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Spatial and spatiotemporal clustering of the COVID-19 pandemic in Ecuador

Aglomeración espacial y espaciotemporal de la pandemia por COVID-19 en Ecuador

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Abstract

Introduction: In Ecuador, the first COVID-19 case, the disease caused by the SARS-CoV-2 virus, was officially reported on February 29, 2020. As of April 2, the officially confirmed numbers of COVID-19 cases and deaths from it were 3 163 and 120, respectively, that is, a mortality rate of 3.8%.
Objective: To identify spatial and spatiotemporal clusters of COVID-19 cases officially confirmed in Ecuador.
Materials and methods: Case series study. An analysis of all COVID-19 cases officially confirmed in Ecuador from March 13, 2020 to April 2, 2020 was performed. Relative Risk (RR) of COVID-19 contagion was determined using the discrete Poisson distribution model in the SaTScan software. Clusters were generated using purely spatial and spatiotemporal scan statistics. Significance of each cluster was obtained through 999 iterations using the Monte Carlo simulation, obtaining the most probable random model.
Results: As of April 2, spatiotemporal clustering allowed identifying two clusters in Ecuador, a main cluster in the Guayas province (area: 15 430 km²; population: 3.6 million inhabitants; RR: 7.08; p<0.000001; calculated annual incidence 1700 cases / 100 000 people) and a secondary cluster in the Pichincha province (area: 88 904 km²; population: 7.1 million; RR: 0.38; p<0.000001; calculated annual incidence 737 cases / 100 000 people.)
Conclusions: The implementation of COVID-19 mitigation strategies should be focused on areas of high transmission risk; therefore, spatial, and spatiotemporal clustering with SaTScan can be extremely useful for the early detection and surveillance of COVID-19 outbreaks.
Keywords: SARS-CoV; COVID-19; Coronavirus; Spatio-Temporal Analysis; Disease Clustering; Quarantine (MeSH).

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Resumen

Introducción. En Ecuador el primer caso de COVID-19, la enfermedad causada por el virus SARS-CoV-2, fue reportado oficialmente el 29 de febrero del 2020, y para el 2 de abril, las cifras oficiales de casos confirmados y de muertes ascendían a 3 163 y 120, respectivamente, con una tasa de mortalidad del 3.8%
Objetivo. Identificar aglomerados espaciales y espaciotemporales de los casos de COVID-19 confirmados oficialmente en Ecuador.
Materiales y métodos. Estudio de series de casos. Se analizaron todos los casos de COVID-19 confirmados oficialmente en Ecuador entre el 13 de marzo y el 2 de abril de 2020. El riesgo relativo (RR) de contagio se determinó en el programa SaTScan de acuerdo con el modelo de probabilidad discreta de Poisson, las aglomeraciones espaciales y espaciotemporales se detectaron con la estadística de rastreo espacial y la significancia estadística de cada aglomerado se determinó mediante 999 iteraciones usando la simulación Monte Carlo, obteniéndose el modelo aleatorio más probable.
Resultados. Al 2 de abril, mediante la aglomeración espaciotemporal, fue posible identificar dos aglomerados en Ecuador, uno principal centrado en la provincia de Guayas (superficie: 15 430 km², población: 3,6 millones de habitantes, RR: 7.08; p<0.000001 e incidencia anual calculada: 1 700 casos/100 000 habitantes) y uno secundario centrado en la provincia de Pichincha (superficie: 88 904 km², población: 7.1 millones de habitantes, RR: 0.38, p<0.000001 e incidencia anual calculada: 737 casos/100 000 habitantes).
Conclusiones. La implementación de las estrategias de mitigación del COVID-19 se debe enfocar en áreas de alto riesgo de transmisión; por tanto, los datos sobre aglomerados espaciales y espaciotemporales obtenidos con el programa SatScan pueden ser de gran utilidad en la detección temprana y vigilancia sanitaria de focos de COVID-19.
Palabras clave: SARS-CoV; Coronavirus; COVID-19; Análisis por conglomerados; Análisis espacio-temporal; Cuarentena (DeCS).

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Introduction

The coronavirus disease 2019 (COVID-19), caused by the SARS-CoV-2 virus, is a major threat to human health worldwide.[1] This disease was first reported in Wuhan, China, in December 2019 and has spread rapidly throughout the world. The pervasive spread of the virus is linked to an evolving situation, which could potentially collapse hospitals and medical facilities in countries with weak health systems. COVID-19 transmission is airborne[2] and its estimated basic reproduction number is 2.24-3.58, with an incubation period of 2 to 14 days.[3] The time the virus remains active on copper surfaces, cardboard, stainless steel, and plastic surfaces is 4, 24, 48, and 72 hours, respectively.[4]

As the number of COVID-19 cases increases, governments accelerate the deployment of countermeasures to stop the spread of the virus. There is a major concern that older adults and people with underlying medical conditions may be at higher risk for serious complications if they develop the disease. Morbidity in COVID-19 is associated with pneumonia, respiratory failure, septic shock, and multiple organ dysfunction.[5] Furthermore, the economically active population, especially young adults, are catching and spreading the virus,[6] and the number of people that are asymptomatic virus carriers is unknown as this population has not been tested and it is not clear if they are staying at home.[7]

Ecuador has two centers of population agglomeration, namely, Quito, the capital of the Pichincha province (population 2 011 388) and administrative capital of the country, and Guayaquil, the capital of the Guayas province (population 1 978 376) and the main market and trade center of the country.[8] Both have busy international airports with heavy traffic of people and commodities.

