ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 12, Issue, 04, pp. 55450-55454, April, 2022
https://doi.org/10.37118/ijdr.24403.04.2022

RESEARCH ARTICLE OPEN ACCESS

ANALYSIS OF THE PULMONARY TOMOGRAPHIC PATTERN BY THE B.1.1.7 AND P.1 VARIANTS OF THE SARS-COV-2 VIRUS

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ARTICLE INFO

Article History:
Received 11th January, 2022
Received in revised form
26th February, 2022
Accepted 14th March, 2022
Published online 27th April, 2022

Key Words:
COVID-19; SARS-CoV-2; Diagnostic; Tomography.

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ABSTRACT

The SARS-CoV-2 virus has undergone several genetic mutations, which culminated in multiple waves of disease transmission. Computed tomography (CT) of the chest may be a diagnostic alternative complementary to RT-PCR to assess pulmonary involvement and assist in the therapeutic approach. To analyze the pulmonary tomographic patterns in the epidemic peaks of COVID-19 caused by the B.1.1.7 and P.1 variants of the SARS-CoV-2 virus. Cross-sectional, descriptive, analytical and retrospective study through the evaluation of 360chest CT scans of patients with COVID-19 in two epidemic peaks of the disease of April–September 2020(B.1.1.7) and October 2020–March 2021(P.1) in an area of the Brazilian Amazon. Were included patients >18 years old of both sexes. The pattern and degree of pulmonary involvement, distribution of lesions, affected segments and other CT findings were evaluated. Gender (p=0.289) and age group (p=0.314) did not vary significantly between periods. In the first, 70.6% had pulmonary involvement10-25% and in the second,43.3%. The presence of interlobular septa thickening was significantly observed in the first epidemic peak (81.9%) (p=0.002). Prevalence of women and age between 45-60 years. All had ground-glass lesions and the typical pattern of involvement prevailed in both analyses. The Alpha variant presented a higher degree of pulmonary involvement in relation to the Gamma variant.

Citation: ***Beatriz Amaral Costa Savino, Eduarda Gabriel Mafra, Andrea Luzia Vaz Paes, Carlos Alberto Costa do Amaral, Marcelo Coelho Simões and Clea Nazaré Carneiro Bichara.*** "Analysis of the pulmonary tomographic pattern by the b.1.1.7 and p.1 variants of the sars-cov-2 virus*", International Journal of Development Research*, 12, (04), 55450-55454.

INTRODUCTION

COVID -19 is caused by SARS-CoV-2 virus and started in China in December 2019. The pathogen quickly spread globally and acquired the status of a pandemic in March 2020, posing a major threat to global public health (SOY*et al*., 2020; ZHOU *et al*. 2020). Since then, the virus has undergone several mutations, culminating in multiple waves of transmission (HANRATH *et al*., 2021). Brazil was one of the epicenters of the pandemic, registering 29.1 million cases and 652 thousand confirmed deaths until the beginning of March 2022 (BRASIL, 2022). The World Health Organization (WHO), in collaboration with other international entities, has been monitoring and evaluating the evolution of SARS-CoV-2 since January 2020. Changes in its structure can modify the transmissibility, epidemiology, virulence or clinical presentation of the disease, altering its severity, the performance of vaccines, drugs, diagnostic tools, among other public health measures (WHO, 2021).

In order to prioritize monitoring and inform the ongoing response to the COVID-19 pandemic, SARS-CoV-2 was stratified into variants considered of concern: Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2), and Omicron (B.1.1.529). In Brazil, there was a prevalence of the Alpha variant during the first epidemiological wave of the disease, circulating from March to October 2020. Since November 2020, however, the Gamma variant broke out and spread the second wave of transmission in the country (WHO, 2021). Real-time reverse transcription polymerase chain reaction (RT-PCR) is the gold standard for SARS-CoV-2 diagnosis. However, this method is not always accessible and has shown variable sensitivity and specificity, due to insufficient viral load, errors in sample collection methods or lack of definitive reference standards (OMER *et al*., 2020; PULIA*et al*., 2020). Thus, computed tomography (CT) of the chest can be a diagnostic alternative complementary to RT-PCR, in addition to serving to assess pulmonary involvement and assist in the therapeutic approach (LI*et al*., 2020; LIU *et al*., 2020). The present study aimed to analyze the main epidemiological characteristics and imaging findings on chest CT in a sample of patients with COVID-19 who performed the screening at a reference diagnostic center, comparing two epidemic peaks of the disease in an area of the Brazilian Amazon in the years 2020 and 2021, caused by the variants B.1.1.7 and P.1 of the SARS-CoV-2 virus.

