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**LEPTOSPIROSIS IN VIETNAM**

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**Резюме.** Лептоспироз представляет серьезную проблему для здравоохранения многих стран, так как в мире ежегодно около 1 млн. людей болеют этой тяжелой инфекцией, часто оканчивающейся летальным исходом. В настоящее время значение этой проблемы возрастает, что связано с развитием интеграционных процессов, обусловленных глобализацией экономики, интенсификацией хозяйственной деятельности, приводящей к антропогенной трансформации ландшафтов и расширению контингента лиц, входящих в угрожаемые профессии, а также глобальными климатическими изменениями. Юго-Восточная Азия, включая Вьетнам, относится к числу самых неблагоприятных в отношении лептоспироза регионов мира. Целью работы является современный анализ литературных данных о распространении лептоспирозной инфекции во Вьетнаме. В ходе данной работы было проанализировано более 100 научных статей. Это позволило констатировать, что основными источниками лептоспирозной инфекции во Вьетнаме являются синантропные грызуны (крысы), сельскохозяйственные (буйволы, крупный рогатый скот, свиньи) и домашние животные (кошки и собаки). Существенной особенностью заражения жителей Вьетнама является употребление ими в пищу крыс, кошек и собак. Из сельскохозяйственных животных в качестве источника инфекции наибольшее значение имеют свиньи. Показатели инфицированности этих животных лептоспирами различаются весьма широко, достигая 73%. Значение этих показателей существенно различаются в зависимости от территории обитания животных, от размера фермы, возраста, пола свиней, от количества осадков и ряда других факторов. У свиней во Вьетнаме было выявлено большое разнообразие сероваров лептоспир среди которых преобладали Tarassovi, Bratislava, Australis, Javanica, Autumnalis, Grippotyphosa и другие. Официальная отчетность о заболеваниях лептоспирозом, основанная на клинических данных, не отражает реальное количество больных во Вьетнаме. В среднем около 10% жителей Вьетнама инфицировано

лептоспирами. Работа в сельском хозяйстве, является доминирующим фактором риска заражения. Наиболее высокие показатели серопревалентности к лептоспирам были выявлены у фермеров - 63,2%. Для Вьетнама характерно большое разнообразие сероваров циркулирующих лептоспир. Наиболее часто у людей выявляются антитела к лептоспирам сероваров Hebdomadis, Wolffii и Icterohaemorrhagiae, но их частота существенно различались между собой в разных регионах, что можно полагать, связано с ландшафтно-климатическим своеобразием территории, а также обусловлены хозяйственной деятельностью людей. Географические, климатические и социальные различия северной, центральной и южной части Вьетнама в значительной степени определяют эпидемиологические особенности лептоспироза и аргументируют целесообразность разработки конкретных мер профилактики этой инфекции для каждой территории с учетом их специфики.

**Ключевые слова:** лептоспироз, лептоспиры, серовары лептоспир, заболеваемость, Вьетнам, крысы, буйволы, крупный рогатый скот, серопревалентность, антитела.

**Abstract.** Leptospirosis poses a serious public health problem in many countries because about 1 million people suffer annually from this severe, often fatal, infection. At present, its importance has been increasing due to development of integration processes, globalization and intensification of economic activities, inevitable anthropogenic transformation of landscapes as well as rise in number of people with occupational risk of pathogen exposure. The burden of human leptospirosis is expected to rise with demographic shifts and climate change that result in heavy rainfall and flooding. Regarding leptospirosis, Southeast Asia, including Vietnam, is among the most vulnerable global regions. The objective of the review was to analyze available published data on the spread of leptospirosis in

