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Original Article

Eroepidemiology of Leptospirosis Among Healthy People in Zanjan, Northwest of Iran

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ABSTRACT

Objective: A tropical disease of zoonotic origin, Leptospirosis is a public health concern, particularly in developing countries. This present investigation sought to determine the seroprevalence of *Leptospira* in healthy people referred to Shahid Motahari Laboratory, Zanjan, Iran.
Methods: 181 healthy people referred to Shahid Motahari laboratory in Zanjan, Iran, were included in the present study. Serum samples were collected from each participant, whose demographic information was gathered using a questionnaire. After being stored -20 °C, the samples were analyzed for Anti-*Leptospira* IgG antibodies using NovaLisa Leptospira IgG ELISA" kit, the results of which were reported as positive, negative, or equivocal.
Results: Out of 181 serum samples, 43 (23.7%) samples were positive, 36 (19.9%) were equivocal, and 102 (56.4%) were negative for anti-*Leptospira* IgG. The average age of the participants was 40.6 years old. No significant difference was shown between age and gender with anti-*Leptospira* IgG. IgG levels were not found to be correlated significantly with the rural residence of the participants, as well as the other demographic characteristics of participants.
Conclusion: The results of this investigation contribute to the understanding of the epidemiological aspects of Leptospirosis in the region and underscore the importance of continued surveillance and awareness efforts.

GRAPHICAL ABSTRACT

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Introduction

A tropical disease of zoonotic origin, Leptospirosis is a public health concern, particularly in developing countries. Caused by the *Leptospira* species of pathogenic bacteria, Leptospirosis was primarily thought to be an infection related to jobs and rural environments, currently, this disease is growing in urban and rural areas [1, 2]. Concerning the impact of leptospirosis on people's health and well-being, and its correlation with low health levels, this infectious disease can cause the continuation of poverty [3]. The epidemiology of leptospirosis is very complicated due to the multiplicity of factors that might affect the likelihood of infection on a regional basis [4]. Risk factors for contracting Leptospirosis are generally associated with factors that contribute to the survival of the bacterium, i.e. exposure to water or dirt which has been contaminated by animal urine [5]. Equally important determinants of disease transmission include skin contact with intermediate animals or their excrement, monsoon, and floods, and occupational exposure [6].

The clinical manifestation may range from a febrile illness of mild severity to high-grade fever with systemic complications and mortality. While Leptospirosis is rather an acute disease in humans, cases of prolonged illness have also been documented [7-9]. Manifestations of this disease vary from fever with an unknown source to potentially fatal complications including Villo disease and severe pulmonary hemorrhage syndrome, which may result in a mortality rate of 5-40%. As such, timely diagnosis coupled with the administration of effective antibiotics is of utmost importance [10]. On a global scale, Leptospirosis is estimated to affect 1.03 million individuals, of whom 58,900 die annually. This marked prevalence is associated with roughly 2.90 million disability-adjusted life years (DALY) [11]. The pathogenic *Leptospira* strain is able to survive in the external environment and kidney tubules of infected animals [12].

The host, humans in this case, usually becomes infected upon exposure to carrier animals or urine-contaminated environments [10].

Potential reservoirs of spirochetes [13] include wild animals such as rodents, along with canine, bovine, swine, and equine families of domesticated animals [10]. Leptospirosis is often diagnosed based on serologic detection of antibodies, which are present at the detectable levels in the blood within 5 to 7 days following the onset of symptoms [14]. Microscopic agglutination test (MAT) and ELISA are the most frequently preferred serologic tests for Leptospirosis diagnosis. Although leptospirosis has the highest prevalence in tropical regions, its prevalence has recently been reported to show an ascending trend in temperate regions as well, which is attributed to increased populations of rodents in urban areas, rainfalls, and floodings and global warming [15, 16].

As of today, the pathogenesis of leptospirosis is yet to be fully explained, as it appears to differ from the other bacterial infections to some extent. In spite of a marked rise in the count of white blood cells or leukocytosis in hospitalized cases, there is no evidence to suggest that neutrophils might be involved in the upregulation of cell markers associated with increased inflammatory response [17].

