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Spatial analysis of COVID-19 hospitalised cases in an entire city: The risk of studying only lattice data

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HIGHLIGHTS
• Areas with higher incidence of COVID-19 hospitalised patients were determined.
• The areas at higher risk were those with greater economic inequality.
• The exclusive use of lattice data could mask high-risk areas.
• Employing random population controls during pandemics is very useful.
• Implementing this analysis allows an early warning system to be set up.

GRAPHICAL ABSTRACT

ABSTRACT
We live in a global pandemic caused by the COVID-19 disease where severe social distancing measures are necessary. Some of these measures have been taken into account by the administrative boundaries within cities (neighborhoods, postal districts, etc.). However, considering only administrative boundaries in decision making can prove imprecise, and could have consequences when it comes to taking effective measures. To solve the described problems, we present an epidemiological study that proposes using spatial point patterns to delimit spatial units of analysis based on the highest local incidence of hospitalisations instead of administrative limits during the first COVID-19 wave.

For this purpose, the 579 addresses of the cases hospitalised between March 3 and April 6, 2020, in Albacete (Spain), and the addresses of the random sample of 383 controls from the Inhabitants Register of the city of Albacete, were georeferenced.

The risk ratio in those hospitalised for COVID-19 was compatible with the constant risk ratio in Albacete (p = 0.49), but areas with a significantly higher risk were found and coincided with those with greater economic inequality (Gini Index). Moreover, two districts had areas with a significantly high incidence that were masked by others with a significantly low incidence.

In conclusion, taking measures conditioned exclusively by administrative limits in a pandemic can cause problems caused by managing entire districts with lax measures despite having interior areas with high significant...
incidences. In a pandemic context, georeferencing disease cases in real time and spatially comparing them to updated random population controls to automatically and accurately detect areas with significant incidences are suggested. This would facilitate decision making, which must be fast and accurate in these situations.

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1. Introduction

In December 2019, a series of cases of pneumonia of unknown cause took place in Wuhan, Hubei, China whose clinical presentations were similar to viral pneumonia (Huang et al., 2020). On 11 March 2020, the World Health Organization declared that COVID-19 was a global pandemic because it rapidly spread among humans (Mizukoshi et al., 2021). The clinical SARS-CoV-2 infection spectrum seems wide. This disease is characterised by a process covering mild symptoms to serious ones that mainly affect a lung or the gastrointestinal tract and can, ultimately, lead to multi-organ failure (Llorens et al., 2021).

Although considerable research has been conducted about COVID-19 etiology, how risk factors can affect COVID-19 incidence and mortality is still being determined (Lipsitt et al., 2021). Apart from risk factors of a medical kind, other risk factors must be considered because they might be important for COVID-19 development and its disease progression. Overall, then, transmission dynamics of viral infectivity, such as COVID-19, is due to systemic causes; general factors that are the same for all regions (e.g., biological characteristics of virus, incubation period, etc.) and specific factors which are different for each region and/or city (Coccia, 2020a).

The spatial differences between incidence and mortality rates have been associated with very different factors, such as the population’s spatial distribution (control pattern) is necessary to compare it to that of cases (Gonzalez-Rubio et al., 2017). Thus a set of area-risk population controls can be randomly selected to estimate its spatial variation (Prince et al., 2001). This determines which areas have a higher incidence and to accurately study if a correlation exists with other variables, such as socio-economic level.

A methodology to identify areas with a high or low incidence of a given disease can be followed by a geo-epidemiological case and controls study to estimate the spatial variation in the disease’s relative risk. We observe spatial variation in the risk when the intensity function of both cases and controls are not proportional. This reflects the probability of someone from a given location possibly being a case or not (Diggle, 2013).

In spatial epidemiology, cases and controls can be managed as if they were the realisations of two separate inhomogeneous Poisson processes (IPP), and Kernel smoothing techniques are applied to estimate the spatial variation in their intensity (Bivand et al., 2013; Gatrell et al., 1996). To estimate the IPP intensity of λ1 cases (X) and λ0 controls (x), the study employs a standard Gaussian Kernel with the same bandwidth, which is determined by cross validation. Bandwidth h measures the level of smoothing. Silverman (2018) provides methods to select the bandwidth of Kernel smoothers in a general configuration. Using several values according to the considered process and selecting a value that is apparently feasible seem reasonable. Finally, estimating the local prevalence of a given phenomenon is the relative risk or the logarithmic reason of the local intensities of the two IPP (Kelsall and Diggle, 1998).