Community mitigation can be interpreted as the tactics and strategies to help slow human-to-human transmission. Social distancing, curfews, and mandatory quarantine and lockdown are among the most effective mitigation strategies.[9] The COVID-19 pandemic can be divided into three phases. The first is the exponential stage, characterized by the growth of contagions without overlapping the detection of cases (that is, since cases start being identified until the end of the outbreak). Then comes the logistic phase, where detection of cases becomes visible; it is dependent on the reproduction rate (R_o) and ends when the fraction of population is x=0.5. Finally, the terminal phase of the pandemic is characterized by a reduction in the number of cases.[10,11]

Community mitigation practices are implemented during the logistic phase of a pandemic because a high proportion of cases is evident at that moment. Governments and health authorities need to balance between taking measurements early before the outbreak (which can have a strong economic impact) or during the logistic phase (with the risk of having a higher number of cases). In fact, community mitigation should be implemented during the exponential phase of a pandemic; however, this does not happen during this phase because the peak of cases is not visible yet. If mitigation tactics are applied in the early stages of a pandemic, before the outbreak, the moment in which the logistic phase of the pandemic is reached will be delayed (buying time for better treatment pathways);[12] additionally, the rate of disease increase will be reduced.

Spatial clusters have become a powerful tool to give an idea of the spatial distribution of a disease using maps. Scan statistics have been developed to test the presence of spatial and spatiotemporal clusters and identify their approximate location.[13] SaTScan (Kulldorf, Cambridge, UK) is a free software to statistically analyze spatial, temporal, or spatiotemporal conglomerates.[14]

To detect clusters, SaTScan moves a circular window around a study region and compares the number of cases found in the window to the number of cases expected under the null hypothesis (random distribution of cases).[15] According to the number of suspected cases, it is established whether they follow a random distribution or if they are distributed according to the Poisson or the Bernoulli probability models.[16]

In this context, the present study seeks to contribute to understanding the COVID-19 pandemic in Ecuador. It could be potentially used in surveillance and to determine clusters that can highlight the heterogeneity of the disease and early detection of COVID-19 outbreaks.

Materials and methods

A case series analysis of confirmed COVID-19 cases reported in Ecuador from March 13, 2020, to April 2, 2020, was performed. Confirmed cases per province were obtained through the situation reports (SITREP) disclosed by the Risk and Emergency Management National Service (SNGRE) - National Emergency Operations Committee (COE) of Ecuador.[17]

To determine the relative risk of a COVID-19 outbreak, the discrete Poisson probability model of the SatScan program was used.[18] The probability model was based on determining the likelihood of finding cases within the cluster over the probability of finding cases outside the cluster.[18] The spatial clusters for cases were generated according to the Kulldorf purely spatial and space-time scan statistics,[14] which consist on determining the most probable cluster radius (likelihood-ratio test) through a circular window of a variable diameter that moves around the study area, with a maximum distance of 50% of the population.[13,16]

For the space-time analysis, the prospective option was used for early detection of disease outbreaks. The analysis made using SITREP data from March 13 to March 15 was purely spatial, with the discrete Poisson scan statistic and scanning for high and low rates. The maximum percentage of the population at risk was the default (50%), high-rate clusters were restricted to have at least 2 cases, temporal trend adjustments and spatial adjustments were not used, and default P-value was utilized for inference. From March 16 to March 26, prospective space-time scan statistics were used; the spatial window allowed 50% of the population at risk, and the maximum temporal cluster size was 50% of the study period. Adjustments for weekly trends, known as relative risks, and spatiotemporal data were not used.

Three datasets were entered into the program: the case file, the population by province obtained from the 2010 Census,[19] and the file with the geographic coordinates for each province.

