

Original Article

## Epidemiological profile of Hantavirus in the Ñuble region period 2002-2018, Chile

Perfil epidemiológico do Hantavirus na região Ñuble período 2002-2018, Chile

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### Abstract

Hantavirus infection is an endemic zoonosis in Chile, with an average lethality of around 36%. The highest lethality (60%) was recorded in 1997. Prevention strategies have been applied since then. Early diagnosis and technologies, such as the use of ECMO (Extracorporeal Membrane Oxygenation) and Hantavirus immune plasma, have contributed to increasing the survival of people due to this disease at the national level. In the newly created Region of Ñuble in Chile, the incidence and lethality of Hantavirus cases are unknown; therefore, the objective of this research is to describe the epidemiological profile of Hantavirus cases in the Region of Ñuble, Chile from 2002 to 2018. This knowledge contributes to substantiating and justifies the need to invest in technology and reinforce interventions related to the early diagnosis and prevention of this disease in the region. Cases reported in the Ñuble region during the period 2002-2018, extracted from the Epidemiological Survey of Environmental Research of Hantavirus cases of the Ministry of Health of Chile, were analyzed retrospectively. The epidemiological profile of the Ñuble region is very similar to the national one in terms of characterizing the individual suffering from the disease. The most affected population is young men, residents in rural areas, and mainly from a low socioeconomic segment. The regional profile of Hantavirus cases makes it possible to identify three communes with the highest number of cases: El Carmen, Coihueco, and San Carlos. A political-administrative response is expected to focus on and optimize strategies and resources to reduce the incidence and lethality of this pathology in the Ñuble region.

**Keywords:** Andes virus, Hantavirus cardiopulmonary syndrome, *Oligorizomys longicaudatus* (long-tailed mouse).

### Resumo

A infecção por hantavírus é uma zoonose endêmica no Chile, com letalidade média em torno de 36%. A maior letalidade (60%) foi registrada em 1997. Estratégias de prevenção vêm sendo aplicadas desde então. O diagnóstico precoce e tecnologias como o uso de ECMO (Extracorporeal Membrane Oxygenation) e plasma imune ao Hantavirus, têm contribuído para aumentar a sobrevivência das pessoas por esta doença em nível nacional. Na recém-criada Região de Ñuble no Chile, a incidência e letalidade dos casos de Hantavírus são desconhecidas; portanto, o objetivo desta pesquisa é descrever o perfil epidemiológico dos casos de Hantavírus na Região de Ñuble, Chile de 2002 a 2018. Esse conhecimento contribui para fundamentar e justificar a necessidade de investir em tecnologia e reforçar as intervenções relacionadas ao diagnóstico precoce e prevenção desta doença na região. Os casos notificados na região de Ñuble durante o período 2002-2018, extraídos do Inquérito Epidemiológico de Pesquisa Ambiental de casos de Hantavírus do Ministério da Saúde do Chile, foram analisados retrospectivamente. O perfil epidemiológico da região de Ñuble é muito semelhante ao nacional no que diz respeito à caracterização do indivíduo acometido pela doença. A população mais afetada são homens jovens, residentes em áreas rurais e, principalmente, de um segmento socioeconômico baixo. O perfil regional dos casos de Hantavírus permite identificar três municípios com maior número de casos: El Carmen, Coihueco e San Carlos. Espera-se uma resposta político-administrativa que enfoque e otimize estratégias e recursos para reduzir a incidência e letalidade desta patologia na região de Ñuble.

**Palavras-chave:** vírus Andes, síndrome cardiopulmonar por hantavírus, *Oligorizomys longicaudatus* (rato de cauda longa).

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## 1. Introduction

Hantavirus is a viral disease considered an emerging zoonosis whose main vectors are wild rodents. The first human cases registered in the American continent were detected in the United States in 1993, identifying the “unnamed virus” as the causal agent (Khan et al., 1996). In Chile, the first case was recorded in 1995 (Baró et al., 1999), although serological studies would have revealed the presence of antibodies in a group of people who survived atypical pneumonia in 1993 (Navarrete et al., 2000). Around 40 variants carried by different species of rodents that can transmit it to humans have been identified globally (Jonsson et al., 2010). Among rodents, there is horizontal transmission, not producing the disease in them (Pavletic, 2000).

The circulating virus in Chile is the Andes variant, which is transmitted by the wild rodent *Oligoryzomys longicaudatus* (long-tailed mouse), a protected species in Chile (Padula et al., 2000). Predators such as Barn Owl (*Tyto alba*) and White-tailed Kite (*Elanus leucurus*) may play an essential role in the biological control of the long-tailed mouse in natural or urban areas of Chile and some other countries in south America, however, further studies have to be done to asseverate it (Muñoz-Pedrerros et al., 2016; Magrini and Fature, 2008). The long-tailed mouse transmits the virus to humans mainly through inhalation of aerosols produced from the urine and feces of infected rodents. Other forms of transmission have been described besides mucosal (nasal, buccal, or conjunctival) inoculation due to contact with virus-contaminated hands (Schmaljohn and Hjelle, 1997). Person-to-person transmission has also been documented, corresponding to a low-frequency situation in which the mode of contagion is not clear (Padula et al., 1998; Martinez-Valdebenito et al., 2014). This disease has an endemic seasonal presentation, that is, the highest incidence of cases occurs in late spring and during the summer period (Reyes et al., 2019).