METHODS

A cross-sectional, descriptive, analytical and retrospective study was carried out through the evaluation of computed tomography scans of the chest of patients diagnosed with COVID-19 divided into two periods: April to September 2020 and October 2020 to April 2021. The study population consisted of 360 patients who underwent chest CT at the same referral radiology service in Belém-PA, Brazil, divided into two groups of 180 patients, selected in the chronological order in which the exam was performed. The patients included in the study were over 18 years old, of both sexes, living in an area of the Brazilian Amazon, with tomographic findings suggestive of COVID-19, presenting some degree of pulmonary involvement. The variables studied were age, sex, pattern of pulmonary involvement (typical, atypical or indeterminate), percentage of pulmonary involvement (<10%, 10-25%, 25-50%, 50-75% and >75%), distribution of lesions (unilateral or bilateral) and other CT findings (ground-glass pattern, conventional consolidation, linear opacity, pleural thickening, air bronchogram sign, nodules, bronchial wall thickening and bronchiectasis). The classification system for chest CT scans chosen to guide this article was based on the Consensus of Experts of the Radiological Society of North America (RSNA) (Table 1) (Ye *et al*., 2020). The epidemiological classification of the disease according to the variants of concern of the SARS-CoV-2 virus was based on information from official bodies after analyzing the dominant genetic variability in each analyzed period. Statistical data were analyzed using the Bioestat 5.0 program, and results with a p-value lower than 0.05 were considered relevant. The Microsoft Word 15.19.1 and Microsoft Excel 15.19.1 programs were used to create graphs and tables.

All research subjects were studied according to the precepts of the Declaration of Helsinki, the Nuremberg Code and the Norms for Research Involving Human Beings (Res. CNS 466/12) of the National Health Council were respected, and the researchers signed the Term of Commitment of Data Usage – TCUD.

RESULTS

The proportions of patients of different genders (p=0.289) or different age groups (p=0.314) did not vary significantly between the two periods (Table 2). There was a significant association between the period and the pattern of involvement (p=0.002): of the individuals in the first period, 34 (18.9%) had an undetermined pattern of involvement and of the individuals in the second period, 92.8% had a typical pattern of involvement.Also, period and involvement were significantly associated (p<0.001): in the second period, 48 (26.7%) had involvement <10%, a proportion higher than expected by chance; of the 180 individuals in the first period, 127 (70.6%) had 10-25% involvement, in a greater proportion than expected (Table 3). Period and laterality were significantly associated (p<0.001): in the second period, 164 (91.1%) were bilateral, in a greater proportion than expected; of the individuals in the first period, 22.8% were unilateral, in a greater proportion than expected by the statistical test (Table 4). Ground glass findings were found in 100% of patients. Period and interlobular septal thickening were significantly associated (p=0.002): of the 85 individuals with other findings in the second period, 33 (38.8%) had no interlobular septal thickening, this proportion being higher than expected; while in the first period, 81.9% had thickening of the interlobular septa, in a significantly higher proportion than expected. Also, there was a significant association between the epidemiological period and the presence of intermingling lattice (p<0.001): of the 85 individuals with other findings in the second period, 100% had no intermingling lattice, this proportion being higher than expected; in the first period, 90 (77.6%) had fine intermingled reticulates, this proportion being higher (†) than expected.

Table 1. RSNA chest CT classification system for reporting COVID-19 pneumonia

CT findings of COVID-19 pneumonia imaging classification	Justification	CT findings
Typical	More specific characteristics for COVID-19 pneumonia	Peripheral, bilateral, ground-glass opacity with or without consolidation or visible intralobular lines (“crazy paving”) Multifocal ground-glass opacity of rounded morphology with or without consolidation or visible intralobular lines (“mosaic paving”) Reverse halo sign or other organizing pneumonia findings (seen later in the disease)
Undetermined	Nonspecific imaging features of COVID-19 pneumonia	Absence of typical features Presence of multifocal, diffuse, perihilar, or unilateral ground-glass opacities with or without consolidation without a specific distribution and are non-rounded or non-peripheral. Few, very small ground-glass opacities with a non-rounded, non-peripheral distribution
Atypical	Unusual or unreported features of COVID-19 pneumonia	Absence of typical or undetermined characteristics Presence of isolated lobar or segmental consolidation without ground-glass opacity Discreet small nodules (centrilobular, "tree bud") pulmonary cavitation Smooth interlobular septum thickening with pleural effusion
Negative for pneumonia	No featuresof pneumonia	No CT resources to suggest pneumonia

Note: Adapted from the Radiological Society of North America Expert Consensus Statement on the reporting of chest CT findings related to COVID-19.