Vietnam. More than 100 research articles were analyzed allowing to state that in Vietnam synanthropic rodents (rats), agricultural (buffaloes, cattle, pigs) and domestic animals (cats, dogs) are the main sources of leptospirosis infection in humans. It is essential that rats (cats and dogs also) in Vietnam are used for food. Among all farm animals, pigs are of maximal importance as a source of infection in humans. In Vietnam, *Leptospira* prevalence in pigs varies widely, up to 73%. It depends significantly on the location, farm size, age and gender of animals, etc. A large variety of *Leptospira* serovars have been identified in pigs in Vietnam: Tarassovi, Bratislava, Australis, Javanica, Autumnalis, Grippytyphosa, and some others. Official Vietnam reporting of leptospirosis cases based on clinical data does not reflect the real-life incidence rate in humans. However, the available seroprevalence studies reveal that, on average, about 10% of the Vietnamese population are infected with *Leptospira*. Work in agriculture is the dominant risk factor for acquiring this infection. The highest *Leptospira* seroprevalence rates were detected in farmers, 63.2%. Serovar diversity is typical for pathogenic *Leptospira* circulating in Vietnam. In humans, the most frequent are antibodies to *Hebdomadis*, *Wolffi* and *Icterohaemorrhagiae*, but the frequency varied markedly across the country depending on the site, possibly with relation to the environment, as well as with economic activity of the local population. In Vietnam, geographic, climatic and social differences between northern, central and southern regions contribute to the specificity of local leptospirosis epidemiology. This emphasizes the advisability of developing special measures for leptospirosis prevention taking into account regional peculiarities.

**Keywords:** antibodies, buffalo, cattle, incidence, *Leptospira*, *Leptospira* serovars, leptospirosis, rats, seroprevalence, Vietnam.

1           **Introduction**

2           Leptospirosis is a globally widespread disease, largely due to the wide range  
3 of reservoir hosts of pathogenic *Leptospira* and animals susceptible to them [9].  
4 Thus, according to the Leptospirosis Burden Epidemiology Reference Group  
5 (LERG), the number of severe leptospirosis cases in humans exceeds 500,000 per  
6 year, though real incidence may be even much higher due to insufficient attention  
7 to this infection and difficulties of its diagnostics [78]. Some other researchers  
8 emphasize that leptospirosis is among the main global zoonoses, and it accounts  
9 for the number of deaths that exceeds mortality due to other causes of hemorrhagic  
10 fever. The annual number of leptospirosis cases exceeds one million, and 58,900 of  
11 fatal outcomes are recorded worldwide annually [26].

12           The highest leptospirosis incidence rate in humans is reported in subtropical  
13 and tropical climatic zones (e.g., in Seychelles, Malaysia, New Caledonia,  
14 Suriname), with 20.0-100.0 per 100 thousand population [4], [31], [46], [86].  
15 Vietnam is a country in Southeast Asia that is one of the most vulnerable regions  
16 in the world with regard to leptospirosis. The region ranks second in the world  
17 (next to Oceania), both for leptospirosis morbidity and mortality [26]. Moreover, it  
18 was possibly in Southeast Asia, under conditions of high humidity and  
19 swampiness, long before the appearance of humans, that certain species of  
20 *Leptospira* adapted to parasitizing the bodies of animals, primarily rodents [5].  
21 Currently, leptospirosis poses a significant public health problem in many  
22 countries, including Russia [9]. However, Southeast Asia, Vietnam particularly,  
23 provides the most favorable conditions for the survival of *Leptospira* as the  
24 pathogen prefers a warm and humid climate. The essential social significance of  
25 leptospirosis lies in the occupational risk of infection to which people are exposed  
26 in connection with the work they perform [15]. The Government of Vietnam has  
27 recognized the priority of five zoonotic diseases, including leptospirosis, and  
28 established a framework to investigate and respond to these diseases through the

29 One Health program [63]. The socio-economic importance of leptospirosis is  
30 increasing due to a number of drivers. The most important of them are as follows.

31 1. Integration is proceeding and developing through: globalization of the  
32 economy; international economic cooperation; and trade, including export/import  
33 of animals (agricultural, domestic, wild), food, and feed [60]. All this favors the  
34 introduction of pathogenic *Leptospira* into virgin territories [2], [3]. Development  
35 of international tourism entails growth in the number of patients infected with  
36 *Leptospira* abroad [57], [14], [45]. Several cases of leptospirosis (including fatal)  
37 have been reported in Russian tourists that had acquired the infection in Vietnam  
38 [7], [10],[6].

39 2. Intensification of economic activity is leading to anthropogenic  
40 transformation of landscapes and a growth in the number of the threatened  
41 workers. More than 50% of the Vietnamese population is employed in the  
42 agricultural sector [24]. In the previous century, it was noted that the cultivation of  
43 rice provides favorable conditions both for survival of *Leptospira* in the  
44 environment and for the habitat of the pathogen's potential carriers [1]. Rice is the  
45 main agricultural crop in Vietnam; its production and export increase steadily.  
46 According to the Ministry of Agriculture and Rural Development of the Socialist  
47 Republic of Vietnam, the country's rice output in 2021 reached over 43.86 million  
48 tons, up 1.1 million tons compared to 2020 [85]. In 2020, Vietnam exported \$2.74  
49 billion worth of rice to many countries, making it the third largest rice exporter in  
50 the world [66]. Leptospirosis in Vietnam (in the Mekong Delta, first of all) may be  
51 considered an environmentally linked disease.

