Innovative Journal of Pediatrics
Volume 34 · Issue 3 · e142968

OPEN PEER REVIEW

Epidemiology, Clinical and Laboratory Findings of Pediatric Leptospirosis in Southeastern Turkey

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SUBMITTED	REVISED	ACCEPTED	DOI
12 Nov 2023	27 Jan 2024	28 Mar 2024	10.5812/ijp-142968

About this report

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Contents

1 **Original submission** Seyed Hossein Shahcheraghi 2
2 **Revision 1** 3
Authors' reply to reviewers 4
Reviewer and editor comments 10
3 **Revision 2** 11
Authors' reply to reviewers 12
Reviewer and editor comments 13

1 Original submission

1 comment · 6 Dec 2023

Seyed Hossein Shahcheraghi Reviewer

MAJOR REVISION 6 Dec 2023

It is a good study, but the writing is poor. Please correct the errors.
Errors in the attached file should be corrected.
The study location is missing.

2

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.

Reviewer 1:

Question: *It should be converted into a short report format. The importance of the topic should be mentioned due to the variety of clinical symptoms. The novelty of the study should be placed at the beginning of the discussion.The exact method of diagnosing the disease should be mentioned. The article should be written in a new format. It is too vague to be judged again.*

Reply: The article has been rewritten in a new format and revised product systems have been uploaded. Relevant explanations are given below.

Reviewer 2:

Question: *It is a good study with writing poor. please revise errors.*
Errors in attached file should be revised.
study place was miss.

Reply: The article has been rewritten in a new format and revised product systems have been uploaded. Relevant explanations are given below.

Reviewer 3:

Question: *Thank you for consider me as a reviewer of this report. Overall though, the study appears to add useful epidemiologic and clinical data on an important infectious disease affecting children in this unique geographic region and population. With some minor revisions to address the above suggestions, I think this could make for an interesting, publishable article for the journal.*
Introduction:
- More details could be given about why the Southeastern region of Turkey specifically was chosen. Are there any geographical, socioeconomic, or cultural factors that increase risk there?

Reply *The Southeastern region of Turkey has fertile soils and the main source of livelihood is farming and animal husbandry. It has a mild and hot climate. The higher proportion of rural population in this region may be a factor in the higher incidence.*

- The authors could cite prior local studies or reports of increased suspected leptospirosis cases to further justify the focus on Southeastern Turkey.

Reply *In our country, which is located in a temperate climate zone, although the actual incidence is unknown, many cases and case series have been reported from Marmara, Black Sea, Eastern Anatolia and Çukurova regions.*

Reference 12 Demiroglu YZ, Turunc T, Kasar M, Boga C, Timurkaynak F. Weil's Disease: Four Cases from Çukurova, Turkey. Klimik Dergisi/Klimik J. 2011 Apr 1;24(1):52–6.

- Very minor, but the objective statement could be made more specific. For example mentioning the study is a retrospective case series over a defined time period.

Reply Between 01.01.2020 and 31.12.2021, the medical files of all patients under 18 years of age diagnosed with leptospirosis were retrospectively reviewed.

Methods:
- More details could be provided on the specific statistical analyses used to characterize and compare the data.

Reply ***Statistical analysis:***

Within the scope of the study, SPSS 25.0 statistical package program was used to analyze the data obtained. Descriptive statistical methods such as percentage, standard deviation, frequency, mean, minimum-maximum values were used to evaluate the data. In addition, Kolmogorov-Smirnov test was performed to evaluate the suitability of the data for normal distribution. As a result of this analysis, it was determined that the data showed a normal distribution.

- The case definition of confirmed leptospirosis could be more clearly defined early on.

Reply *Urine and blood samples were sent for microscopic agglutination test and PCR. Patients with positive PCR results were included in the study.*

- More specifics could be given for the PCR testing methodology itself and interpretative criteria.

Reply *Molecular methods such as Polymerase Chain Reaction (PCR), which are based on the detection of bacterial DNA in leptospirosis and have higher sensitivity/specificity rates compared to other diagnostic methods, have been accepted in recent years. due to the advantages of these methods, their use in the diagnosis of leptospirosis is increasing.*

Reference 13 Bergmann M, Llewellyn JR, Hartmann K. Epidemiologie und Prophylaxe der Leptospirose beim Hund [Epidemiology and prevention of leptospirosis in dogs]. Tierarztl Prax Ausg K Kleintiere Heimtiere. 2017 Jun

20;45(3):163-168. German. doi: 10.15654/TPK-160964. Epub 2017 May 3. PMID: 28466955.

