Syndemic and syndemogenesis of low back pain in Latin-American population: a network and cluster analysis

On behalf of GEEMA (Grupo de Estudio Epidemiológico de Enfermedades Músculo Articulares) and Group COPCORD-LATAM (Explicar la

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ORIGINAL ARTICLE

Syndemic and syndemogenesis of low back pain in Latin-American population: a network and cluster analysis

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Abstract

Introduction Although low back pain (LBP) is a high-impact health condition, its burden has not been examined from the syndemic perspective.

Objective To compare and assess clinical, socioeconomic, and geographic factors associated with LBP prevalence in low-income and upper-middle-income countries using syndemic and syndemogenesis frameworks based on network and cluster analyses.

Methods Analyses were performed by adopting network and cluster design, whereby interrelations among the individual and social variables and their combinations were established. The required data was sourced from the databases pertaining to the six Latin-American countries.

Results Database searches yielded a sample of 55,724 individuals (mean age 43.38 years, SD = 17.93), 24.12% of whom were indigenous, and 60.61% were women. The diagnosed with LBP comprised 6.59% of the total population. Network analysis showed higher relationship individuals' variables such as comorbidities, unhealthy habits, low educational level, living in rural areas, and indigenous status were found to be significantly associated with LBP. Cluster analysis showed significant association between LBP prevalence and social variables (e.g. Gender inequality Index, Human Development Index, Income Inequality).

Conclusions LBP is a highly prevalent condition in Latin-American populations with a high impact on the quality of life of young adults. It is particularly debilitating for women, indigenous individuals, and those with low educational level, and is further exacerbated by the presence of comorbidities, especially those in the mental health domain. Thus, the study findings demonstrate that syndemic and syndemogenesis have the potential to widen the health inequities stemming from LBP in vulnerable populations.

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Key points

• *Syndemic and syndemogenesis evidence health disparities in Latin-American populations, documenting the complexity of suffering from a disease such as low back pain that is associated with comorbidities, unhealthy habits, and the social and regional context where they live.*

• *The use of network and cluster analyses are useful tools for documenting the complexity and the multifaceted impact in health in large populations as well as the differences between countries.*

• *The variability and impact of socioeconomic indicators (e.g., Gini index) related to low back pain and comorbidities could be felt through the use of cluster analysis, which generates evidence of regional inequality in Latin America.*

• *Populations can be studied from different models (network and cluster analysis) and grouping, presenting new interpretations beyond geographical groupings, such as syndemic and inequity in health.*

Keywords Latin-American population · Low back pain · Network analysis · Syndemic · Syndemogenesis

Introduction

Low back pain (LBP) is a complex musculoskeletal condition that is increasingly becoming prevalent in the global population because of sedentary lifestyles. It is thus considered the leading cause of disability worldwide, as it adversely affects the quality of life and compromises one's ability to engage in everyday activities, thus limiting productivity and economic independence of affected individuals [1]. LBP is recognized as a major public health problem in high-income countries, due to its high prevalence in the population strata that are in the most productive stage of life and the financial burden that it imposes on the public health systems [2, 3].

The worldwide LBP prevalence has been estimated at 7.3% [2]. The Global Burden Disease (GBD) group has assessed LBP, along with 315 other conditions, in 195 countries with different levels of development. The findings yielded by these investigations indicate that, between 1990 and 2016, the years lived with disabilities (YLDs)—as an important measure of disability burden on an individual—has increased by 54% in LBP [3, 4]. Moreover, the GBD group reported that 20% of adults suffering from acute LBP will develop chronic pain, and although fewer than 28% of these individuals have a severe disability, they account for 77% of the recorded YLDs [2–4].

Numerous individual-level factors (such as high body mass index, renal disorders, smoking, sugary drink intake, occupational hazards, and ergonomic risks) have been associated with LBP chronicity and severity [4, 5].

Syndemic is a process that allows documenting the disease impact on human health in the presence of other exacerbating factors, such as individual characteristics or socioeconomic conditions that undermine human health and lead to health disparities within the society [6, 7]. The synergistic interplay between various medical conditions and other individual and societal factors is the focus of the syndemic approach, pertaining to the "interacting, co-present, or sequential disease and the social environment factors that promote and enhance the negative effects of diseases interaction" [6]. Similarly, syndemogenesis is defined as the "process, pathway, and stages of syndemic development involving a disease-social context and disease-disease interactions, to acknowledge the health or social conditions that underlie the syndemic-causing illness" [7].

In 2018, the Latin American Group on the Study of Rheumatic Diseases in Native Peoples (*Grupo Latino Americano de estudio De Enfermedades Reumáticas en Pueblos Originarios*—GLADERPO) published a study that demonstrated the syndemic relationship among rheumatic diseases, comorbidities, and socioeconomic status [8]. These findings, obtained by using big data tools and syndemic concepts, have motivated the present study as a part of which the same analytic and conceptual strategies were applied to a larger sample of Indigenous and Mestizo populations in six Latin-American countries.

The study was guided by the hypothesis that LBP is a syndemic condition that produces syndemogenesis, which was tested by performing complex analyses on regional datasets containing community-level data. Specifically, Community Oriented Program for Control of the Rheumatic Diseases (COPCORD) [9] methodology was applied to examine the prevalence and syndemogenesis of LBP in six Latin-American countries.

Objective

The objective of this study was to compare and assess clinical, socioeconomic, and geographic factors associated with LBP prevalence in low-income and upper-middle-income countries using syndemic and syndemogenesis frameworks based on network and cluster analyses.