52 Obviously, the spread of leptospirosis is underestimated in Southeast Asia  
53 and, possibly, in other rice-growing countries [81]. Animal husbandry is an  
54 important sector of the Vietnamese national economy, and livestock is potentially  
55 an important reservoir for pathogenic *Leptospira* [36]. Significant changes have  
56 recently taken place in this sector in Vietnam. These resulted both in a notable  
57 increase in the number of farm animals (pigs alone about 29 million heads) and in

58 an improvement in technologies of meat processing and trade in supermarkets.  
59 However, infection with some *Leptospira* serovars may reduce one live pig born  
60 per litter, equivalent to 8% loss of production [18].

61 3. Global climate change may soon transform Vietnam into one of the  
62 countries most affected by weather [53], [31]. This means more extensive flooding  
63 of agricultural land during the rainy season and increased salinization during the  
64 dry season as a result of sea level rise and higher river flooding. In the Mekong  
65 Delta, about 590,000 hectares of rice land would be lost due to flooding and  
66 salinization; that is about 13 percent of rice growing fields in the region [87].  
67 Leptospirosis is commonly considered a flood-related infection [47]. Some  
68 findings support the hypothesis that soils may be the original habitat of the genus  
69 *Leptospira* and a possible environmental reservoir, or at least a temporary carrier,  
70 of pathogenic strains [75], [76], [23]. Rains wash the surface of the soil,  
71 transferring particles including *Leptospira* into suspension [70], [74]. Thus,  
72 *Leptospira* penetrate freshwater bodies, where it survives even under unfavorable  
73 conditions [77], potentially infecting people on rice plantations. On the other hand,  
74 during the dry season, salinity will grow due both to sea level rise and higher river  
75 flooding.

76 The objective of this review was to analyze the literature data on the spread  
77 of leptospirosis infection in Vietnam.

78

### 79 **Materials**

80 Articles were sought from Web of Science and international databases:  
81 Medline (through PubMed), Science Direct, and Google Scholar. We used a  
82 combination of the following search terms: [Leptospirosis AND Vietnam]. The  
83 total number of references exceeded 100, but we excluded those non-essential and  
84 added a number of important references (mostly in Russian) not available in those  
85 databases.

86

87 **Geography**

88 Vietnam is situated at the southeastern tip of the Indochinese Peninsula. On  
89 the east side, Vietnam contacts the South China Sea. The geographical position of  
90 Vietnam has a pronounced, elongated meridional character. The nation stretches  
91 along the 105th meridian in a narrow strip. This specific feature of Vietnamese  
92 geography, together with alternation of highlands and lowlands, results in a  
93 significant variety of climatic conditions.

94 Vietnam has both a tropical climate zone and a temperate climate zone, with  
95 all of the country experiencing the effects of the annual monsoon. Rainy seasons  
96 correspond to monsoon circulations, which bring heavy rainfall in the north and  
97 south from May to October, and in the central regions from September to January.  
98 In the northern regions, average temperatures range from 22–27.5°C in summer to  
99 15–20°C in winter. The southern areas have a narrower range of 28–29°C in  
100 summer to 26–27°C in winter. Vietnam's climate is also impacted by the El Niño  
101 Southern Oscillation (ENSO), which influences monsoonal circulation, and drives  
102 complex shifts in rainfall and temperature patterns which vary spatially at a sub-  
103 national level. Due to such different geographical and climatic features, which to a  
104 certain extent determine socio-economic characteristics, Northern, Central and  
105 Southern Vietnam are usually considered separately. This has prompted  
106 researchers to analyze the impact of abiotic, biotic, and social factors on the spread  
107 of leptospirosis infections in those different regions of Vietnam [54].