- The case definition could be more clearly and explicitly defined early in the methods.

Reply *There was no history of travel in our patients. All of them were found to be working at the wells in the corn fields, helping their families with the irrigation work or being related to the well works.*

- Statistical tests used to characterize and compare data are not elaborated on.

Reply *Statistical analysis section added.*

- More details on the data quality/completeness from medical records would strengthen reliability.

Reply *The data obtained from the files were retrospectively evaluated in detail.*

Results:
- Lack of temporal analysis: Cases are summarized over the 2-year period as a whole. No data is provided on seasonal, monthly or other temporal trends. As an environmental infection, understanding temporal patterns could be valuable.

Reply *Leptospirosis is more common in summer and early fall. Our patient group included children working in irrigation, and all cases occurred in the summer.*

- Limited statistical testing: Summary statistics like means and percentages are reported, but statistical analyses comparing groups or assessing significant correlates are not presented. This limits interpretability of potential risk factors.

Reply *Information about the epidemiology, clinical and laboratory findings of pediatric leptospirosis is given.*
- No clinical outcome data: While hospitalization rates are noted, quantitative or qualitative details on clinical recovery, complications, or longer term outcomes of identified cases are not provided. This misses an opportunity for more thorough description.

Reply *There were no additional problems in the outpatient clinic controls.*
- No pathogen or genomic analysis: Details on infecting Leptospira species/strains from testing could provide useful characterization but are not included.

Reply *With the PCR method used, results were obtained as leptospira spp negative or positive.*
- Representativeness of the cases to overall pediatric burden in the region is unable to be assessed fully without understanding the population base and catchesment area clearly.

Reply *In a region with a population of around half a million in southeastern Turkey, 36 confirmed cases under the age of 18 were detected. Although comparisons cannot be made as there are no available data for Turkey as a whole, the higher proportion of rural population in the southeastern region may be effective in the higher incidence.*

Discussion:
- Propose reasons for higher incidence rate estimates compared to other temperate region reports. Is there something specific occurring locally? Are rates truly elevated or an overestimate? Explore possible explanations more fully.

Reply *Farmers, those in contact with livestock, those in close contact with rodents and people living in areas with poor sanitation are at risk (15).*

Reference 2 Costa F, Hagan JE, Calcagno J, Kane M, Torgerson P, Martinez-Silveira MS, Stein C, Abela-Ridder B, Ko AI. Global Morbidity and Mortality of Leptospirosis: A Systematic Review. PLoS Negl Trop Dis. 2015 Sep 17;9(9):e0003898. doi: 10.1371/journal.pntd.0003898. PMID: 26379143; PMCID: PMC4574773.

Special precautions should be taken for rodents, which are the most important hosts of the disease, to prevent transmission between disease-carrying animals and humans. Protective equipment such as boots, gloves and goggles should be used in occupational, touristic and sportive activities. Special protective measures should be taken in cases where skin integrity is impaired. It is estimated that these precautions are less followed in the pediatric age group.

- Comment on the 100% male proportion and predominantly rural residence. Elaborate on unique cultural, behavioral, or occupational factors locally that may have contributed to this finding. Compare to studies in similar population groups.

Reply As we determined in our study, all cases were found to be male because the cause of contamination was related to well and field irrigation, and boys were helping their family with these tasks in the foreground.
- Note any outstanding or unusual clinical manifestations compared to expects typical manifestations in pediatric leptospirosis cases. Explain possible reasons for similarities/differences.

Reply *In accordance with the literature, the disease was milder in our patients compared to the adult group. none of the patients required intensive care.*

- Discuss microbiological characteristics and infecting strains if possible. How do common strains in this region compare to worldwide reports? Insert local context.

Reply *With the PCR method used, results were obtained as leptospira spp negative or positive.*

- Consider temporal trends and seasonality patterns witnessed clinically. How

might factors like climate, rain patterns or agriculture cycles have influenced cases over the 2-year span?

Reply *Leptospirosis is more common in summer and early fall (6). Our patient group included children working in irrigation, and all cases occurred in the summer.*

- Suggest specific prevention opportunities, control measures, or health policy changes locally that could impact risk based on suspected exposures and transmission sources. Provide more pointed public health recommendations.

Reply *Leptospirosis is an important public health problem. Special precautions should be taken for rodents, which are the most important hosts of the disease, in order to prevent the transmission of the disease between carrier animals and humans. Protective equipment such as boots, gloves and goggles should be used in occupational, touristic and sportive works.*

- Additional limitations of the retrospective study design could be acknowledged.