Generally regarded as an occupational disease associated with activities with certain levels of exposure to contaminated water and infected animals, Leptospirosis has also been reported in individuals performing recreational activities in humid environments without apparent exposure to presumed contaminated sites [18, 19]. Individuals who travel from other parts of the world to tropical regions are thought to be highly vulnerable to Leptospirosis [20].

As such, early diagnosis is a prerequisite for timely administration of antibiotics, which is highly important in cases with severe disease [21].

The disease could be prevented by avoiding contact with contaminants either directly or indirectly, which is not a feasible preventive measure for individuals whose job mandates continued exposure to such contaminants [22]. Concerning the zoonotic nature of leptospirosis and its well-established prevalence in neighboring provinces, it is important to have a better understanding of the frequency of

Leptospirosis in Zanjan province, which may prove useful in the proper management of patients presenting with fever and jaundice, and differentiation of the bacterial illness from hemorrhagic fevers of viral origin. Here, we sought to investigate the seroprevalence of *Leptospira* in healthy people referred to Shahid Motahari Laboratory, Zanjan, Iran**.**

Materials and Methods

Study population

The present work was a prospective cross-sectional investigation carried out from February to April 2020 to assess the seroprevalence of *Leptospira* among healthy people referred to Shahid Motahari Laboratory, Zanjan, Iran for checkup. This laboratory is located in a rural immigrant area. Inclusion criteria of participants in this study were (1) healthy people aged ≥ 18; and (2) willingness to participate in the study (all participants were asked to provide written informed consent). We did not limit our inclusion criteria to a particular sex or occupation. Participants were selected using simple random sampling method. The study design was approved by the Research Ethics Committee of Zanjan University of Medical Sciences (IR.ZUMS.REC.1398.460).

Sample size

According to Araghian *et al.* and Naddaf *et al.* studies [23, 24] that the seroprevalence of leptospirosis in Iran was reported at about 48-50%, and assuming a confidence level of 98%, and a margin of error (precision) of 5%, the estimated sample size was determined to be 181.

Blood samples and data collection

Two milliliters of blood sample were collected from a peripheral vein of each participant under aseptic precautions, coagulated at room temperature and then centrifuged at 4500 rpm for 5 min. The obtained serum samples were stored at -20 °C for serological analysis. All participants were interviewed using a questionnaire including age, gender, educational level, occupation, history of fever or underlying diseases, and contact history of exposure to domestic animals.

IgG-ELISA

Anti-*Leptospira* IgG antibodies were measured in sera of participants using "NovaLisa *Leptospira* IgG ELISA" kit (NovaTec Immundiagnostica GmbH, Dietzenbach, Germany). Briefly, *Leptospira* antigen-coated microwells were incubated with 100 µl of serum diluted with a ratio of 1:100 using IgG sample diluent for 1 h at 37 °C. Once the wells were washed using phosphate buffer (0.2 M), bound antibodies were detected with *Leptospira* anti-IgG Conjugate (100 µl per well) and 3,3',5,5'-tetramethylbenzidine (TMB) substrate (100 µl per well). Following 30 minutes from the addition of the Stop solution, the light absorbance of the specimens was measured at wavelengths 450 and 620 nm. Positive and negative controls, along with cut-off controls and substrate blank samples were analyzed in each run. Results were expressed by Cut-off calculation. The cut-off was set to mean absorbance value of the cut-off control determinations. Results were reported to Unit [NovaTec Unit = NTU] as follows: [NovaTec Unit = NTU] = patient absorbance value × 10/ Cut-off. The results were interpreted as follows: NTU> 11 was interpreted as positive; NTU between 9-11 was interpreted as equivocal and NTU< 9 was interpreted as negative. Based on the information provided by the manufacturer, the "NovaLisa *Leptospira* IgG" kits were > 98% sensitive and 97.4% specific in terms of diagnostic accuracy.

Statistical analysis

The data were analyzed using IBM SPSS version 17.0 (SPSS, Inc., Chicago, IL). Statistical significance was determined based on the chi-square test. A P-value < 0.05 was assumed to be the threshold of significance.