The hypotheses that were analyzed were 1) null hypothesis: there are no differences in the relative risk of a COVID-19 outbreak in the geographic area analyzed, and 2) alternative hypothesis: there are differences in the relative risk of a COVID-19 outbreak in the geographic area analyzed. The statistical significance of each cluster was obtained through 999 iterations of the most probable model using the Monte Carlo simulation.[20]

Results

In Ecuador, as of March 27, patients with COVID-19 had a median age of 20-49 years. Cumulative deaths and cases are summarized in Figure 1. The highest percentage of cases was found in patients between 20 to 49 years (61%), followed by patients between 50 to 64 years (23%). On March 27, of the 1 627 cases reported at that point, 887 were males (54%) and 750 females (46%). Patient zero arrived in Guayaquil, Ecuador, from Spain on February 14 and was in contact with 175 people during the flight and another 27 people upon arrival. Then, patient zero travelled to the Los Rios province and stayed with his family. On February 29, patient zero was confirmed as positive for COVID-19. The second cluster of infection started with a tourist that arrived in Quito and went to the Sucumbios province. On March 10, ten cases were reported by the Ministry of Public Health of Ecuador. The first official SITREP provided by the national authority was from February 29 to March 13 at 15:00, informing of 23 confirmed cases (11 in Los Rios, 7 in Guayas, 4 in Pichincha, and 1 Sucumbios) (Figure 1, Figure 2a).

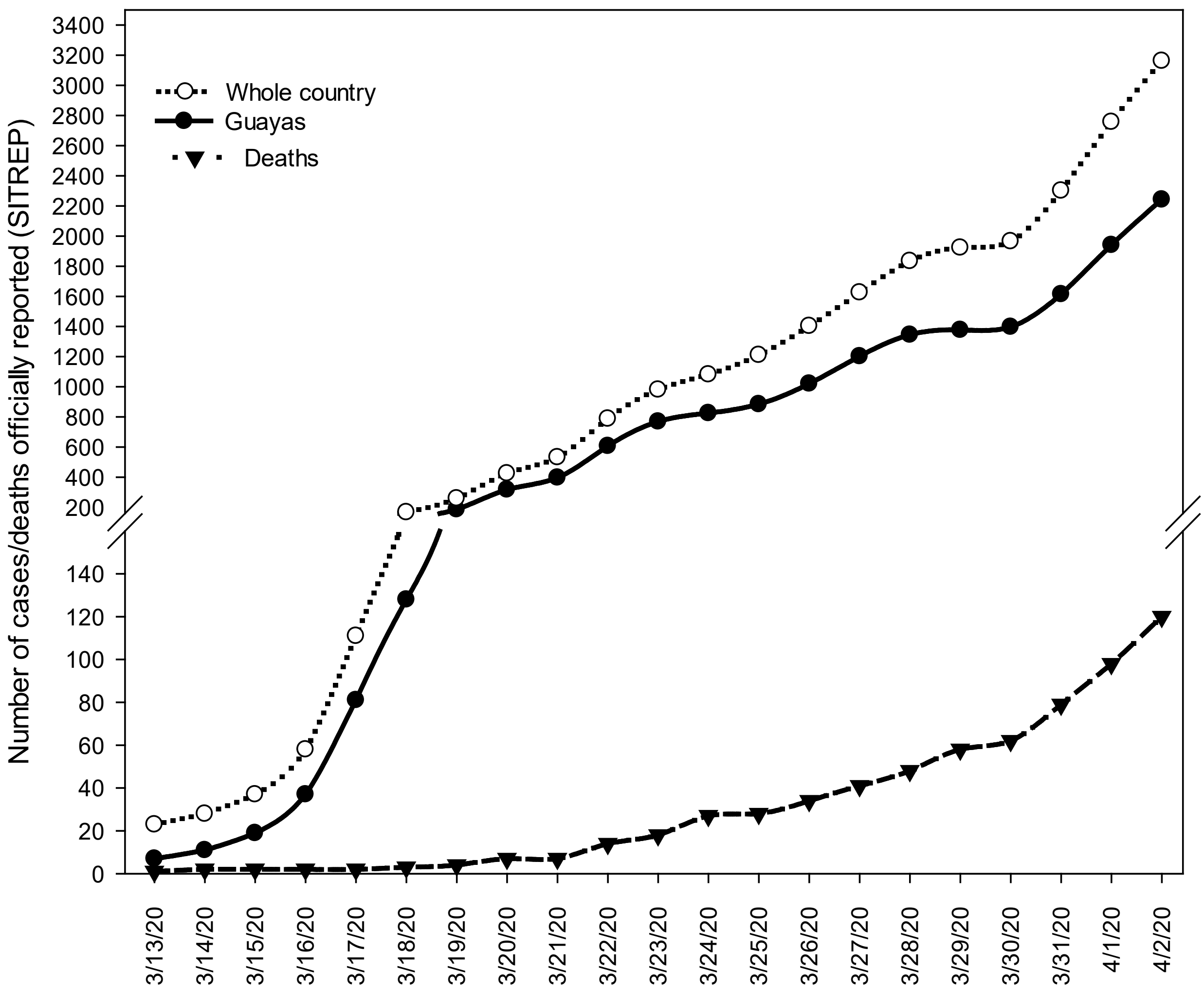

Figure 1. Cumulative number of cases and deaths by COVID-19 in Ecuador and in the Guayas cluster (epicenter of the pandemic in the country), from March 13 (first official situation report - SITREP) to April 2, 2020.
Source: Taken from the National Risk and Emergency Management Service.[21]

The spatial analysis was done in 24 provinces, with a population of 14 451 115 people. As of March 13, the annual incidence of COVID-19 in Guayas was 0.19 cases/100 000 people. Two significant clusters were detected, the main cluster in Los Rios and a secondary cluster in multiple provinces, with the epicenter in Pichincha (Table 1, Figure 2a). For the spatial distribution of the main cluster, a total of 11 cases were detected from a total population of 778 115 in an area of 7 205km^2 (RR=16.11; p=5e-7; log-likelihood ratio 16.89). The secondary conglomerate was generated for a radius of 172.4km (RR=0.22; p=0.084; log-likelihood ratio 4.99) (Table 1, Figure 2a).