The human population has invaded the rodent habitat; therefore, the greatest risk of contagion is for people who live in rural areas and those who visit these places for recreational or work activities (Jonsson et al., 2010). The disease can be classified as mild Hantavirus or Hantavirus cardiopulmonary syndrome (HCPS); in either case begins with a flu-like syndrome, with fever, myalgia, and headache and sometimes accompanied by gastrointestinal symptoms progressively establishing itself, triggering HCPS (Pan American Health Organization, 2011). The incubation period ranges from 7 to 45 days, with an average of 18 days (Vial et al., 2006; MINSAL, 2012; 2013). The treatment for this disease consists of life support through mechanical ventilation and vasoactive drugs, which may require ECMO (Extracorporeal Membrane Oxygenation) and the administration of immune serum, which must be inoculated in case of well-founded suspicion of Hantavirus (MINSAL, 2018). There is no specific antiviral treatment or vaccine for this disease. The year 2000 marks the date for the surveillance of this pathology in Chile, the annual incidence has fluctuated between 40 and 60 cases (Reyes et al., 2019). The notification of Hantavirus cases from 2012 to 2016 has registered a median of 39 cases per year, with an incidence rate between 0.3 and 0.4 per hundred thousand inhabitants (MINSAL, 2017a, b).

The regions with the highest incidence rates, ordered in decreasing order, are Aysén, Los Lagos, Araucanía, and Bío-Bío (Sotomayor and Aguilera, 2000). Due to its large population, the latter has lower incidence rates than other regions; however, it is the region with the highest number of infections (Reyes-Zaldívar and Ferrés, 2019). The Bío-Bío region has historically been the region that has registered the highest number of Hantavirus cases nationwide (Reyes-Zaldívar and Ferrés, 2019). Until 2017, this region was politically and administratively constituted by four provinces: Concepción, Arauco, Bío-Bío, and Ñuble. At that time, the Ñuble province represented 45% of the cases of this disease in the whole region of Bío-Bío. Since 2018 the province of Ñuble was separated from the Bío-Bío Region and began to be called the Ñuble Region.

In 1997, Chile registered a lethality rate of 60%, which is considered the highest to date, and the average lethality in Chile is around 36% (Toro et al., 1998). However, due to the different strategies and technologies implemented in Chile, such as prevention, early diagnosis, the use of ECMO, and Hantavirus immune plasma, survival from this disease has been increasing.

The description of the epidemiological profile of Hantavirus cases in the Ñuble region is justified considering the high lethality of this disease, the high incidence of cases, and the absence of studies in the Ñuble region. A study of this nature supports the need to invest in technology and strengthen interventions related to early diagnosis. Consequently, the patient would access better therapy, and the importance of community-oriented interventions in terms of prevention and recognition of symptoms for timely consultation in health centers would be revealed. This study will contribute to implementing strategies for the reduction of the incidence and lethality of this disease in the Ñuble region.

## 2. Materials and Methods

A cross-sectional mixed-type study was conducted. The study population was obtained from a secondary database of cases generated by the Ministry of Health of Chile (MINSAL) applying the “Epidemiological survey and environmental investigation of cases of Hantavirus infection” under the Hantavirus Surveillance Circular B51/July 24, 2012 (Martinez-Valdebenito et al., 2014). The database was requested by the transparency code A0001T0008511 from the MINSAL epidemiology unit under the State transparency law, Law 20,285. The database, delivered according to legislation, did not include sensitive or private data, under Law 19,628 on the protection and treatment of sensitive information.

The sample comprises all the cases in the base, excluding one case for having incomplete data and twenty cases that were excluded for being outside the period analyzed (2000, 2001, and 2019). The data from the secondary information source was reviewed and refined, which avoided the entry of repeated information or incomplete information, increasing reliability. The information was handled in a digital device protected with a security key and after being analyzed in a computer, all traces of the database were eliminated. Furthermore, the study was submitted for approval by the Bioethics and Biosafety Committee of the Universidad del Bío-Bío.

Any person notified and confirmed with Hantavirus by ELISA or PCR laboratory technique, during the period 2002-2018 and, who registered the Ñuble Region as the place of contagion, regardless of the place where the notification was made, was considered as an inclusion criterion. As exclusion criteria, cases with incomplete or duplicate data and cases outside the 2002-2018 periods were considered.

The sociodemographic variables characterizing the individual were: Sex, age, province of infection, commune of infection, and month of occurrence. The clinical variables were: fever, headache, myalgia, gastrointestinal symptoms, chest X-ray, and blood count (thrombocytopenia (<150,000), elevated hematocrit (>50%), atypical leukocytosis (>10% of immunoblasts)), Puumala test, lethality due to Hantaviruses. The Puumala test it is an immunochromatographic rapid test linked to enzymes (ELISA) to detect antigens, not available for Ñuble region.

The risk factors considered were: resident in the rural sector, a worker in the rural sector, such as a forestry worker and farmers, entry to closed or abandoned buildings, a hiker or tourist in endemic areas, and contact with a confirmed case of Hantavirus.

### 2.1. Data processing

Once the secondary database containing 122 cases was reviewed, the non-existence of repeated or incomplete data was confirmed. The presence of 21 cases that were outside the period that includes 2002-2018 was detected, for which 101 notified cases were worked on.

The total number of confirmed and notified cases of Hantavirus between the years 2002 and 2018 that had as a place of infection any of the 21 communes of the Ñuble Region as described. The description of the information was made from the median as a measure of central tendency, also using absolute and percentage frequencies for the categorical variables. For the temporal variables, incidence rates were calculated where the numerator was made up of the number of cases reported for each year and the denominator by the INE (National Statistics Institute) population as of June 30 of each year.

## 3. Results

According to the data extracted from the secondary database, during the period 2002 to 2018 in the Ñuble Region, 101 notified cases of Hantavirus were identified. The percentage distribution by sex was 73.23% in men and 26.73% in women (Figure 1).

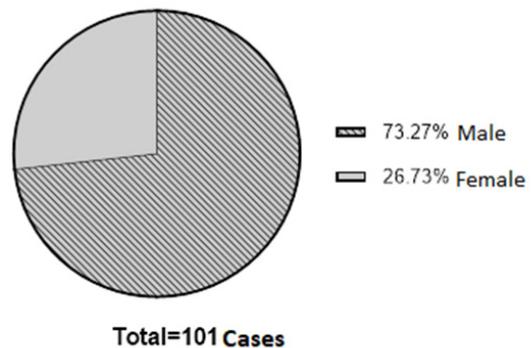
The Ñuble region is administratively constituted of three Provinces (Itata, Diguillín, Punilla) and 21 communes. According to the province of occurrence of the cases between the years 2002 to 2018 in the Ñuble region, the highest concentration (53 cases) was seen in Diguillín province, sixteen more cases than Punilla and 42 more cases than Itata (Figure 2).