This study aimed to better understand the factors associated with the heterogeneity of hospitalisation for COVID-19 in the city of Albacete (Spain), one of the city most affected countries by COVID-19 in the first months of this pandemic. The randomness of hospitalised cases in the city was studied and those areas with a statistically significant incidence were sought.

The correlation among the areas with levels of income and inequality was studied. Finally, the advantage of using spatial point patterns analyses, as opposed to the generalised use of works with aggregate data by administrative areas, was analysed in a pandemic context.

2. Material and methods

2.1. Sample, data, and measures of variables

This study was approved by the Ethics Committee of the University Hospital Complex of Albacete. Cases were those patients hospitalised in this complex for COVID-19 during the first wave of the pandemic between 3 March and 6 April 2020 (Romero-Sánchez et al., 2020).

All the cases were diagnosed with COVID-19, as confirmed by a laboratory either by positive serology with immunoglobulin G (IgG)/immunoglobulin M (IgM) antibodies against SARS-CoV-2 in blood or RNA detection of SARS-CoV-2 in nasopharyngeal samples by a real-time polymerase chain reaction (rt-PCR) with reverse transcriptase. From this database, the following were obtained: address (street name and number), the date and time admitted to hospital, sex and
The sample included 946 hospitalised patients. Of them, the cases whose addresses were not located in Albacete or outside its city centre were eliminated. This left a sample of 579 positive SARS-CoV-2 patient cases admitted to hospital.

In order to perform a suitable analysis, it is necessary to have a big enough number of representative controls to acquire information about population characteristics. Moreover, georeferencing these controls informs us about the population density in each area, among other factors. This was how the controls were obtained from a random inhabitants sample obtained from the municipal Inhabitants Register held by the Albacete City Council. European legislation about personal data protection was taken into account. A necessary sample size was determined for a 95% confidence level and a 5% estimation error for a city with 174,000 inhabitants. The inhabitants register provided the anonymous data of 400 randomly selected people, which indicated their address, sex and age. For the purpose of respecting their anonymity, the inhabitants register randomly added or deducted 0 or 2 to the street number. This operation minimally modified (e.g., a dwelling to the left or the right) controls’ locations but did not affect the spatial analysis. It also ensured controls’ anonymity.

After acquiring the data, the controls whose addresses were located in boroughs of Albacete were removed. This left 383 controls located in the city centre. Each event (cases and controls) was georeferenced by Coordinates X and Y using coordinates UTM, ETRS 89 ZONE 30 to study spatial randomness by point patterns.

2.2. Data analysis procedure

The spatial randomness study was performed according to the methodology described for the spatial variation in relative risk in accordance with Bivand et al. (2013). The Monte Carlo test (Kelsall and Diggle, 1998), which is based on the null hypothesis that the cases (hospitalised for COVID-19) and controls (randomly selected from the population) have the same spatial distribution, means that cases have a random spatial distribution. If we randomly simulated (several times) the labelling of the cases and controls for all the events in the study area, the new series of cases and controls would have the same spatial distribution as the original one. If this were not so, relabelling cases and controls would lead to different patterns, and the random distribution of cases hospitalised for COVID-19 would be ruled out.

After studying the spatial randomness in the city as a whole, the areas with a significant incidence were sought. This meant that the contour lines served to delimit the areas for which the associated p-value was over or below the given threshold value (0.05 and 0.95) using the R software. In this study, we preferred using automatic methods as a guide to estimate bandwidth.

After determining the areas with a significant incidence, the correlation with the socio-economic level was studied. To do so, the different layers of the Atlas of the Distribution of Household Incomes were used, prepared by Spanish National Statistics Institute (INE [data can be accessed at https://www.ine.es/experimental/atlas/experimental_atlas.htm]) data from the Spanish Tax Agency (INE), were employed:

1. A person’s mean income. For each home, it is calculated by dividing the home’s total income by the number of members living at that home.
2. The Gini Index. The Gini Coefficient is a measure of income inequality distribution (presented as a value between 0 and 1, where 0 represents a perfectly equal geographical region where all incomes are equally shared, and 1 represents a perfectly unequal society where everybody’s incomes are obtained by only one person).