Results and Discussion

A total of 181 participants, comprising 91 males (50.3%) and 90 females (49.7%), with a mean age of 40.6, were included in the study. The Anti-Leptospira IgG results were categorized as positive, equivocal, or negative. Among the 181 serum samples, 43 (23.7%) tested positive for anti-Leptospira IgG, 36 (19.9%) were equivocal, and 102 (56.4%) were negative.

Table 1 lists the sociodemographic characteristics of the participants and their correlation with anti-Leptospira IgG. In terms of age distribution, 60 participants (33.1%) were aged 18-30 years old, 69 participants (38.1%) were aged 31-60 years old, and 52 participants (28.7%) were over 60. The analysis revealed no significant difference between age and gender concerning anti-Leptospira IgG, based on the chi-square test (P> 0.05). Regarding occupation, approximately 44.2% of participants were housewives, and 36.5% were employed. However, our investigation did not identify any statistically significant correlation between occupation and anti-Leptospira IgG, based on the chi-square test (P> 0.05). Regarding medical history, 99.4% of participants had no prior history of fever, and 71.8% had no underlying diseases. Nevertheless, our analysis found no significant association between these risk factors and anti-Leptospira IgG, based on the chi-square test (P> 0.05). Out of 181 participants, 59 (32.6%) had a village living history and 27.6% of individuals had a contact history of exposure to domestic animals.

Table 1: Demographic information of the participants

Variable	Number of participants (n=181)	Anti-*Leptospira* IgG			*P*-value
		Positive	Equivocal	Negative	
Gender					
Male	91	19 (26.7%)	14 (24.4%)	58 (48.9%)	0.118**
Female	90	24 (20.9%)	22 (15.4%)	44 (63.7%)	
Age groups (years)					
18-30	60	15 (25%)	12 (20%)	33 (55%)	0.08**
31- 60	69	17 (24.6%)	15 (21.7%)	37 (53.6%)	
>60	52	11 (21.2%)	9 (17.3%)	32 (61.5%)	
Educational level					
No education	37	4 (10.8%)	10 (27%)	23 (62.2%)	0.149**
Primary school	46	11 (23.9%)	5 (10.9%)	30 (65.2%)	
Secondary/High school	43	10 (23.3%)	9 (20.9%)	24 (55.8%)	
University/Postgraduate	55	18 (32.7%)	12 (21.8%)	25 (45.5%)	
Occupation					
Employeda	66	16 (24.2%)	10 (15.2%)	40 (60.6%)	0.903**
Student	14	4 (28.6%)	2 (14.3%)	8 (57.1%)	
Housewife	80	19 (23.8%)	20 (25%)	41 (51.3%)	
Soldier	6	1 (16.7%)	2 (23.3%)	3 (50%)	
Retired	13	3 (23.1%)	1 (7.7%)	9 (69.2%)	
Unemployed	2	0	1 (50%)	1 (50%0	
History of fever					
Yes	1	1 (100%)	0	0	0.436**
No	180	42 (23.3%)	36 (20%)	102 (56.7%)	
History of underlying diseases					
Yes	51	12 (23.5%)	9 (17.6%)	30 (58.8%)	0.879**
No	130	31 (23.3%)	27 (20.8%)	72 (55.4%)	
Exposure to domestic animals					
Yes	50	12 (24%)	11 (22%)	27 (54%)	0.894**
No	131	31 (23.7%)	25 (19.1%)	75 (57.3%)	
History of village living					
Yes	59	14 (23.7%)	13 (22%)	32 (54.3%)	0.873**
No	122	29 (23.8%)	23 (18.8%)	70 (57.4%)	

However, none of these factors were found to be significantly correlated with anti-*Leptospira* IgG, based on the chi-square test ($P > 0.05$).

The findings revealed that 23.7% of the 181 serum samples were positive for anti-Leptospira IgG antibodies, 19.9% were equivocal, and 56.4% were negative. The average age of the participants was 40.6 years old, and no significant correlation was observed between age, gender, rural residence, or other demographic characteristics and anti-Leptospira IgG levels. According to our findings, 43 (23.7%), 36 (19.9%), and 102 (56.4%) subjects had positive, suspected, and negative leptospirosis serology, respectively, which, to some extent, is in agreement with the results of Regmi *et al.*'s study 21% and Delmas *et al.* (19%) [25, 26]. Meanwhile, the overall prevalence of leptospirosis in an investigation by Gonwong *et al.* in Thailand was reported to be 28%, which is higher than the overall prevalence of leptospirosis in the present study.

