UNIVERSIDAD DE INVESTIGACIÓN DE TECNOLOGÍA EXPERIMENTAL YACHAY

Escuela de Ciencias Biológicas e Ingeniería

TÍTULO: "EXPLORATORY EPIDEMIOLOGICAL ANALYSIS IN PNEUMONIA PATIENTS IN IESS SOUTHERN QUITO HOSPITAL"

Trabajo de integración curricular presentado como requisito para la obtención del título de Biólogo

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Urcuquí, Septiembre 2020

Urcuquí, 2 de diciembre de 2020

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CARRERA DE BIOLOGÍA
ACTA DE DEFENSA No. UITEY-BIO-2020-00041-AD

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Dedicatoria

A Dios, mi amada familia y José,

Gracias por su infinito amor

Lizbeth Xiomara Quiroz Cabascango

Dedication

To God, my beloved family and José,

Thank you for your infinite love

Lizbeth Xiomara Quiroz Cabascango

Agradecimiento

Agradezco a mis profesores Santiago Ballaz PhD e Isidro Amaro PhD, tutor y co-tutor, personas de gran sabiduría, conocimiento y paciencia, siempre dispuestas a resolver mis dudas.

Agradezco enormemente al Dr. Francisco Mora y al Dr. Marco Bonifaz por permitirme acceder a la recolección de los datos en el Hospital del IESS Quito-Sur para realizar esta investigación.

Al profesor Diego Peluffo PhD. y mis compañeros estudiantes de TICs por todo su apoyo en la recolección de los datos. ¡Dios les pague!

A mis amigas y amigos de la universidad, por todos los momentos compartidos.

Finalmente, y no menos importante, agradezco a mi familia por su apoyo y amor incondicional a lo largo de toda mi vida.

Lizbeth Xiomara Quiroz Cabascango

Acknowledgment

I am grateful Santiago Ballaz PhD. and Isidro Amaro PhD, tutor and co-tutor, people of great wisdom, knowledge and patience, always ready to solve my doubts.

I greatly thank Dr. Francisco Mora and Dr. Marco Bonifaz for allowing me access to IESS Southern Quito Hospital data collection to carry out this research.

To Professor Diego Peluffo PhD. and my fellow TICs students for all their support in collecting the data.

To my friends from university, for all the shared moments.

Finally, but not least, I thank my family for their unconditional love and support throughout my life.

Lizbeth Xiomara Quiroz Cabascango

ABSTRACT

Pneumonia is a public health problem worldwide due to its high mortality rate and the high costs it generates for governments, especially in underdeveloped countries. A significant increase in cases of pneumonia has been observed in IESS Southern Quito Hospital. For this reason, the objective of this study was to carry out an exploratory epidemiological and descriptive analysis of people diagnosed with pneumonia during December 2018. It will establish correlations between demographic variables such as gender, people who consume alcohol and tobacco, and quantitative variables such as vital signs, blood count, and age. For this, a principal component analysis (PCA) is carried out. Alcoholic patients have a high correlation between their neutrophils and age and a tendency to develop bacterial pneumonia. It showed us that, even though the PCA analysis does not allow us to establish causality, it gave us the guideline to investigate the existing scientific evidence and to observe that bacterial pneumonia may be associated with alcohol consumption. It was also shown that few smoking patients (4) compared to non-smokers (179), so, in that case, the conclusions obtained from this analysis would not be correct due to this great inequality in the comparison of patients. Finally, based on our analysis it cannot concluded any sex effects in the risk for pneumonia.

Key words: PCA, correlation, bacterial pneumonia, neutrophils, age

RESUMEN

La neumonía es un problema de salud pública a nivel mundial debido a su alta mortalidad y a los grandes costos que genera a los gobiernos, especialmente en los países subdesarrollados. En el Hospital del IESS Quito-Sur se ha observado un incremento significativo de los casos de neumonía. Por tal motivo, el objetivo de este estudio fue realizar un análisis exploratorio epidemiológico y descriptivo de las personas diagnosticadas con neumonía durante diciembre del 2018. Esto nos permitirá establecer correlaciones entre variables demográficas como género, personas que consumen alcohol y tabaco junto con variables cuantitativas como signos vitales, biometría hemática y edad. Para ello se realizó un análisis de componentes principales (ACP). Se encontró que los pacientes alcohólicos tenían una alta correlación entre sus neutrófilos y edad, además de una tendencia a presentar neumonía bacteriana. Esto nos mostró que, pese a que el análisis de ACP no nos permite establecer causalidad, si nos da una pauta para indagar en la evidencia científica existente y observar que en efecto la neumonía bacteriana puede estar asociada al consumo del alcohol. También se evidenció que existen pocos pacientes fumadores (4) frente a pacientes no fumadores (179) por lo que, en ese caso, las conclusiones obtenidas de este análisis no serían correctas, debido a esta gran desigualdad en la comparación de los pacientes. Finalmente, basándonos en nuestros análisis, no se puede concluir ningún efecto sexual en el riesgo de neumonía.

Palabras clave: ACP, correlación, neumonía bacteriana, neutrófilos, edad.

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INTRODUCTION

In 2013, pneumonia was included in Priority Medicines for Europe and the World Report as new priority diseases due it major cause of morbidity and mortality in adults and children in low and middle income countries (Nga Tong, BA, 2013; Zar et al., 2013). Only in 2017, was registered more than 2 million people died by pneumonia, where the third part of them, where children younger than 5 years. According to World Health Organization, pneumonia implies great costs for each country government, nearly $ 109 million per year (World Health Organization, 2019)

Pneumonia is a severe infectious disease that causes inflammation of the alveoli sacs, limiting the entry of oxygen into the body, causing problems in breathing (Nga Tong, BA, 2013), mainly among children under 5 years and adults over 65 years (Dang et al., 2014). Pneumonia can be caused by a wide variety of bacteria, viruses, and fungi in the air we breathe (Bartlett & Mundy, 1995; Mandell, 2015) where *Streptococcus pneumoniae* is the most common microorganism of bacterial pneumonia.

There are many risk factors to acquire pneumonia. For instance: age, gender, alcohol consumption, cigarette smoking, heart failure, diabetes, and other chronic diseases (Caldeira, 2012). In Ecuador, several studies on pneumonia have been carried out, but very few risk factors such as alcohol and tobacco consumption are considering. It is important to carry out this research because, in Ecuador, pneumonia is one of the leading causes of mortality (Siguenza & Webster, 2015).

In the diagnosis, doctors evaluate several clinical characteristics (vital signs) especially temperature and respiratory rate. However, it is also important to perform X-rays films to detect the disease and assess its severity through a blood count examination (Musher & Thorner, 2014). Therefore, this research will focus on mentioned factors (gender, alcohol consumption, cigarette smoking) and analyze with vital signs, blood count, and age.