According to the probable place to acquire the infection, the cases occurred mainly in the communes of El Carmen (17 cases), Coihueco (16 cases), and San Carlos (15 cases).

The commune of Ninhue did not register cases during the characterized period (Figure 3).

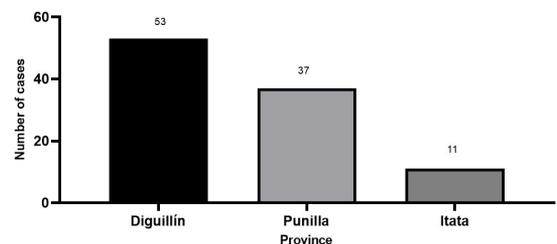
A marked seasonal presentation is observed in the spring-summer months, constituting 89% of the total cases in these seasons. According to the onset of the symptoms of the cases, the first ones appear in October of each year with a marked increase as the summer period advanced in the southern hemisphere (September to March). The number of symptomatic individuals begins to decline at the end of May; only isolated cases were observed during the winter months of June, July, and August. In September there were no cases of Hantavirus (Figure 4).

**Hantavirus cases by sex, Ñuble region 2002-2018**



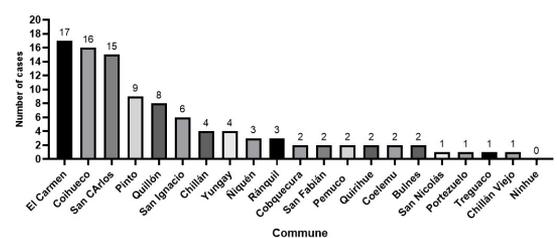
**Figure 1.** Hantavirus cases by sex, in Ñuble Region 2002-2018.

**Hantavirus cases by province of occurrence, Ñuble region 2002-2018**

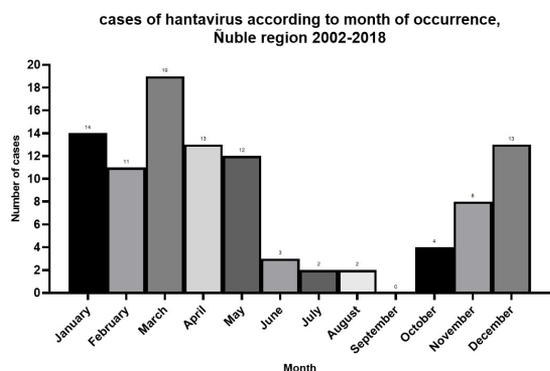


**Figure 2.** Hantavirus cases by the province of occurrence, Ñuble Region 2002-2018.

**Hantavirus cases according to occurrence commune, Ñuble region 2002-2018**



**Figure 3.** Hantavirus cases according to the commune of occurrence, Ñuble Region 2002-2018.



**Figure 4.** Hantavirus cases according to the month of occurrence, Ñuble Region 2002-2018.

The highest incidence rates correspond to the year 2003 (11 cases), 2004 (10 cases), 2012 (10 cases), and 2014 (10 cases). The lowest incidence rate was recorded in 2006 (Figure 5).

The median age of all cases in the region was 17 years (range: 0 to 69 years). The greatest risk of contracting Hantavirus is present in the age range of 15 to 34 years.

The age groups with the highest concentration of cases correspond to those between 20-24 and 30-34 years-old group, with 14 cases registered for each group, with an incidence rate of three per hundred thousand inhabitants each. Younger people (0-14 years) and older people (over 70) were the least affected (Figure 6).

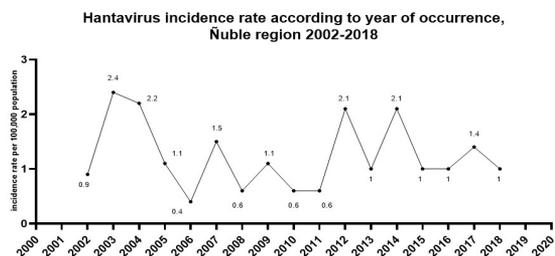
Hantavirus case fatality is fluctuating, presenting a downward trend as of 2014. Case-fatality peaks are observed in 2006, 2010, 2013, and 2014, reaching 100% in 2006, but a low number of cases every year, except the year 2014 with 10 cases and 60% lethality. In the years 2002, 2008, 2016, and 2018, the lethality was 0% (Figure 7).

As for lethality due to Hantavirus according to the place of residence, it is reported that the communes with the highest lethality correspond to Chillán Viejo (100%), Quillón (63%), San Fabián, Cobquecura, and San Ignacio (50%). The communes in which there are no reported deceased cases correspond to Ninhue, Chillán, San Nicolás, Bulnes, Coelemu, Quirihue, Portezuelo, Treguaco, and Pemuco.

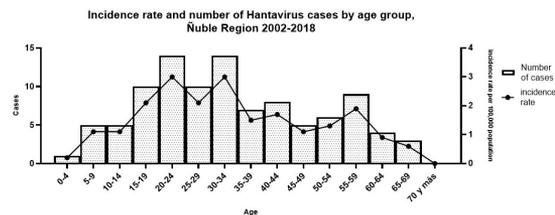
In Cobquecura, San Fabián, and Chillán Viejo, where lethality reaches one of the highest figures, it is observed that the number of cases is markedly lower (2, 2, and 1 case respectively). On the other hand, in communes that register a greater number of cases, such as San Carlos, Coihueco, and El Carmen, with 15, 16, and 17 cases, respectively, the lethality is lower compared to the other communes that report deceased cases (Figure 8).

Although the incidence in women (27 cases) is lower than in men (74 cases), the lethality is higher in women, presenting 40.7% during the period 2002-2018 in the Ñuble region, compared to men who present a lethality of 28% during the same period in the region (Figure 9).