Materials and methods

Secondary analysis based on network and cluster analyses were conducted using the data sourced from the database created as a part of COPCORD collaboration with Latin-American countries [8, 10].

Case definition

LBP was defined as pain in the lumbar region during the last seven days or at some point in their life whether or not associated with trauma, and then the rheumatologist reviewed these patients to corroborate the diagnosis of LBP classifying it into two groups: (1) mechanical and (2) inflammatory in the original studies [10].

Data sources

A model was developed for the present study, incorporating both individual- and community-level data. The individual variables of interest were obtained directly from the respondents, and included socioeconomic factors (age, educational level, ethnicity, access to health services), pain (current and historical), self-reported comorbidities, self-reported LBP corroborated by a rheumatologist, and functional capacity (Health Assessment Questionnaire-Disability Index, HAQ-DI) [11]. The aforementioned information was obtained from the epidemiological database created by the GEEMA (*Grupo de Estudio Epidemiológico de Enfermedades Músculo Articulares*) based on the previous studies conducted in five regions of Mexico [12], as well as the COPCORD-LATAM (Latin-American) database consisting of information gained through epidemiological studies conducted in Colombia [13], Ecuador [14], Perú [15], and Venezuela [16]. In addition, the GLADERPO base was consulted to access information obtained through epidemiological studies focusing on eight Indigenous communities in Argentina [17], Ecuador [18], México [19–21], and Venezuela [22]. The information obtained through these prior investigations pertained to adults (i.e., $\geq$ 18 years old) affected by musculoskeletal discomfort and/or diagnosed with rheumatic diseases. These studies were conducted at the community level using COPCORD methodology. Briefly, trained community personnel applied COPCORD questionnaire (pain characteristics, disability, coping strategies, and health seeking behavior) in a door-to-door survey. Individuals reporting musculoskeletal pain, stiffness, or swelling in the last seven days and/or at any point during their lifetime were evaluated by participating physicians to classify or diagnose any rheumatic disease and socioeconomic variables, as well as items included in the Health Assessment Questionnaire-Disability Index (HAQ-DI) [9, 12]. The definition of LBP for the calculation of prevalence and all other analysis was LBP including mechanic and inflammatory.

The social-level or collective/contextual variables that represent the average behavior per country incorporated in the model developed as a part of this investigation included the carbon dioxide emissions per capita, Human Development Index (HDI), income inequality, Gini coefficient, income inequality quintile ratio, inequality in life expectancy, life expectancy at birth, mean years of educational attainment, and total unemployment rate (as well as female to male ratio), as explained in more detail in Supplementary File 1 [23].

Analysis

A descriptive analysis was performed on the variables included in the theoretical model, and the findings are reported as measures of central tendency (media and median) and dispersion (standard deviation, SD, and interquartile range, IQR) for continuous variables and as absolute and relative frequencies for ordinal as well as nominal or categorical variables. For each of the study variables, a bivariate analysis was performed as a part of analysis of variance (ANOVA), reporting two-tailed *p* value for continuous variables and the chi-squared test was used to compare prevalence and percentages, while the comparison of mean values was done by Student's *t* test. *p*-values ≤ 0.05 were considered significant; 95% confidence intervals (95% CI) were reported.

A multivariate analysis using a multiple stepwise logistic regression analysis was used which included the LBP (with or not with) as the dependent variable and we included sociodemographic, disability, and self-reported comorbidities with clinical relevance and/or statistical significance ($p \leq 0.05$) as independent variables. The logistic models were evaluated using the Hosmer–Lemeshow test. Stata v16 for Mac statistical software was used (StataCorp, College Station, TX, USA).

Network analysis

As the dataset used in the current analyses was derived from databases pertaining to six countries, some variations existed in their scope and format. To mitigate these discrepancies, a data standardization process was implemented, whereby the dataset related to the Mexican population served as the standard against which the datasets related to other countries were assessed and modified as needed.

The standardized datasets were subsequently subjected to network analysis, the aim of which was to establish relationships between the model variables. In this approach, in line with standard network representation, variables of interest are represented as nodes, while edges represent the connectivity between them.

Two types of network analyses models were conducted, aiming (1) to evaluate the group behavior of each variable of interest in each country and the general relation between countries, and (2) to establish individual-level relationships, whereby the resulting network was subjected to cluster analysis to determine the properties of each group and how they relate to socioeconomic variables.

The odds ratio (OR) was obtained considering LBP as the outcome for two different groups, individual countries and connected countries. The OR values were obtained using R [24] and the "Odds Ratio" package [25].

The first OR was obtained by individual countries network whereby diabetes mellitus, hypertension, cardiovascular disease, gastritis, anxiety–depression, smoking, alcohol intake, obesity, disability (i.e., HAQ-DI > 0.8), and trauma in the last seven days served as exposure variables of interest. For the second OR values, pertaining to the individual network and connected countries, the exposure variables included diabetes mellitus, hypertension, cardiovascular disease, anxiety–depression, smoking, and obesity. Here, gastritis and alcohol consumption were excluded since that information was not available for Colombia. Similarly, although disability (HAQ-DI) and trauma were considered for the connected countries analysis, they were excluded from the individual network since these variables were examined further in the cluster analysis.

In the group behavior models, the OR of each variable served as the weight of the respective nodes. The edge size was obtained by counting the number of individuals that are diagnosed with LBP in each group, whereby each of the exposure variables was normalized by the total number of individuals in each group. For the individual network, each node represents an individual, and the weight of the nodes is equal to the number exposure variables for which a definite diagnosis exists for that individual. Moreover, an edge is created between two individuals for each exposure variable they have in common.

