

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Acute poisoning in Shenyang, China: a retrospective and descriptive study from 2012 to 2016
<b>AUTHORS</b>	Zhang, YaJie; Yu, Boxin; Wang, Nana; Li, Tiegang

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Odd Martin Vallersnes University of Oslo, Department of General Practice
<b>REVIEW RETURNED</b>	01-Feb-2018

<b>GENERAL COMMENTS</b>	<p>Dear authors,</p> <p>your manuscript reports a descriptive retrospective study of acute poisonings treated at a tertiary hospital in North East China. Descriptive studies like this are needed to keep track of trends and developments in the panorama of poisoning, and your study provides valuable information. However, there are some problems with the presentation of the study in the manuscript.</p> <p>The major problem is the lack of discussion of the limitations of the study, e.g.:</p> <ol style="list-style-type: none"><li>1. To what extent does your patients reflect the patients treated for poisoning in your area? Are your patients a select group as they are treated at a tertiary hospital? Do they differ from the patients treated at the other hospitals, are they more severely ill, are other toxic agents involved etc.</li><li>2. Concerning trends and comparison with the previous study, was there any changes in the population in your catchment area or in the number of patients treated at your hospital? Any changes in the logistics of local health services?</li><li>3. How was diagnosis of toxic agent made? Clinically? With laboratory confirmation?</li></ol> <p>At the end of Introduction you state that you aim to describe the clinical and sociodemographic patterns of acute poisoning at your hospital, as you then proceed to do. In addition, you describe trends, both in the time period covered by your study and in comparison to a previous study. This should also be stated as one of your aims. Furthermore, the comparison to the previous study is not as clearly presented as it could be, but spread about here and there. I think this comparison warrants a paragraph or a subsection on its own both in Results and in Discussion.</p> <p>Methods: How did you identify the relevant medical records? Could any have been missed?</p>
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	<p>What is relative recovery? The term is not defined.</p> <p>Intentional: This term is a bit difficult. For substance abuse related poisoning, I agree that the exposure is intentional. Whether the poisoning is intentional is debatable. If the intention was to get high, poisoning (or death) could be said to be accidental.</p> <p>Results: Your total cases is 5009. However, in table 4, the total is stated to be 5018. Furthermore, the sum of the subtotals in table 4 is 5016.</p> <p>To me, the proportion of patients staying longer in hospital than 48 hours is surprisingly large compared to regular practice in Europe. Please comment in Discussion.</p> <p>The legends in the figures are unreadable or missing.</p> <p>The category of analgesics would be more informative if opioids were listed separately from other analgesics.</p> <p>What are Mixed drugs? Please provide a definition.</p> <p>Please provide more detailed results on treatment.</p> <p>Patients leaving against medical advice are a quite different group from patients transferred to other hospitals. Please provide separate figures.</p> <p>Your explanations for the high number of poisonings among females need to be substantiated by references to relevant research. As do your explanations concerning young adults.</p> <p>Conclusion: Rather than stating that the pattern of poisoning is altered, it would be more interesting in what way it was altered.</p> <p>Minors: Abstract - Conclusion: The first sentence is not a conclusion. The second sentence is not covered by the results presented in the abstract.</p> <p>The age limit of 11 years or older is not stated as an inclusion criterion in Methods in the main text, though it is in the abstract.</p> <p>The third sentence in the second paragraph in Methods stating what information can be obtained from the HIS is unnecessary, as you go on to state what information you actually will retrieve.</p> <p>I find medians and interquartile ranges more informative than means and standard deviations when presenting results like yours. I concede that this is a matter of taste.</p> <p>You vary between one and two decimals when stating percentages. One will do.</p> <p>The poisonings in the ED-rate for your hospital is a result and should be presented as such.</p> <p>Pharmaceutical drugs or therapeutic drugs? Please be consistent.</p> <p>References 4-6 do not quite seem the best choice to cover the</p>
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	statements in their sentence in the first paragraph in Introduction.
<b>REVIEWER</b>	Omid Mehrpour Birjand University of Medical Sciences, Birjand,Iran
<b>REVIEW RETURNED</b>	16-Feb-2018