For statistical analysis, the multivariate technique called principal component analysis (PCA) will be used. An exploratory analysis describes an extensive data set in a simpler dimension called principal components, collecting the original variables' greatest variability. It also allows us to study the relationships that occur between variables

(correlated or uncorrelated) and thus measure their strength and directionality (Santos et al., 2019; Zhang & Castelló, 2017)

LITERATURE REVIEW

There is few research which use PCA in epidemiological analysis. However, here it is intended to show that this type of exploratory analysis can give us good results, which, although they cannot be taken as conclusive, can lay solid foundations and give step to future research.

It is important to mention the advantages and disadvantages of this exploratory study. Therefore, an exploratory analysis's main advantage is that it does not have a mandatory and strict research structure to follow, so the researcher can choose the simplest process according to her criteria. In this case, the design that we follow is quite simple, elaborate PCA to choose the most determining variables, and then use them in a new PCA to evaluate the individuals' behavior against the different variables.

The main disadvantage is that its results can be taken as inconclusive because the objective is to explore the problem and its environment. The conclusions drawn cannot be definitive, but instead can be of great help for future research.

PCA analysis

Principal component analysis is a multivariate tool that transforms the largest number of variables in a smaller number of variables called principal components (Paul et al., 2013). These principal components $(u_1 \dots u_p)$ are obtained through a linear transformation of the m original variables $(x_1 \dots x_m)$. The i-th principal component is calculated as follows:

$$u_i = w_{i1}x_1 + w_{i2}x_2 + \cdots + w_{im}x_m$$

Where $w_{i1} \dots w_{im}$ are the loadings (weights of the original variables on the linear combination) (Cova et al., 2013).

The cophenetic correlation coefficient used for variables selection calculates the correlation between the Euclidean distances in the reduced space and the same distances in the original dimension space given by the number of original variables. Therefore, the value can be used as a measure of the quality of the reduction achieved (Balzarini et al., 2008).

For the criterion of evaluation and analysis of the behavior of the variables and the individuals, the book “Methods of Multivariate Analysis” by Alvin Rencher is taken into account.

According PCA analysis, if the angle between two variables is small (less than 90º), there is a high positive correlation. It means that if one decreases those of the other

also and if those values increase, those of the other variable will also increase (Rencher, 2005). If the angle between two variables is close to 90°, then the correlation between those two variables is small. In that case we say that there is no correlation between the two variables. If the angle between two variables is close to 180 °, there is a high negative correlation. It indicates that while the values of one variable increase, the other decreases (Rencher, 2005).

PROBLEM STATEMENT

Pneumonia is a constant public health problem, especially in underdeveloped countries (Zar et al., 2013). Thus, it is important to carry out studies on pneumonia in Ecuador, especially because no research evaluates alcohol consumption and tobacco use. This way, we can assess the incidence of this disease to better treat it and reduce its cases.

In the IESS Southern Quito Hospital has been detected an epidemic of transmissible respiratory diseases in the last two years. In fact, around the 80% of the respiratory diseases admissions are primary diagnosed with pneumonia. Therefore, the objective of this study is to perform a high-throughput exploratory epidemiological analysis that can identify the role of demographic variables as gender, alcohol consumption, and cigarette smoking with quantitative variables such as vital signs, blood count and age. To this end, around 2000 clinical records from the archives of the Hospital Quito Sur, filed during December 2018 will be analyzed using statistical multivariate as PCA.

OBJECTIVES

General

To conduct an exploratory (descriptive) analysis of patients with pneumonia admitted in the emergency room in IESS Southern Quito Hospital (IESS-HQS) using the multivariate PCA technique, which establishes differences between patients with pneumonia based on their gender, alcohol and tobacco consumption.

Specific

- Select the most useful and representative variables from the data collected through the PCA analysis through their loadings.
- Analyze the correlation between demographic variables (age, sex, alcoholic people and cigarette smoking), vital signs and blood count.

METHODOLOGY

Ethical statement

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975 (Shrestha, 2012). Informed consent was obtained from all patients for being included in the study. The study was approved by the Ethics Committee IESS Southern Quito Hospital conducted in accordance with the rules of ethics of the Ecuadorian legislation (Public Health Ministerial order from December 31st 2014). The authors declare they had no access to identifying patient information when analyzing the data.

Study zone

This study was carry out in IESS Southern Quito Hospital, a city located at 2,850 m.a.s.l. Inaugurated in 2017, this hospital benefits around 1.2 million people, mainly in the surroundings of Quito's southern area (Edición Médica, 2017).

Diagnosis

The diagnosis was carried out and recorded by qualified medical staff with expertise in pneumology of IESS-HQS. Clinical diagnosis relied on the Man Management of Community-acquired Pneumonia in Older Adults guide (Simonetti et al., 2014), which mentions as the main criteria for the diagnosis of community-acquired pneumonia (CAP) the following main symptoms: fever, tachypnea, continuous sputum production in the absence of oropharyngeal irritation and rhinorrhea, with signs of condensation of the alveolar space. Additionally, X-radiography, blood count and renal function exams were also carried out. X-ray films helped to detect pneumonia through the presence of air bronchogram, single or multilobar infiltrates, and pleural effusion (Musher & Thorner, 2014). Blood count and renal function exams allow to measure severity, the presence of systemic inflammatory response, and the scaling of the therapeutic interventions (Menéndez et al., 2010).

Data collection and categorization

The data base was extracted from 583 patient files dated in December 2018 and stored in the AS400 patient’s digital database of the IESS-HQS. It was collected information regarding qualitative (sex, alcohol consumption, and smoking people) and

quantitative variables (vital signs, blood count and age). The variables (29) were defined as follow:

Demographic variables

Age was categorized as: children (1-14 years), young (15-25 years), adult (26-64 years), or elder (≥65 years) (Government of Canada SC., 1998); gender categorized as women and men; habits as alcoholic consumption and use of tobacco.

Vital signs variables

Temperature (°C), pulse (PPM), respiration rate (BPM), weight (Kg), oxygen saturation (%), arterial pressure (mmHg). Reference values according (Ball, Jane; Dains, Joyce; Flynn, John; Solomon, Barry; Stewart, 2014)

Blood count

Including leukocyte (WBC)(K/µL), hemoglobin (HGB)(g/dL), hematocrit (HCT)(%), mean corpuscular volume (MCV)(fl), mean corpuscular hemoglobin (MCH)(pg), medium corpuscular hemoglobin concentration (MCHC)(g/dL), mean platelet volume (MPV)(fL), red blood cell distribution width (RDW) (%), monocytes (K/µL), eosinophils (K/µL), lymphocytes (K/µL), neutrophils (K/µL), basophils (K/µL), platelets (K/µL), red blood cell (RBC) (M/µL), monocytes (%), eosinophils (%), lymphocytes (%), neutrophils (%), basophils (%), erythrocyte distribution width based on the coefficient of variance (GRCV) (%), platelet distribution width (PDW) (%). Reference values according (Failace, 2011; UNAM, 2012).