For the data analysis, ArcGis 10.8. (developed by the Environmental Systems Research Institute) and R Software R-4.0.5 were employed. ArcGis has been employed to process maps in the shapefile (shp) format, while R has been used to make statistical calculations (analyses of spatial point patterns) and to work with the maps in the shp format created with ArcGis. The most used R packages in this work were: splancs, spatstat, sp., maptools, rgdal, RColorBrewer, lattice, nortest, Rcmdr and spdep.

3. Results

Table 1 shows the number of hospitalisations during the first wave per week (from 3 March to 6 April 2020), who were included in the study using ALBACOVID data (Romero-Sánchez et al., 2020). As we previously indicated, 593 cases were included, made up of 341 men (57.5%) and 252 women (42.5%), with a statistically significant difference (p < 0.05). The number of cases rose in the first 4 study weeks and reached 256 hospitalisations in a single week. In week 5, they lowered to 35. As not all the cases were discharged weekly, healthcare pressure peaked in week 5. The mean age of those in hospital was 66.9 years over the 5 weeks. This age was not constant with a maximum mean age of 75.3 years in week 1.

3.1. Spatial analysis

Fig. 1 shows the 579 georeferenced cases hospitalised for COVID-19 from 3 March to 6 April 2020 and the 383 controls from the city of Albacete. These points are limited by a window (shp of the polygon) developed by ArcGis to delimit the analysed area and to allow subsequent analyses.

First of all, we studied if randomness appeared in the spatial distribution of cases in the city of Albacete as a whole. The Monte Carlo test is based on the fact that cases and controls are equally distributed according to the null hypothesis. The results were not significant (p-value of 0.49), which indicates that the observed risk ratio was consistent with a constant risk ratio. Cases were randomly distributed in the city on the whole.

When we repeated the process only with men (cases and controls) and only with women (cases and controls), the results were not significant (p-value: 0.36 and p-value: 0.70); that is, distributions were also random.

Then the areas inside the city where the incidence was significant were searched. Fig. 2 shows the main (red) and minor (blue) contours of significant incidence. Four areas where the incidence was higher were identified: two in the central zone and two on the outskirts (NE and S areas). Six regions with a less significant incidence were identified, which generally lay on the outskirts.

Fig. 3 depicts the areas with a significant incidence on a layer with districts of Albacete. The areas with high and low incidences do not coincide with administrative limits.

The four areas with a significantly higher incidence cover part of the  La Estrella, Polígono de San Antón, La Pajarita, Carretas, El Pilar, Industria, Feria, Fátima, Villacerrada, Franciscanos, Santa Teresa, Pedro Lamata, Sepúlcalo, Universidad, Parque Sur, Hospital and Medicina districts. The six areas with a significantly lower incidence correspond to a part of the Universidad, la Milagrosa, Hospital, Industria, San Antonio Abad, Villacerrada, Los Llanos, Cañicas, El Pilar, Feria, San Pablo, Vereda and San Pedro districts. In this way, we find districts with areas with

| Table 1 |
| HOSPITALISED CASES IN WEEKS 1 TO 5 OF THE FIRST WAVE PER SEX, ALONG WITH THEIR MEAN AGE PER WEEK. |
| Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Total |
|---|---|---|---|---|---|
| Cases |
| Men | 4 | 35 | 107 | 149 | 34 | 329 |
| Women | 5 | 23 | 71 | 120 | 31 | 250 |
| Total | 9 | 58 | 178 | 269 | 65 | 579 |
| Age |
| Mean (years) | 4 | 35 | 107 | 149 | 34 | 329 |
higher and lower incidences. A description containing only areas of incidence per district or administrative limit would not be suitable.

Another way of representing the areas with a higher incidence is by a Kernel density map, like those depicted in Fig. 4. Three maps are shown: one with the total incidence (A) and two for sex (B men and C women). They represent incidence by different tones of red, whereby darker areas have a higher incidence and lighter ones a lower incidence. The zones delimited by a white dashed line are those with a significantly higher incidence than the average in the study area. The areas delimited by a black line have a significantly lower incidence. In qualitative terms, no large differences appear in the distribution of incidence per sex.