<b>GENERAL COMMENTS</b>	<p>This is a Cross-sectional study that describes pattern of acute poisoning patients admitted to the emergency department over a five-year period from 2012 to 2016. Below are some suggestions and questions which may help guide the authors with this effort. I hope the comments prove helpful in improving your work and allowing acknowledgement of limitations while getting the most out of what you have done</p> <ol style="list-style-type: none"> <li>1. Perhaps the most important limitation is that the authors retrospectively analyzed admissions due to acute poisonings from the hospital information system which can cause the bias</li> <li>2. Did you include data related to patients with the history of co-ingestion of poisons? Please explain your inclusion criteria more clearly. How did you considered the cases with co ingestion of drugs/poisons in your statistical analysis?</li> <li>3. The number of admission and outcomes of patients referred to other wards or intensive care units can be obtained from HIS. Were you included such data in your statistical analysis?</li> <li>4. Please provide more details about sampling method.</li> <li>5. Please describe the omitted group of patients and missing information (those initially screened but not ultimately included)</li> <li>6. Please do not leave p-values standing alone in the text without supporting information. In the text, present the name of the test, its value, and statistics for all significant and important non-significant results</li> <li>7. The limitations of study should be covered in the text</li> <li>8. In table 4 the number of poisoned patients with therapeutic drugs has been noted as 1637 cases. This does not appear to work out with the numbers given and it seems that the correct number is 1635.also The total number of toxic agent over the five years seems to be 5016 not 5018 persons.</li> <li>9. Please explain about the inconformity between the reported number of table 1 and 2. According to table 1, the Number of patients in 20-29 age-group is 1547. But in table 2 the reported total number is 1560.</li> <li>10. What is the significance level adopted by the authors?</li> <li>11. It has been noted" The four most common toxic agent group in decreasing order were therapeutic drugs, pesticides, alcohol, fumes" but in page 11 it has been mentioned" The pesticide poisoning presented a growing trend from 2012 to 2015" again for alcohol it has been noted" There was a stable trend in the alcohol poisoning" which of them is correct about the pesticides and alcohol?</li> <li>12. What is your definition of relative recovery in this study? It should be explicitly defined in the method section</li> <li>13. The discussion is not link with the results of manuscript in some parts. Please clarify and elaborate at the beginning of the discussion, it has been mentioned" In the present study, annual rates of ED visits was about 0.65% ". First, this is not mentioned in the result section. Second, it seems that the reported rates were based on total entries (829,808) and number of poisoned patients (5,375) over the five years but it has been discussed with annual rates of ED visits across the world. The same problem occurs numerous times throughout the manuscript for example in page 14, it has been noted "We found a lot of suicidal behaviors were initiated after an acute interpersonal conflict. It was consistent with a</li> </ol>
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	<p>multivariate analysis about suicide reason in a research performed in China” but in the result section it has not been addressed</p> <p>14. Figures have visible imperfections. The axes labels should be presented and units should be included in parentheses</p> <p>15. The results of various studies on the most common toxic agent have not been well discussed. The authors should highlighted the Common Substance poisoning in other parts of the world especially in Asian countries. Below you can see title of some studies may be related to your study:</p> <ul style="list-style-type: none"> <li>♣ Rajapakse T, Griffiths KM, Christensen H, Cotton S. A comparison of non-fatal self-poisoning among males and females, in Sri Lanka. BMC psychiatry. 2014 Dec;14(1):221.</li> <li>♣ Alizadeh AM, Hassanian-Moghaddam H, Shadnia S, Zamani N, Mehrpour O. Simplified acute physiology score II/acute physiology and chronic health evaluation II and prediction of the mortality and later development of complications in poisoned patients admitted to intensive care unit. Basic Clin Pharmacol Toxicol. 2014 Sep;115(3):297-300</li> <li>♣ Alinejad S, Zamani N, Abdollahi M, Mehrpour O. A narrative review of acute adult poisoning in Iran. Iranian journal of medical sciences. 2017 Jul;42(4):327.</li> <li>♣ Zöhre E, Ayrik C, Bozkurt S, Köse A, Narcı H, Çevik İ, Toker İ, Demir F, Ovla D. Retrospective analysis of poisoning cases admitted to the emergency medicine. Archives of Iranian Medicine (AIM). 2015 Feb 1;18(2).</li> <li>♣ Moradi M, Ghaemi K, Mehrpour O. A hospital base epidemiology and pattern of acute adult poisoning across Iran: a systematic review. Electronic physician. 2016 Sep;8(9):2860.</li> <li>♣ Nair PK, Revi NG. One-year study on pattern of acute pharmaceutical and chemical poisoning cases admitted to a tertiary care hospital in Thrissur, India. Asia Pac J Med Toxicol. 2015 Apr 1;4:79-82.</li> <li>♣ Tagwireyi D, Chingombe P, Khoza S, Maredza M. Pattern and epidemiology of poisoning in the East African region: a literature review. Journal of toxicology. 2016;2016.</li> </ul> <p>16. Dimensional figures are not appropriate because it is difficult to give the Reader a quick visual impression of the results</p> <p>17. More reference are needed to support author’s statements in the discussion section of manuscript.</p> <p>18. The key words should be taken from the Medical Subject Headings (MeSH) list of Index Medicus</p>
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### VERSION 1 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Odd Martin Vallersnes

