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Could the SARS-CoV-2 Outbreak Cause an Increase in Rickettsia Infection? North Cyprus Observation

Meryem Guvenir[1](ID), Emrah Guler[2](ID), Kaya Suer[3](ID)

[1]Near East University, Vocational School of Health Services, Department of Medical and Clinical Microbiology, Nicosia, Cyprus
[2]Near East University, Faculty of Health Sciences, Department of Medical and Clinical Microbiology, Nicosia, Cyprus
[3]Near East University, Faculty of Medicine, Depatment of Infectious Diseases and Clinical Microbiology, Nicosia, Cyprus

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Abstract

Objective: The aim of the study was to determine the prevalence rate of the Rickettsiae infection during the Turkish Republic of North Cyprus SARS-CoV-2 pandemic according to years.

Methods: This cross-sectional study was carried out during 2016 to 2020. Weil-Felix test is based on cross-reactions which occur between antibodies produced in acute rickettsial infections with antigens of OX (OX 19, OX 2, and OXK) strains of Proteus species. On a lam surface, a small 100 µL of the patient's serum is placed. A single drop of the desired antigen (OX19, OX2 ve OXK) is added, and the resulting suspension is mixed and then rotated for one minute. Visible agglutination is indicative of a positive result and corresponds roughly to a titer of 1:20. Statistical analysis of the data obtained was conducted with SPSS (Statistical Package for the Social Sciences) Demo Ver 22.0 (SPSS Inc., Chicago, IL, USA) program.

Results: Total patient number were 369 (Male: 192, 52%; Female: 177, 48%) and the mean age was 33.40±21.37. The number of patients who found as positive for any of the Rickettsiae infection (OX19, OX2 and OXK) were 15.4% in 2016; 21.1% in 2017; 22.9% in 2018 %; 23% in 2019 and 37.3% in 2020. It has been observed that OX19 and OX2 positivity has increased significantly over the years. It is seen that the Proteus OX19 positive cases in 2020 are significantly higher than in other years (p=0.026). It is found that the positive cases of OX2 positivity in 2020 are significantly higher than in other years (p=0.036). Additionaly, considering the distribution over the years, it was seen that Rickettsiae positive patients increased significantly between 2016 and 2020 (p=0.017). Additionaly, considering the distribution over the years, it was seen that Rickettsiae positive patients increased significantly between 2016 and 2020 (p=0.017).

Conclusion: Our hypothesis is the because of the SARS-CoV-2 pandemic due to the people staying at home the animal population such as rodents' population caused an increase. Therefore, the increase in zoonotic infections should not be ignored and it should not be forgotten that necessary precautions should be taken to prevent these infections from getting out of control.

Keywords: Rickettsiae, SARS-CoV-2, North Cyprus

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Address for correspondence/reprints:
Meryem Guvenir

Telephone number: +90 (542) 850 06 43
E-mail: meryemguvenir@hotmail.com

INTRODUCTION

Rickettsiae are Gram negative obligate intracellular bacteria which include several zoonotic pathogens distributed in the worldwide (1). Rickettsiae genus consist of four group. Typus group Rickettsiae (TGR) include the *R. prowazekii* and the *R. typhi*. Except for the rickettsial diseases inluded the epidemic typhus (*R. prowazekii*), Rocky Mountain spotted fever caused (*R. rickettsii*), Mediterranean spotted fever caused (*R. conorii*), and murine typhus caused (*R. typhi*), at least 10 other rickettsial diseases have been described and attributed to Rickettsia species within the Spotted Fever Group (2,3).

The reservoir of the R. typhi infection are rats (*Rattus rattus* and *Rattus norvegicus*) and the vector is the oriental rat flea (*Xenopsylla cheopis*). The way of transmission is percutaneous inoculation of the microorganisms presentin flea feces (4). Its distribution is worldwide however in the southern areas of the USA, South America, Australia, Southeast Asia, and Southern Europe has been reported as endemic (5). *R. conorii* infection is transmitted to humans by the bite of the brown dog tick name as the *Rhipicephalus sanguineus* and endemic in some areas of Spain and other Mediterranean countries (6). So main transmission way of the TGR are the invasive rodents, specifcally the black rats (*Rattus rattus*), and the brown rats (*Rattus norvegicus*), serve as primary reservoirs. Humans are infected by the contamination of disrupted skin, respiratory tract, or conjunctivae with infected fea faeces (7).

Cyprus is a third largest country in the Eastern Mediterranean and located south of Turkey, west of Syria and Lebanon, North of Egypt, Israel and southeast of Greece. The North part of the Cyprus is consisting of approximately 375 000 population who are Turkish Cypriots (8). The aim of the study was to determine the prevalence rate of the Rickettsiae infection during the SARS-CoV-2 pandemic and compare the other years.