Factors such as high rodent population, high humidity, close contact, and constant contact with animals and working without protection have been reported as the most pressing predisposing factors for leptospirosis in Thailand [27]. In some studies, including the investigation performed by Vargas *et al.* in Colombia, the overall prevalence of leptospirosis was lower than in the present study (12.2%) [28]. In the current study, we did not observe any relationships between gender and the results of leptospirosis serological tests, which fell in line with the findings of Regmi *et al.*'s study and Alikhani *et al.*'s study [29]. While other investigations have reported differences in terms of the prevalence of leptospirosis and mentioned that leptospirosis is more common in men [30, 31].

Nevertheless, we were not able to find any significant relationships between gender and positive serological results, which could be due to the presence of women in agriculture and animal husbandry almost equal to men in the studied geographical area. No relationship was found between age and the results of serological tests, which is in agreement with the findings reported by Alikhani *et al.* [29]. While other studies including the study of Gonwong *et al.* in Thailand [27] and Delmas *et al.* in France [26] reported a significant correlation between age and the results of serological tests. The highest number of positive cases were reported among individuals aged 31-60, while the study of Etienne *et al.* reported the highest number of positive cases among participants aged 51-61 [23]. Our findings did not indicate any relationship of potential significance between the level of education and the results of serological tests, while the study conducted by Gonwong *et al.* reported a significant inverse correlation between education and the results of leptospirosis serological tests [27]. No relationship was found between job status and the results of leptospirosis serological tests, while most of the investigations conducted demonstrated a significant relationship between job and leptospirosis. As Regmi *et al.*'s study [25] reported the most positive cases of leptospirosis serology in farmers; Etienne *et al.*'s study [32] also reported the most positive cases of leptospirosis serology among livestock farmers.

No significant relationship was found between the results of leptospirosis serological tests in terms of residence, which is in agreement with the findings of other studies [31, 33].

While Gonwong *et al.*'s study in Thailand demonstrated positive cases of leptospirosis in rural areas [27]. In other studies in Tanzania and Nicaragua, a statistically significant relationship has been reported between the place of residence and the results of leptospirosis serological tests [33, 34]. Similarly, we did not observe any correlations between the history of contact with domestic animals and the results of leptospirosis serological tests. While other studies such as Regmi *et al.*'s study have found a significant relationship between the history of contact with domestic animals and the results of leptospirosis serological tests [35, 36].

According to the high seroprevalence of *Leptospira* in healthy people in our study, disease control and prevention policies are necessary for people with high risk of infection. Furthermore, comprehensive studies using Microscopic Agglutination Technique (MAT) are suggested for the leptospirosis diagnosis due to its diagnostic accuracy for seroepidemiologic identification of

the disease. MAT uses panels of live Leptospira, ideally recent isolates, representing circulating serovars from the patient's area of residence. ELISA-based serological tests with complementary molecular detection (PCR) are a practical and robust alternative method for diagnosing leptospirosis with new infections in countries with a higher burden of the disease. It will be possible to prevent the disease by increasing the awareness of the people at risk and the personnel of the regional health and treatment systems, and by preventing human contact with contaminated materials, as well as by vaccinating livestock and animals.

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No potential conflict of interest was reported by the authors.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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References

[1]. Bharti A.R., Nally J.E., Ricaldi J.N., Matthias M.A., Diaz M.M., Lovett M.A., Levett P.N., Gilman R.H., Willig M.R., Gotuzzo E., Vinetz J.M. Leptospirosis: a zoonotic disease of global importance, *The Lancet infectious diseases*., 2003, **3**:757 [Crossref], [Google Scholar], [Publisher]

[2]. Bello S., Rodríguez M., Paredes A., Mendivelso F., Walteros D., Rodríguez F., Realpe M.E. Epidemiological surveillance of human leptospirosis in Colombia, 2007-2011, *Biomedica*., 2013, **33**:153 [Crossref], [Google Scholar], [Publisher]