Institution and Country: Associate professor, University of Oslo, Norway

Please state any competing interests: None declared.

Please leave your comments for the authors below

Dear authors,

your manuscript reports a descriptive retrospective study of acute poisonings treated at a tertiary hospital in North East China. Descriptive studies like this are needed to keep track of trends and developments in the panorama of poisoning, and your study provides valuable information. However, there are some problems with the presentation of the study in the manuscript.

The major problem is the lack of discussion of the limitations of the study, e.g.:

1. To what extent does your patients reflect the patients treated for poisoning in your area? Are your patients a select group as they are treated at a tertiary hospital? Do they differ from the patients treated at the other hospitals, are they more severely ill, are other toxic agents involved etc.

Our hospital was one of the regional tertiary care hospitals with three branches, in Shenyang. Patients with poisoning seeking for treatment visit or are referred to this hospital. The patients we treated are representative but statistics of a single centre teaching hospital might not present reflection of the generalized and precise situation in this region. We discussed this in the limitations.

2. Concerning trends and comparison with the previous study, was there any changes in the population in your catchment area or in the number of patients treated at your hospital? Any changes in the logistics of local health services?

The number of patients treated at our hospital was increased and health services got better, but we didn't get the data standardization, so this comparison was rough and we discussed this in the limitations.

3. How was diagnosis of toxic agent made? Clinically? With laboratory confirmation?

The diagnosis was established by patients' history, physical examination, routine and toxicological laboratory evaluation.

At the end of Introduction you state that you aim to describe the clinical and sociodemographic patterns of acute poisoning at your hospital, as you then proceed to do. In addition, you describe trends, both in the time period covered by your study and in comparison to a previous study. This should also be stated as one of your aims. Furthermore, the comparison to the previous study is not as clearly presented as it could be, but spread about here and there. I think this comparison warrants a paragraph or a subsection on its own both in Results and in Discussion.

I revised the manuscript according to the advice.

Methods:

How did you identify the relevant medical records? Could any have been missed?

We retrieved the relevant medical records through searching HIS using the following keywords: poisoning, alcohol, carbon monoxide and organophosphate. This work was performed by two people so the records were retrieved twice. If there were any omissions, it must be very less.

What is relative recovery? The term is not defined.