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Table 1. Significant spatial and spatiotemporal COVID-19 clusters in Ecuador from March 13 to April 2, 2020.

Date	cluster	method	Centered	time frame	No. cases in cluster	Expected No. of cases	Annual cases / 100 000	Relative risk	p-value
3/13	Main	spatial	Los Rios[1]	NA	11	1.24	516.3	16.11	<0.0001
	Secondary	spatial	Pichincha	NA	4	11.25	20.7	0.22	0.084
3/14	Main	spatial	Los Rios	NA	11	1.56	258.2	10.74	<0.0001
	Secondary	spatial	Pichincha	NA	4	14.19	10.3	0.17	0.0029
3/15	Main	spatial	Guayas - Los Rios[2]	NA	30	11.94	82.6	7.56	<0.0001
	Secondary	spatial	Pichincha[3]	NA	6	19.08	10.3	0.19	<0.0001
3/16	Main	spatiotemporal	Los Rios	3/13-3/13	11	0.79	516.3	16.8	<0.0001
	Secondary	spatiotemporal	Guayas[4]	3/15-3/16	27	7.44	135.3	5.85	<0.0001
	Secondary	spatiotemporal	Pichincha	3/14-3/15	2	14.43	5.2	0.11	0.0033
3/17	Main	spatiotemporal	Guayas-Santa Elena	3/16-3/17	65	12.15	300.2	11.5	<0.0001
	Secondary	spatiotemporal	Pichincha	3/14-3/15	2	21.72	5.2	0.078	<0.0001
3/19	Main	spatiotemporal	Guayas	3/17-3/19	834	176.8	730.7	7.94	<0.0001
	Secondary	spatiotemporal	Pichincha	3/14-3/16	30	342.99	22.1	0.26	<0.0001
3/26	Main	spatiotemporal	Guayas	3-20/3-26	1 021	353.67	1 193.7	10.41	<0.0001
	Secondary	spatiotemporal	Pichincha	3-20/3-26	209	685.97	77.1	0.18	<0.0001
3/27	Main	spatiotemporal	Guayas	3/21-3/27	884	191.3	1 265.3	8.92	<0.000001
	Secondary	spatiotemporal	Pichincha	3/21-3/27	179	371.49	132.1	0.42	<0.000001
3/31	Main	spatiotemporal	Guayas	3/23-3/31	1 008	275.07	1 122.1	5.74	<0.000001
	Secondary	spatiotemporal	Pichincha	3/23-3/31	255	533.52	146.4	0.41	<0.000001
4/2	Main	spatiotemporal	Guayas	3/26-4/2	1 358	303.97	1 700.7	7.08	<0.000001
	Secondary	spatiotemporal	Pichincha	3/26-4/2	327	736.95	736.95	0.38	<0.000001

1 Cluster centered in the Los Rios province: 7 205km^2, population: 778 115 (1.801900 S, 79.534600 W).
2 Cluster centered between the Los Rios province and the Guayas province: 22 635km2; population: 4 423 598 (2.189400 S; 79.889100 W); radius: 58.4km.
3 Cluster centered in the Pichincha province: 88 904km^2; population: 7 070 647; (0.253800 S, 79176300 W); radius: 172.46km.
4 Cluster centered in the Guayas province: 15 430km^2; population 3 645 483; (2.189400 S, 79.889100 W).
Source: Own elaboration.

As of March 15, the observed annual incidence was 32.9 cases/100 000 people. The purely spatial scan statistics with the discrete Poisson model detected two clusters. The main cluster was in Guayas and Los Rios with coordinates 2.189400 S, 79.8891000 W and a radius of 58.35km. The total population within the cluster was 4 423 598; the number of expected cases was 11.94 and the calculated annual incidence was 82.6 cases/100 000 people (RR=7.56; p<0.000001; log-likelihood ratio 17.73.) The second cluster was in Santo Domingo, Pichincha, Cotopaxi, Tungurahua, Imbabura, Esmeraldas, Bolivar, Carchi, Chimborazo, Manabí, and Napo. The coordinates were 0.253800 S, 79.176300 W, with a radius of 172.46km and the calculated annual incidence was 10.3 cases/100 000 people (RR=0.19; p=0.00087; log-likelihood ratio 9.72) (Table 1; Figure 2b).