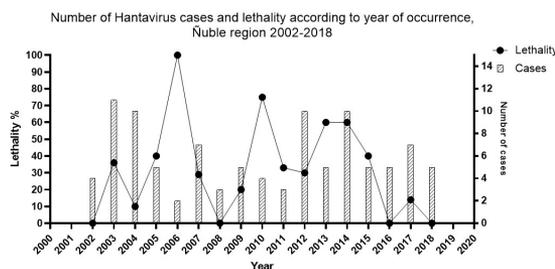
People, regardless of gender, took an average of two days between the onset of the first symptom and the first contact with medical assistance (Table 1).



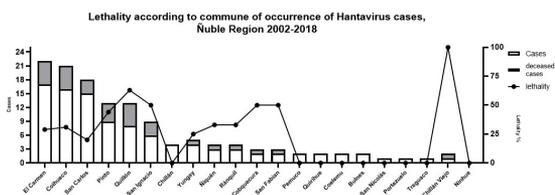
**Figure 5.** Hantavirus incidence rate according to the year of occurrence, Ñuble Region 2002-2018.



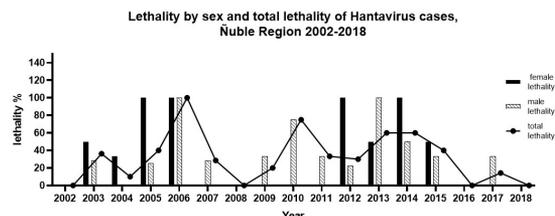
**Figure 6.** Incidence rate and the number of Hantavirus cases by age group, Ñuble Region 2002-2018.



**Figure 7.** Number of Hantavirus cases and lethality according to the year of occurrence, Ñuble Region 2002-2018.



**Figure 8.** Lethality according to commune of occurrence of Hantavirus cases, Ñuble Región 2002-2018.



**Figure 9.** Lethality by sex and total lethality of Hantavirus cases, Ñuble Region 2002-2018.

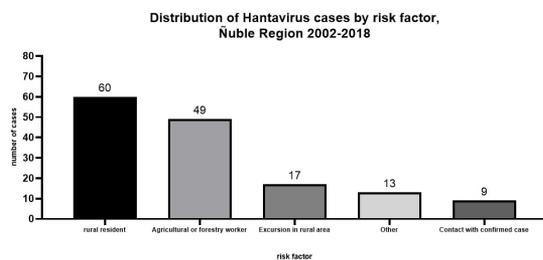
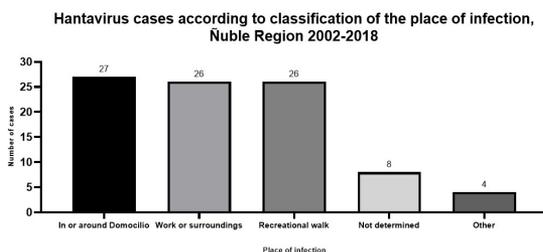
**Table 1.** The difference in days between the date of onset of symptoms and the date of the first consultation, according to sex, according to the cases of Hantavirus registered between 2002 and 2018 in the New Region of Ñuble.

Sex	Average of days delaying consultation.
Males	2.2
Women	2.6

**Table 2.** Description of clinical variables according to the sex of Hantavirus cases in the New Region of Ñuble 2002-2018.

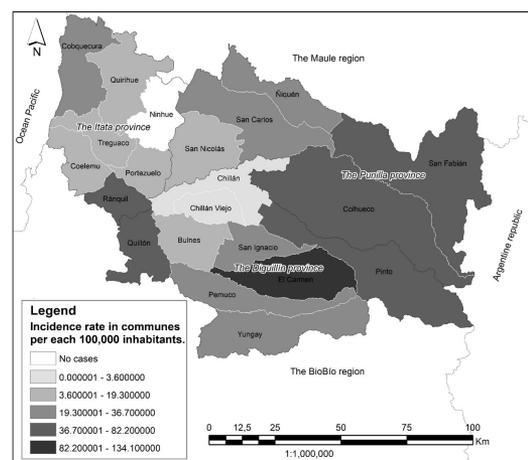
Clinical Variable	Percentage Frequency Men (%)	Percentage Frequency Women (%)	Total Percentage Frequency (%)
SCPH* symptoms	94.6	85.2	92.1
Fever	90.5	85.2	89.1
Myalgias	77.0	66.7	74.3
Headache	75.7	66.7	73.3
Thrombocytopenia	77.0	63.0	73.3
Chest x-ray	60.8	66.7	62.4
Gastrointestinal symptoms	48.6	40.7	46.5
Left deviation	28.4	22.2	26.7
Mild Hanta symptoms	5.4	14.8	7.9

\*SCPH: hantavirus cardiopulmonary syndrome.

**Figure 10.** Distribution of Hantavirus cases by risk factor, Ñuble region 2002-2018.**Figure 11.** Hantavirus cases according to the classification of the place of infection, Ñuble Region 2002-2018.

It is observed that the presentation of the disease for both sexes is mainly HCPS (Hantavirus cardiopulmonary syndrome). When comparing the presentation of mild Hantavirus disease concerning sex, women present a higher percentage. In male cases, the predominant signs and symptoms in decreasing order correspond to fever, myalgia, thrombocytopenia, and headache. While in women, the predominant signs and symptoms are fever, myalgia, headache, chest X-ray, and thrombocytopenia (Table 2).

The most frequent risk factors related to acquiring Hantavirus infection are: residing in rural areas (60 cases),

**Hantavirus incidence rate according to infection commune in the Ñuble region, in the period 2002 - 2018****Figure 12.** Hantavirus incidence rate according to infection commune in the Ñuble region, in the period 2002-2018.

being a farmer or forestry worker (49 cases), going on excursions (17 cases), others (13 cases), and being a contact of one confirmed case (9 cases) (Figure 10).