Statistics

Statistics were automatically computed using the Rstudio desktop software (version 4.0.2). After of the selection of patients (183) and the identification of possible outliers with the *winsorization* method and then missing data were filled through the mean substitution (Kwak & Kim, 2017)**.** Finally, it was carried out a normalization of the treated data. After then, it was proceeded to select the most representative variables using the Jolliffe's method with PCA and cophenetic correlation (Rencher, 2005). We subsequently worked with these and other variables that further were selected at the researcher's discretion based on the scientific evidence. PCA analysis was conducted with all the variables considering the following grouping: alcoholic, non-alcoholic, smokers, non-smokers, men and women. The PCA was carry out using the Info Stat (Statistical Software).

RESULTS AND DISCUSSION

Selection of patients

From a total of 532 patients suffering from respiratory conditions during December 2018, 305 were diagnosed with pneumonia. Because many of these pneumonia cases had many missing data in the 29 quantitative (vital signs, blood count and age) variables under scrutiny. Only the patients who had at least 60% completion of these variables were selected. The size of our sample was reduced to 183 patients. Even after this data depuration, there were still patients whose empty variables exceed the allowed 10% (Dong & Peng, 2013; Salgado et al., 2016). It was then decided that the data depuration was no longer performed by patients, but by variables so that the variables presenting more than 10% of absences were removed from the analysis. The eliminated variables were 5: oxygen saturation, weight, arterial pressure, RDW and PDW.

In this way, we proceeded to work with 24 variables: age, temperature (°C), pulse (PPM), respiration rate (BPM), WBC (K/µL), HGB (g/dL), HCT (%), MCV (fl), MCH (pg), MCHC (g/dL), MPV (fL), monocytes (K/µL), eosinophils (K/µL), lymphocytes (K/µL), neutrophils (K/µL), basophils (K/µL), platelets (K/µL), RBC (M/µL), monocytes (%), eosinophils (%), lymphocytes (%), neutrophils (%), basophils (%), GRCV (%).

Selection of representative variables

In this exploratory statistical analysis, the original data matrix contained 24 quantitative variables. Therefore, first, a selection of the most representative variables was made using the procedure described by Jolliffe's. This method is based on selecting the variables corresponding to the largest coefficient (loadings) in absolute value in the principal components (Rencher, 2005). For this reason, a PCA was carried out with the original matrix, and it was observed that the first seven principal components (Table 1) explain 78% of the total variability. These seven principal components are enough to perform the selection of variables. Therefore, 7 variables with the largest coefficient were select in the first seven principal components mentioned before. These were: lymphocytes (K/µL), RBC (M/µL), basophils (%), eosinophils (K/µL), MCHC (g/dL), monocytes (%) and MPV (fL) (Table 2).

Continuing with the selection of significantly relevant variables, temperature and respiratory rate were chosen because they are clinical characteristics on which the doctor bases the diagnosis for pneumonia (Miettinen et al., 2008; Strauß et al., 2014). Age was also selected, since many authors refer to it as a main risk factor for pneumonia (Pham et al., 2010; Torres et al., 2013). Neutrophils (%) was finally taken into consideration because of being a gold standard inflammation biomarker in pneumonia (Menéndez et al., 2010; Ning et al., 2016) and because, along with lymphocytes, it is a good predictor of bacteremia (de Jager et al., 2012) . From now onward, these four variables will be referred as "particular variables" in the text. Taking in mind this configuration (the 4 "particular variables" plus the 7 variables chosen above), the PCA analysis showed that the percentage of variance explained by the first two axes was very low (41.2%), while the coefficient of cophenetic correlation was 0.730 (Table 3). When considering only the variables with the highest loadings in the PC1 and PC2 analysis (lymphocytes and RBC, Table 2) and the 4 "particular variables", it turned out that the percentage of variance that was accounted for the two first axes was 64.8%, and the coefficient of cophenetic correlation is 0.870 (Table 3). It was then concluded that the later configuration had a better fit goodness than the former one. For these reasons, from here onward, and as a function of the objectives established in this research, it was decided to focus the analysis to the most relevant variables for the research: lymphocytes (K/µL), RBC, temperature, respiratory rate, age and neutrophils (%).

Table 1

Eigenvalues and percentage of variance explained by the first 7 principal components

Lambda	Value	Proportion	Cumulative Proportion
1	6,09	0,25	0,25
2	2,90	0,12	0,37
3	2,89	0,12	0,49
4	2,28	0,10	0,59
5	1,96	0,08	0,67
6	1,55	0,06	0,74
7	1,15	0,05	0,78

The seven principal components were obtained from the 24 variables of the 183 patients.

Table 2
Eigenvectors with loadings of 24 variables

Variables	E1	E2	E3	E4	E5	E6	E7
Age	-0.33	-0.03	0.04	0.22	-0.07	0.06	0.01
Temperature (°C)	0.01	0.12	0.01	-0.29	0.31	0.29	-0.09
Pulse (PPM)	0.26	0.08	-0.06	-0.25	0.15	0.13	0.18
Resp. rate (BPM)	0.22	-3.6E-03	-0.06	-0.12	0.16	0.08	0.30
WBC (K/µL)	0.10	0.37	-0.24	0.17	0.23	-0.20	0.20
HGB (g/dL)	-0.12	0.36	0.34	-0.22	-0.07	-0.12	-0.01
HCT (%)	-0.12	0.39	0.32	-0.19	-0.14	-0.10	-0.03
MCV (fl)	-0.32	-0.12	0.11	-4.3E-03	0.17	0.09	0.16
MCH (pg)	-0.30	-0.14	0.16	-0.10	0.26	0.06	0.18
MCHC (g/dL)	-3.6E-03	-0.11	0.18	-0.34	0.35	-0.04	0.14
MPV (fL)	-0.17	0.04	-0.06	-0.04	-0.10	0.01	0.43
Monocytes (K/µL)	0.21	0.23	-0.02	0.12	0.29	0.28	-0.17
Eosinophils (K/µL)	0.04	-0.03	0.31	0.34	0.33	-0.31	-0.08

Table 2 (Cont.)