METHODS

Study Group

This cross-sectional study was carried out during 2016 to 2020. Samples were analyzed in a micobacteriology laboratory at Near East Hospital, in North Cyprus. All the suspected cases of Rickettsiae infection visiting the microbiology laboratory of the hospital were enrolled. Samples that were not suitable for transfer or not approved by the center expert were excluded from the study. The study were approval of the Near East University Hospital Ethics Committee (decision number: YDU/2021/94-1390)

Serology

Weil-Felixtest is a nonspecific agglutination test which detects anti-rickettsial antibodies in patient's serum. Weil-Felix test is based on cross-reactions which occur between antibodies produced in acute rickettsial infections with antigens of OX (OX 19 (Code: 524005A, Lorne Laboratory), OX 2 (Code: 522005A, Lorne Laboratory), and OXK (Code: 526005A, Lorne Laboratory)) strains of Proteus species. Typhus group rickettsiae (*Rickettsia prowazekii, R. typhi*) react with *P. vulgaris* OX19, and scrub typhus (*Orientia tsutsugamushi*) reacts with *P. mirabilis* OXK. The spotted fever group rickettsiae (*R. rickettsii, R. africae, R. japonica*, etc.) react with *P. vulgaris* OX2 and OX19, to varying degrees, depending on the species. On a solid surface, a small 100 µL of the patient's serum is placed. A single drop of the desired antigen is added, and the

resulting suspension is mixed and then rotated for one minute. Visible agglutination is indicative of a positive result and corresponds roughly to a titer of 1:20.

Statistical Analysis

Statistical analysis of the data obtained was conducted with SPSS (Statistical Package for the Social Sciences) Demo Ver 22.0 (SPSS Inc., Chicago, IL, USA) program. Person Chi-Square, Fisher's Exact test and Binary Logistic Regression Analysis were used to determine statistical significance and the significance was evaluated at $p < 0.05$.

RESULTS

According to our results between 2016-2020, total patient number were 369 (Male: 192, 52%; Female: 177, 48%) and the mean age was 33.40±21.37. The mean age of Rickettsiae positive patient (95/369, 25.7%) was 33.15±20.28. The number of OX19, OX2 and OXK positive patients were 2/52 (3.8%); 5/52 (9.6%) and 2/52 (3.8%), retrospectively in 2016. The number of OX19, OX2 and OXK positive patients were 1/76 (1.3%); 12/76 (15.8%) and 3/76 (3.9%), retrospectively in 2017. The number of OX19, OX2 and OXK positive patients were 1/70 (1.4%); 13/70 (18.6%) and 5/70 (7.1%), retrospectively in 2018. The number of OX19, OX2 and OXK positive patients were 2/61 (3.3%); 9/61 (14.8%) and 9/61 (14.8%), retrospectively in 2019. The number of OX19, OX2 and OXK positive patients were 3/59 (5.1%); 22/59 (37.3%) and 2/59 (3.4%), retrospectively in 2020.

The number of patients who found as positive for any of the Rickettsiae infection (OX19, OX2 and OXK) were 15.4% in 2016; 21.1% in 2017; 22.9% in 2018 %; 23% in 2019 and 37.3% in 2020.

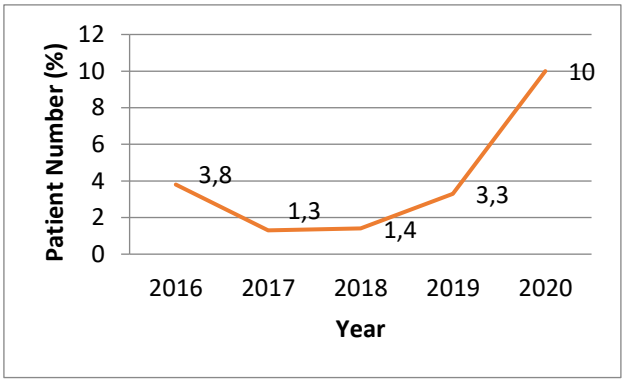

Figure 1. Distrubition of the OX19 positive patient number accrording to the years

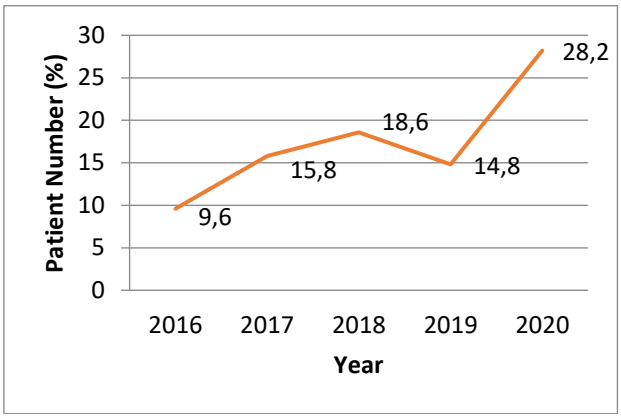

Figure 2. Distrubition of the OX2 positive patient number accrording to the years