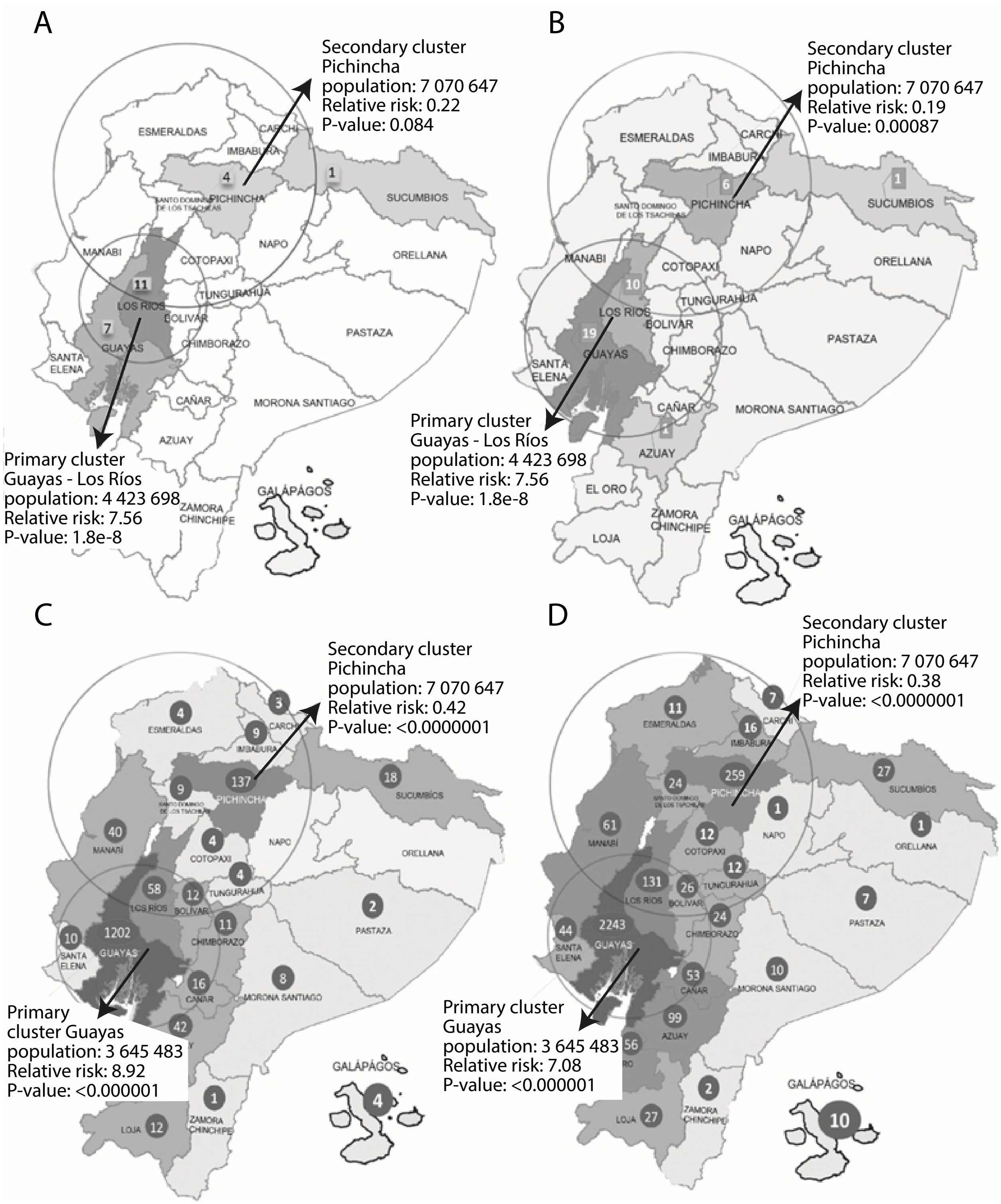

Figure 2. Map of Ecuador (not to scale) showing the main and secondary spatial clusters of the COVID-19 pandemic as of A) March 13, 2020, B) March 15, 2020, and spatiotemporal clusters from C) March 13, 2020 - March 26, 2020, and D) March 13, 2020 to April 2, 2020. Numbers are cases per province.
Source: Taken from the National Risk and Emergency Management Service.[22]

As of March 19, a total of 263 cases reported in 14 provinces were analyzed. Incidence reached 95/100 000. Spatiotemporal analysis with the discrete Poisson probability model detected two clusters. The main cluster included Guayas, Azuay, Cañar, Morona, and Loja with coordinates 2.900100 S, 79.059000 W and a radius of 125km. The time frame of the cluster was from March 17 to 19, with an RR=7.94; p<0.00001; log-likelihood ratio of 167.8, and a recurrence interval of $1x10^{16}$ units. A second cluster was detected, including the provinces of Pichincha, Carchi, Imbabura, Esmeraldas, Pastaza, Chimborazo, and a part of the province of Sucumbíos, with coordinates 0.502700 N, 77.904300 W and a radius of 254.9km. The time frame for the secondary cluster was from March 14 to March 16, with an RR=0.26; p=6.4e-8; log-likelihood ratio of 17.7; and recurrence interval of $1.5x10^7$ units (Table 1).