Conditions where patients recovered with normal symptoms and signs but the laboratory findings were abnormal or not available on discharge were categorized as relative recovery

Intentional: This term is a bit difficult. For substance abuse related poisoning, I agree that the exposure is intentional. Whether the poisoning is intentional is debatable. If the intention was to get high, poisoning (or death) could be said to be accidental.

I have altered the category of type for exposure in Method section.

Results:

Your total cases is 5009. However, in table 4, the total is stated to be 5018. Furthermore, the sum of the subtotals in table 4 is 5016.

5009 is correct data, while the total 5018 in table 4 included 9cases that were calculated tautologically. We have made an explanation below the table4.

We checked the initial data and found the previous sum of the subtotals 5016 was a wrong number, and we have modified the wrong number.

To me, the proportion of patients staying longer in hospital than 48 hours is surprisingly large

compared to regular practice in Europe. Please comment in Discussion.

It was related to the complex doctor-patient environment in China, patients with poisoning usually were asked to remain in the observing room (available in our ED) for 48h to 72h. This has been explained in discussion.

The legends in the figures are unreadable or missing.

We have re-uploaded new readable figures.

The category of analgesics would be more informative if opioids were listed separately from other analgesics.

The opioids poisoning in our study was only 13 cases and we have made a annotation below the Table 4.

What are Mixed drugs? Please provide a definition.

The mixed drugs were defined as two or more drugs being ingested. It was defined in Method section.

Please provide more detailed results on treatment.

Detailed results on treatment were supplemented in Treatment and Outcome.

Patients leaving against medical advice are a quite different group from patients transferred to other hospitals. Please provide separate figures.

Separate figures were provided in Table 1.

Your explanations for the high number of poisonings among females need to be substantiated by references to relevant research. As do your explanations concerning young adults.

Relevant references have been supplemented. Listed in [26-28],[34,35] in references.

Conclusion: Rather than stating that the pattern of poisoning is altered, it would be more interesting in what way it was altered.

It has been explained in Conclusion section.

Minors:

Abstract - Conclusion: The first sentence is not a conclusion. The second sentence is not covered by the results presented in the abstract.

Conclusion in abstract has been revised.

The age limit of 11 years or older is not stated as an inclusion criterion in Methods in the main text, though it is in the abstract.

It has been added in the Methods section.

The third sentence in the second paragraph in Methods stating what information can be obtained from the HIS is unnecessary, as you go on to state what information you actually will retrieve.

It has been revised and deleted.

I find medians and interquartile ranges more informative than means and standard deviations when presenting results like yours. I concede that this is a matter of taste.

You vary between one and two decimals when stating percentages. One will do.

Two decimals were adopted.

The poisonings in the ED-rate for your hospital is a result and should be presented as such.

It has been revised.

Pharmaceutical drugs or therapeutic drugs? Please be consistent.

It has been modified.

References 4-6 do not quite seem the best choice to cover the statements in their sentence in the first paragraph in Introduction.

New references have replaced the previous.

Reviewer: 2

Reviewer Name: Omid Mehrpour

Institution and Country: Birjand University of Medical Sciences, Birjand,Iran

Please state any competing interests: None

Please leave your comments for the authors below

This is a Cross-sectional study that describes pattern of acute poisoning patients admitted to the emergency department over a five-year period from 2012 to 2016. Below are some suggestions and questions which may help guide the authors with this effort. I hope the comments prove helpful in improving your work and allowing acknowledgement of limitations while getting the most out of what you have done

1. Perhaps the most important limitation is that the authors retrospectively analyzed admissions due to acute poisonings from the hospital information system which can cause the bias

It was true that our study was primarily limited by its retrospective nature. We discussed this in limitation.

2. Did you include data related to patients with the history of co-ingestion of poisons? Please explain your inclusion criteria more clearly. How did you considered the cases with co ingestion of drugs/poisons in your statistical analysis?

(1) Yes, we included these data. Patients admitted to the ED with a diagnosis of drug poisoning, aged  $\geq 11$  years, were enrolled for this study. Cases of poisoned patients  $< 11$  years admitted to pediatrics ward, animal bites (snake, insect) for its infrequency and chronic poisoning were excluded from the study.