The largest number of Hantavirus infections (29.6% of cases) occurs in or around the home. Hantavirus infections that occur at work or in surroundings represent 28.6% of cases, and infections in recreational outing activities represent 28.6% of cases. In 13% of cases, there is no report of the site of infection (Figure 11).

The commune with the highest incidence rate of Hantavirus is registered in El Carmen, with 130 per hundred thousand inhabitants, Pinto with 82.4 per hundred thousand inhabitants, and Coihueco with 63.2 per hundred thousand inhabitants (Figure 12).

#### 4. Discussion

Hantavirus disease has undoubtedly been a public health problem in Chile since the late 1990s, which was made known through epidemiological surveillance.

The knowledge that has been generated during these years regarding the disease focuses on prevention behaviors in the community. Also, critical patients have been managed with strict protocols, and the expansion of the ECMO technology in other centers in the country (Reyes et al., 2019).

The objective of the study was to epidemiologically characterize individuals diagnosed with Hantavirus in the Ñuble region, according to the registry of mandatory notifications that have accumulated from 2002 to 2018 in the region. Therefore, allowing support for the implementation and reinforcement of public health policies with local relevance.

This profile exhibits the clinical characteristics, as well as those who are most affected, considering their age, place of residence, risk conditions, and work they usually perform, among others.

This epidemiological profile presents the possibility of observing changes at the regional level indicating guidelines in which the reinforcement of ministerial protocols for patient care is emphasized, from the first stages of diagnosis. Therefore, it is suggested to implement protocols such as strengthening the training of health personnel regarding the early suspicion of the pathology, through the clinical picture, examinations, and epidemiological history. Protocols have been followed to accelerate timely referral to an intensive care unit that has ECMO. A good interpretation of the blood count has an excellent predictive value but requires the availability of both, the test and trained personnel to interpret it (Navarrete et al., 2016).

The time to intervene between the appearance of the first symptoms and the development of the disease and death is very short. The rapid progression of the disease, with only three days between the appearance of the first symptoms and the first consultation, and only two more days between the first consultation and death, make it necessary for health personnel to have widely disseminated and internalized knowledge. Therefore, the health personnel know that there must be always a high suspicion of Hantavirus diagnosis (Ferrés et al., 2010).

Likewise, the rapid test technology is done at the Ñuble regional hospital which is located in the capital city (Chillán). However, to avoid loss of time in the transfer from distant communes to the base hospital and obtain a timely presumptive diagnosis it would be necessary to implement the rapid test technology at least in the care centers of communes with the highest incidence.

Furthermore, it is desirable to have a confirmatory diagnostic test at the Ñuble regional hospital to avoid delays in transporting samples to the ISP (Chilean Institute of Public Health), located 400 km. up north in Santiago de Chile, which is the one that currently confirms the diagnosis of the samples from the region, in an average time of three days. It would be not only useful for the patient who is suffering from the disease, but it would be highly beneficial for the close contacts of the case and those exposed to the source.

It is known that all those who became ill had a positive molecular diagnosis up to fifteen days before starting the prodromal phase (Ferrés et al., 2007). Consequently, allowing early diagnosis and intensive management of severe cases, would reduce lethality (Juneja et al., 2011).

Timely diagnosis and the start of support therapies are the fundamental pillars for the survival of infected patients (Reyes et al., 2019). Therefore, it is important to reinforce the healthcare network in the region with technologies such as ECMO or mobile ECMO, to provide the best care and generate a higher probability of survival in patients with Hantavirus cardiopulmonary syndrome (Wernly et al., 2011; Bugeo et al., 2016; Reyes-Zaldívar and Ferrés, 2019).

The epidemiological profile of the Hantavirus cases in the Ñuble Region shows that its distribution by sex is very similar to that published at the national level: constituting 73% of the cases of the male sex in the region, and 71% of the cases for males in the nation. When disaggregating the age groups of the patients, the regional figures are quite similar to the national reality. The most affected groups at the regional level are those between 20-24 and 30-34 years, with an incidence rate of 3.0 x 100,000 inhabitants each one, and at the national level the age range group 20-29 years old (0.40 x 100,000 inhabitants) and 30-39 years old (0.36 x 100,000 inhabitants) (Sotomayor and Aguilera, 2000). Concerning the most affected age groups in the region, about half of the cases are concentrated between 15 and 34 years.

The incidence rates of the Ñuble region (3.0 x 100,000 inhabitants) are higher than the national incidence rates (0.4 x 100,000 inhabitants) (Reyes et al., 2019). The highest incidence of cases during the period analyzed in the Ñuble region occurred during the years 2003, 2004, 2012, and 2014, with almost half of the total cases accumulated in those years, unlike the country data, which concentrates the highest incidence in the years 2001 and 2002 (MINSAL, 2013).

The lethality in the region, reached the highest value in 2006 at 100%, although with a low incidence (two cases). During the last four years of the period, the incidence has been steadily low and with a downward trend. On the other hand, in the region, there is evidence of a marked lethality in the female sex with 40.7%, above the male, with 28%.

While the lethality caused by Hantavirus in Chile shows a downward trend from 60% in 1997 to 32% in 2011, with some variations in 2006 (43.6%), to reach the lowest figure in 2008 with 20%. Historically, the high lethality in women stands out, reaching 55% in 2006, while in men it was 38% (MINSAL, 2013). A situation that can be related as much as with ecological factors of the Andes virus, the flowering of the quila (*Chusquea quila*) that leaves a large number of seeds, the reproduction and occurrence of "ratadas" (increase in the population of mice) due to the high food availability (Holza and Palma, 2012). Other reasons might be, delay to attend a health service or delay to detect the disease by health members, greater exposure to the virus by individuals visiting places of risk, deficiencies in the health system, or the virulence of the agent itself.

In the Ñuble region the risk factors for acquiring the infection, are mostly being a resident in the rural sector, and a farmer or forestry worker. At the national level, the infection risk rises for people living in the rural sector (Vial et al., 2019).