Community mitigation strategies began with the national emergency declaration on March 3. As of March 17, the national decree of state of exception began with a curfew from 21:00 to 5:00, a lockdown, school and work cancellation, restriction of inter-province transport for 14 days, and restriction of mobility for private transport (curfew order). In Pichincha, the spreading of the virus was controlled by delaying the logistic phase of the COVID-19 pandemic. However, the Guayas province did not follow such restriction measurements, and there was a relaxed lockdown policy in the province, normal activity of public and private transportation, people moving around without personal protection equipment (PPE) or especially masks, and no restrictions on economic activities (street vendors and itinerant sales).

Consequently, a severe outbreak occurred in the Guayas province. As of March 27, the total number of officially reported cases was 1 202 compared to 1 627 total cases in the country. The spatiotemporal analysis detected a significant cluster for Guayas (RR=10.17; p<0.0000001; log-likelihood ratio 856.9; recurrence interval $1x10^{16}$,) and a calculated annual incidence of 1 194 cases/100 000 people (Figure 2c). As of April 2, a total of 9 604 samples were taken, 3 163 cases were confirmed, and 71% (n=2 243) of the cases were reported in the Guayas province. Two highly significant clusters were detected (Figure 2d); the main cluster, Guayas, had a calculated incidence of 1 700/100 000 (RR=7.08; p<0.000001) (Table 1).

Discussion

Evidence of the COVID-19 pandemic in Ecuador, as well as genome clusters with viruses from Europe and New Zealand,[23] support a European origin. Based on the official information, there were two potential clusters for COVID-19 infection in Ecuador. After the positive confirmation of patient zero, two clusters developed within the next 72 hours, from February 29 to March 2. Patient zero was related to the development of the Guayas cluster, and a tourist infected with the virus that traveled from Quito - Pichincha to Sucumbíos was related to the development of the Pichincha cluster. Patient zero traveled from Guayas to Los Rios, and, as of March 3, the incidence in the province of Guayas was low and no significant clusters had been detected. The spread of COVID-19 in the country may have been sudden because there was misinformation that only older adults and people with underlying diseases could become sick; therefore, young people believed that they could not get ill and were not likely to carry the virus.

As of March 27, of the 1 637 cases, 887 cases were males (54%) and 750 were females (46%). Interestingly, demographic data from the Wuhan pandemic showed a similar trend with higher infection rates in males than in females.[24-26] In a study conducted to investigate sex differences in patients with COVID-19, there were significantly more deaths in men compared to women (70.3 % vs. 29.7%; $\chi^2 = 4.45$; p<0.05).[27]

Mathematical modeling of the pandemic, predicting the number of infected patients, and estimating the basic reproduction rate using simple counts of the confirmed cases could be misleading as the actual number of cases is unknown.[28,29] Therefore, more evidence is needed for further pandemic modeling.

The Pichincha cluster was successfully controlled due a strict lockdown and adequate management by the authorities of the COVID-19 emergency. An analysis made by Cereda *et al.*[30] at the epicenter of the outbreak in Codongo- Italy, showed that quarantine played a critical role in reducing the net reproduction rate. However, due to the high number of expected cases (736.95 on April 2), mitigation measures should continue to be practiced.

Relative risk considers the probability of an event (case) in relation to the individual's exposure to the virus.[15] Therefore, as of March 26, there were 10.41 times more probability of finding a case inside the cluster (Guayas province) than outside (p<0.0000001). At the beginning of the pandemic, as of March 16, the main cluster grouped the cases from Guayas and Los Rios, as well as areas from the provinces of Manabí (1 case), and Bolivar and Santa Elena (both provinces with zero cases, respectively), even though a higher number was expected for these provinces. The behavior of the population who did not comply with the mandatory lockdown could jeopardize the mitigation strategies.[31] In Wuhan, epicenter of the global pandemic, the suspension of public transport (inter- and intra-cities), public health interventions and strict mitigation strategies were associated with a delay in the spread of COVID-19 of 2.91 days.[32]

Data from 23 Ecuadorian hospitals and 31 intensive care units showed that 1.27% of total hospital beds were used for the intensive care units, with an average nurse-to-patient ratio of 1:3.4.[33] As the disease spread, an outbreak of cases was reported in the province of Guayas, as well as a collapse of the province's health care system. The number of cases in the main cluster (Guayas province) alarmed the authorities as the mitigation strategies were not effective in controlling the spread of COVID-19. It should be noted that, in 2018, according to the National Institute of Statistics and Censuses (INEC, for its acronym in Spanish), the number of hospital beds per 1 000 people was 1.4,[34] which implied that that they were insufficient to treat severe COVID-19 cases.