108

109 **Leptospira reservoirs**

110 Small synanthropic mammals, rats first of all, are the most important  
111 reservoirs of pathogenic *Leptospira*. The principal feature of their behavior is  
112 living close to humans, in residential premises or commercial facilities (livestock  
113 farms, enterprises for the processing of animal raw materials, warehouses, etc.).  
114 Moreover, rats penetrate natural foci, easily contact wild animals, and can  
115 exchange *Leptospira*. Infection in rodents proceeds mostly in chronic, non-fatal



116 forms, but causes very long, often lifelong, excretion of the pathogen in the animal  
117 urine. In Vietnam, the risk of human infection with *Leptospira* from those animals  
118 is especially high, since rats, including those imported from abroad, are  
119 traditionally used for food [41]. In 1962 in the south of Vietnam (Saigon, currently  
120 Ho Chi Minh City), *Leptospira* were isolated from *Rattus norvegicus*. Those  
121 *Leptospira* were assigned to *L. bataviae* by the cross agglutination lysis and cross  
122 absorption tests, although they were not antigenically identical to the reference  
123 strain or its variant subserotype [40]. Those synanthropic mammals serve as an  
124 important source of human infection in the cities of Vietnam, as *Leptospira*  
125 prevalence in rats is high.

126 Thus, in January 2011 in northern Vietnam (urban areas of Hanoi and Hai  
127 Phong), 22% of 100 studied rats were found to have antibodies to *L. interrogans*  
128 [44]. In a later study, another group of researchers in Vietnam not only confirmed  
129 such high infection prevalence in rats, but also isolated *Leptospira* from 3 rats [43]  
130 and from 144 rats (135 *R. norvegicus*, 8 *R. rattus*, 1 *R. argentiventer*) captured in  
131 Vietnam. In total, 17 *L. interrogans* were isolated, of which 16 isolates belonged to  
132 the *Bataviae* serogroup [42]. More recent studies conducted in southwestern  
133 Vietnam used not only serological, but also molecular genetic methods (using RT-  
134 PCR for the *lipL32* gene, confirmed by 16S rRNA, as well as by the microscopic  
135 agglutination test- MAT). The results also bear witness to a high prevalence of  
136 *Leptospira* in those synanthropic animals. Antibodies to *Leptospira* were detected  
137 in 18.3% of rats, namely in *Rattus norvegicus* (33.0%), *Bandicota indica* (26.5%),  
138 *Rattus tanezumi* (24.6%), *Rattus exulans* (14.3%), and *Rattus argentiventer* (7.1%).  
139 The most common serovars, in descending order, were: *Javanica* (4.6% of rats),  
140 *Louisiana* (4.2%), *Copenhageni* (4.2%), *Cynopterie* (3.7%), *Pomona* (2.9%), and  
141 *Icterohaemorrhagiae* (2.5%). A total of 16 rats (5.8%) tested positive by RT-PCR.  
142 There was considerable agreement between the MAT and PCR, although  
143 significantly more rats were positive by MAT. *Leptospira* seroprevalence in rats

144 caught during the rainy season was higher than in those caught in the dry season  
145 [52].

146 The results of a study performed by a Russian-Vietnamese group of  
147 researchers in seven northern provinces of Vietnam (Dien Bien, Laitiau, Lao Cai,  
148 Ha Giang, Lang Son, Cao Bang, Quang Ninh) confirmed the high infection of  
149 small wild mammals with *Leptospira*. PCR-based study of lung and kidney  
150 suspensions of 158 animals revealed 16S rRNA of pathogenic *Leptospira* in 22  
151 (13.9%) samples [8]. Another Russian-Vietnamese group investigated by real-time  
152 PCR 133 rodents (of 25 species) trapped in 2010, 2013, 2014, and 2018 in three  
153 provinces of northern Vietnam (Ha Giang, Cao Bang, Lao Cai); 24 rodents (18%)  
154 were positive for *Leptospira*. Those were: *Callosciurus erythraeus*, *Bandicota*  
155 *savilei*, *Berylmys bowersi*, *Niviventer fulvescens*, *Rattus nitidus*, *Rattus cf. rattus*,  
156 and *Rattus tanezumi*. The Tanezumi rat (*Rattus tanezumi*), also known as the Asian  
157 rat or Asian house rat, dominated: 11 of 44 animals (33.1%) were infected [12].  
158 When comparing the results of a study on sera of 156 rats from different provinces  
159 of Vietnam, it was found that *Leptospira* seroprevalence in the southern province  
160 (Can Tho) was higher than in the central (Ha Tinh) or in the northern (Tai Binh):  
161 24.6%, 10.0%, and 11.4%, respectively. The average value was 16.0% [54].  
162 Therefore, *Leptospira* prevalence in rats was close to those obtained in earlier  
163 studies conducted in the Mekong Delta region [52], [58], [17]. Their findings were  
164 at the level of those for other countries of Southeast Asia, such as Thailand, Lao  
165 PDR and Cambodia; the mean prevalence was about 7.1% [25].