Eigenvectors with loadings of 24 variables

Variables	E1	E2	E3	E4	E5	E6	E7
Lymphocytes (K/µL)	0.35	2.2E-03	0.03	0.02	-0.01	-0.19	0.23
Neutrophils (K/µL)	-0.13	0.38	-0.29	0.12	0.23	-0.05	0.07
Basophils (K/µL)	0.09	0.23	0.19	0.35	-0.02	0.29	0.39
Platelets (K/µL)	0.26	0.03	-0.06	0.11	0.16	-0.06	-0.10
RBC (M/µL)	0.10	0.43	0.23	-0.14	-0.24	-0.14	-0.16
Monocytes (%)	0.15	-0.03	0.22	-1.2E-03	0.13	0.45	-0.39
Eosinophils (%)	0.01	-0.09	0.34	0.32	0.29	-0.29	-0.11
Lymphocytes (%)	0.31	-0.19	0.17	-0.10	-0.13	-0.14	0.18
Neutrophils (%)	-0.32	0.19	-0.21	0.08	0.09	0.08	-0.11
Basophils (%)	0.02	0.02	0.35	0.25	-0.17	0.40	0.27
GRCV (%)	0.13	0.03	-0.12	0.27	-0.26	0.13	-0.09

Table 3

Percentage of variance explained and cophenetic correlation of 6 and 11 variables

	Total variance explained	Cophenetic correlation
Variables selected according loadings and particular variables (11 variables).	41.2%	0.730
Particular variables and 2 variables with highest loadings in PC1 and PC2 (6 variables)	64.8%	0.870

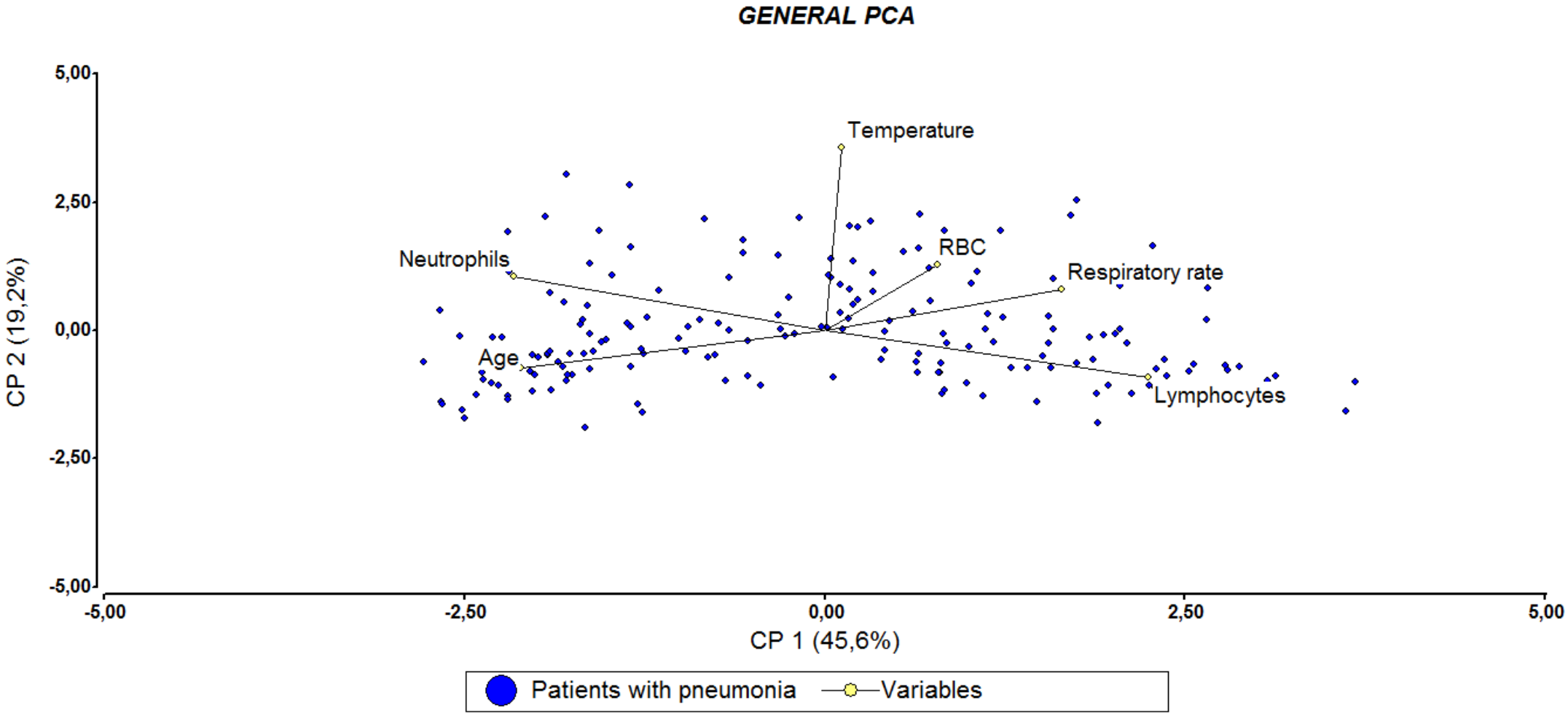

Figure 1. General PCA for the six variables selected. (It shows the correlation between the representative variables and the patients with pneumonia)

Sample overview

After performing a general analysis of the patients having pneumonia, there were identified 110 children (0-14 years old); 3 young people (15-25 years old), 11 adults (26-64 years old) and 56 elder (≥ 65 years old). It coincides with the well-known evidence that children and the elder are the most prone, vulnerable patients to community-acquired pneumonia (Bartlett & Mundy, 1995; Dang et al., 2014; Mandell, 2015).

General PCA

As shown in Figure 1, the PCA analysis was carried out on the 6 selected variables. The Principal component 1 (PC1) explained the 45.6 % of variance, while the Principal Component 2 (PC2) did only 19.2% of variance. The sum of these 2 Principal Components explained 64.8% of the total variance, which means that it was working with the 64.8 % of the total information. The first principal component separates the lymphocytes and respiration rate (right of the Figure 1) and neutrophils and age (left of the Figure 1). Patients with high neutrophil levels and older ages would have low values of lymphocytes and respiration rate. On the other hand, RBC and Temperature showed a significant positive correlation with Principal Component 2.

Lymphocytes and respiration rate demonstrated a high positive correlation with each other. It means that if values of lymphocyte levels are elevated, the respiration rate will also increase. On the contrary, if the lymphocyte count decrease, the respiration rate will also diminish (Figure 1). Neutrophils and age had high positive correlation each other, therefore, the values of neutrophils increase with the age or decrease when the age too (Figure 1). A similar high positive correlation was found between RBC and temperature present a correlation (Figure 1), but they were not correlated with neutrophils, age, respiratory rate and lymphocytes.