The final network based on the aforementioned principles was obtained using the Gephi [26] software and the node positions within Gephi graphs were solved using the Graph Layout Algorithm ForceAtlas2 [27]. It is worth noting that, in this algorithm, nodes repel each other with the force equivalent to their weight (which is treated as a property of a charged particle), while edges attract nodes as springs. For the individual networks, the spatial position on the network pertaining to each node was used to obtain the groups using the density-clustering algorithm [28] implemented in the R package DBSCAN [29].

The country inequality index was also considered during modeling in order to evaluate the relationship between global socioeconomic variables and the key comorbidities. Pertinent models where obtained from social-level or collective/contextual variables *from 2018 Statistical Update* (2018), and the values pertaining for each variable were captured in the models (Table 2 and supplementary file) [23].

Ethics approval

As the present investigation involves data collected as a part of prior studies, no specific study protocol approval was needed, as all Institutional and Ethics Committees of each participating institution had already approved pertinent studies. Moreover, all participants in the original studies were informed of the study procedures and voluntarily signed informed consent forms prior to taking part in data collection. All data was blinded for the secondary analysis. The datasets from the different countries contain variables that are related to patient personal information that was deleted for the leader researcher before the computer scientist manages the data. The algorithm developed to create the ultimate database contains a filter to remove those columns from all the calculations; each user is identified by a randomly generated identification (ID) key that can be used by clinicians to find the specific person if needed.

Results

The total sample included in this report comprised of 55,724 individuals, and 33,772 (60.61%) of whom were women. The mean age for the entire sample was 43.38 years (SD = 17.4), and the mean number of years of educational attainment was 6.52 years (SD = 4.89). Moreover, 13,444 (24.12%) individuals self-reported as being of Indigenous background and 17,379 (32.29%) respondents were rural residents. The most prevalent self-reported comorbidities were hypertension (8705 individuals, or 16.17% of the sample), anxiety-depression (7306, 13.92%), smoking (7010, 13.02%), alcohol consumption (3875, 8.22%), diabetes (4016, 7.46%), and cardiovascular disease (1890, 3.51%), as indicated in Table 1.

LBP was diagnosed in 3673 participants (6.59%; 95% CI = 6.28–6.69) and mechanical LBP was noted in 3235/3673 individuals (88.0%; 95% CI = 86.98–89.10). The prevalence of LBP showed significant difference between countries at $p > 0.001$, whereby 460 of 2300 individuals were affected in Argentina (20.00%; 95% CI = 18.38–21.69), 237/6688 (3.54%; 95% CI = 3.11–4.02) was reported for Colombia, 474/7549 (6.28%; 95% CI = 5.74–6.84) for Ecuador, 2126/32,726 (6.50%; 95% CI = 6.23–6.76) for México, 15/955 (1.57%; 95% CI = 0.8–2.5) for Peru, and 305/5507 (5.54%; 95% CI = 4.94–6.17) for Venezuela.

The analyzed socioeconomic variables varied among countries. For example, the environmental pollution indicator (CO_2 emissions per capita) was the highest in Argentina, whereas inequality (Gini coefficient) was the greatest in Colombia, where a 2:1 ratio was noted for the income gap between men and women. Education level was similar across all countries, while the highest health expenditure as a percentage of GDP was reported for Ecuador at 8.5%, followed by Argentina at 6.8%, as indicated in Table 2.

Logistic regression analysis of the variables associated with each LBP dimension (ethnicity, country, schooling, health coverage, and community type) after controlling for age and gender revealed that living in a rural area (OR 1.56; 95% CI = 1.37–1.77, $p < 0.001$); anxiety/depression symptoms (OR 1.66; 95% CI = 1.46–1.88, $p < 0.001$), gastritis (OR 1.57; 95% CI = 1.39–1.76, $p < 0.001$), alcoholism (OR 1.27; 95% CI = 1.05–1.41, $p < 0.001$), and obesity (1.21; 95% CI = 1.05–

Table 1 Comparison of sociodemographic and clinical variable in subjects with low back pain and controls (individual level)

