post-TBI hormonal disorders" (source: Abstract; Introduction; Results).***

*Answer: The post-TBI hormonal disorders was changed to post-TBI endocrine disorders.*

***Reporting Deficiencies: The manuscript omits a limits section, a crucial component of every scientific research, and utilizes generic, non-standard keywords that hinder its discoverability***

*Answer: Thank you for this very important comment. We added new section (6.limitation) in manuscript to cover the limitations of study.*

***Q3. Correct and fully report the contingency-table groups and epidemiological formulas (STROBE: statistical methods):***

***The methods state that patients were divided into four groups, but groups C and D are both labeled as TBI–, H-, even though group C is described as patients with hormonal disorder without TBI (source: Materials and methods, Data analysis). In addition, the prevalence and***

***incidence formulas are introduced but not displayed, making it impossible to verify how the reported rates were calculated.***

***Correct the four contingency-table group definitions so that each TBI/hormonal-disorder category is distinct (source: Materials and methods, Data analysis).***

*Answer: We correct the contingency-table group D, which is TBI+/H+.*

***Display the exact prevalence formula and define every numerator and denominator (source: Materials and methods, Data analysis).***

*Answer: We explained the numerator and denominator as the follow:*

Prevalence was calculated as the follows:

$$\text{Prevalence} = \frac{A}{C}$$

Where, A is TBI+, H+ and C is TBI–, H+.

The incidence was calculated using following equation (8):

$$\text{Incidence} = \frac{A}{A+B}$$

Where, B is TBI–, H- patients.

*This was applied in MS.*

***Display the exact incidence formula and define whether the denominator is person-time, population at risk, or another denominator (source: Materials and methods, Data analysis).***

*Answer: Thank you for this important observation. We have revised the Data Analysis section to clarify our calculations. We corrected the prevalence formula.*

*Regarding incidence: because this was a retrospective study relying on clinical documentation with imprecise dates of endocrine onset, we could not reliably calculate person-time incidence rates. Instead, we report cumulative incidence over the fixed 5-year study period (2020–2024). We have explicitly defined this denominator as the population at risk and have clarified that*

*cumulative incidence — not incidence rate — was the measure used. This has been added to the revised Methods section.*

***Ensure that Table 1 labels match the corrected contingency-table definitions (source: Table 1).***

*Answer: The Table 1 was checked accordingly.*

***Q4. Strengthen statistical analysis beyond descriptive comparisons (STROBE: statistical methods and main results):***

***The manuscript reports sex and age differences in prevalence, incidence, and time gap, but it does not report statistical tests, confidence intervals, regression models, or adjustment for potential confounders such as age, sex, calendar year, TBI severity, skull fracture, or hospitalization factors (source: Materials and methods, Data analysis; Results). The current analysis therefore cannot distinguish descriptive differences from statistically supported associations.***

***Author to-do list:***

***Report statistical tests used to compare prevalence or incidence across sex and age groups (source: Materials and methods, Data analysis; Results).***

*Answer: We analyzed the mean time gap between genders by unpaired T-Test and mentioned it in results section and Figure 2 as well as in the data analysis section of MS. Moreover, the prevalence of endocrine disorders after traumatic brain injury was compared based on the age using ANOVA procedure, followed by Tukey's post hoc test.*

***Provide confidence intervals for prevalence and incidence estimates (source: Results; Tables 1–2; Figures 1–2).***

*Answer: We provided 95% CI for the results of prevalence and time gap.*

***Consider multivariable regression or stratified analysis to assess whether sex and age differences persist after adjustment (source: Results; Discussion).***

*Answer:*

***Clearly distinguish descriptive findings from inferential conclusions (source: Results; Discussion; Conclusion).***

*Answer: We added P-values for inferential statistics in Results section and discussed them in discussion section of MS.*

***Q5. Define and analyze the time gap from TBI to hormonal disorder diagnosis more rigorously (STROBE: variables and outcome data):***

***The manuscript reports that the mean time gap between TBI onset and hormonal disorder diagnosis was shorter in women than men, but it does not explain how TBI onset date and endocrine diagnosis date were extracted, whether follow-up time differed by patient, or whether delayed diagnosis could reflect healthcare access rather than biological onset (source: Results, Figure 3; Discussion). This limits interpretation of the conclusion that onset is earlier in women.***

***Author to-do list:***

***Define "time gap" operationally and specify the exact dates used for calculation (source: Results, Figure 3).***

*Answer: The time gap was measured by subtracting the year of diagnosis of endocrine disorders from the year of TBI injury. This was added in data analysis section of MS.*

***Report the sample size used for the time-gap analysis by sex (source: Results, Figure 3).***

*Answer: The sample size by sex for time gap analysis was added in Figure 3 legends.*