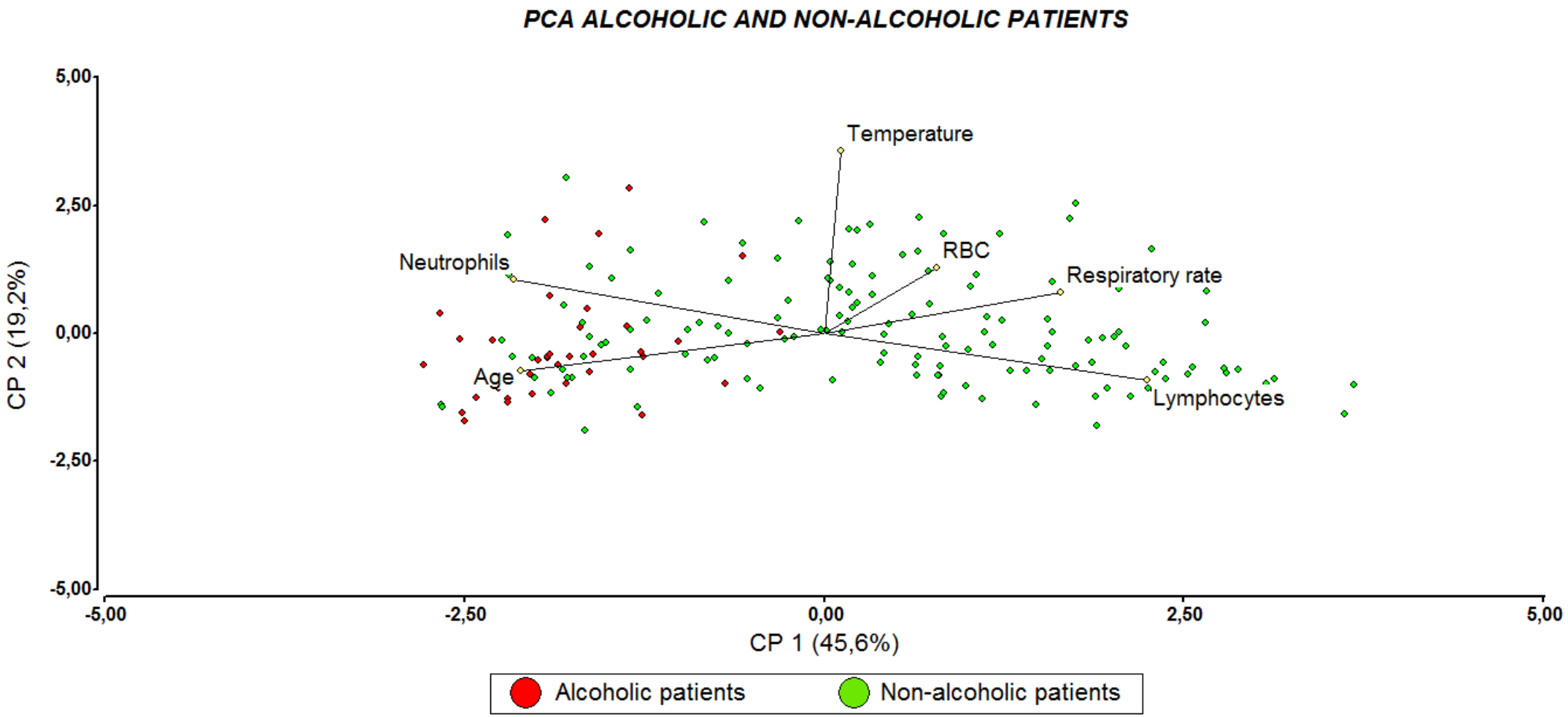

Figure 2. PCA analysis for alcoholic and non-alcoholic patients with pneumonia

Table 4

Registration of the incidence of the types of pneumonia in December 2018, by alcoholic, non-alcoholic patients, age groups and totals.

Pneumonia	Alcoholic (n=35)					Non-alcoholic (n=148)				
	Children 0-14 years old	Young 15-24 years old	Adults 25-64 years old	Elder ≥ 65 years old	**Total alcoholic**	Children 0-14 years old	Young 15-24 years old	Adults 25-64 years old	Elder ≥ 65 years old	**Total non-alcoholic**
J12: Viral pneumonia, not elsewhere classified	-	-	-	-	**-**	15	-	-	-	**15**
J15: Bacterial pneumonia, not elsewhere classified	-	-	5	15	**20**	10	1	1	15	**27**
J16: Pneumonia due to other infectious organisms, not elsewhere classified	-	-	-	-	**-**	-	-	-	1	**1**
J17: Pneumonia in diseases classified elsewhere	-	-	-	1	**1**	1	-	-	-	**1**
J18: Pneumonia, organism unspecified	-	-	1	13	**14**	83	2	4	15	**104**
Total	**0**	**0**	**6**	**29**		**109**	**3**	**5**	**31**	

Diseases were classified according to: ICD-10 Version:2019

Table 5

Mean and standard deviation of variables selected in alcoholic and non-alcoholic patients

Variable	Alcoholic (n=35)		Non-alcoholic (n=148)	
	Mean	SD	Mean	SD
Age (years)	77.71	15.98	20.45	33.02
Temperature (°C)	37.00	1.02	37.23	0.98
Lymphocytes (K/uL)	1.17	0.63	3.33	2.19
Neutrophils (%)	78.55	12.39	58.14	21.44
Respiration rate (BPM)	19.91	5.52	28.93	11.06

Reference categories: lymphocytes 1.1-3.2 K/uL, neutrophils 40-65%, respiration rate 12-18/min and 20-30/min in children.

Alcoholic and non-alcoholic patients

In this set of statistics, there were included a total of 183 pneumonia patients, 35 of which (19.13%) declared to frequently consume alcohol, while 148 (80.87%) were classified as non-habitual alcohol consumers. In the Figure 2, the alcoholic patients (red) are grouped near age and neutrophils variables. These variables present high positive correlation, thus suggesting that neutrophils increased as the age increase. Among the 82.86% of the alcoholic patients with high levels of neutrophils were elder (≥ 65 years old), whereas the others (17.14%) were adults (25-64 years old). Interestingly, most of the alcoholic patients grouped near of the neutrophils and age variables, especially the elder patients, had acquired bacterial pneumonia, (Table 4). As the first principal component separates the lymphocytes and respiration rate (right of the Figure 1) and neutrophils and age (left of the Figure 1). It means that if the neutrophils and age increase, the lymphocytes and respiration rate decrease.

Elder and alcoholic patients

As shown in Table 4, in the section of alcoholic patients, there are 2 groups. The first one show 6 out 35 alcoholic patients which are adults (17.74%) and the second one show 29 out of 35 alcoholic patients which are elder (82.26%). Of these last ones, 15 presented "Bacterial pneumonia, not elsewhere classified", 13 presented "Pneumonia, organism unspecified" and just 1 presented "Pneumonia in diseases classified elsewhere" (Table 4). These data were in agreement with a previous report (Yoshikawa et al., 2000), where it was found that *Streptococcus pneumoniae* is the most frequent agent causing pneumonia in the elder. Accordingly, elder patients admitted to be treated with antimicrobial therapy against bacterial pathogens (Stupka et al., 2009).