The incidence according to the place of infection has a homogeneous distribution trend between home, work, and outings in the region. While at the national level, infection in the home or surroundings is present in more than 50% of cases (Vial et al., 2019). The distribution of cases in the Ñuble region occurs mainly in communes with high rurality, especially the foothills of Ñuble, and the communes with the highest number of visitors in the summer. These sectors meet the habitat conditions for the rodent, such as food, shelter, and watercourses. Exceptionally, the commune of Ninhue has never presented cases to date, which could be related to the low presence of the rodent in that area, making it necessary to carry out studies in this regard. The incidence rates in the region correspond to 3.0 per 100,000 inhabitants, while at the national level it represents 0.4 per 100,000 inhabitants. In Chile, the cases are geographically distributed from the southern limit of the Atacama region to the Magallanes region, as in the region, in mainly foothill areas characterized by a high density of vegetation and watercourses (MINSAL, 2017a).

The temporal distribution of cases during the year in the region is similar to that reported in the literature (Puerta et al., 2006). The incidence begins to increase in the spring months and decreases in the autumn months. Isolated cases occur during the winter months, reducing the incidence to zero in September.

Regarding the symptoms present in patients in the Ñuble region, fever and cardiopulmonary syndrome due to Hantavirus stand out, which are found in more than 90% of patients. Concerning other symptoms and signs, myalgias, headache and thrombocytopenia were almost equally frequent, followed by an altered chest X-ray. This is highly correlated with the suspicion algorithm described in the regulations issued by the Ministry of Health of Chile (Reyes et al., 2019; MINSAL, 2017a, b; Ramos et al., 2001).

In the Ñuble region, the analysis of the cases according to symptomatology shows that the investigation of cases of mild Hantavirus occurs in a very low percentage. This can be explained by the lack of detection of mild or oligosymptomatic cases (MINSAL, 2013).

From the onset of symptoms to medical consultation, which is affordable, takes an average of only two or three days, regardless of the person's gender. This could be because the population has been educated in seeking timely medical help when the symptoms are consistent with Hantavirus, or because the symptoms are rapidly progressive and disabling.

Finally, it is necessary to highlight the quality of the records of the ministerial database of the Ñuble region, which allows us to infer that there is optimal notification and registration of cases classified as Hantavirus, which are collected through epidemiological surveillance by the SEREMI Health teams. Records that allowed access to all the information necessary to carry out this study, which provided valuable information to know the profile and distribution of patients, to promote knowledge for the development and implementation of public health policies, both in prevention and treatment, with territorial relevance.

Hantavirus is an endemic disease not easy to eradicate since the species of rodent that transmits it is a protected species and the extreme level of rurality of affected people.

The Ñuble region, according to its social determinants of health, is the most rural in Chile and the second most impoverished according to the MINISTERIO DE DESARROLLO SOCIAL, CHILE CASEN 2017 survey (National Socioeconomic Characterization of Chile).

## 5. Conclusion

The epidemiological profile of the Ñuble region is similar to the national one in terms of the characterization of the individual suffering from the disease. Affected young men are residents in rural areas and mostly from a low socioeconomic segment. Total registered cases of Hantavirus in Chile (45%) are found in the Ñuble region. The communes with the highest number of cases are El Carmen (Diguillin province), Coihueco (Punilla province) and San Carlos (Punilla province). The incidence rate of Hantavirus disease is 7.5 times higher in Ñuble than at the national level.

Consequently, the regional epidemiological profile of Hantavirus cases will make it possible to identify the most affected areas and individuals, thus targeting and optimizing strategies and resources, such as implementing rapid test at communes with higher incidence and have a confirmatory diagnostic test at the Ñuble regional hospital to reduce the incidence and lethality of this pathology in the Ñuble region.

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## References

- BARÓ, M., VERGARA, J. and NAVARRETE, M., 1999. Hantavirus en Chile: revisión y análisis de casos desde 1975. *Revista Médica de Chile*, vol. 127, no. 12, pp. 1513-1523. <http://dx.doi.org/10.4067/S0034-98871999001200015>. PMID:10835761.
- BUGEDO, G., FLOREZ, J., FERRÉS, M., ROESSLER, E. and BRUHN, A., 2016. Hantavirus cardiopulmonary syndrome was successfully treated with high-volume hemofiltration. *Revista Brasileira de Terapia Intensiva*, vol. 28, no. 2, pp. 190-194. <http://dx.doi.org/10.5935/0103-507X.20160032>. PMID:27410413.
- FERRÉS, G.M., SANDOVAL, C.C., DELGADO, B.I., SOTOMAYOR, P.V., OLEA, N.A. and VIAL, C.P.A., 2010. Hantaviriosis: caracterización clínica-epidemiológica de pacientes pediátricos en Chile. *Revista Chilena de Infectología*, vol. 27, no. 1, pp. 52-59. <http://dx.doi.org/10.4067/S0716-10182010000100009>. PMID:20140316.
- FERRÉS, M., VIAL, P., MARCO, C., YAÑEZ, L., GODOY, P., CASTILLO, C., HJELLE, B., DELGADO, I., LEE, S.J. and MERTZ, G.J., 2007. Prospective evaluation of household contacts of persons with hantavirus cardiopulmonary syndrome in Chile. *The Journal of Infectious Diseases*, vol. 195, no. 11, pp. 1563-1571. <http://dx.doi.org/10.1086/516786>. PMID:17471425.
- HOLZA, A. and PALMA, E., 2012. Floraciones de bambúes en Chile y Argentina: actual floración masiva del colihue, historia natural y riesgos asociados. *Revista Bosque Nativo*, vol. 50, pp. 40-46.