***Provide a statistical comparison and confidence intervals for the sex-specific time-gap estimates (source: Results, Figure 3).***

*Answer: The statistical comparison and CI were reported in results section of MS as well as in data analysis section of Materials and Methods.*

***Reframe "earlier onset" as "shorter time to recorded diagnosis" unless true biological onset was measured (source: Results; Discussion; Conclusion).***

*Answer: The suggestion was applied in all section of MS.*

***Minor Comments:***

***1. Tables and figures:***

***The manuscript contains two tables and three figures. Table 1 and Table 2 are cited in the Results; Figure 1, Figure 2, and Figure 3 are also cited in the Results, so all tables and figures appear to be cited in the main text (source: Results; Tables 1–2; Figures 1–3). Please improve table formatting, define all abbreviations in table footnotes, and ensure that figure captions include enough information to be understood without returning to the main text.***

*Answer: We improved Tables and Figures legends by adding some information.*

***2. Early-stage editorial and language red flags:***

***Several wording problems should be corrected during revision. "TBI is one of the common cause of death" should be revised to "TBI is one of the common causes of death" (source: Introduction). "During five years (2020-2024), 39709 patients were suffered from TBI" should be revised to "During the five-year period from 2020 to 2024, 39,709 patients experienced TBI" (source: Results). "The prevalence and incidence for endocrine dysfunction after TBI calculated" should be revised to "The prevalence and incidence of endocrine dysfunction after TBI were calculated" (source: Materials and methods, Data analysis). "B) TBI with without following hormonal disorder" should be revised to "TBI without subsequent hormonal disorder" (source: Materials and methods, Data analysis).***

*Answer: Thank you for improving our article grammatically. All changes were applied in MS.*

***3. Terminology consistency:***

***The manuscript alternates between "hormonal disorders," "endocrine disorders," "endocrine dysfunction," "endocrinopathies," and "hormonal disturbance" (source:***

***Abstract; Materials and methods; Results; Discussion). Please select one main term and use it consistently, defining any narrower terms such as hypopituitarism separately.***

*Answer: We used endocrine disorders in all sections of MS.*

***4. Title and keyword consistency:***

***The manuscript title uses "hormonal disorders," while the keywords include "Trauma" and "Damage," which are too broad and less informative than standard indexing terms (source: Title; Keywords). Please revise the keywords to include more specific terms such as "Traumatic brain injury," "Endocrine dysfunction," "Hypopituitarism," "Incidence," and "Prevalence."***

*Answer: The title and Keywords were changed accordingly and highlighted by red color.*

***5. Reference currency:***

***Several references were published before 2010 and should be reviewed for replacement with newer and more directly relevant sources where appropriate, while retaining seminal references only when necessary. These include older references from 1959, 1977, 2002, 2005, 2006, and 2009 (source: References 4, 11, 12, 15, 16, 17). Please also review whether older mechanistic references are essential to the argument or can be replaced by recent reviews.***

*Answer: Thank you for this comment. All old references were changed with new ones and highlighted by red color.*

***6. Reference-list cleanup:***

***The reference list appears to contain a duplicate or near-duplicate pair for the Arizona pediatric TBI study, listed as both Ref 6 and Ref 8 (source: References 6 and 8). Please remove duplicate entries, renumber citations if needed, and ensure that each reference is cited only once in the final reference list***

*Answer: The duplicated reference was corrected in manuscript.*

**Response to respected reviewer** #2

***2-1- Ethical approval and consent status are not acceptable as currently reported:***

**** What the author wrote: The manuscript states that data were collected and analyzed and that there is no need for an ethical code, and it does not report informed consent or a formal waiver of consent. (source: Metadata ethical approval field; Materials and methods)***

**** Why correction is required: This must be corrected because the manuscript is not compliant with basic editorial requirements regarding ethical oversight for retrospective research using patient records. (source: Metadata ethical approval field; Materials and methods)***

**** To do: Provide the ethics committee approval code, or provide an official exemption or waiver statement from the relevant institutional review board, and clarify the consent or consent-waiver status. (source: Metadata ethical approval field; Materials and methods).***

*Answer:* *This study was approved by the Ethics Committee of Hamadan University of Medical Sciences (Code: IR.UMSHA.REC.1403.463).*

***2-2-Source population and database coverage are unclear:***

**** What the author wrote: The manuscript refers to hospitals in Hamadan and patients of Hamadan city, but the methods state that the database of Besat Hospital, Hamadan, was reviewed. (source: Abstract; Materials and methods, Study design)***

**** Why correction is required: This must be corrected because internal inconsistency currently prevents reliable assessment of whether the prevalence and incidence estimates represent one hospital, multiple hospitals, or the city population. (source: Abstract; Materials and methods; Results)***