Alcohol consumption (acute and chronic consumption) emerges as the main risk factor for bacterial pneumonia since there is evidence that alcohol diminishes the ciliary function and bacterial clearance, the innate primary line of defense against lung infections (Bhatty et al., 2011; Bradley, 2019). After infection has started, the first cells to arrive at the infection site are neutrophils, where they accumulate in large quantities for controlling and clearing infection (Pechous, 2017). It could explain why in alcoholic and elder patients (whose majority presented bacterial pneumonia) were grouped close to the variables neutrophils and age (Figure 2). It means an increase the values of this variables in that alcoholic and elder patients (Table 5).Alcohol compromises the functions of cytokines, macrophages and neutrophils (De Roux et al., 2007). It follows that alcohols makes the body more vulnerable to viral or bacterial infections causing pneumonia

(Bustamante-Marin & Ostrowski, 2017). Considering the non-alcoholic patients, they surprisingly showed a greater tendency to acquire "organism unspecified Pneumonia" (Table 4), and the values of neutrophils and age decrease related with alcoholic patients (Table 5). It could indicate that alcohol consumption in the elder may be associated with a greater probability of acquire bacterial pneumonia which is the most severe of pneumonia in terms of morbility and mortality (Sattar & Sharma, 2020). At the time of the infection, it is produced an endotoxemia (Cangemi et al., 2016), then the number of neutrophils increases while lymphocyte counts decrease (de Jager et al., 2012). The decrease of lymphocytes in patients with pneumonia is known as lymphopenia. Several studies have already been reported where patients with pneumonia suffer from lymphopenia (Bermejo-Martin et al., 2017; Marrie & Wu, 2005). This could be due lymphocyte's massive migration to the lungs, adhesion to the vascular endothelium, etc (Bermejo-Martin et al., 2017). Moreover, the association between neutrophils and lymphocytes is called neutrophil-lymphocyte count ratio (NLCR) and are used to evaluate the severity of several infectious diseases (de Jager et al., 2012).

In addition, Figure 2 show a high positive correlation between lymphocytes and respiratory rate. However, there are no meta-analysis or biological reports that explain this correlation between respiratory rate and lymphocytes. For this reason, it is essentially carry out more analysis to find responses. The respiratory rate is a key predictor of pneumonia and it is likely to be associated with mortality rates (Strauß et al., 2014). Respiratory rates in patients with pneumonia are generally found to be high, a condition called tachypnea (Park, 2020). However, in Table 5, different values were found (non-alcoholic patients: 28, 93 ± 11, 06, alcoholics: 19, 91 ± 5, 52; Table 5). This difference may be due to the fact that non-alcoholic patients are mostly children between 0 and 5, whose normal respiratory rates are usually higher than those of adults or elders.

In Figure 2, the temperature and RBC present high positive correlation. However, the right angles formed by the variables RBC, temperature with age and neutrophils, indicates that it does uncorrelated with them, or is very low. Alcoholic patients close to these variables (neutrophils, age) seemed to indicate that these patients are uncorrelated with variables such as temperature and age. In other words, it can find alcoholic patients who have high RBC values as well as low ones. In the same way we can find alcoholic patients who have normal temperature values as well as high. For this reason, in the case of alcoholic patients, the variables temperature and RBC are inconclusive. Although some

authors relates alcohol consumption with RBC (Nikiforov et al., 2017), that was not the case in this analysis since it was even observed normal RBC (Table 5).

Adults and alcoholic patients

Of the 35 alcoholic patients, 6 where adults (17.74%), which 5 of them presented "Bacterial pneumonia, not elsewhere classified" and 1 presented "Pneumonia, organism unspecified". Despite the Bacterial pneumonia is frequent in elder people, there are 5 cases, which show the strong relation of this kind of pneumonia with alcoholic consumption and the adults.

Non-alcoholic patients

The non-alcoholic patients represent the 80.87% of the pneumonia patients, however with this graphic (Figure 2), we can only explain the variables related to alcoholic people because they present a uniform distribution near of neutrophils and age variable. On the contrary, the non-alcoholic patients are distributed throughout all planes and are difficult to predict the association of these patients with a specific variable.

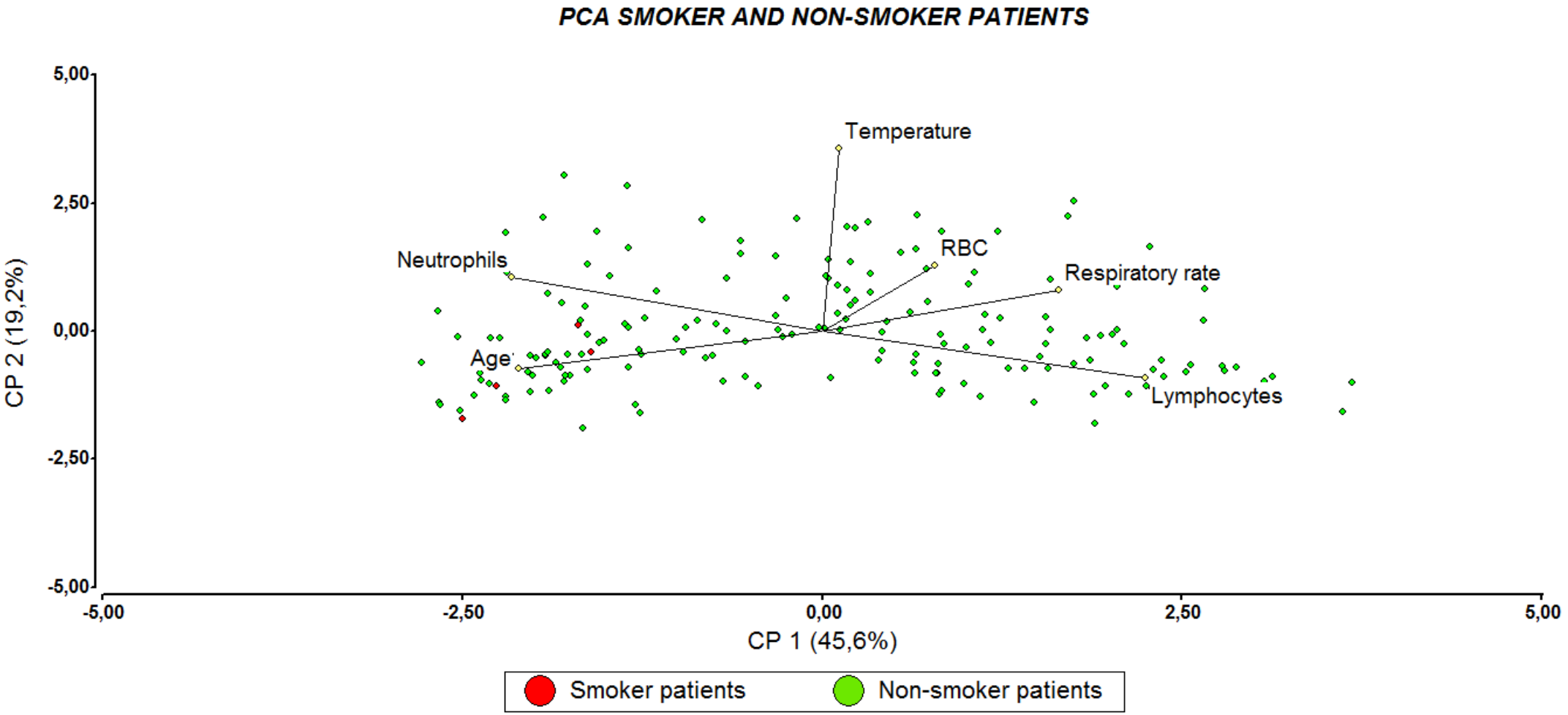

Figure 3. PCA analysis for smokers and non-smokers patients with pneumonia

Table 6

Registration of the incidence of the types of pneumonia in December 2018, by smoker and non-smoker, age groups and totals.