- JONSSON, C.B., FIGUEIREDO, L.T.M. and VAPALAHTI, O., 2010. A global perspective on hantavirus ecology, epidemiology, and disease. *Clinical Microbiology Reviews*, vol. 23, no. 2, pp. 412-441. <http://dx.doi.org/10.1128/CMR.00062-09>. PMID:20375360.
- JUNEJA, D., NASA, P., SINGH, O., JAVERI, Y., UNIYAL, B. and DANG, R., 2011. Clinical profile, intensive care unit course, and outcome of patients admitted in intensive care unit with dengue. *Journal of Critical Care*, vol. 26, no. 5, pp. 449-452. <http://dx.doi.org/10.1016/j.jcrr.2011.05.007>. PMID:21737238.
- KHAN, A.S., KSIAZEK, T.G. and PETERS, C.J., 1996. Hantavirus pulmonary syndrome. *Lancet*, vol. 347, no. 9003, pp. 739-741. [http://dx.doi.org/10.1016/S0140-6736\(96\)90082-3](http://dx.doi.org/10.1016/S0140-6736(96)90082-3). PMID:8602007.
- MAGRINI, L. and FACURE, K.G., 2008. Barn owl (*Tyto alba*) predation on small mammals and its role in the control of hantavirus natural reservoirs in a periurban area in southeastern Brazil. *Brazilian Journal of Biology = Revista Brasileira de Biologia*, vol. 68, no. 4, pp. 733-740. <http://dx.doi.org/10.1590/S1519-69842008000400007>. PMID:19197490.
- MARTINEZ-VALDEBENITO, C., CALVO, M., VIAL, C., MANSILLA, R., MARCO, C., PALMA, R.E., VIAL, P.A., VALDIVIESO, F., MERTZ, G. and FERRÉS, M., 2014. Person-to-person household and nosocomial transmission of andes Hantavirus, Southern Chile, 2011. *Emerging Infectious Diseases*, vol. 20, no. 10, pp. 1637-1644. <http://dx.doi.org/10.3201/eid2010.140353>. PMID:25272189.
- MINISTERIO DE SALUD DE CHILE – MINSAL, 2013 [viewed 21 February 2023]. *Guía clínica de prevención, diagnóstico y tratamiento del síndrome cardiopulmonar por Hantavirus* [online]. Santiago: MINSAL. Available from: [https://www.minsal.cl/sites/default/files/files/HANTA\\_imprimir.pdf](https://www.minsal.cl/sites/default/files/files/HANTA_imprimir.pdf)
- MINISTERIO DE SALUD DE CHILE – MINSAL, 2017a [viewed 21 February 2023]. *Boletín de brotes* [online]. Santiago: Ministerio de Salud de Chile, vol. 1, no. 2. Available from: [http://epi.minsal.cl/wp-content/uploads/2017/08/Bolet%C3%ADn\\_Brotes\\_1.pdf](http://epi.minsal.cl/wp-content/uploads/2017/08/Bolet%C3%ADn_Brotes_1.pdf)
- MINISTERIO DE SALUD DE CHILE – MINSAL. DEPARTAMENTO DE EPIDEMIOLOGÍA, 2017b [viewed 21 February 2023]. *Informe síndrome cardiopulmonar por Hantavirus. Situación epidemiológica SE 1-52, año 2017* [online]. Santiago: MINSAL. Available from: [http://epi.minsal.cl/wp-content/uploads/2018/01/hantavirus\\_SE522017.pdf](http://epi.minsal.cl/wp-content/uploads/2018/01/hantavirus_SE522017.pdf)
- MINISTERIO DE SALUD DE CHILE – MINSAL. DIVISIÓN DE PREVENCIÓN Y CONTROL DE ENFERMEDADES. DEPARTAMENTO DE ENFERMEDADES TRANSMISIBLES, 2018 [viewed 21 February 2023]. *Manual de procedimientos para administración de plasma inmune para infección por hantavirus* [online]. Santiago: MINSAL. Available from: [https://diprece.minsal.cl/wrdprss\\_minsal/wp-content/uploads/2018/03/Manual-Administraci%C3%B3n-Plasma-Inmune-Hantavirus.-Versi%C3%B3n-2.0.pdf](https://diprece.minsal.cl/wrdprss_minsal/wp-content/uploads/2018/03/Manual-Administraci%C3%B3n-Plasma-Inmune-Hantavirus.-Versi%C3%B3n-2.0.pdf)
- MINISTERIO DE SALUD DE CHILE – MINSAL. SUBSECRETARIA DE SALUD PÚBLICA, 2012 [viewed 21 February 2023]. *Circular B51/24: vigilancia y control de la infección por Hantavirus* [online]. Santiago: MINSAL. Available from: <https://www.ispch.cl/sites/default/files/documento/2013/04/CIRCULAR%20B51-24%20VIGILANCIA%20Y%20CONTROL%20HANTA%202012.pdf>
- MUÑOZ-PEDREROS, A., GIL, C., YAÑEZ, J., RAU, J.R. and MÖLLER, P., 2016. Trophic ecology of two raptors, Barn Owl (*Tyto alba*) and White-tailed Kite (*Elanus leucurus*), and possible implications for biological control of Hantavirus reservoir in Chile. *The Wilson Journal of Ornithology*, vol. 128, no. 2, pp. 391-403. <http://dx.doi.org/10.1676/wils-128-02-391-403.1>
- NAVARRETE, C., SALDIAS, N.F., MANCILLA, G.M.R., ZAROR, T.M.L. and FERRES, G.M., 2000. Evidencia clínico epidemiológica de la existencia de síndrome pulmonar por hantavirus en Valdivia-Chile desde 1993. *Revista Chilena de Infectología*, vol. 17, no. 3, pp. 233-240. <http://dx.doi.org/10.4067/S0716-10182000000300007>
- NAVARRETE, M., HOTT, M., CAROCA, J., LEYTON, L., VENEGAS, N., ISMAIL, K., SAAVEDRA, F. and OTTH, C., 2016. Correlación entre criterios clínicos y de laboratorio de casos notificados por sospecha de hantavirosis y el resultado de la técnica de referencia. *Revista Chilena de Infectología*, vol. 33, no. 3, pp. 275-281. <http://dx.doi.org/10.4067/S0716-10182016000300004>. PMID:27598275.
- PADULA, P.J., COLAVECCHIA, S.B., MARTÍNEZ, V.P., VALLE, M.O.G., EDELSTEIN, A., MIGUEL, S.D., RUSSI, J., RIQUELME, J.M., COLUCCI, N., ALMIRÓN, M. and RABINOVICH, R.D., 2000. Genetic diversity, distribution, and serological features of hantavirus infection in five countries in South America. *Journal of Clinical Microbiology*, vol. 38, no. 8, pp. 3029-3035. <http://dx.doi.org/10.1128/JCM.38.8.3029-3035.2000>. PMID:10921972.
- PADULA, P.J., EDELSTEIN, A., MIGUEL, S.D., LÓPEZ, N.M., ROSSI, C.M. and RABINOVICH, R.D., 1998. Hantavirus pulmonary syndrome outbreak in Argentina: molecular evidence for person-to-person transmission of Andes virus. *Virology*, vol. 241, no. 2, pp. 323-330. <http://dx.doi.org/10.1006/viro.1997.8976>. PMID:9499807.
- PAN AMERICAN HEALTH ORGANIZATION, 2011. *El control de las enfermedades transmisibles*. 19th ed. Washington: Pan American Health Organization, 976 p.
- PAVLETIC, B.M.V.C., 2000. Hantavirus: su distribución geográfica entre los roedores silvestres de Chile. *Revista Chilena de Infectología*, vol. 17, no. 3, pp. 186-196. <http://dx.doi.org/10.4067/S0716-10182000000300002>
- PUERTA, H., CANTILLO, C., MILLS, J., HJELLE, B., SALAZAR-BRAVO, J. and MATTAR, S., 2006. Hantavirus del nuevo mundo: ecología y epidemiología de un virus emergente en Latinoamérica. *Medicina*, vol. 66, no. 4, pp. 343-356. PMID:16977974.
- RAMOS, M.M., OVERTURE, G.D., CROWLEY, M.R., ROSENBERG, R.B. and HJELLE, B., 2001. Infection with Sin Nombre hantavirus: clinical presentation and outcome in children and adolescents. *Pediatrics*, vol. 108, no. 2, p. e27. <http://dx.doi.org/10.1542/peds.108.2.e27>. PMID:11483837.
- REYES, R., YOHANNESSEN, K., AYALA, S. and CANALS, M., 2019. Estimaciones de la distribución espacial del riesgo relativo de mortalidad por las principales zoonosis en Chile: enfermedad de Chagas, hidatidosis, síndrome cardiopulmonar por hantavirus y leptospirosis. *Revista Chilena de Infectología*, vol. 36, no. 5, pp. 599-606. <http://dx.doi.org/10.4067/S0716-10182019000500599>. PMID:31859801.
- REYES-ZALDÍVAR, F.T. and FERRÉS, M., 2019. Hantavirus: descripción de dos décadas de endemia y su letalidad. *ARS Med: Revista de Ciencias Médicas*, vol. 44, no. 1, pp. 30-39. <http://dx.doi.org/10.11565/arsmed.v44i1.1522>.
- SCHMALJOHN, C. and HJELLE, B., 1997. Hantaviruses: a global disease problem. *Emerging Infectious Diseases*, vol. 3, no. 2, pp. 95-104. <http://dx.doi.org/10.3201/eid0302.970202>. PMID:9204290.
- SOTOMAYOR, V. and AGUILERA, X., 2000. Epidemiología de la infección humana por Hantavirus en Chile. *Revista Chilena de Infectología*, vol. 17, no. 3, pp. 220-232. <http://dx.doi.org/10.4067/S0716-10182000000300006>
- TORO, J., VEGA, J.D., KHAN, A.S., MILLS, J.N., PADULA, P., TERRY, W., YADÓN, Z., VALDERRAMA, R., ELLIS, B.A., PAVLETIC, C., CERDA, R., ZAKJ, S., SHIEH, W.J., MEYER, R., TAPIA, M., MANSILLA, C., BARO, M., VERGARA, J.A., CONCHA, M., CALDERÓN, G., ENRIA, D., PETERS, C.J. and KSIAZEK, T.G., 1998. An outbreak of hantavirus pulmonary syndrome, Chile, 1997. *Emerging Infectious Diseases*, vol. 4, no. 4, pp. 687-694. <http://dx.doi.org/10.3201/eid0404.980425>. PMID:9866751.