Table 2. Comparison between the demographic characteristics of COVID-19 positive patients undergoing chest CT in a reference laboratory, from April to September 2020 (first period) and October 2020 to April 2021 (second period), Amazon-Brazil

Variable	1st Period(n=180)	2nd Period(n=180)	p-value
Gender			0,289
Female	94 (52,2)	105 (58,3)	
Male	86 (47,8)	75 (41,7)	
Age			0,314
18 - 25 years	2 (1,1)	5 (2,8)	
25 - 35 years	10 (5,6)	16 (8,9)	
35 - 45 years	30 (16,7)	38 (21,1)	
45 - 60 years	74 (41,1)	66 (36,7)	
+60 years	64 (35,6)	55 (30,6)	

Table 3. Comparison of the pattern of involvement and dimensions of involvement of patients positive for COVID-19 undergoing chest CT in a reference laboratory, from April to September 2020 (first period) and October 2020 to April 2021 (second period), Amazon-Brazil

Variable	1st Period (n=180)	2nd Period (n=180)	p-value
Patterno f involvement			0,002
Undetermined	*34 (18,9) †*	*13 (7,2) **	
Typical	*146 (81,1) **	*167 (92,8) †*	
Involvement			<0,001
<10%	*16 (8,9) **	*48 (26,7) †*	
10-25%	*127 (70,6) †*	*78 (43,3) **	
25-50%	26 (14,4)	36 (20,0)	
>50%	11 (6,1)	18 (10,0)	

Categorical variables are displayed as n (%). The percentages are relative to the total of each column. In all cases the chi-square was used. *: this frequency was lower than what would be expected by chance. †: this frequency was higher than expected.
Source: authors.

Table 4. Comparison of laterality of lung lesions in COVID-19 positive patients undergoing chest CT in a reference laboratory, from April to September 2020 (first period) and October 2020 to April 2021 (second period), Amazon-Brazil

Variable	1st Period (n=180)	2nd Period (n=180)	p-value
Laterality			<0,001
Bilateral	*139 (77,2) **	*164 (91,1) †*	
Unilateral	*41 (22,8) †*	*16 (8,9) **	

Categorical variables are displayed as n (%). The percentages are relative to the total of each column. Chi-square was used. *: this frequency was lower than what would be expected by chance. †: this frequency was higher than expected.
Source: authors.

Table 5. Comparison of the prevalence of other changes among COVID-19 positive patients undergoing chest CT in a reference laboratory, from April to September 2020 (first period) and October 2020 to April 2021 (second period)), Amazon-Brasil

Variable	1st Period (n=180)	2nd Period (n=180)	p-value
Thickening of the Interlobular Septa	*95 (81,9)†*	*52 (61,2)**	0,002
Fine IntermediateReticulate	*90 (77,6)†*	*0 (0,0)**	<0,001
Nodules	33 (28,4)	22 (25,9)	0,808
Atelectasis	2 (1,7)	6 (7,1)	0,073
Bronchiectasis	3 (2,6)	5 (5,9)	0,287
Lymph node enlargement	3 (2,6)	5 (5,9)	0,287
Micronodules	7 (6,0)	1 (1,2)	0,142
Stretchmarks	1 (0,9)	4 (4,7)	0,165
Parenchymalbands	3 (2,6)	0 (0,0)	0,264
Pleural effusion	1 (0,9)	2 (2,4)	0,575
Air bronchogram	0 (0,0)	2 (2,4)	0,178
Pulmonary Cyst	2 (1,7)	0 (0,0)	0,509

For thickening of the septa, intermingling reticulate and nodules, the chi-square was used. In other cases, Fisher's exact test. Information on the absence of each finding is omitted for brevity in the Table. Categorical variables are displayed as n (%). The percentages are relative to the total of each column.
Source: authors.

The presence of nodules (p=0.808), atelectasis (p=0.073), bronchiectasis (p=0.287), lymph node enlargement (p=0.287), micronodules (p=0.142), striae (p=0.165), parenchymal bands (p=0.264), pleural effusion (p=0.575), air bronchogram (p=0.178) or pulmonary cyst (p=0.509) (Table 5).