Pneumonia	Smoker (n=4)					Non-smoker (n=179)				
	Children 0-14 years old	Young 15-24 years old	Adults 25-64 years old	Elder ≥ 65 years old	**Total smoker**	Children 0-14 years old	Young 15-24 years old	Adults 25-64 years old	Elder ≥ 65 years old	**Total non-smoker**
J12: Viral pneumonia, not elsewhere classified	-	-	-	-	**-**	15	-	-	-	**15**
J15: Bacterial pneumonia, not elsewhere classified	-	-	-	3	**3**	10	1	6	27	**44**
J16: Pneumonia due to other infectious organisms, not elsewhere classified	-	-	-	-	**0**	-	-	-	1	**1**
J17: Pneumonia in diseases classified elsewhere	-	-	-	-	**0**	1	-	-	1	**2**
J18: Pneumonia, organism unspecified	-	-	-	1	**1**	83	2	5	27	**117**
Total	**0**	**0**	**0**	**4**		**109**	**3**	**11**	**56**	

Diseases were classified according to: ICD-10 Version:2019

Table 7

Mean and standard deviation of variables selected in smoker and non-smoker patients

Variable	Smoker (n=4)		Non-smoker (n=179)	
	Mean	SD	Mean	SD
Age (years)	87.00	10.00	30.16	37.39
Temperature (°C)	36.60	0.39	37.20	0.99
Lymphocytes (K/uL)	1.00	0.24	2.96	2.17
Neutrophils (%)	79.08	7.50	61.66	21.63
Respiration rate (BPM)	22.00	9.93	27.32	10.84

Reference categories: lymphocytes 1.1-3.2 K/uL, neutrophils 40-65%, respiration rate 12-18/min and 20-30/min in children.

Smoker and non-smokers patients

This section analyzes 183 patients who have acquired pneumonia, of which only 4 were classified as people who smoke cigarettes constantly (2.19 %) and 179 classified as people who do not smoke cigarettes constantly (97.81%). These 4 smoker patients (red color) were near to neutrophils and age variables. At the same time, these patients presented low values in the lymphocytes and respiration rate. Due to low rate of smokers (4 vs. 179 non-smokers) it was not possible to establish associations with these patients with most studied variables.

The use of tobacco is a risk factor for bacterial pneumonia (De et al., 2013) even in passive smokers (Almirall et al., 2014). The smoking alters mucociliary clearance and buccal epithelial surfaces, facilitating the adherence of pathogens. It leads to a large oropharyngeal colonization, thus increasing the risk of acquire pneumonia (Baskaran et al., 2019). Of this way, tobacco inhibits the innate and adaptive immune system response. It includes toll-like receptors, lymphocytes, maturation of dendritic cells, opsonization and phagocytosis capacities (Campagna et al., 2016). In fact, 3 out of 4 patients with pneumonia that are smokers, presented "Bacterial pneumonia, not elsewhere classified", and 1 presented "Pneumonia, organism unspecified" (Table 6). It shows that both alcohol consumption and tobacco smoking increase the risk for acquire bacterial pneumonia. Moreover, every patients classified as smokers were also alcoholics, so the risk of acquire bacterial pneumonia or another pneumonia could increases even more (Wyatt et al., 2012). In general terms, smoking patients' results are similar to those of alcoholics, high values of neutrophils and age while lymphocytes and respiratory rate decreases (Figure 3). (Table 7). The RBC and temperature variables, as they are not correlate with the other variables, may have high as well as low values, therefore these two variables are not conclusive in our study with smoking patients.

Even if we would account for the smokers' behavior against the selected variables, these were not conclusive because of having only 4 smokers. It was presumed that the population evaluated has few tobacco smoking habits. It is important to mention that both in Tables 4 and 7 of alcoholic, non-alcoholic patients and smoker, non-smoker patients respectively, has been observed that there are child patients who have a tendency to acquire viral pneumonia. This could explain why the variable lymphocytes have a negative correlation with age since viral pneumonia is characterized by an increase in lymphocytes and is very common in children (Kim et al., 2014). In fact, according to

Ruuskanen et al., this type of pneumonia is very common in children so in this way we compare our results with the existing scientific evidence (Ruuskanen et al., 2011).