[3]. a) World Health Organization., Report of the second meeting of the leptospirosis burden epidemiology reference group, 2011 [Google Scholar], [Publisher]; b) Edache E., Dawi H., Ugbe F. 3D-QSAR, Molecular Docking, Molecular Dynamics Simulations and Structural Studies of Some Selected Inhibitors of the Glycoprotein (GPC) of Lassa Virus. *Journal of Applied Organometallic Chemistry*, 2023, **3**:224 [Crossref], [Publisher]; c) Khalil M., Noor S., Ahmad Z., Ahmad F. Fate of Pakistani Exported Mango due to Its Toxicity (Heavy Metals, Pesticides, and Other Toxic Organic Components). *Journal of Applied Organometallic Chemistry*, 2023, **3**:86 [Crossref], [Publisher]

[4]. Lau CL., Smythe L.D., Craig SB., Weinstein P. Climate change, flooding, urbanisation and leptospirosis: fuelling the fire?, *Transactions of the Royal Society of Tropical Medicine and Hygiene*., 2010, **104**:631 [Crossref], [Google Scholar], [Publisher]

[5]. a) Lomar A.V., Diament D., Torres J.R. Leptospirosis in Latin America, *Infectious Disease Clinics*., 2000, **14**:23 [Crossref], [Google Scholar], [Publisher]; b) Lahhob Q., Al-sanaf A., Mohammed N., Abbas H., Ibrahim Z., Najim M., Malik Z., Budaiwi Z., Abdul-Jabbar Z., Kadham M. Mineral and trace elements, dietary sources, biological effects, deficiency, and toxicity: a review. *J. Med. Pharm. Chem. Res*., 2023, **5**:536 [Publisher]; c) A. Shatie A., Hasan Mathkor T. Assessment of hormone levels and some heavy metals of Iraqi traffic-warden policemen exposed to vehicle exhausts. *J. Med. Pharm. Chem. Res*., 2022, **4**:441 [Publisher]; d) Maleki Dizaj S., Sharifi S., Shahi S., Montazersaheb S., Salatin S., Ahmadian E., Khezri K., Rahbar Saadat Y., Dalir Abdolahinia E., Ghavimi M.A. The most important consideration in clinical usage of curcumin. *J. Med. Pharm. Chem. Res*., 2022, **4**:1224 [Publisher]; e) Sharma S. A Short Review of Past, Present, and Future of Metallocene and Its Derivatives as an Effective Therapeutic Agent. *Journal of Applied*