DISCUSSION

In the first year of the pandemic, there has been a great concern in the scientific community regarding two variants of the SARS-CoV-2 virus, known in the dynamic nomenclature proposed by Rambaut *et al.* (2020) as B.1.1.7 (alpha) and P.1 (gamma), initially identified in infected patients, respectively, in the United Kingdom and Manaus, Brazil (RAMBAUT *et al*., 2021; TEGALLY *et al*., 2020; FARIA *et al*., 2021). These variants need monitoring due to the presence of a set of mutations that lead to an increase in transmissibility and to the deterioration of epidemiological situations in the areas where they are established. In this sense, this study analyzed chest CT scans in the first two epidemic peaks of the disease, characterized by each of the variants: B.1.1.7 of April - September 2020 and P.1 of October 2020 - March 2021, in an area of the Brazilian Amazon. Despite having the same origin, the different strains have different mutations (FREITAS *et al*., 2021), justifying the sometimes differentiated clinical and epidemiological aspects of the disease. In the study, it was observed that the proportions of patients of different genders and age groups did not vary significantly in the two analyzed periods. There was a slight prevalence in women 94 (52.2%) and 105 (58.3%), respectively in the first and second epidemic period. In addition, the most affected age group was between 45-60 years in both periods: 74 (41.1%) and 66 (36.7%), findings observed in almost all published studies, such as those by Ding *et al.* (2020) (Female 54.46%: 53.7 years ± 15.9 and Men 45.54%: 58.3 years ± 16.2).

The prevalence of involvement in people aged between 45-60 years can be explained by the fact that this is an economically active age with a large presence in more exposed social and professional groups. In this way, in a period in which social isolation was recommended, it assumed a greater risk of contagion and spread of the SARS-CoV-2 virus (LIU *et al*., 2020). It is known that in addition to identifying signs and symptoms, the diagnosis of COVID-19 is a priority for the treatment and control of the disease in its early stages. RT-PCR is currently the gold standard for the diagnosis of SARS-CoV-2. However, due to the lack of availability during the beginning of the pandemic, its application was limited in the first epidemic period of the disease in the study area (YE *et al*., 2020). For this reason, chest CT, as a sensitive, practical and fast method, was temporarily adopted as an adjuvant for the indirect diagnosis of SARS-CoV-2 infection in the second largest regional metropolis of the Legal Amazon (YE *et al*., 2020). The high sensitivity of chest CT assists in the detection of early signs of disease as it allows the assessment of the nature of the extent of the lesions as well as detecting fine alterations that are not normally seen in other exams with lower resolution, such as chest X-ray (YANG *et al*., 2020).These early findings, while subtle, are of significant help when there is a clinical suspicion of severe pneumonia and potentially life-threatening respiratory diseases such as COVID-19 (YANG *et al*., 2020).