166 However, it should be mentioned that in Southeast Asia, Vietnam included,  
167 the prevalence of *Leptospira* in rats was found to be rather low as compared to  
168 other southern countries. The highest *Leptospira* prevalence in rats (>70%) was  
169 reported in Brazil [62], [29], [26], [27], Mexico [59], Egypt [69], and some other  
170 countries [17]. The study conducted in three provinces of Vietnam [54] revealed  
171 that the seroprevalence in animals other than rats was much higher: 44.2% in  
172 buffalo (n= 52), 32.9% in dogs (n=219), 24.9% in cattle (n=233), while only

173 12.2% in cats (n=164), and 10.2% in pigs (n=381). In total, it means that  
174 *Leptospira* seroprevalence in animals in the northern province (Tai Binh) was  
175 higher than in the central (Ha Tinh) or the southern (Can Tho): 25.9%, 13.3%, and  
176 19.8%, respectively. However, consideration of seroprevalence in individual  
177 animal species clarifies significantly our knowledge about the infection of animals  
178 with *Leptospira* in different regions of Vietnam.

179 It should be noted that the sera of buffaloes, in the samples of which  
180 antibodies to *Leptospira* were found more often than in other animal species, were  
181 not examined in Can Tho, as buffalo are not common in this province. Naturally,  
182 the lack of data on those animals in the southern Vietnam had an impact on the  
183 total seroprevalence in animals of the region. Moreover, it was found that in Can  
184 Tho *Leptospira* seroprevalence in cattle (n=69) was higher than in Tai Binh (n=80)  
185 or Hatin (n= 84): 30.4%, 22.5%, and 22.6%, respectively. *Leptospira*  
186 seroprevalence in dogs, cats and pigs in Tai Binh exceeded that in both other  
187 provinces. Thus, in dogs it was 46.7% in Tai Binh (n=60), 15.2% in Hatin (n=79),  
188 and 40.0% in Can Tho (n=32). The same figures for cats were 25.0% in Tai Binh  
189 (n=60), 4.8% in Hatin (n= 42), and 4.8% in Can Tho (n=62). *Leptospira*  
190 seroprevalence in pigs was 20.5% in Tai Binh (n=122), 3.3% in Hatin (n=121), and  
191 7.2% in Can Tho (n=138).

192 *Hebdomadis*, *Louisiana*, and *Javanica* were the most common serovars  
193 detected in buffalo, while in pigs it was *Castelloni*, and in rats *Louisiana*. In cattle,  
194 15 different serovars were detected, *Hebdomadis* and *Canicola* being the most  
195 frequent. Thirteen serovars were identified in dogs, but *Hardjobovis* was the most  
196 frequently detected. Six serovars were detected in cats; *Louisiana*, *Hebdomadis*,  
197 and *Castellonis* dominated.

198 Using a low dilution threshold for sera containing antibodies to *Leptospira*  
199 (1:100), 17 *Leptospira* serovars were detected in the studied animals, of which  
200 *Hebdomadis* (2.3%), *Molasses* (1.6%), *Castelloni* (1.5%), and *Javanica* (1.4%)  
201 were the most frequent. *Panama*, *Tarassovi*, *Australis*, and *Autumnalis* were found

202 in all three provinces, while Bratislava was found only in Can Tho. It should be  
203 pointed out that all 17 *Leptospira* serovars were present in Can Tho, while only 12  
204 and 8 serovars were found in Taibin and Hatin, respectively [54].