- VIAL, C.C., VALDIVIESO, F.R., CUIZA, A.V., DELGADO, I.B., RIBEIRO, G.E., LLOP, E.R., FERRÉS, M.G., REPETTO, G.M.L., RIQUELME, R.O., RIOSECO, M.L.Z., CALVO, M.A., MERTZ, G. and VIAL, P.A.C., 2019. Factores de riesgo socio-demográficos del síndrome cardiopulmonar por hantavirus. *Revista Chilena de Infectología*, vol. 36, no. 4, pp. 428-432. <http://dx.doi.org/10.4067/S0716-10182019000400428>. PMID:31859765.
- VIAL, P.A., VALDIVIESO, F., MERTZ, G., CASTILLO, C., BELMAR, E., DELGADO, I., TAPIA, M. and FERRÉS, M., 2006. Incubation period of hantavirus cardiopulmonary syndrome. *Emerging Infectious Diseases*, vol. 12, no. 8, pp. 1271-1273. <http://dx.doi.org/10.3201/eid1208.051127>. PMID:16965713.
- WERNLY, J.A., DIETL, C.A., TABE, C.E., PETT, S.B., CRANDALL, C., MILLIGAN, K. and CROWLEY, M., 2011. Extracorporeal membrane oxygenation support improves survival of patients with Hantavirus cardiopulmonary syndrome refractory to medical treatment. *European Journal of Cardio-Thoracic Surgery*, vol. 40, no. 6, pp. 1334-1340. <http://dx.doi.org/10.1016/j.ejcts.2011.01.089>. PMID:21900022.