Organometallic Chemistry, 2023, **3**:142 [Crossref], [Publisher]
[6]. Levett P. Leptospirosis, *Clinical microbiology reviews.*, 2001, **14**:296 [Crossref], [Google Scholar], [Publisher]
[7]. Herrmann-Storck C., Saint Louis M., Foucand T., Lamaury I., Deloumeaux J., Baranton G., Simonetti M., Sertour N., Nicolas M., Salin J., Cornet M. Severe leptospirosis in hospitalized patients, Guadeloupe, *Emerging infectious diseases.*, 2010, **16**:331 [Crossref], [Google Scholar], [Publisher]
[8]. Papa A., Theoharidou D., Antoniadis A. Pulmonary involvement and leptospirosis, Greece, *Emerging infectious diseases.*, 2009, **15**:834 [Crossref], [Google Scholar], [Publisher]
[9]. Gouveia E.L., Metcalfe J., De Carvalho A.L.F., Aires T.S., Villasboas-Bisneto J.C., Queirroz A., Santos A.C., Salgado K., Reis M.G., Ko A.I. Leptospirosis-associated severe pulmonary hemorrhagic syndrome, Salvador, Brazil, *Emerging infectious diseases.*, 2008, **14**:505 [Crossref], [Google Scholar], [Publisher]
[10]. Croda J., Ramos JG., Matsunaga J., Queiroz A., Homma A., Riley L.W., Haake D.A., Reis M.G., Ko A.I. Leptospira immunoglobulin-like proteins as a serodiagnostic marker for acute leptospirosis, *Journal of Clinical Microbiology.*, 2007, **45**:1528 [Crossref], [Google Scholar], [Publisher]
[11]. Torgerson P.R., Hagan J.E., Costa F., Calcagno J., Kane M., Martinez-Silveira M.S., Goris M.G., Stein C., Ko A.I., Abela-Ridder B. Global burden of leptospirosis: estimated in terms of disability adjusted life years, *PLoS neglected tropical diseases.*, 2015, **9**:e0004122 [Crossref], [Google Scholar], [Publisher]
[12]. Shang E.S., Exner M.M., Summers T.A., Martinich C., Champion C.I., Hancock RE., Haake D.A. The rare outer membrane protein, OmpL1, of pathogenic Leptospira species is a heat-modifiable porin, *Infection and Immunity.*, 1995, **63**:3174 [Crossref], [Google Scholar], [Publisher]
[13]. Tangkanakul W., Tharmaphornpil P., Plikaytis B.D., Bragg S., Poonsuksombat D., Choomkasien P., Kingnate D., Ashford D.A. Risk factors associated with leptospirosis in northeastern Thailand, 1998, *The American journal of tropical medicine and hygiene.*, 2000, **63**:204 [Crossref], [Google Scholar], [Publisher]
[14]. Levett PN., Branch S.L., Whittington C.U., Edwards C.N., Paxton H. Two methods for rapid serological diagnosis of acute leptospirosis, *Clinical Diagnostic Laboratory Immunology.*, 2001, **8**:349 [Crossref], [Google Scholar], [Publisher]
[15]. Pijnacker R., Goris M.G., Te Wierik M.J., Broens E.M., van der Giessen J.W., de Rosa M., Wagenaar J.A., Hartskeerl R.A., Notermans D.W., Maassen K., Schimmer B. Marked increase in leptospirosis infections in humans and dogs in the Netherlands, 2014, *Eurosurveillance.*, 2016, **21**:30211 [Crossref], [Google Scholar], [Publisher]
[16]. Dupouey J., Faucher B., Edouard S., Richet H., Kodjo A., Drancourt M., Davoust B. Human leptospirosis: an emerging risk in Europe?, *Comparative immunology, microbiology and infectious diseases.*, 2014, **37**:77 [Crossref], [Google Scholar], [Publisher]
[17]. Raffray L., Giry C., Vandroux D., Kuli B., Randrianjohany A., Pequin A.M., Renou F., Jaffar-Bandjee M.C., Gasque P. Major neutrophilia observed in acute phase of human leptospirosis is not associated with increased expression of granulocyte cell activation markers, *PLoS One.*, 2016, **11**:e0165716 [Crossref], [Google Scholar], [Publisher]
[18]. Haake D.A., Levett P.N. Leptospirosis in Humans. *Curr Top Microbiol Immunol.*, 2015, 387:65
[Crossref], [Google Scholar], [Publisher]
[19]. Radl C., Müller M., Revilla-Fernandez S., Karner-Zuser S., de Martin A., Schauer U., Karner F., Stanek G., Balcke P., Hallas A., Frank H. Outbreak of leptospirosis among triathlon participants in Langau., Austria., 2010., *Wiener klinische Wochenschrift.*, 2011., **123**:751 [Crossref], [Google Scholar], [Publisher]
[20]. Lau C., Smythe L., Weinstein P. Leptospirosis: an emerging disease in travellers., *ravel medicine and infectious disease.*, 2010, **8**:33 [Crossref], [Google Scholar], [Publisher]
[21]. Guidigli F., Castro A.A., Atallah A.N. Antibiotics for leptospirosis., *The Cochrane database of systematic reviews.*, 2003, 2 [Crossref], [Google Scholar], [Publisher]
[22]. Regmi L., Pandey K., Malla M., Khanal S., Dev Pandey B. Sero-epidemiology study of leptospirosis in febrile patients from Terai region