205 In Vietnam, infection of humans with *Leptospira* occurs not only through  
206 direct contacts with dogs and cats (or the use of water or food contaminated by  
207 them), but also through consumption of their meat, as those animals are used for  
208 food [13], [11]. Pigs are of great importance in Vietnam because of their  
209 contribution to human nutrition, their role in agricultural production systems, and  
210 their economic function. Vietnam's pig herd is the largest in Southeast Asia [51].  
211 In 2020 it exceeded 27 million head, and about 7 million Vietnamese people were  
212 involved in pigs raising in 2016 [34]. Therefore, pigs are considered the main  
213 source of leptospirosis in humans. In addition, leptospirosis in pigs leads to large  
214 economic losses due to abortion and infertility of animals [48].

215 In Vietnam, *Leptospira* seroprevalence in pigs ranged up to 73% among  
216 sows (n=424) in the Mekong Delta, where leptospirosis is endemic. [18]. High  
217 *Leptospira* prevalence in pigs was also confirmed by pathogen detection in pig  
218 kidneys. Thus, in the Mekong Delta (south Vietnam), *Leptospira* were detected by  
219 immunofluorescence in 22 of 32 pigs (69%), and *Leptospira* serovar Bratislava  
220 was isolated from the kidney of one pig [19]. A serological survey was conducted  
221 among sows in the Mekong Delta in southern Vietnam in 1999 to investigate  
222 variations in *Leptospiral* seroprevalence over a one-year period. In this region,  
223 leptospirosis is endemic, and a high *Leptospiral* seroprevalence has been shown in  
224 the pig population [20].

225 However, a rather low prevalence (8.17%) was detected in a seroprevalence  
226 study of pigs (n=1959) randomly selected in five provinces (Son La, Hanoi, Nghe  
227 An, Dak Lak, An Giang) [48]. The low *Leptospira* prevalence, according to those  
228 authors, was due to a number of reasons, as follows. Serum was sampled during  
229 dry or early wet seasons, when seroprevalence is likely to be lower than in the  
230 rainy season [71]. Most of other studies were conducted in the Mekong Delta of

231 southern Vietnam, relatively close to riverine areas, which provide more exposure  
232 to contaminated water and hence higher levels of *Leptospira* prevalence. Sera were  
233 sampled at slaughterhouses, from rather young animals (aged 6–9 months), while  
234 older pigs are more likely to be infected with *Leptospira* [18]. Animals chosen for  
235 slaughter usually look healthy and probably are less infected with *Leptospira*.

236 However, some other researchers do not share the conclusion about  
237 favorable conditions for infection of pigs with *Leptospira* in the Mekong Delta.  
238 Thus, in a study of 2000 sera from 10 provinces, the average *Leptospira*  
239 seroprevalence was 21.05%, while that of the samples from three provinces lying  
240 in the Mekong Delta was much lower: 10.0% in Soc Trang and 11.5% in Dong  
241 Thap. The highest detected seroprevalence values were 37.5% in Quang Ngai  
242 (Central region), 32.5% in Binh Duong (South), and 30.5% in Bac Giang (North)  
243 [49]. There is probably some impact from the amount of precipitation, as has  
244 already been proven for Brazil [68], India [71], and Korea [39]. In addition to the  
245 aforementioned drivers of *Leptospira* prevalence in pigs, it is likely that animal  
246 gender should be taken into account as well [48]. The size of the farms involved  
247 into the study is also important, including possible herd movements [50].

248 Some downtrend in *Leptospira* prevalence in pigs may be due to co-infection  
249 and reduction in the number of those animals due to the outbreak of African swine  
250 fever in 2019, which led to culling and death of approximately 5.9 million pigs  
251 (about 22%) [21],[88]. In 2021, ASF outbreaks were ongoing in 48 out of 63  
252 provinces in Vietnam, resulting in the death and culling of nearly 280,000 pigs  
253 with a total weight of about 11,678 metric tons, about 3.6-fold higher than the  
254 culled numbers in the same period of 2020 [22].

255 A wide variety of *Leptospira* serovars were identified in pigs: Tarassovi,  
256 Bratislava, Australis, Javanica, Autumnalis, Grippytyphosa, etc. [18], [19], [20]. In  
257 particular, Pyogenes and Panama serovars were isolated [49] that already had been  
258 detected in cattle in some other countries [56], [61], [33]. It should be noted that  
259 the Pyogenes serovar was detected in Quang Ngai, the province known for its

260 large herd of cattle. One may assume the cattle to be a source of *Leptospira* in local  
261 pigs. In addition, it has been suggested that since *Leptospira* of Bratislava and  
262 Tarasovi serovars are common in wild boars [37], [80], those animals may also  
263 contribute to pathogen transmission to farm pigs [50].