**** To do: Reconcile the setting description and clearly state whether the data came from Besat Hospital only, multiple hospitals, or a population-level registry for Hamadan city. (source: Abstract; Materials and methods; Results)***

*Answer: We used all databases of hospitals in Hamadan city, Iran. This was mentioned in all parts of manuscript.*

***2-3- Diagnostic definitions for hormonal disorders are incomplete:***

**** What the author wrote: The manuscript reports endocrine disorders, hormonal disorders, endocrinopathies, and hormonal disturbance after TBI but does not define the included diagnoses, ICD codes, laboratory thresholds, or diagnostic criteria. (source: Abstract; Materials and methods)***

**** Why correction is required: This must be corrected because the manuscript is not fully evaluable without reproducible outcome definitions and clear diagnostic criteria. (source: Materials and methods)***

**** To do: Define all included endocrine or hormonal disorders, provide the codes or clinical/laboratory criteria used for diagnosis, and use one consistent outcome term throughout the manuscript. (source: Materials and methods; Results)***

*Answer: The ICD codes, clinical criteria, or laboratory thresholds used to identify each endocrine outcome were added in study design section of MS and highlighted by red color.*

***2-4 Contingency-table categories and epidemiological formulas require correction:***

**** What the author wrote: The manuscript contains four patient groups, but group C and group D are both labeled as TBI–, H-, and the prevalence and incidence equations are introduced but not displayed. (source: Materials and methods, Data analysis)***

**** Why correction is required: This must be corrected because internal inconsistency currently prevents reliable assessment of the prevalence and incidence calculations. (source: Materials and methods, Data analysis; Table 1)***

**** To do: Correct the four TBI/hormonal-disorder categories, display the exact prevalence and incidence formulas, and define each numerator and denominator used in the calculations. (source: Materials and methods, Data analysis; Table 1).***

*Answer: This section of manuscript completely revised.*

***2-5 Statistical analysis is insufficient for the stated comparisons:***

**** What the author wrote: The manuscript reports differences by sex, age, year, and time gap, but does not report statistical tests, confidence intervals, adjusted models, or control for confounding factors. (source: Materials and methods, Data analysis; Results)***

**** Why correction is required: This must be corrected because the manuscript is not fully evaluable without statistical evidence supporting the reported group differences and trend interpretations. (source: Results; Discussion)***

**** To do: Add appropriate statistical comparisons, confidence intervals, and, where possible, adjusted analyses for sex, age, year, and relevant clinical covariates. (source: Materials and methods; Results)***

*Answer: We added suitable statistical analysis in both Materials and Methods and Results sections of manuscript, reporting p-values and 95% CI.*

***2-6 Data availability and supplementary material are not addressed:***

**** What the author wrote: The manuscript does not report a data availability statement and does not state whether supplementary files, coding lists, extraction forms, or statistical outputs are available. (source: Metadata; Full manuscript)***

**** Why correction is required: This must be corrected because the manuscript is not fully verifiable without information on data availability and supporting materials. (source: Metadata; Materials and methods)***

**** To do: Add a data availability statement and clarify whether supplementary materials, diagnostic code lists, database extraction details, or analysis outputs are submitted. (source: Metadata; Materials and methods)***

*Answer: During submission, we added Data availability statement (Data available upon request by authors).*

***2-7 Reference integrity and recency require correction:***

**** What the author wrote: The manuscript contains 20 references; all references contain DOI and/or PMID information, but 7 references were published in 2011 or earlier, one local citation entry contains an implausible PubMed ID format, and one duplicate or near-duplicate reference pair is present. (source: References)***

**** Why correction is required: This must be corrected because the manuscript is not fully verifiable without a current, nonduplicated, and internally consistent reference list. (source: References)***

**** To do: Correct the affected reference entries, remove duplicate or near-duplicate entries, and replace older references with newer sources unless a strong justification exists for retaining them. (source: References)***

**** References with DOI/PMID: Ref 1 - Izzy et al., Ref 2 - Emelifeonwu et al., Ref 3 - Lauzier et al., Ref 4 - Cohan et al., Ref 5 - Mele et al., Ref 6 - Ortiz et al., Ref 7 - Maleki et al., Ref 8 - Ortiz et al., Ref 9 - Oruganti et al., Ref 10 - Aljboor et al., Ref 11 - Labrie et al., Ref 12 - Daniel et al., Ref 13 - Yang et al., Ref 14 - Wagner et al., Ref 15 - Berry et al., Ref 16 - Hoffman et al., Ref 17 - Feldman et al., Ref 18 - Zhong et al., Ref 19 - Mahajan et al., Ref 20 - Tanriverdi et al. (source: References)***

**** References requiring further review:***

**** Ref 4 - Cohan et al. — published in 2005; contains an implausible PubMed ID format in the manuscript reference list; correct the citation details and replace with a newer study unless a strong justification exists for retaining it. (source: References 4)***