of Nepal. *BMC Infect Dis*., 2017, **17**:628 [Crossref], [Google Scholar], [Publisher]
[23]. Araghian A., Elmi A., Farahbakhsh M., Hosseini S., Faezi S. Seroepidemiology of leptospirosis in Guilan province., northern Iran: comparison between MAT and IgM-ELISA techniques., *The Journal of Infection in Developing Countries*., 2018, **12**:109 [Crossref], [Google Scholar], [Publisher]
[24]. Naddaf S.R., Mohabati R., Vahabpor R., Naeimi S., Eybpoosh S. Diagnosis of leptospirosis in febrile patients of Golestan Province., Iran: Serology versus PCR., *Journal of Medical Microbiology and Infectious Diseases*., 2020., **8**:98 [Crossref], [Google Scholar], [Publisher]
[25]. Regmi L., Pandey K., Malla M., Khanal S., Pandey B.D. Sero-epidemiology study of leptospirosis in febrile patients from Terai region of Nepal, *BMC Infectious Diseases*., 2017, **17**:1 [Publisher]
[26]. Delmas B., Jabot J., Chanareille P., Ferdynus C., Allyn J., Allou N., Raffray L., Gaüzere B.A., Martinet O., Vandroux D. Leptospirosis in ICU: a retrospective study of 134 consecutive admissions., *Critical care medicine*., 2018, **46**:93 [Crossref], [Google Scholar], [Publisher]
[27]. Gonwong S., Chuenchitra T., Khantapura P., Islam D., Ruamsap N., Swierczewski B.E., Mason C.J. Nationwide seroprevalence of leptospirosis among young Thai men, 2007–2008, *The American journal of tropical medicine and hygiene*., 2017, **97**:1682 [Crossref], [Google Scholar], [Publisher]
[28]. Escandón-Vargas K., Osorio L., Astudillo-Hernández M. Seroprevalence and factors associated with Leptospira infection in an urban district of Cali., Colombia, *Cadernos de saude publica*., 2017, **33**:e00039216 [Crossref], [Google Scholar], [Publisher]
[29]. Alikhani A., Babamahmoodi F., Alian S., Zameni F., Ghorbani A., Shojaeefar A. Sero-epidemiological study of leptospirosis in healthy people in qaemshahr, Iran, 2015, *Journal of Mazandaran University of Medical Sciences*., 2016, **26**:78 [Google Scholar], [Publisher]
[30]. Plank R., Dean D. Overview of the epidemiology, microbiology, and pathogenesis of Leptospira spp. in humans, *Microbes and infection*., 2000, **2**:1265 [Crossref], [Google Scholar], [Publisher]
[31]. Benacer D., Thong K.L., Min N.C., Verasahib K.B., Galloway R.L., Hartskeerl R.A., Souris M., Zain S.N.M. Epidemiology of human leptospirosis in Malaysia, 2004–2012, *Acta tropica*., 2016, **157**:162 [Crossref], [Google Scholar], [Publisher]
[32]. Ntabanganyimana E., Giraneza R., Dusabejambo V., Bizimana A., Hamond C., Iyamuremye A., Nshizirungu P., Uzabakiriho R., Munyengabe M., Wunder Jr E.A., Page C. Sero-prevalence of anti-Leptospira antibodies and associated risk factors in rural Rwanda: A cross-sectional study, *PLoS Neglected Tropical Diseases*., 2021, **15**:e0009708 [Crossref], [Google Scholar], [Publisher]
[33]. Ashford D.A., Kaiser R.M., Spiegel R.A., Perkins B.A., Weyant R.S., Bragg S.L., Plikaytis B., Jarquin C., Reyes J.D.L., Amador J.J. Asymptomatic infection and risk factors for leptospirosis in Nicaragua, *The American journal of tropical medicine and hygiene*., 2000, **63**:249 [Google Scholar], [Publisher]
[34]. Assenga J.A., Matemb L.E., Muller S.K., Mhamphi G.G., Kazwala R.R. Predominant leptospiral serogroups circulating among humans, livestock and wildlife in Katavi-Rukwa ecosystem, Tanzania, *PLoS neglected tropical diseases*., 2015, **9**:e0003607 [Crossref], [Google Scholar], [Publisher]
[35]. Galan D.I., Roess A.A., Pereira S.V.C, Schneider M.C. Epidemiology of human leptospirosis in urban and rural areas of Brazil, 2000–2015, *PloS one*., 2021, **16**:e0247763 [Crossref], [Google Scholar], [Publisher]
[36]. Muñoz-Zanzi C., Mason M.R., Encina C., Astroza A., Romero A. Leptospira contamination in household and environmental water in rural communities in southern Chile, *International journal of environmental research and public health*., 2014, **11**:6666 [Crossref], [Google Scholar], [Publisher]

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