The classic chest CT findings of COVID-19 patients are ground-glass opacities with peripheral distribution, multilobar, usually most prominent in the lower middle lobes and posterior lung areas. The reported prevalence of ground glass varies between 46% and 100% and predominates in the early stages of the disease (UFUK *et al*., 2020). Pathophysiologically, this change is justified during the initial stage of viral pneumonia, when inflammation of the interstitial alveolar wall occurs, which contains various degrees of cellular infiltrates, but no collagen tissue forms interstitial fibrosis (ZHU *et al*., 2020). It is important to emphasize that the frequency of imaging findings depends on the chronology of the infectious period in which the examination was performed. Most individuals have a normal CT during the first 2 days after the onset of symptoms and, with disease progression, ground-glass findings usually develop, peaking at 6 – 13 days (SIMPSON *et al*., 2020). Around the 14th day after the begining of the symptoms, when resorption of the inflammatory process occurs, the mosaic paving pattern tends to regress, but ground-glass opacities persist. The disappearance of tomographic findings is usually slow and tends to extend after a month of illness. However, even so, persistent scar alterations can be described (SIMPSON *et al*., 2020). With the progression of the infectious process, there is a decrease in inflammatory cells and the proliferation of fibroblasts, responsible for the thickening of the alveolar wall and septa (ZHU *et al*., 2020). At this moment, the appearance of areas of consolidation and/or thickening of the interlobular septum with a fine intermingled reticulate (mosaic paving pattern) within the ground-glass areas is observed on CT (XIONG *et al*., 2020). These tomographic findings of COVID-19 infection are nonspecific and may be very similar to those of other lung infections. As they also vary according to the stage of disease involvement, it is of great importance for such findings to be correlated with clinical and laboratory evidence of infection (SIMPSON *et al*., 2020). In this sense, during the first epidemic period in the region, chest CT scans were performed earlier, since most individuals were in the acute and subacute stages of the infection and the attempt at early diagnosis was essential for clinical management. In the present study, ground-glass lesions were observed in 100% of chest CT scans, in both epidemic peaks, without distinction, similar to the analyzes by Xie *et al*. (2020), Guan *et al*. (2020) and Xiong *et al*. (2020). Another relevant finding was the significant association (p=0.002) between the two periods and interlobular septa thickening. During the first period, there was a greater presence of lesions in a mosaic paving pattern (81.9%) compared to the second (61.2%). Such results were similar to those of Zhou *et al*. (2020) (62.9%) and Pan *et al*. (2020) (81%). The presence of other changes, such as nodules (p=0.808), atelectasis (p=0.073), bronchiectasis (p=0.287), lymph node enlargement (p=0.287), micronodules (p=0.142), striae (p=0.165), parenchymal bands (p=0.264), pleural effusion (p=0.575), air bronchogram (p=0.178) or lung cyst (p=0.509) (Table 13). These findings are unusual in images of patients with COVID-19, both in this study and in analyzes performed by Pan *et al.* (2020) and Guan *et al*. (2020). The presence of changes such as pleural effusion and atelectasis in patients with COVID-19 has a higher incidence in patients with more severe conditions and may suggest a worse prognosis of the disease (CHATE *et al*., 2020). Thus, the low frequency of these changes in the present study suggests the possibility of milder to moderate cases of infection, since the sample consisted of outpatients. About the laterality of the lesions, in the first epidemic period, 77.2% of the patients observed had bilateral pulmonary involvement and the remaining percentage was divided into 15% of right unilateral involvement and 7.8% on the left side. Data similar to this were found by Brito *et al*. (2020), in which the peripheral and bilateral distribution of COVID-19 lesions are among the most frequent radiological findings in observation. There was a significant association between the period and the pattern of tomographic involvement of the individuals (p=0.002), although in both epidemic peaks the typical pattern prevailed. In the first period, 18.9% presented an undetermined pattern of involvement, while in the second period, 92.8% of the individuals presented a typical pattern of involvement, with these proportions being higher than expected by the statistical test.

Retrospective observational studies estimated an increased risk of death (35%) associated with the alpha (WHO, 2021) variant, which is also observed through data from the Ministry of Health, recording 6,751 deaths from April to September 2020 and 3,752 deaths from October 2020 to March 2021 in the metropolitan region of Belém-PA-Brazil (BRAZIL, 2022). In this study, this information translates into the degree of involvement of lung lesions in chest CT scans. Of the 180 individuals observed in the first period, 127 (70.6%) had involvement between 10-25%, in a greater proportion than expected in relation to the second period, where only 78 (43.3%) had involvement between 10-25% and 48 (26.7%) of the first period. Finally, this work showed important findings in the areas studied, however, it worked with limitations because it was a retrospective, single-center and outpatient study and, therefore, it was not possible to carry out the study in critically ill patients. To assess the differences in lung CT pattern between the two COVID-19 epidemic peaks in the region, a broader survey would be necessary. However, the most striking aspect of this analysis was to show the daily medical reality during the pandemic, when, with the scarcity of RT-PCR for the diagnosis of SARS-CoV-2, chest computed tomography was used as a complementary tool for diagnosis, prognosis and treatment of the disease.

CONCLUSION

This study was relevant for understanding the reality of the COVID-19 pandemic in Brazil, more specifically the epidemic peaks and the effects of the different strains (B.1.1.7 and P.1) in one of the largest metropolises in the Amazon, Belém- PA. It was observed that the proportions of individuals of different sexes and different age groups did not vary significantly between the two analyzed periods, with a prevalence of women and individuals aged between 45-60 years. The characterization of the sample consisted of mild to moderate patients, considering that they attended a low-complexity private diagnostic center, on an outpatient basis. According to the tomographic findings, 100% of the individuals had ground glass lesions and the prevalence of the mosaic paving pattern was 81.9% in the first period compared to 61.2% in the second period (p=0.002). The other changes did not differ between the different moments. There was a prevalence of the typical tomographic pattern in relation to the two periods, with this proportion being higher than expected in the second period (92.8%) (p=0.002). The alpha variant showed a higher degree of involvement in relation to the gamma variant. Of the individuals observed in the first period, 127 (70.6%) had involvement between 10-25%, in a greater proportion than expected in relation to the second period, where only 78 (43.3%) had involvement between 10-25 % and 48 (26.7%) had <10% (p=<0.001).

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