(2) The mixed drugs were defined as two or more drugs being ingested. It was defined in Method section.

3. The number of admission and outcomes of patients referred to other wards or intensive care units can be obtained from HIS. Were you included such data in your statistical analysis?

Generally, patients with poisoning were all treated in ED in our hospital, where specialized poisoning wards exist, and were not transferred to other wards or ICU. So the data obtained in ED was the whole number.

4. Please provide more details about sampling method.

We retrieved the relevant medical records through searching HIS using the following keywords: poisoning, alcohol, carbon monoxide and organophosphate. This work was performed by two people so the records were retrieved twice. If there were any omissions, it must be very less.

5. Please describe the omitted group of patients and missing information (those initially screened but not ultimately included)

Cases of poisoned patients  $< 11$  years admitted to pediatrics ward, animal bites (snake, insect) for its infrequency and chronic poisoning were excluded from the study. It was expounded in method section.

6. Please do not leave p-values standing alone in the text without supporting information. In the text, present the name of the test, its value, and statistics for all significant and important non-significant results

We have revised and presented the name of the test, its value.

7. The limitations of study should be covered in the text

New discussion of limitations was revised.

8. In table 4 the number of poisoned patients with therapeutic drugs has been noted as 1637 cases. This does not appear to work out with the numbers given and it seems that the correct number is 1635. also The total number of toxic agent over the five years seems to be 5016 not 5018 persons.

(1) We checked the initial data and found the wrong number in 2012 and 2014, 1 missing in other drugs in 2012 and wrong calculation of subgroup of therapeutic drugs, which resulted in wrong final calculation. The correct number was 1637.

(2) The previous sum of the subtotals 5016 was a wrong number, and we have modified the wrong number.

9. Please explain about the inconformity between the reported number of table 1 and 2. According to table 1, the Number of patients in 20-29 age-group is 1547. But in table 2 the reported total number is 1560.

(1)The previous number1560 in table 2 was wrong and the correct number was 1550. The number of alcohol in 20-29 age-group was 429, we made a mistake in this number and have modified it to the correct number.

(2) Among 1550 cases, 3 cases were calculated tautologically for a combination of alcohol poisoning and other drugs poisoning.

10. What is the significance level adopted by the authors?

A p value of less than 0.05 was considered to be significant.

11. It has been noted” The four most common toxic agent group in decreasing order were therapeutic drugs, pesticides, alcohol, fumes” but in page 11 it has been mentioned” The pesticide poisoning presented a growing trend from 2012 to 2015” again for alcohol it has been noted” There was a stable trend in the alcohol poisoning” which of them is correct about the pesticides and alcohol?

Maybe it was improper expression that brought about this contradiction. Every expression was based on its corresponding data. When it came to the total of various toxic agent groups, the number of therapeutic drugs, pesticides, alcohol and fumes was decreased in sequence. However, when it came to the change of certain specific substance, such as pesticides, the number of pesticides increased year by year on the whole, and it was just a rough trend.

If you think these expressions are ill-considered, please tell us and we will make a change.

12. What is your definition of relative recovery in this study? It should be explicitly defined in the method section

Conditions where patients recovered with normal symptoms and signs but the laboratory findings were abnormal or not available on discharge were categorized as relative recovery. It has been added in the method section.

13. The discussion is not link with the results of manuscript in some parts. Please clarify and elaborate at the beginning of the discussion, it has been mentioned” In the present study, annual rates of ED visits was about 0.65% “. First, this is not mentioned in the result section. Second, it seems that the reported rates were based on total entries (829,808) and number of poisoned patients (5,375) over the five years but it has been discussed with annual rates of ED visits across the world. The same problem occurs numerous times throughout the manuscript for example in page 14, it has been noted “We found a lot of suicidal behaviors were initiated after an acute interpersonal conflict. It was consistent with a multivariate analysis about suicide reason in a research performed in China” but in the result section it has not been addressed

We have revised the relevant section to make it consistent in results and discussion section.