3.2. Correlation with socio-economic variables

Fig. 5 depicts the mean income per person (A) and inequality or the Gini Index (B) overlapping the map of districts, and they overlap on the areas with a higher incidence (C and D, respectively). Fig. 5A and C shows the areas with a lower mean income per person (red) and those with a higher mean income per person (green). Most of the areas with a higher incidence correspond to the areas with a lower mean income per person, except some regions or districts where incomes exceed the mean. This effect is corrected in Fig. 5B and D by including the Gini Index, which illustrates inequalities. These districts include very different income areas that are masked when considering the district’s mean value. Thus, Fig. 5D indicates that the maximum incidence areas, where income was higher, correspond to the areas with more economic inequality. The joint interpretation of Fig. 5C and D shows that the maximum incidence occurs in those areas with lower mean incomes per person or with more economic inequalities.

3.3. Temporary evolution

Finally, to study spatio-temporary evolution, Fig. 6 includes three Kernel density maps that correspond to weeks 1 (from 3 to 8 March 2020), 3 (from 16 to 22 March) and 5 (from 30 March to 6 April) during the first COVID-19 wave in Albacete. The first infection points (week 1) specifically concentrate in three zones or districts. With time (weeks 3 and 5), the spatial distribution of the number of cases or incidence at these points increases.

3.4. Comparing spatial point patterns to aggregate data

Fig. 7A shows the value obtained by dividing the number of cases in each district by the sum of cases and controls. This provides the districts of Sepulcro (value of 1, no controls), La Estrella (value of 0.89), Pedro Lamata (0.91), Feria (0.73), Polígono San Antón (0.71) and La Pajarita (0.70). They all have a higher incidence if we bear in mind only the data of the administrative limits according to cases and controls. This
figure also includes the areas with a higher (red lines) and lower (blue lines) significant incidence determined by the spatial point patterns analysis; that is, without considering administrative limits. **Fig. 7B** and **C** provides details of two districts in which the calculated incidence value, namely district El Pilar with 0.56 and district Universidad with 0.57, is a relatively low mean value. This coincides with two areas with a high (red line) and low (blue line) significant incidence. Thus, by considering only the mean incidence per district, their reality would be masked by two zones with a very different incidence.

### 4. Discussion

This work studied the spatial distribution of cases hospitalised for COVID-19 during the first wave in the city of Albacete (Spain). Areas
with a statistically significant incidence were sought. The possible correlation of these areas with levels of income and inequality was also studied. Finally, the advantage of employing a spatial point patterns analysis over the widespread use of administrative zones in a pandemic context was analysed.

The fact that grouping geographical cases could help to identify the cause of disease is well-established, which is the basis of modern epidemiology (Gonzalez-Rubio et al., 2018). During a pandemic, grouping cases can help to take measures to a greater or lesser extent in well-delimited areas with a higher incidence. Administrative limits are often used to study case clusters to evaluate incidences in closed areas, which conditions decision making. However, these administrative limits can be arbitrary and based on the structure of cities or their administrative units, which may lead to mistaken results when studying how a pandemic evolves. Moreover, and more often than not, they do not coincide with the limits that the population dynamics itself would generate (Zhong et al., 2014). The mistakes that would arise by exclusively processing only aggregate data might be due to either the edge effect, or areas with a significantly low incidence compensating those areas with a significantly high incidence in the same district, which was the case in our study. Here we show two examples: districts El Pilar (0.56) and Universidad (0.57) do not have the highest incidence in the city and, if measures are taken by administrative limits, they might not be included in possible mobility restrictions or limitations. However, according to the spatial point patterns analysis these two districts have internal areas with a significantly high incidence (Fig. 7B and C).

Thus, we obtained areas with a significantly high incidence that were masked in districts with the lower mean incidences calculated...
for the administrative area. If measures had been taken per district, measures could have been lax in those areas with a significantly high incidence, which would pose a public health problem. The point patterns analysis is more accurate when seeking disease clusters. In a pandemic context, having up-to-date and georeferenced random population controls available would be very useful for accurately detecting disease clusters in cities. Once these clusters are detected, layers can be overlapped with the desired administrative limits. Thus, apart from increasing the accuracy when delimiting areas, it is also possible to better study their relation to other variables, as we did by studying the spatial correlation with levels of income and inequality.