	Total group *n* = 55,724	Low back pain *n* = 3673 (6.59%)	Without low back pain *n* = 52,051 (93.51%)	*p*
Gender				0.64
Female (%)	33,772 (60.61%)	2213 (60.25%)	31,559 (60.63%)	
Male (%)	21,952 (39.39%)	1460 (39.75%)	20,492 (39.37%)	
Age (years), mean (SD)	43.38 (17.93)	44.06 (17.08)	43.33 (18.99)	< 0.001
Community type *n* = 53,825		*n* = 3490	*n* = 50,335	< 0.001
Rural (%)	17,379 (32.29%)	1636 (46.88%)	15,743 (31.28%)	
Urban (%)	36,446 (67.71%)	1854 (53.12%)	34,592 (68.72%)	
Ethnicity				
Indigenous (%)	13,444 (24.12%)	1546 (42.09%)	11,897 (22.86%)	< 0.001
Non-indigenous (%)	42,281 (75.88%)	2127 (57.91%)	40,154 (77.14%)	< 0.001
Educational level, mean number of years (SD) (*n* = 47,033)	6.52 (4.89)	5.81 (4.39)	6.5 (4.92)	< 0.001
Social coverage (*n* = 47,371)				< 0.001
None (%)	10,853 (22.91%)	999 (34.64%)	9854 (22.15%)	
Public (%)	24,021 (50.71%)	1334 (46.26%)	22,687 (51.0%)	
Social cover (%)	4626 (9.77%)	243 (8.43%)	4383 (9.85%)	
Private (%)	4796 (10.12%)	149 (5.17%)	4647 (10.45%)	
Public/private (%)	2972 (6.27%)	157 (5.44%)	2815 (6.33%)	
Others (%)	103 (0.22%)	2 (0.07%)	101 (0.23%)	
Comorbidities (*n* = 53,837)				
Diabetes (%)	4016 (7.46%)	255 (7.05%)	3761 (7.49%)	0.33
Hypertension (%)	8705 (16.17%)	624 (17.25%)	8081 (16.09%)	0.06
Cardiovascular disease (%)	1890 (3.51%)	165 (4.56%)	1725 (3.43%)	< 0.001
Anxiety/depression (%) (*n* = 52,476)	7306 (13.92%)	886 (25.47%)	6420 (13.10%)	< 0.001
Smoking (%)	7010 (13.02%)	485 (13.41%)	6525 (12.99%)	0.47
Alcoholism (*n* = 47,149) (%)	3875 (8.22%)	489 (14.47%)	3386 (7.74%)	< 0.001
Disability (HAQ-DI ≥ 0.8) (%)	4634 (9.50%)	414 (13.21%)	4220 (9.24%)	< 0.001

SD, standard deviation; *RIQ*, interquartile range; *HAQ-DI*, Health Assessment Questionnaire-Disability Index

1.41, $p < 0.001$) were the main LBP comorbidities, alongside disability (HAQ-DI > 0.8) (OR 1.45; 95% CI = 1.25–1.69, $p < 0.001$).

Figure 1 shows the networks resulting from the global analysis of individual countries and all six countries as a single group. The central node represents the country of interest (non-significant measures are represented at this node), with other nodes representing each of the exposure variables, whereby the color and size is equal to the OR for each group. The edge size represents the number of individuals with LBP and each one of the specific exposure variables.

Figure 2 depicts the network analysis of the key comorbidities (diabetes mellitus, hypertension, cardiovascular disease, anxiety–depression, smoking, and obesity), disability (HAQ-DI), and trauma in the last seven days and their connections to each country. Here, the LBP prevalence in each country determines the node size and color, and the exposures nodes' OR is used as the node size. Similarly, the edge size is the number of individuals in each country that is affected by each of the exposure variables, whereby its color corresponds to the color of the source node (country).

The individual network analysis results are shown in Fig. 3, in which the colors denote the groups stemming from the cluster analysis performed by the density cluster method implemented in R DBSCAN [29]. Here, each group shows the nodes of the most closely linked individuals due to the attractions among the edges, since each edge is obtained by comparing the diagnoses pertaining to the two nodes it connects, and each group contains nodes with similar combinations of morbidities. The network shown in Fig. 3 consists of 1971 nodes and 812,708 edges.

The resulting clusters represent the relationship between LBP and the key comorbidities. The obtained clusters using the comorbidities model can be used to study the distribution of global socioeconomic variables per country in each cluster, and evaluate how each country compares with the average value across all Latin-American countries of the study.

Table 2 Description of collective/contextual variables by countries (social level)

	Argentina $n = 2300$	Colombia $n = 6688$	Ecuador $n = 7549$	Mexico $n = 32{,}726$	Perú $n = 955$	Venezuela $n = 5507$
Low back pain ($p > 0.001$)	460 (20.0%)	237 (3.54%)	474 (6.28%)	2126 (6.50%)	15 (1.57%)	305 (5.54%)
Carbon dioxide emissions per capita (in tonnes) for 2014	4.7	1.8	2.8	3.9	2	6
Income inequality, Gini coefficient	42.4	50.8	45	43.4	43.8	46.9
Coefficient of Human Inequality for 2017	13.9	22.9	19.4	20.8	18.9	16.2
Current health expenditure (% of gross domestic product) for 2015	6.8	6.2	8.5	5.9	5.3	3.2
Education Index for 2017	0.816	0.676	0.697	0.678	0.689	0.741
Estimated gross national income per capita, female (2011 PPP$) for 2017	12,395	10,271	7388	11,065	8446	7401
Estimated gross national income per capita, male (2011 PPP$) for 2017	24,789	15,692	13,307	22,873	15,140	13,976
Expected years of schooling (years) for 2017	17.4	14.4	14.7	14.1	13.8	14.3
Expected years of schooling, female (years) for 2017	16.2	14.3	13.9	13.8	13.6	13.2
Gender Development Index for 2017	0.997	0.997	0.978	0.954	0.95	1.011
Gender Inequality Index for 2017	0.358	0.383	0.385	0.343	0.368	0.454
Human Development Index for 2017	0.825	0.747	0.752	0.774	0.75	0.761
Human Development Index, female for 2017	0.816	0.747	0.741	0.752	0.728	0.762
Human Development Index, male for 2017	0.764	0.749	0.757	0.789	0.766	0.754
Income inequality, quintile ratio	9.5	14.3	10.7	8.8	10.6	15.8
Inequality in life expectancy (%)	9.5	13.2	13.9	12.3	13.2	10.5
Life expectancy at birth (years)	76.7	74.6	76.6	77.3	75.2	74.7
Life expectancy at birth, female (years)	80.4	78.2	79.3	79.7	77.9	78.9
Life expectancy at birth, male (years)	73	71	73.9	74.9	72.6	70.8
Mean years of schooling (years)	9.9	8.3	8.7	8.6	9.2	10.3
Mean years of schooling, female (years)	10.1	8.5	8.6	8.4	8.7	10.7
Mean years of schooling, male (years)	9.7	8.1	8.8	8.8	9.7	10
Population, total (millions)	44.3	49.1	16.6	129.2	32.2	32
Total unemployment rate (female to male ratio)	1.49	1.58	1.59	1.03	1.03	1.22