14. Figures have visible imperfections. The axes labels should be presented and units should be included in parentheses

We have modified and re-uploaded new figures.

15. The results of various studies on the most common toxic agent have not been well discussed. The authors should highlighted the Common Substance poisoning in other parts of the world especially in Asian countries. Below you can see title of some studies may be related to your study:

We made a new discussion on the most common toxic agent

♣ Rajapakse T, Griffiths KM, Christensen H, Cotton S. A comparison of non-fatal self-poisoning among males and females, in Sri Lanka. *BMC psychiatry*. 2014 Dec;14(1):221.

♣ Alizadeh AM, Hassanian-Moghaddam H, Shadnia S, Zamani N, Mehrpour O.

Simplified acute physiology score II/acute physiology and chronic health evaluation II and prediction of the mortality and later development of complications in poisoned patients admitted to intensive care unit. *Basic Clin Pharmacol Toxicol*. 2014 Sep;115(3):297-300

♣ Alinejad S, Zamani N, Abdollahi M, Mehrpour O. A narrative review of acute adult poisoning in Iran. *Iranian journal of medical sciences*. 2017 Jul;42(4):327.

♣ Zöhre E, Ayrik C, Bozkurt S, Köse A, Narcı H, Çevik İ, Toker İ, Demir F, Ovla D. Retrospective analysis of poisoning cases admitted to the emergency medicine. *Archives of Iranian Medicine (AIM)*. 2015 Feb 1;18(2).

♣ Moradi M, Ghaemi K, Mehrpour O. A hospital base epidemiology and pattern of acute adult



poisoning across Iran: a systematic review. Electronic physician. 2016 Sep;8(9):2860.

♣ Nair PK, Revi NG. One-year study on pattern of acute pharmaceutical and chemical poisoning cases admitted to a tertiary care hospital in Thrissur, India. Asia Pac J Med Toxicol. 2015 Apr 1;4:79-82.

♣ Tagwireyi D, Chingombe P, Khoza S, Maredza M. Pattern and epidemiology of poisoning in the East African region: a literature review. Journal of toxicology. 2016;2016.

16. Dimensional figures are not appropriate because it is difficult to give the Reader a quick visual impression of the results

We have re-uploaded new planar figures.

17. More reference are needed to support author's statements in the discussion section of manuscript.

Relevant references have been added.

18. The key words should be taken from the Medical Subject Headings (MeSH) list of Index Medicus It has been modified and new key words were all taken from 2018 Mesh list of Index Medicus.

#### FORMATTING AMENDMENTS (if any)

Uniform format was adopted.

Required amendments will be listed here; please include these changes in your revised version:

- Kindly re-upload FIGURES with at least 300 dpi resolution.

New figures with 300 dpi resolution were re-uploaded.

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Odd Martin Vallersnes University of Oslo, Norway
<b>REVIEW RETURNED</b>	29-Mar-2018

<b>GENERAL COMMENTS</b>	<p>Dear authors,</p> <p>I am satisfied with most of the changes in your revised manuscript, but some issues remain:</p> <p>I am not convinced about the usefulness of the relative recovery category, especially since it also includes patient discharged without available laboratory results. Presumably, these patients had fully recovered?</p> <p>The categories of type of exposure differs in the second and fourth paragraphs in Methods.</p> <p>Was toxicological laboratory analyses done in all patients? And if not, do you know in how many cases such analyses were done?</p> <p>The number of opioid poisonings is surprisingly small. Please comment in Discussion.</p> <p>I do not think it is proper to label females in general as 'emotionally fragile'.</p> <p>One decimal will do when stating results.</p> <p>The English in the manuscript still needs major improvement.</p>
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<b>REVIEWER</b>	Omid Mehrpour
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	Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences, Moallem Avenue, Birjand, Iran
<b>REVIEW RETURNED</b>	07-Apr-2018

<b>GENERAL COMMENTS</b>	Dear authors: Thanks for revision of the manuscript. I am much in line with the revised manuscript. And now it looks much clearer and well organized.
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### VERSION 2 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Odd Martin Vallersnes

Institution and Country: University of Oslo, Norway

Please state any competing interests: None declared.