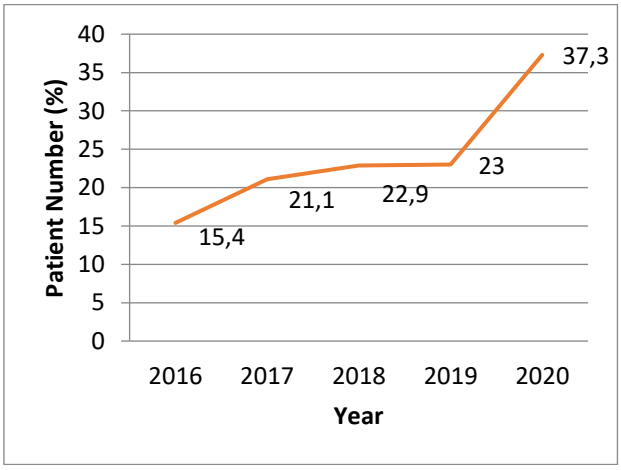

Figure 3. Distrubition of the Rickettsiae positive patient number accrording to the years

It is seen that the Proteus OX19 positive cases in 2020 are significantly higher than in other years ($p=0.026$) (Figure 1). It is found that the positive cases of OX2 positivity in 2020 are significantly higher than in other years ($p=0.036$) (Figure 2).

Additionaly, considering the distribution over the years, it was seen that Rickettsiae positive patients increased significantly between 2016 and 2020 (p=0.017) (Figure 3).

DISCUSSION

Murine typhus (endemic typhus) is a zoonotic infectious disease caused by *R. typhi* (*R. mooseri*), which is an obligate intracellular bacterium. The main syptoms of the disease is headache, rash, and fever (8). The life cycle of murine typhus inluded rats (*Rattus norvegicus* and *R. rattus*) as reservoirs, and their fleas and the main vector is the oriental rat flea *Xenopsylla cheopis* (9). Studies reported that three Rickettsiae spesies have been detected as *R. conorii*, *R. typhi* and *Rickettsia felis* in Southern Cyprus (10,11,12,13). However, enough information is not available on the presence and distribution of fleaborne rickettsiae in in Southern Cyprus. In the study of Christou C et. al, fleas collected from rats between 2000–2003 in 51 areas of all provinces of Southern Cyprus. They were studied with the molecular analysis to distinguish the prevalence and identification of fleaborne rickettsiae. They reported that *R. typhi* was found in 4% of the *Xenopsylla cheopis* and in 6.6% in the *Leptopsylla segnis*. This is the first report of *R. typhi* in *X. cheopis* and *L. segnis* from rats in Southern Cyprus. This study results indicated that the geographic distribution of fleas coexit with the geographic distribution of the pathogen they can harbor, which indicate the potential risk of flea-transmitted infections in Southern Cyprus (14).

Although we are not enough information about the Rickettsiae infections in North Cyprus, we are realized that the Rickettsiae infections has been increases during the SARS-CoV-2 pandemi in North Cyprus. Therefore, the aim of the study was to determine the prevalence rate of the Rickettsiae infection during the SARS-CoV-2 pandemic and compare the prevalence with other years. It is seen that the positive cases of OX2 positivity in 2020 are significantly higher than in other years (p=0.036). Additionaly, considering the distribution over the years, it was seen that Rickettsiae positive patients increased significantly between 2016 and 2020 (p=0.017).

One of the few studies that Economides P. reported that 44.6% of the human population were seropositive to *R. conorii* and 46.8% of the human population were seropositive to *R. typhi* in Southern Cyprus. Also, they indicated that *R. typhi* were isolated from humans with clinical symptoms of rickettsioses during the study (15).

Although there is no explanation about the increase of rodent prevalence from local governments in North Cyprus, patients who participated in our study during SARS-CoV-2 pandemic indicated that they lived in places and / or had contact with a high rodent population in their anamnesis. Bedoya-Perez et al indicated that after ‘lock dowm’ for SARS-CoV-2 pandemic, some local governments and public health authorities related the closures of restaurants and food-related venues to increased prevalence of rats (16). Also, Centers of Disease Control and Prevention was published the report about the Rodent Control during SARS-CoV-2 pandemic on 21 May 2020 (17). Although these study results support our hypothesis, this interaction might be increased the zoonotic infections such as Rickettsiae infections in North Cyprus

Study Limitation

The fact that the study was conducted retrospectively in a single center and the small number of cases are limiting the study.

CONCLUSION

To reduce human mobility in order to prevent transmission during the SARS-CoV-2 pandemic process, all countries were 'lock down'. It has been observed that there is an increase in animal populations as a result of the decrease in human mobility. Therefore, the increase in zoonotic infections should not be ignored and it should not be forgotten that necessary precautions should be taken to prevent these infections from getting out of control.

Ethics Committee Approval: The study was approved by the decision of the Near East University Clinical Research Ethics Committee (26.08.2021 and no: 2021/94).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept: HK, Design: HK, MG Literature search: EG, MG, HK, Data Collection and Processing: MG, HK, EG Analysis or Interpretation: EG, Writing: EG, MG, HK

Conflict of Interest: No conflict of interest was declared by the authors.

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