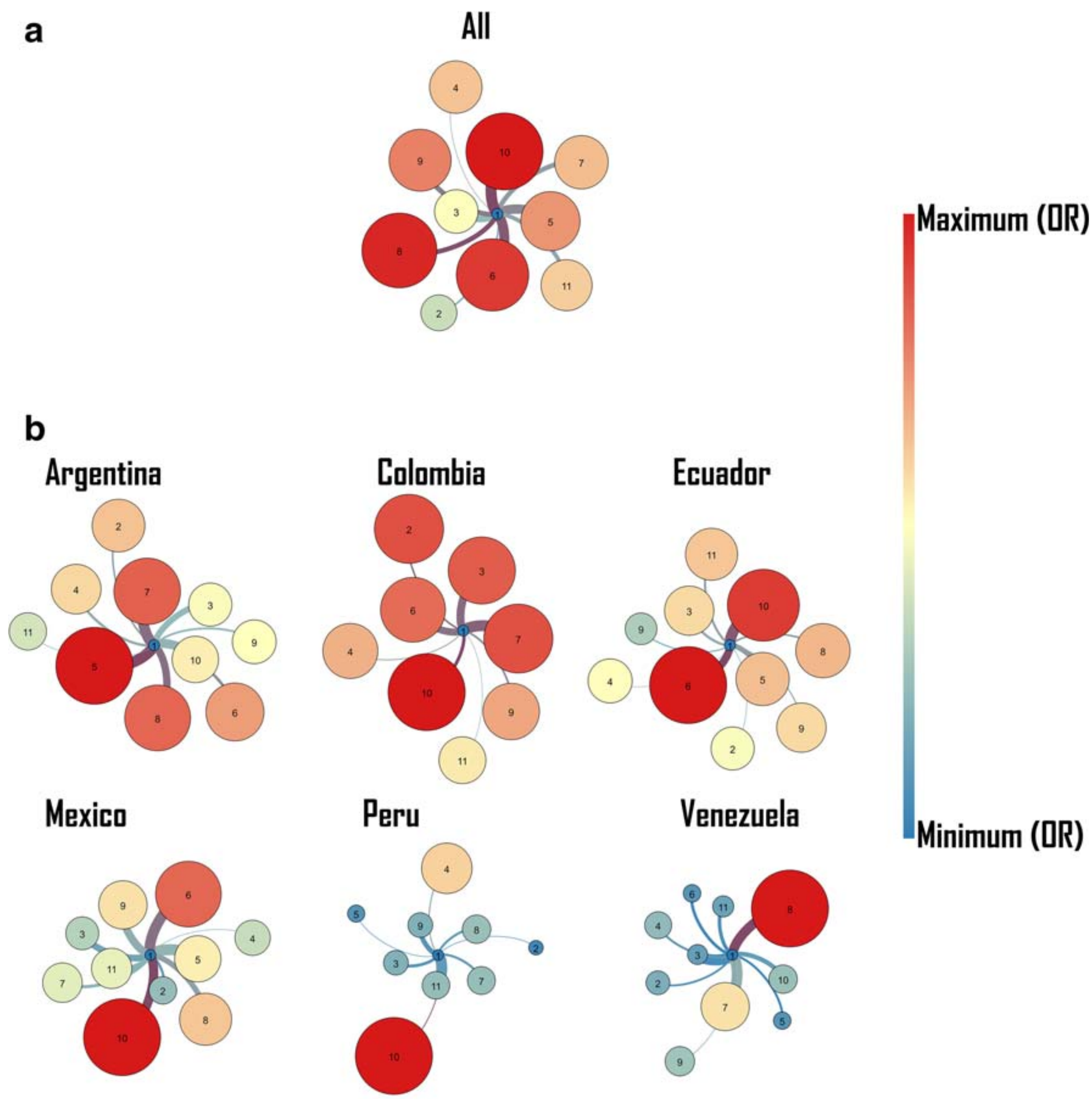
Figure 4 shows a categorical value of each one of the socioeconomic variables, the categorical values of each entry are obtained by calculating the average value of each socioeconomic variable for each cluster, then each one of these variables is divided by the average value of the same variable in the total LBP population, and the resulting values are normalized between 0 and 1. Then, the values are categorized in six groups: the first three indicated to the average value of the variable at that cluster is below the average value of the variable in the total LBP population and the last three indicates that the value is higher.

For the final cluster analysis, the results are presented on Fig. 4 together with the normalized values of the comorbidities.

The normalization of the comorbidities is obtained with respect the total number of subjects per cluster that contain the comorbidity, so to obtain a prevalence value per cluster in percentage of the total number of individuals per cluster.

For brevity, only the most extreme clusters are discussed here, i.e., cluster 0 and cluster 4 involving a single morbidity, and cluster 9 and cluster 10, in which more than five comorbidities are associated with LBP, and the bigger difference between the two clusters is that cluster 10 contains individuals that report anxiety or depression.