The pandemic in Guayas had 2 phases. The first occurred from February 29 to March 13, where the number of reported cases was moderate. However, on April 2, the pandemic exploded; this could be comparable to the 2010 cholera epidemic in Port-au-Prince, Haiti, which also had a two-phase behavior.[15] As of April 2, the spread of the disease in the Guayas province was fast, and the emergency overwhelmed the response capacity of the health system. The Ecuadorian authorities provided additional resources, transferred critical patients to sentinel hospitals, and adapted existing infrastructure to accommodate new diagnosed patients with COVID-19. At this point, it became critical to monitor closely the emerging and active cluster (higher RR).

A similar study conducted in the United States found 8 significant spatiotemporal clusters from January 22 to March 9, 2020. The spatial scan statistics detected the most likely cluster in the epicenter of the U.S.

COVID-19 pandemic, clustering counties in New York, Connecticut, and New Jersey (RR=96.8).[35]

The cluster technique is effective to understand the spatial distribution of an active pandemic. Although this information is useful, more surveillance is needed to understand better which areas are prone to COVID-19 outbreaks. A major limitation of the spatiotemporal analysis, as well as of any kind of prediction or modeling of the disease, is the requirement of accurate data and that, in order to establish adequate and focalized countermeasures, it is necessary to have the actual and up-to-date number of cases.

Conclusions

Mitigation strategies should be enforced in areas with a high risk of transmission. The Guayas province, due to its population and commercial flow, played a significant role in the COVID-19 pandemic in Ecuador. Although mitigation strategies were successfully implemented in the second cluster, that was not the case of the main cluster. This could explain the reduced incidence and delay of the COVID-19 growth in the secondary cluster compared to the main cluster. The COVID-19 behavior evidenced in Ecuador and the findings of this study could be used for implementing better containment or mitigation strategies. Early detection of outbreaks is critical for restarting activities after the lockdown. Finally, spatial and spatiotemporal clustering with SaTScan can be used for surveillance and early detection of COVID-19 outbreaks.

Conflicts of interest

None stated by the authors.

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References

1. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. Nat Med. 2020;26:450-2. http://doi.org/ggn4dn.
2. Zhang R, Li Y, Zhang AL, Wang Y, Molina MJ. Identifying airborne transmission as the dominant route for the spread of COVID-19. Proc Natl Acad Sci U S A. 2020;117(26):14857-63. http://doi.org/ggz2gz.
3. Lai CC, Shih TP, Ko WC, Tang HJ, Hsueh PR. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and corona virus disease-2019 (COVID-19): the pandemic and the challenges. Int J Antimicrob Agents. 2020;55(3):105924. http://doi.org/ggpj9d.
4. España. Centro de Coordinación de Alertas y Eergencias Sanitarias. Información científica-técnica. Enfermedad por coronavirus, COVID-19. Ministerio de Salud; 2020 [cited 2020 Mar 27]. Available from: https://bit.ly/2VGgIYQ.
5. Chang D, Lin M, Wei L, Xie L, Zhu G, Cruz CS, *et al.* Epidemiologic and clinical characteristics of novel coronavirus infections involving 13 patients outside Wuhan, China. JAMA. 2020;323(11):1092-3. http://doi.org/ggkjnh.
6. Velavan TP, Meyer CG. The COVID-19 pandemic. Trop Med Int Health. 2020;25(3), 278-80. http://doi.org/ggpb3j.
7. Bai Y, Yao L, Wei T, Tian F, Jin DY, Chen L, *et al.* Presumed asymptomatic carrier transmission of COVID-19. JAMA. 2020;323(14):1406-7. http://doi.org/ggmbs8.
8. Carvajal AM. Quito se convirtió en la ciudad más poblada del Ecuador con más de 2,7 millones de habitantes en el 2018. El Comercio. 10 de enero de 2019 [cited 2020 Mar 27]; Actualidad. Available from: https://bit.ly/2YSrtt1.
9. Anderson RM, Heesterbeek H, Klinkenberg D, Hollingsworth TD. How will country-based mitigation measures influence the course of the COVID-19 pandemic? Lancet. 2020;395(10228), 931-4. http://doi.org/ggnm7x.
10. Tuite AR, Fisman DN. Reporting, pandemic growth, and reproduction numbers for the 2019 novel coronavirus (2019-nCoV) pandemic. Ann Intern Med. 2020;172(8):567-8. http://doi.org/ggpxzh.
11. Roosa K, Lee Y, Luo R, Kirpich A, Rothenberg R, Hyman JM, *et al.* Short-term forecasts of the COVID-19 pandemic in Guangdong and Zhejiang, China: February 13-23, 2020. J Clin Med. 2020;9(2):596. http://doi.org/ggpxs4.
12. Wu JT, Leung K, Bushman M, Kishore N, Niehus R, de Salazar PM, *et al.* Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. Nat Med. 2020;26:506-10. http://doi.org/dqbq.
13. Kulldorff M. A spatial scan statistic. Communications in Statistics - Theory and Methods. 1997;26(6):1481-96. http://doi.org/dh4cnw.
14. SaTScan v 9.6. Software for the spatial and space-time scan statistics. Boston, MA: SaTScan; 2005 [cited 2020 Jul 2]. Available from: https://bit.ly/2YRIzHG.
15. Piarroux R, Barrais R, Faucher B, Haus R, Piarroux M, Gaudart J, *et al.* Understanding the cholera pandemic, Haiti. Emerg Infect Dis. 2011;17(7):1161-8. http://doi.org/fht9gm.
16. Kulldorf M. Prospective time periodic geographical disease surveillance using a scan statistic. J. R. Statist. Soc. A. 2001;164(Part 1):61-72.
17. Ecuador. Servicio Nacional de Gestión de Riesgos y Emergencias. Samborondón: Gobierno de la República de Ecuador; 2020 [cited 2020 Apr 20]. Available from: https://bit.ly/38nqt3f.
18. Kulldorf M, Nagarwalla N. Spatial disease clusters: Detection and Inference. Stat Med. 1995;14(8):799-810. http://doi.org/cs37sd.
19. Ecuador. Instituto Nacional de Estadísticas y Censos (INEC). Población y Demografía. Quito: INEX; [cited 2020 Mar 27]. Available from: https://bit.ly/2AuHTPa.
20. Mooney CZ. Quantitative Applications in the Social Sciences: Monte Carlo simulation. Thousand Oaks, CA: Sage publications; 1997. http://doi.org/b7hn2m.
21. Ecuador. Servicio Nacional de Gestión de Riesgos y Emergencias. Informes de Situación e Infografias – COVID 19 – desde el 29 de Febrero del 2020. Samborondón: Gobierno de la República de Ecuador; 2020 [cited 2020 Apr 20]. Available from: https://bit.ly/31EUdY4.