Reply ***Limitations of the Study***

The limitations of the study are that it is a retrospective study and includes data obtained from a single center. The study was conducted in a hospital in the southeastern region and cannot be generalized to the whole population. There are very few studies on leptospirosis in pediatric patients. Epidemiologic studies with more comprehensive data on this subject should be performed

- The conclusion mostly restates information from earlier sections; it could be expanded with implications of the findings.

Reply *The conclusion section was written as a separate title. revisions were added.*

6. Conclusion

Leptospirosis is an important public health problem. Special precautions should be taken for rodents, which are the most important hosts of the disease, in order to prevent the transmission of the disease between carrier animals and humans. Protective equipment such as boots, gloves and goggles should be used in occupational, touristic and sportive works.

Our study is the first study on the epidemiology, clinical, laboratory findings and treatment of leptospirosis in southeast Turkey. Due to the retrospective nature of the study, the results should be evaluated carefully. PCR-positive symptomatic patients were included in our study, and since the clinical picture of leptospirosis in children is milder, the actual incidence of the disease may be higher than that detected. Although there is not enough data on the incidence of leptospirosis in Turkey, it should be considered that the incidence in the southeast region may be

higher than the incidence in Turkey, since our study was conducted in a region where well water is used intensively.

The clinical presentation of leptospirosis varies widely, and clinical symptoms and findings may be milder and more uncertain in children. For this reason, clinicians should keep leptospirosis in mind when approach patients and should not hesitate to request a test, especially in patients with risk factors such as occupational encounters.

References:
- The balance of dated foundational papers and new, location-specific studies helps reinforce key points on pediatric leptospirosis. The authors could consider any very latest 2022/2023 epidemiology data if available.

Reply *References have been revised. additions have been made. relevant sections are shown in yellow.*

Thank you for your interest

2 Revision 1

0 comments

No public comments in this round.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

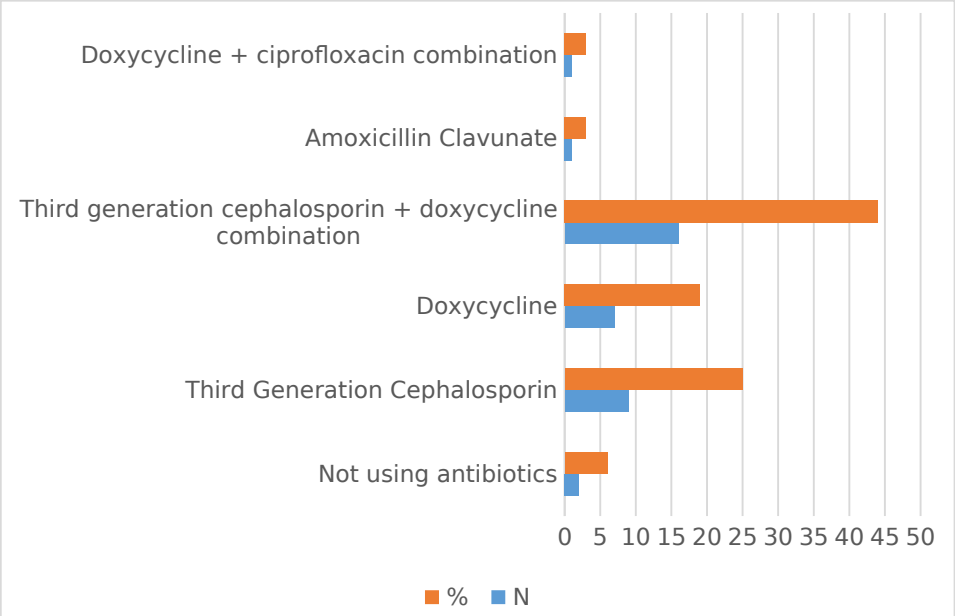
The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewer 1:

Question:

1. *Fig. 2 should be described more with %.*

Reply: Figure 2 has been revised by adding percentage expressions.



2. *first paragraph in Discussion has addition describe. You should make bold your results.*

   The first paragraph of the discussion section has been revised. '' In an area of about half a million inhabitants in southeast Turkey, 36 confirmed cases under the age of 18 have been identified. The number of cases detected in our study is well above 0.14 per 100,000 population in the leptospirosis annual epidemiology report published by the European Center for Disease Prevention and Control in 2020, and is evaluated above the 0.1-1 estimated for temperate regions''

   In the conclusion section, suggestions were added to the last paragraph.

Thank you for your interest

3 Revision 2

0 comments

No public comments in this round.