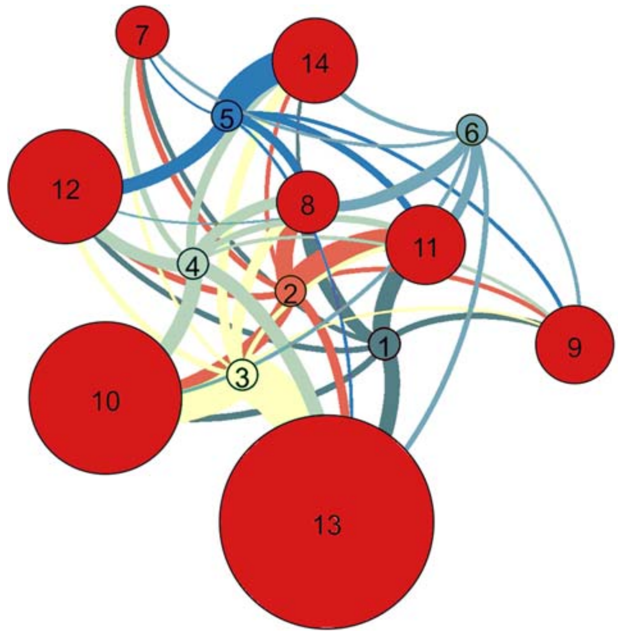
Cluster 0, for example, involves 299 individuals that share the following characteristics compared with the overall LBP population: younger age (category 2), a higher average years of schooling (category 4), prevalence of smokers (100%), gender (category 2, more males), being of Indigenous and Mestizos background (category 3, below or equal to the overall relation between Mestizos and Indigenous), and lower prevalence of disability score positive (HAQ-DI of 7.4%). This cluster is also characterized by the following global variables: less inequality Gini value (category 3), higher HDI (category 4), and less spending on health per capita (category 3) than in the overall LBP population. The other cluster at the lower extreme, cluster 4, was formed by 401 individuals, characterized by younger age (category 3) and a lower average years of education (category 2), as well as lower anxiety, depression, and disability scores (HAQ-DI of 14.5%); lower



		COUNTRY (OR)						
ID	Label	All	Argentina	Colombia	Ecuador	Mexico	Peru	Venezuela
1	Backpain	-	-	-	-	-	-	-
2	Diabetes mellitus	0.712	0.876	0.953	0.938	0.678	0.292	0.516
3	Hypertension	0.911	0.679	0.921	1.115	0.882	1.122	0.366
4	Cardiovascular disease	1.142	0.812	0.724	0.967	0.975	3.247	0.644
5	Gastritis	1.316	1.381	-	1.23	1.401	0.51	0.264
6	Anxiety - Depression	1.655	0.987	0.884	1.917	2.148	-	0.27
7	Smoking	1.167	1.163	0.951	0.607	1.139	1.389	1.491
8	Alcohol	1.722	1.149	-	1.259	1.624	1.433	2.641
9	Obesity	1.389	0.692	0.748	1.119	1.48	1.13	0.741
10	Trauma 7D	1.778	0.745	1.082	1.77	2.585	5.425	0.702
11	HAQ - DI	1.105	0.556	0.59	1.196	1.17	1.362	0.41

Fig. 1 The network analysis shows the differences in the OR values for each variable. (A) shows the OR for all the individuals in the dataset. (B) shows the OR for the variables grouped by country. In Venezuela, for example, alcoholism is associated with the greatest OR, and this is also the only variable for which a positive relationship with low back pain was noted across all countries

Fig. 2 Network of the relations between countries and exposure variables, whereby the position of each country is governed by the exposure variables with the greatest impact on the population. For example, the highest number of individuals diagnosed with low back pain that are also affected by disability (HAQ-DI) was noted for Peru, while the strongest association between anxiety/depression and trauma was established for Ecuador. On the other hand, Venezuela is on the perimeter of the network due to low associations among the examined variables



ID	Label	Prevalence	OR	Color
1	Argentina	0.2	-	
2	Colombia	0.035	-	
3	Ecuador	0.062	-	
4	Mexico	0.064	-	
5	Peru	0.074	-	
6	Venezuela	0.055	-	
7	Diabetes mellitus	-	0.712	
8	Hypertension	-	0.911	
9	Cardiovascular disease	-	1.142	
10	Anxiety - Depression	-	1.655	
11	Smoking	-	1.167	
12	Obesity	-	1.389	
13	Trauma 7D	-	1.778	
14	HAQ - DI	-	1.105	

inequality Gini value (category 3); lower HDI (category 2); and lower health expenditure per capita (category 3) than in the overall LBP population.

Cluster 9, as one of the clusters that have the highest number of comorbidities associated with LBP, contains 85 individuals and is formed by individuals younger than the overall age distribution of the individuals with LBP (category 3), with lower educational attainment (category 3), with more males (category 3), with a similar distribution of Mestizos and indigenous population than the overall distribution in the LBP population, without any self-report anxiety/depression and a prevalence of disability scores (HAQ-DI of 11.8%) and a lower economic Gini inequity (category 2) with a HDI in category 3, and lower spending on health per capita (category 3).