**** Ref 6 - Ortiz et al. — duplicate or near-duplicate of Ref 8; correct duplication and retain only one complete reference entry. (source: References 6 and 8)***

**** Ref 8 - Ortiz et al. — duplicate or near-duplicate of Ref 6; correct duplication and retain only one complete reference entry. (source: References 6 and 8)***

**** Ref 11 - Labrie et al. — published in 1977; replace with a newer study unless a strong justification exists for retaining it. (source: References 11)***

**** Ref 12 - Daniel et al. — published in 1959; replace with a newer study unless a strong justification exists for retaining it. (source: References 12)***

**** Ref 14 - Wagner et al. — published in 2011; replace with a newer study unless a strong justification exists for retaining it. (source: References 14)***

**** Ref 15 - Berry et al. — published in 2009; replace with a newer study unless a strong justification exists for retaining it. (source: References 15)***

**** Ref 16 - Hoffman et al. — published in 2006; replace with a newer study unless a strong justification exists for retaining it. (source: References 16)***

**** Ref 17 - Feldman et al. — published in 2002; replace with a newer study unless a strong justification exists for retaining it. (source: References 17)***

***Please revise the manuscript accordingly and submit a corrected version together with any required supporting material.***

*Answer: All old references (≤2005) were changed by new ones and duplicated reference was corrected in MS.*

**Response to respected reviewer** #3

***1. The study design is mentioned as a retrospective review, but it is not explicitly labeled as cross-sectional.***

*Answer: Thank you for this important comment. We added cross sectional in abstract of article.*

***2. The abstract does not provide detailed eligibility criteria or methods of participant selection.***

*Answer: In study design section, we completely describe the detailed eligibility criteria or methods of participant selection.*

***3. Data were sourced from hospital databases, but specific measurement methods are not detailed in the method.***

*Answer: The study design section detailed methods was provided by complete rewritten this section.*

***4. The abstract does not mention any efforts to address potential sources of bias.***

*Answer: This was described in methods and limitation sections of MS.*

***5. The method does not explain how the study size was determined.***

*Answer: We used all patients records and the frequencies are reported in Table 1.*

***6. The method does not provide details on the handling of quantitative variables.***

*Answer: We completely revised Data analysis section to provide details on the handling of quantitative variables.*

***7. Statistical methods are mentioned, with data analyzed using SPSS software, but specific methods to control for confounding are not detailed.***

*Answer: Due to the retrospective design and sample size constraints, multivariable adjustment was not feasible. To address confounding, results were stratified by age group and sex. We acknowledge that residual confounding by unmeasured factors (e.g., TBI severity, comorbidities) cannot be ruled out, which is noted as a limitation.*

***8. The abstract does not report the number of individuals at each stage of the study.***

*Answer: The number of patients used in this study is reported in results section of manuscript.*

**Best regards,**

**Dr. Kiumarth Amini**

## 2 Revision 1

1 comment · 10 Jul 2026

### Editor-in-Chief

MINOR REVISION 10 Jul 2026

Thank you for submitting the revised version of your manuscript to CHBS. We appreciate the time and effort you have dedicated to addressing the reviewers' comments.

I am pleased to inform you that the revisions have been satisfactory, and all major concerns raised by the reviewers have been adequately addressed. Your point-by-point response letter was comprehensive and clear.

However, before we can proceed to final acceptance, please make the following minor corrections:

1. Numbering of reactions
Please assign consecutive numbers (e.g., Equation 1, 2, 3, ...) to all equations presented in the manuscript.

2. Placement of the ethics code
The ethics approval code / ethical considerations section should be placed at the end of the manuscript.

Please see the guidance and a recently published article.

3

# Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

**Response letter**

I am pleased to inform you that the revisions have been satisfactory, and all major concerns raised by the reviewers have been adequately addressed. Your point-by-point response letter was comprehensive and clear.

***Answer:*** *We would like to express our gratitude and appreciation to the respected editor of the journal.*

However, before we can proceed to final acceptance, please make the following minor corrections:

1. Numbering of reactions

Please assign consecutive numbers (e.g., Equation 1, 2, 3, ...) to all equations presented in the manuscript.

***Answer:*** *We assigned consecutive numbers to all equations presented in the manuscript and highlighted by red color.*

2. Placement of the ethics code

The ethics approval code / ethical considerations section should be written in the end of the manuscript.

***Answer:*** *The ethical code transferred to end of manuscript and highlighted by red color.*

## 3 Revision 2

1 comment · 17 Jul 2026

### Editor-in-Chief

ACCEPT 17 Jul 2026

It is my great pleasure to inform you that your manuscript has been accepted for publication in CHBS.