Please leave your comments for the authors below

Dear authors,

I am satisfied with most of the changes in your revised manuscript, but some issues remain:

I am not convinced about the usefulness of the relative recovery category, especially since it also includes patient discharged without available laboratory results. Presumably, these patients had fully recovered?

As the clinical conditions are complex, some patients can get a relief of symptoms and signs but don't have laboratory examinations on discharge, making the laboratory results unavailable, and we just have the laboratory results at admission or before discharge, and these results may be abnormal.

This condition is not indicated to be a full recovery, so we categorize it into relative recovery.

The categories of type of exposure differs in the second and fourth paragraphs in Methods.

Relevant revision has been done to make it uniform.

Was toxicological laboratory analyses done in all patients? And if not, do you know in how many cases such analyses were done?

Not all patients had toxicological laboratory analyses, in our hospital, generally, patients with organophosphates, or paraquat, or fluoroacetamide, or diazepam, or carbamazepine poisoning will be advised to have toxicological laboratory analyses. However, final decision depends on patients or their relatives.

The number of opioid poisonings is surprisingly small. Please comment in Discussion.

It has been discussed in the ending of fifth paragraph in Discussion.

I do not think it is proper to label females in general as 'emotionally fragile'.

It is indeed ill-considered to label females in general as 'emotionally fragile', and relevant revision has been done.

One decimal will do when stating results.

I revised the manuscript according to the advice.

The English in the manuscript still needs major improvement.

I have worked to improve the quality of English with the assistance of a professional copyediting agency.

We sincerely appreciate for your review and advice.

Reviewer: 2

Reviewer Name: Omid Mehrpour

Institution and Country: Medical Toxicology and Drug Abuse Research Center (MTDRC), Birjand University of Medical Sciences, Moallem Avenue, Birjand, Iran

Please state any competing interests: None declared

Please leave your comments for the authors below

Dear authors:

Thanks for revision of the manuscript. I am much in line with the revised manuscript.

And now it looks much clearer and well organized.

We sincerely appreciate for your review and advice.

### VERSION 3 – REVIEW

<b>REVIEWER</b>	Odd Martin Vallersnes University of Oslo, Norway
<b>REVIEW RETURNED</b>	30-Apr-2018

<b>GENERAL COMMENTS</b>	Dear authors  I am happy with the changes made in your revised manuscript.  Just two minor issues: I appreciate that you have limited the number of decimals to one in the text, but I think one decimal also will suffice in the tables. In the first of your suggestions you refer to the weak coping capacity of females. Is that a fair characterization? If suicide attempt is seen as a result of external stress exceeding coping capacity, the amount of external stress could also be the factor causing the difference between males and females.
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### VERSION 3 – AUTHOR RESPONSE

Reviewer(s)' Comments to Author:

Reviewer: 1

Reviewer Name: Odd Martin Vallersnes

Institution and Country: University of Oslo, Norway

Please state any competing interests: None declared.

Please leave your comments for the authors below

Dear authors

I am happy with the changes made in your revised manuscript.

Just two minor issues:

I appreciate that you have limited the number of decimals to one in the text, but I think one decimal also will suffice in the tables.

The number of decimals in the tables has been revised to one.

In the first of your suggestions you refer to the weak coping capacity of females. Is that a fair characterization? If suicide attempt is seen as a result of external stress exceeding coping capacity,

the amount of external stress could also be the factor causing the difference between males and females.

It is indeed non-objective and ill-considered to refer to the weak coping capacity of females while leaving out of consideration of the amount of external stress females may suffer, we have revised relevant part.

We sincerely appreciate for your review and advice again.