264

### 265 **Leptospirosis in humans**

266 *Leptospirosis* was first identified in Vietnam in 1930 [82], [28]. At the end  
267 of the twentieth century, prevalence in humans was rather high: 18.8% of the  
268 inhabitants in the Mekong Delta aged 15-60 years had antibodies to *Leptospira*  
269 [81]. Moreover, it should be highlighted that even now leptospirosis is  
270 underdiagnosed in many countries, Vietnam included. Due to significant  
271 polymorphism of its clinical course and shortcomings in laboratory diagnostics,  
272 leptospirosis is often misdiagnosed as some other febrile illnesses such as dengue,  
273 scrub typhus, or chikungunya [30], [32], [38], [65]. In Vietnam, nation-wide  
274 reporting on infectious diseases is carried out by the General Department of  
275 Preventive Medicine of the Ministry of Health. Their statistics are built on the  
276 basis of clinical information, resulting in significant underdiagnosis of  
277 leptospirosis. Therefore, in 2014-2017, the Vietnamese Ministry of Health reported  
278 roughly less than 20 cases nationwide per year. In 2018, both morbidity and  
279 mortality due to leptospirosis were reported to be zero [35], [84].

280 However, some scientific publications on *Leptospira* seroprevalence in  
281 humans contradict the official statistics on leptospirosis in Vietnam [46],[83]. In  
282 2019 (November-December), a serological examination of 600 practically healthy  
283 residents of three provinces (representing North, Central North and South  
284 Vietnam) revealed antibodies to *Leptospira* in 9.5% of them. Antibodies to  
285 *Leptospira* serovars Hebdomadis (14.0%), Pomona (14.0%), Saxkoebing (12.3%),  
286 and Panama (8.8%) were most frequently detected. *Leptospira* seroprevalence  
287 varied significantly: from 5.5% in Can Tho City, to 9.0% in Thai Binh, and 14% in  
288 Ha Tinh province. The highest rate of *Leptospira* seroprevalence, 63.2%, was

289 found in farmers. [79]. The seropositivity in Vietnam seemed rather low compared  
290 to other Southeast Asian countries.

291 For instance, in Malaysia the seroprevalence of Leptospiral antibodies in  
292 high-risk groups was up to 28.6% (in planters) and 33.6% (wet market workers)  
293 [64],[67]. However, the difference may be related to the choice of humans under  
294 study. The difference in prevalence might be due to the fact that in Malaysia the  
295 occupationally high-risk group was examined, while in Vietnam they "randomly"  
296 selected healthy residents aged above four, and the highest rate of seroprevalence  
297 to *Leptospira* (63.2%) was revealed in farmers [79].

298 In our opinion, the detection of antibodies to *Leptospira* in almost 10% of  
299 healthy humans in three different provinces clearly indicates that the official data  
300 on the registration of leptospirosis do not reflect the real spread of this infection in  
301 Vietnam. This is confirmed by the results of a study of sera sampled from 3815  
302 patients with suspected leptospirosis. The patients were examined in 11 public  
303 hospitals from three provinces (Thai Binh, Ha Tinh, Can Tho), representing three  
304 different geographical and climatic zones of Vietnam. The result proved that the  
305 conclusions of the authors about the unsatisfactory diagnosis of leptospirosis were  
306 valid not only for individual territories, but for the whole of Vietnam. [55].  
307 Surveillance revealed that in 68 (1.8%) and 248 (6.5%) cases, a leptospirosis  
308 diagnosis was confirmed, or regarded as likely, according to the microscopic  
309 agglutination test (MAT) or enzyme immunoassay (ELISA-IgM), respectively. In  
310 addition, more than 30% of patient serum samples contained IgM antibodies  
311 (according to ELISA data) to *Leptospira*. The number of laboratory-confirmed  
312 leptospirosis cases was highest in Thai Binh (2.3%), while somewhat lower in Ha  
313 Tinh (2.0%) and Can Tho (1.0%). Laboratory values considered "probable for  
314 leptospirosis" were even higher: 8.5% in Ha Tinh, 7.1% in Can Tho, and 7.0% in  
315 Thai Binh.