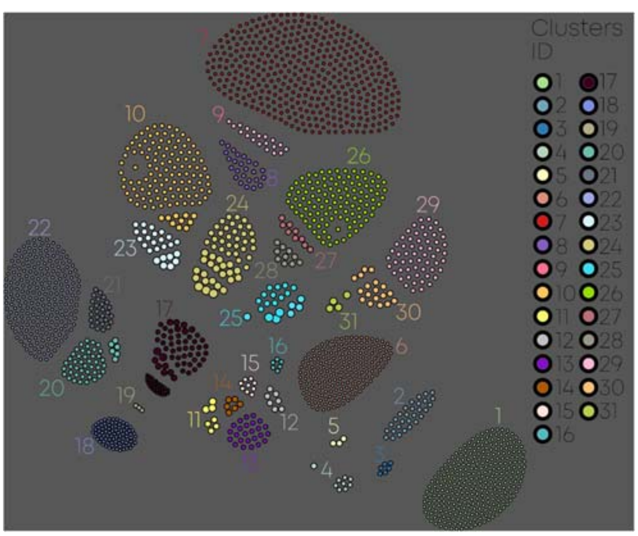


Fig. 3 Clusters allowing for visualization of the individual networks using a model of comorbidities, whereby the central individual is affected by the highest number of comorbidities. The external nodes denote individuals suffering from low back pain and a single comorbidity. The *x* and *y* coordinates are not presented in any specific scale, due to which the cluster positions are only valuable for representation purposes

Cluster 10 is formed by 57 individuals and is formed by individuals younger than the overall age distribution of the individuals with LBP (category 3), with more females (category 4), with a lower educational attainment (category 2) that have a lower number of indigenous individuals compared with the overall LBP population distribution (category 2), who are also affected by several comorbidities (diabetes, hypertension, cardiovascular disease, obesity, and anxiety/depression), and more severe disability (HAQ-DI of 31.6), with a Gini in category 3 and HDI in category 2, and a health expenditure per in category 3, as shown in Supplementary File 1.

Discussion

The syndemic approach was adopted in the present study to evaluate the interrelationships among health and lifestyle indicators globally (e.g., smoking, living in a rural area, inequity), demonstrating the specific weight of each of the examined indicators and their synergy with LBP. The results yielded by network and cluster analyses were utilized to elucidate the syndemic relationships and depict them as processes ranging from the individual level to the social level, thus revealing the syndemogenesis of LBP [6, 7].

Syndemogenesis is observed individually in those affected by LBP, as the analysis revealed its relationship with comorbidities (anxiety/depression, obesity, hypertension, and

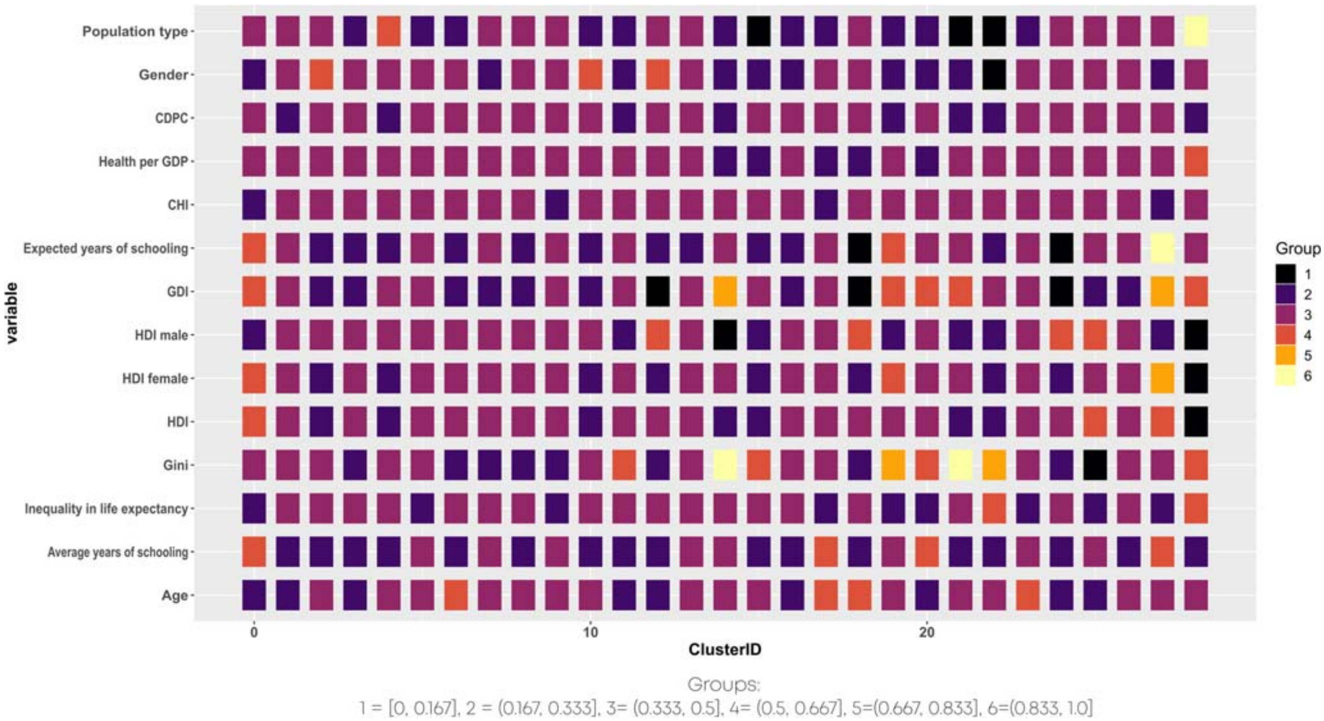


Fig. 4 Graph of the different socioeconomic variables per cluster. The indicated values represent averages per cluster divided by the average value of the variable in the LBP population. Values in the 0–1 range indicate that the average is below the value reported for the overall population, 1 is equal to the overall population, and higher values indicate that the averages exceed values reported for the overall population. CDCP carbon dioxide emissions per capita, GDP gross domestic product, CHI coefficient of human inequality, GDI Gender Development Index, HDI Human Development Index, GINI income inequality, Gini coefficient

gastritis), unhealthy behaviors (Figs. 1 and 2), and some key social variables, such as low education, ethnicity (i.e., belonging to Indigenous population), living in a rural area, and having limited access to healthcare (Fig. 3). However, it is also evident at the societal level, as LBP is more common in countries characterized by greater inequity, as measured by the Gini coefficient and HDI.