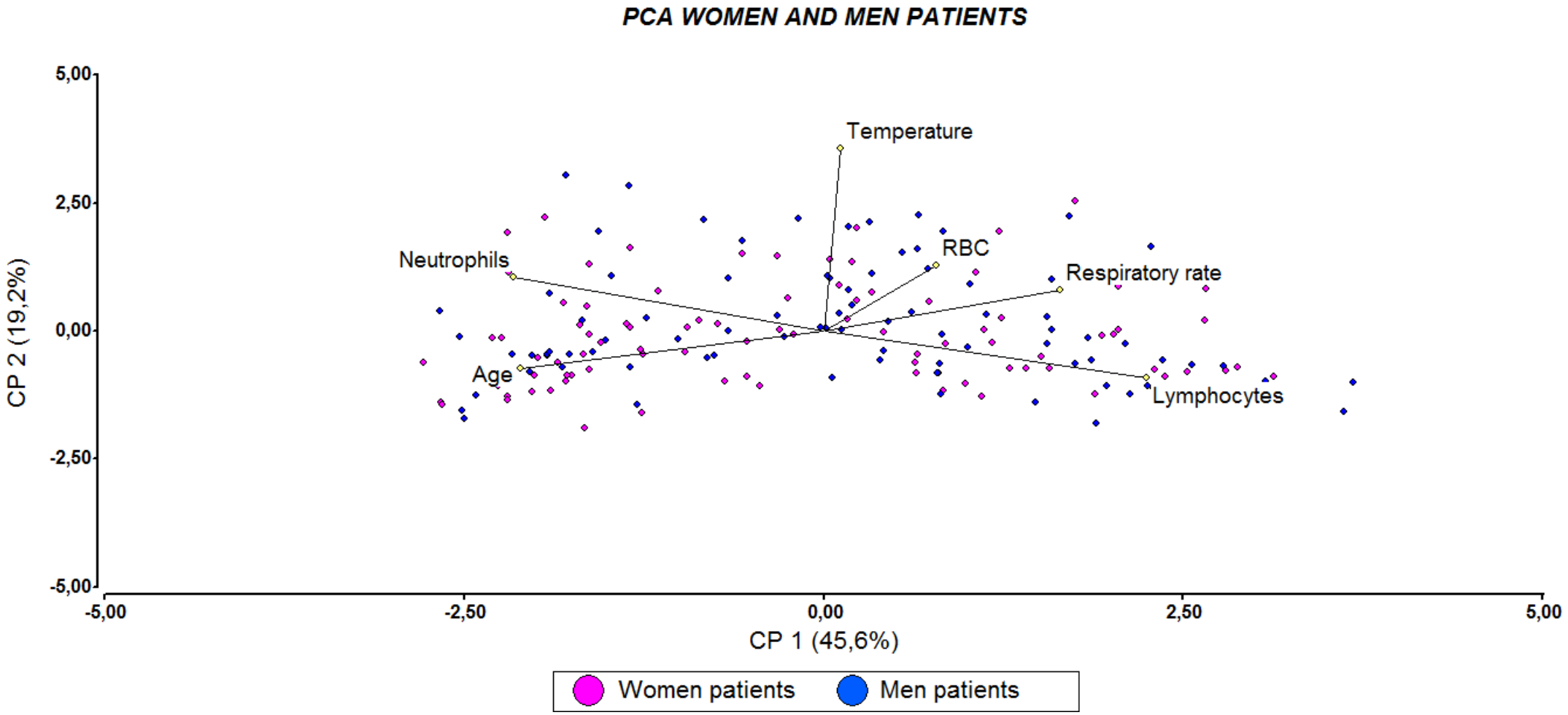

Figure 4. PCA analysis for women and men patients with pneumonia

Table 8

Registration of the incidence of the types of pneumonia in December 2018, by genders, age groups and totals.

Pneumonia	Women (n=94)					Men (n=89)				
	Children 0-14 years old	Young 15-24 years old	Adults 25-64 years old	Elder ≥ 65 years old	**Total women**	Children 0-14 years old	Young 15-24 years old	Adults 25-64 years old	Elder ≥ 65 years old	**Total men**
J12: Viral pneumonia, not elsewhere classified	9	-	-	-	**9**	6	-	-	-	**6**
J15: Bacterial pneumonia, not elsewhere classified	4	1	4	18	**27**	6	-	2	12	**20**
J16: Pneumonia due to other infectious organisms, not elsewhere classified	-	-	-	-	**0**	-	-	-	1	**1**
J17: Pneumonia in diseases classified elsewhere	1	-	-	1	**2**	-	-	-	-	**0**
J18: Pneumonia, organism unspecified	37	-	2	17	**56**	46	2	3	11	**62**
Total	**51**	**1**	**6**	**36**		**58**	**2**	**5**	**24**	

Diseases were classified according to: ICD-10 Version: 2019

Table 9

Mean and standard deviation of variables selected in women and men patients

Variable	Women (n=94)		Men (n=89)	
	Mean	SD	Mean	SD
Age (years)	36.56	39.50	25.94	35.61
Temperature (°C)	37.10	0.94	37.28	1.03
Lymphocytes (K/uL)	2.82	2.14	3.02	2.19
Neutrophils (%)	61.26	21.72	62.87	21.48
Respiration rate (BPM)	27.31	11.04	27.10	10.66

Reference categories: lymphocytes 1.1-3.2 K/uL, neutrophils 40-65%, respiration rate 12-18/min and 20-30/min in children.

Women and Men patients

This section analyzes 183 patients who have acquired pneumonia, of which only 94 are women (51.37%), and 89 are men (48.63%). According to Yancey et al., respiratory diseases are more frequent in men (Yancey et al., 2001). It includes pneumonia, which affects principally children under 5 years old and elder people over 65 (Comes Castellano et al., 2005). In most research investigating the incidence of pneumonia according to gender, the following parameters are evaluated: the severity, the probability of hospitalization, and the death of the patient. And all these parameters are more frequent in men than women (Barbagelata et al., 2020; Gonzalez Quero et al., 2017).

In addition, it is necessary to take in mind the life expectancy of men which is lower than the women (Reade et al., 2009) due the physiological and social factors (Falagas et al., 2007). Physiological factors there are: develop chronic conditions earlier (Reade et al., 2009), hormones (Falagas et al., 2007), immune response of the body to infection (Barbagelata et al., 2020) etc. Moreover, in the social context, men tend to consume alcohol and cigarettes more often than women (Falagas et al., 2007). Although in the studies mentioned above, differences are shown between men and women in terms of the probability of acquiring pneumonia, severity, and hospitalization. This study only shows men and women who have acquired pneumonia and their most important variables. They are not evenly distributed but rather dispersed throughout the plane (Figure 4), so no conclusive criteria have been established. At the same time, table 10 shows that both male women have similar values in the temperature, lymphocytes, neutrophils, and respiration rate. Similarly, Table 9 shows that both men and women tend to acquire the same pneumonia types.

CONCLUSIONS

By using PCA analysis, it was found a grouping between elder patients and the increase of the neutrophils, which is the hallmark of any infection. Within this subsample, both alcoholic and smoker patients showed the greatest tendency to develop bacterial pneumonia, although given the reduced number of smoker patients (only 4) precluded us to state that smoking directly promotes pneumonic infection. As to the sex effects in the risk for pneumonia, the results neither were conclusive. Finally, significant correlations were found between the respiratory rate and lymphocyte count variables, as well as between temperature and RBCs. Although no straightforward mechanistic/physiological accounts that give support these correlations have been found, it should be considered that high respiratory rate and temperature denote the severity of pneumonia, which in light to our mathematical findings may be associated with these particular blood counts. Future research is then guaranteed on the putative links of these variables, which may help understand the physiopathology of the pneumonic infection.

RECOMMENDATIONS

This research is the first attempt to analyze pneumonia from an exploratory and epidemiological point of view that allows us to evaluate the damages caused by the consumption of alcohol and tobacco, in addition to evaluating age and sex. For this reason, it is important that more studies like these are carried out in Ecuador, where pneumonia is one of the main causes of death, and alcohol consumption is quite ingrained in its inhabitants.

ABREVIATIONS

GRVC	Erythrocyte distribution width based on the coefficient of variance
HCT	Hematocrit
HGB	Hemoglobin
IESS-HQS	IESS Southern Quito Hospital
MCH	Mean Corpuscular Hemoglobin
MCV	Mean Corpuscular Volume
MCHC	Medium Corpuscular Hemoglobin Concentration
MPV	Mean Platelet Volume
PCA	Principal Component Analysis
PDW	Platelet Distribution Width
PC1	Principal Component 1
PC2	Principal Component 2
RBC	Red Blood Cell
RDW	Red Blood Cell Distribution Width
WBC	Leukocyte

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