316 In three provinces, 20 different serovars (with a titer threshold of 1:100 to  
317 1:400) were detected using MAT, indicating diversification of *Leptospira* serovars

318 circulating in Vietnam. Of those 20 serovars, 17 were found in Hatin, 16 in Taibin,  
319 and 12 in Can Tho. In general, the serovars Wolffi (14.2%), Hebdomadis (13.8%),  
320 and Icterohaemorrhagiae (12.6%) prevailed, but their incidence varied significantly  
321 in the three provinces. Castellonis (12.3%), Djasiman (12.3%), and Wolffi (12.3%)  
322 dominated in Taibin. Icterohaemorrhagiae (19%) and Wolffi (15%) dominated in  
323 Khatin. Hebdomadis (23.6%) and Wolffi (15.3%) prevailed in Can Tho.

324 According to aggregate findings in those three provinces, leptospirosis was  
325 more common in women (57.9%) than in men (42.1%). It is not typical for most  
326 countries and may be explained by the fact that 85.9% of women in Vietnam are  
327 employed in agriculture. Of the probable and confirmed cases of leptospirosis,  
328 approximately two-thirds were farmers, and most of them were involved in raising  
329 agriculture or domestic animals. Working in agriculture is probably the main risk  
330 factor for contracting leptospirosis in Vietnam. Thus, 53.5% and 83.2% of patients  
331 with probable or confirmed leptospirosis were farmers in Taibin and Hatin,  
332 respectively.

333 About two thirds of patients with leptospirosis were people of working age,  
334 24 to 60 years [55]. Although adults are more frequently infected with *Leptospira*  
335 due to their professional activities, children also acquire this pathogen. Thus, a  
336 serological study of children in the south of Vietnam revealed an average  
337 *Leptospira* prevalence of 12.8% [72]. It ranged from 11% in 7 years-old up to 25%  
338 in 12-year-old children [73]. It is possible that walking barefoot in the mud,  
339 swimming in polluted water, etc., may cause *Leptospira* infection in children [55].  
340 There is evidence that virulent *Leptospira* survive in the environment for several  
341 months [16].

342

### 343 **Conclusion**

344 The main sources of leptospirosis infection in Vietnam are synanthropic  
345 rodents (rats), agricultural animals (buffaloes, cattle, pigs) and domestic animals  
346 (cats, dogs). Among all farm animals, pigs are the most important source of



347 *Leptospira* in Vietnam, as about 7 million of the country's population work in the  
348 pig breeding sector. The seroprevalence of leptospirosis in pigs is up to 73% in  
349 some locations (Mekong Delta), though it varies significantly depending on the  
350 territory, farm size, animal age and gender, amount of precipitation, etc. A specific  
351 and essential feature of the infection in Vietnam is human consumption of cats,  
352 dogs, and rats.

353 Official reporting of leptospirosis cases based on clinical data does not  
354 reflect the actual number of patients in Vietnam. On average, about 10% of the  
355 population was found to be infected with *Leptospira*. Work in the agriculture sector  
356 is the dominant risk factor for acquiring the infection. The highest *Leptospira*  
357 seroprevalence was detected in farmers. Women are infected more often than men.  
358 About two thirds of patients with leptospirosis were people of working age (24 to  
359 60 years), but antibodies to *Leptospira* were also detected in 12.8% of children. A  
360 very wide variety of pathogenic *Leptospira* serovars was detected in Vietnam. The  
361 list of pathogenic *Leptospira* varies significantly depending on the region. This is  
362 due to variation of environment, landscape and climatic features of the territory, as  
363 well as the economic profile of the province. Geographic, climatic and social  
364 differences in the northern, central and southern regions of Vietnam largely  
365 determine the epidemiological features of leptospirosis within the territory. This  
366 argues for the advisability of developing measures to prevent this infection in each  
367 region, taking into account their specifics.

**ТИТУЛЬНЫЙ ЛИСТ**

Лептоспироз во Вьетнаме

Leptospirosis in Vietnam

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**Ключевые слова:** лептоспироз, лептоспиры, серовары лептоспир, заболеваемость, Вьетнам, крысы, буйволы, крупный рогатый скот, свиньи, серопревалентность; антитела, Вьетнам,

**Keywords:** Leptospira, Leptospira serovars, leptospirosis, rats, antibodies, buffaloes, cattle, pigs, incidence, seroprevalence, antibodies, Vietnam.

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