The syndemic approach supports and complements the findings previously published in GBD initiative reports in which LBP is described as a musculoskeletal condition that harms population health [4, 30, 31]. As a part of the present study, data pertaining to a significant number of members of Indigenous and Mestizo populations residing in six Latin-American countries was analyzed, revealing that the LBP prevalence (6.59%) is actually lower than that reported at the global level (ranging from 7.3 to 39.9% depending on the population studied) [2, 30, 32, 33].

In Latin America, lower back pain is considered a condition that most severely affects young adults [33, 34]. While other authors reported 20.6 as the average age at which LBP first manifests, 43.38 years was obtained for the sample examined in the present study, which was still below the value reported by Dutmer et al. (46.3 years) [35] and Gouveia et al. (58.9 years) [36]. The LBP prevalence among males and females also varies across the world, whereby it is found to affect mostly men in African countries [2] while being more prevalent (by around 60%) among women Latin America [31, 35, 36], supporting the findings obtained in the present study.

LBP is linked to different comorbidities. Consequently, in the present study, a number of health indicators were evaluated and the results indicated that LBP is associated with high blood pressure (16.17%), anxiety/depression (13.92%), and smoking (13.02%). Moreover, when groups with and without LBP were compared, a significant difference in anxiety/depression, alcoholism, and cardiovascular disease prevalence was observed. This association with different comorbidities (depression and anxiety in particular) has been documented in the literature [1–3, 31, 34].

These associations are observed in all countries included in the analysis, probably due to a degree of similarity in lifestyle, socioeconomic conditions, cultural context, schooling, and accessibility to health services (Fig. 4). Latin America is among the regions of the world characterized by the highest social inequity, which tends to increase psychosocial stress in the population and may lead to lower back pain that can evolve to a disability, as a result of which earning potential declines and social position deteriorates. The present study findings also indicate that ethnicity, rural residence, low educational level, and inadequate access to health services are the key syndemic factors with the greatest impact on the lumbar pain experienced by the population of the six Latin-American countries studied. In sum, LBP is not only linked to some key comorbidities but also to vulnerability (i.e., low educational level, being female, self-recognized as Indigenous, and having limited access to a health system) and level of social inequity in the country of residence (i.e., high Gini coefficient and low HDI), as revealed by the cluster analysis (Fig. 4 and Supplementary File 1).

This inequity in health has been described in extant GBD publications [1] and the Global Alliance for Musculoskeletal Health, formerly known as the Bone and Joint Decade [37] and World Spine Care [38] initiative, albeit in a disaggregated form. Thus, the key contribution of the present study is evidence supporting presence of several aggravating factors that lead to LBP.

Limitations

The key limitation affecting the present study pertains to the data sources utilized, as the consulted databases were incongruent with respect to the type and number of variables included. Thus, to develop regression models, data standardization had to be performed. Nonetheless, loss of information was inevitable as, for example, alcoholism was not measured in Colombia, and thus had to be excluded from per-country OR models.

The self-reported diseases can generate some biases in the interpretation of the health impact in biomedical terms. However, diseases such as diabetes mellitus, hypertension, and cardiovascular diseases were confirmed that a physician has established them or that they received treatment; this did not apply to mental health conditions such as anxiety and depression. Still, people considered these manifestations to be diseases.

In addition, the design of this secondary analysis could have led to an ecological fallacy, where our inferences on individual data could have been distorted by the aggregate data utilized [39]. It is also worth noting that the samples included in the analyses may not be representative of the respective countries, since in Argentina, for example, the participating individuals were Indigenous, and Mestizos predominated in Colombia.

Conclusions

Low back pain is a highly prevalent condition in Latin-American populations. However, it most adversely affects young adults, women in particular, and is found to be disproportionately prevalent among Indigenous communities, those with low educational levels, and persons suffering from different comorbidities, especially in the area of mental health. Also, the association of these variables with social inequity indices underpins the raised hypothesis of LBP's syndemic and syndemogenesis through complex analysis such as network and cluster analysis.

The study of syndemic and syndemogenesis in rheumatology using sophisticated analytic strategies (big data, artificial intelligence, network, and cluster analysis) makes its visibility into the complexity of rheumatic diseases.

Compliance with ethical standards

As the present investigation involves data collected as a part of prior studies, no specific study protocol approval was needed, as all Institutional and Ethics Committees of each participating institution had already approved pertinent studies. Moreover, all participants in the original studies were informed of the study procedures and voluntarily signed informed consent forms prior to taking part in data collection. All data was blinded for the secondary analysis. The datasets from the different countries contain variables that are related to patient personal information that was deleted for the leader researcher before the computer scientist manages the data. The algorithm developed to create the ultimate database contains a filter to remove those columns from all the calculations; each user is identified by a randomly generated identification (ID) key that can be used by clinicians to find the specific person if needed.

Disclosures None.

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