22. Ecuador. Servicio Nacional de Gestión de Riesgos y Emergencias. Situación Nacional por COVID-19 (coronavirus). Samborondón: Gobierno de la República de Ecuador; 2020 [cited 2020 Apr 20]. Available from: https://bit.ly/3dPO25T.
23. Nextstrain. Real-time tracking of pathogen evolution. Nextstrain.org; 2020 [cited 2020 Apr 20]. Available from: https://bit.ly/2AnpovM.
24. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet. 2020;395(10223): 470-3. http://doi.org/ggjr42.
25. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, *et al.* Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13. http://doi.org/ggjvv6.
26. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al.* Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9. http://doi.org/ggkh48.
27. Jin JM, Bai P, He W, Wu F, Liu XF, Han DM, *et al.* Gender differences in patients with COVID-19: Focus on severity and mortality. Front Public Health. 2020;8:152. http://doi.org/ggx248.
28. Lipsitch M, Swerdlow DL, Finelli L. Defining the epidemiology of Covid-19—studies needed. N Engl J Med. 2020;382(13): 1194-6. http://doi.org/ggmzsq.
29. Remuzzi A, Remuzzi G. COVID-19 and Italy: what next? Lancet. 2020;395(10231):1225-8. http://doi.org/ggnz74.
30. Cereda D, Tirani M, Rovida F, Demicheli V, Ajelli M, Poletti P, *et al.* The early phase of the COVID-19 outbreak in Lombardy, Italy. arXiv. 2020. [cited 2020 Apr 1]. Available from: https://bit.ly/2yhNCjG.
31. Hafiz H, Oei SY, Ring DM, Shnitser N. Regulating in Pandemic: Evaluating Economic and Financial Policy Responses to the Coronavirus Crisis. Boston College Law School Legal Studies Research Paper [working paper]. Boston: Boston College Law School; 2020 [cited 2020 Mar 26]. Available from: https://bit.ly/3ismEyi.
32. Tian H, Liu Y, Li Y, Wu CH, Chen B, Kraemer MU, *et al.* An investigation of transmission control measures during the first 50 days of the COVID-19 pandemic in China. Science. 2020;368(6491):638-42. http://doi.org/ggqs7x.
33. Ochoa-Parra M, Martínez-Reyes F, Camacho-Alarcón R, Jibaja-Vega M, Morales-Alava, F, Salgado-Yépez *et al.* Prestación de cuidados críticos en Ecuador: características actuales y resultados clínicos. Acta Colombiana de Cuidado Intensivo. 2016;16(3):136-43. http://doi.org/d2wc.
34. Ecuador. Instituto Nacional de Estadísticas y Censos (INEC). Boletín técnico N°-01-2019-ECEH. Registro Estadístico de Camas y Egresos Hospitalarios. Quito: INEC; 2019 [cited 2020 Apr 1]. Available from: https://bit.ly/2NNqPqw.
35. Desjardins MR, Hohl A, Delmelle EM. Rapid surveillance of COVID-19 in the United States using a prospective space-time scan statistic: Detecting and evaluating emerging clusters. Applied Geography. 2020;118:102202. http://doi.org/ggr6tr.