In the presence of the novel Coronavirus Disease and other new viral agents, one of the fundamental problems in science is the evaluation of environmental and social weaknesses of cities/regions. (Coccia, 2020b). The COVID-19 pandemic has evidenced vast inequality at all socioeconomic levels. The findings obtained by this study suggested a correlation between income inequality and COVID-19 hospitalisations. Our results revealed that most areas with a higher hospitalisations incidence corresponded to areas with a lower mean income per person, which also clearly appeared when the Gini index was applied, which illustrates inequalities (Fig. 5).

With the obtained data, we found that the socio-economic level can influence the risk of being hospitalised. The spatio-temporal analysis also pointed out that the areas with a higher hospitalisations incidence, which continued throughout the first wave, were apparently related to the socio-economic level. This stressed the impact that income inequalities can have on the risk of being hospitalised for COVID-19. The inequalities we observed in Albacete have also been described elsewhere (Mari-Dell'Omo et al., 2021; Mollalo et al., 2020; Whittle and Diaz-Artiles, 2020), and are linked with living and working conditions, and certainly increase the already present underlying inequalities. Structural inequalities also contribute to heightened exposure to COVID-19. Minorities and people living in low-income households are more likely to work in industries that have remained open during nonessential business closures. They are also more likely to live in crowded conditions and multigenerational households that may elevate exposure and limit options for quarantining family members (Raifman and Raifman, 2020).

Moreover, people with higher income are capable of staying in housing types that favor social distancing (Clouston et al., 2021), while more unfavoured urban areas have a higher population density, which makes social distancing difficult.

Besides, the more unfavoured individuals suffer more chronic disorders and are more vulnerable to COVID-19. Finally, data about prevent measures and containing diseases might not be communicated or diffused in a uniform manner to the whole population (Mari-Dell'Omo et al., 2021). We must bear in mind that COVID-19 started spreading to the population, and the corresponding information was also transmitted among individuals, which doubtlessly influenced the spread pattern and distribution of this disease throughout cities (Liu et al., 2016; Zhan et al., 2018).

Finally for future studies, it would be interesting to know the number of deceased patients instead of hospitalised patients to be able to calculate death rates per zone. It must be taken into account that these mortality data were not available during the first wave and, what more importantly, the certainty that the deaths that occurred outside hospitals were actually caused by COVID-19 was unknown because services and PCR tests were lacking then.

4.1. Study limitations

Only the data of the patients admitted to the city's public hospital complex for COVID-19 were analysed. This means that no cases were included who did not have to be hospitalised or were in private hospitals. During the first wave, lack of means and not being able to make a quick and reliable diagnosis made it practically impossible to confirm if outpatients were actually positive for COVID-19. Moreover, not including cases hospitalised in private centres could have biased the result because these patients with private healthcare insurance policies tend to be more economically well-off and would, therefore, live in areas with a higher mean income per person. Nonetheless, very limited data were published at that time, which made it impossible to differentiate between some hospitalised cases and others.

We are unaware if the distribution of cases followed the same pattern for the population with less serious symptoms and did not have to be hospitalised.

Finally, the elderly are at more risk of being hospitalised if they are infected by SARS-CoV-2. As our study was based on hospitalised cases, perhaps those areas in which more elderly citizens concentrate have a higher incidence, which coincides with more city centre areas.

5. Conclusions

Areas with a significantly many or a few hospitalised patients for COVID-19 incidence can be sought. Those areas at significantly low risk of being hospitalised lie on the outskirts and coincide with areas with less economic inequality, whereas areas with a significantly higher risk coincide with those with more economic inequality according to the Gini index, and not with administrative limits. This needs to be considered when contemplating prevention policies.

Making decisions during a pandemic based exclusively on administrative limits is unsuitable because certain lax measures could be taken in some districts despite including areas with a very high incidence by being masked by others with a lower incidence.

In the pandemic context, georeferencing disease cases in real time and performing their spatial analysis by comparing to up-to-date random controls are suggested as an epidemiological follow-up tool. This would automatically and accurately allow the detection of those areas with a significant incidence and would help decision making. In any case, evaluating its practical application in the future would be necessary because it could imply many difficulties.

CRediT authorship contribution statement

Marta Garcia-Morata: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization, Supervision
Jesus Gonzalez-Rubio: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration
Tomas Segura: Formal analysis, Investigation, Data curation, Supervision
Alberto Najera: Conceptualization, Methodology, Formal analysis, Investigation, Writing – review & editing, Visualization, Supervision, Project administration

Declaration of competing interest

We have no conflicts of interest to disclose.

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