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COVID-19 SUSPICIOUS CASES IN PEDIATRICS: AN ANALYSIS IN A TERTIARY HOSPITAL OFBRAZIL

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ABSTRACT

Objective: Define the COVID-19 suspicious cases profile in children and teenagers in a tertiary hospital in the state of Sergipe, due to the similarity of signals and symptoms with other viral respiratory infections prevalent in pediatrics. **Methods:** sectional study realized through data extraction of medical records of the Santa Isabel Hospital and Maternity, in Sergipe, between March 24 and September 28 of 2020. To this data analysis, continuous and categoric variants was created. **Results:** 302 patients were attended, during that analyzed period time and classified as COVID-19 suspicious cases, of that, 54 children (17.9%) presented one or more subjacent comorbidities, which the most prevalent was related to respiratory system, like asthma. Most of suspicious COVID-19 cases were excluded, and only 95 (31,5%) was diagnosed with the disease. Signs and symptoms did not show significative difference among patients with and without SARS- CoV-2, as we can see in dyspnea (37,9% vs 38,1%. P=1,000). **Final considerations:** the similarity in clinical presentation between the SARS-Cov-2 infection and acute respiratory infections in pediatrics makes the differential diagnosis even harder, needing the use of laboratory tests. Beyond that, there is an increase in the COVID-19 suspicious cases, because of this similarity.

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INTRODUCTION

The acute respiratory infections (ARI) have the viral agents as the main etiology, and although exists more than 200 viral serotypes, there is a prevalence of *Influenza A*, *Rhinovirus*, *Coronavirus* and Respiratory Syncytial Virus (RSV) (Veronesi; Focaccia, 2016). It is known that in Latin American countries, like Brazil, there is a seasonal pattern in the incidence of RI, observed in the first peak in April and the second in July (Calegari; *et al.,* 2005). The virus allocates in columnar epithelial cells of respiratory system and then replicate itself in a way that mixes with the respiratory secretions, being expelled in small aerosol particles generated during the act of sneeze, cough or talk (Forleo *et al.,* 2003). In December of 2019, in China, COVID-19 was identified, a disease characterized by infection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), and with the crescent number of notifications all over the world, in March 2020, the World Health Organization (WHO) decreed a pandemic state.The SARS-CoV-2 is part of the coronavirus lineage and has a single positive strand RNA of the betacoronavirus genus, it infects the epithelial cells of pulmonary alveolus trough endocytosis, mediated by angiotensin II converting enzyme (ACE2). Even though being predominant in pulmonary tissue, the ACE2 can be found in multiple organs tissues like heart, liver, kidneyand gastrointestinal tract, besides blood vessels (Esakandari *et al.,* 2020; Velavan; Meyer, 2020). Moreover, the COVID-19 transmission occurs through respiratory droplets emission of an infected individual that contacts directly or indirectly with the mucosa of a non-infected person. In general, the droplets do not keep suspended in the air and don't reach more than 2 meters distance (Lotfi; Hamblin; Rezaei, 2020; Velavan; Mcintosh; Hirsch; Bloom, 2020). In pediatrics, the initial scenario is that the children, in general, presents only light manifestations of COVID-19, and the infant younger than a year contains bigger risk in this group (Lotfi; Hamblin; Rezaei, 2020). Due to the lack of studies about the treatment of COVID-19 and the effectiveness in children, the management is about nutrition, hydration and if needed, oxygen supplement and ventilatory support (Lima, 2020; Ouassou; *et al.,* 2020; Safadi, 2020). Otherwise, due to the lack of maturity in the immune system, there is a higher susceptibility to infection and complications, like bronchiolitis, that elevates the disease's morbimortality in this age group (Sudbrack; *et al.,* 2007). The bronchiolitis, rhinitis, sinusitis, flu, common cold, pharyngitis and

tonsillitis emphasize themselves inside the most common respiratory cases, as well as pneumonia, once that the viral infection makes the bacterial co-infection more susceptible. The symptoms in thesepresentations may show, in general, with rhinorrhea, sneezes, cough, chest pain, headaches, nose obstruction, fever or odynophagia (Gordillo; Woerner, 2018). It is evident that COVID-19, due to its pathophysiology, may show with many unspecific symptoms and risk factors, in addition to be a recent disease that still lack enough studies about the clinical aspects, especially in pediatrics. Therefore, this study has the objective of relate the profile of suspicious COVID-19 cases in children and teenagers in a tertiary hospital in the state of Sergipe, once the signals and symptoms of this new infection is similar with other prevalent viral respiratory infections in pediatrics.

METHODS

This is a cross-sectional analytical documentary study carried out between March 24 to September 28, 2020 at the Maternal and Child Care Hospital located in Aracaju-Sergipe, which is a reference for general surgery (gynecological), childbirth care and birth, pediatrics (urgency/emergency and pediatric surgery). The hospital has a Pediatric Urgency and Emergency Unit that is responsible for approximately 3,500 monthly visits, in addition to 22 beds in the Pediatric Ward and 7 beds in the Pediatric Intensive Care Unit (PICU). This article was made through medical records consultation of patients with SARS-CoV-2 suspicious infection, to describe the profile and the clinic outcome. In a way to confirm the hypothesis that, although the peak of cases of COVID-19 in Brazil was happening during this study season, other infections such as Influenza virus, is still prevalent in the children and teenagers, which according to the World Health Organization the age range is since birth to 19 years (Brasil, 2007). The inclusion criteria used for this research was people younger than 20 years, both sexes, living in Sergipe, tested to the virus detection. The exclusion criteria were the cases that the medical record was not filled properly. It is important to mention that the definition of suspicious case and confirmed case of COVID-19 was extracted from the Guidelines for the diagnosis and treatment of COVID-19 of Health Ministry (Brasil, 2020).To the data extraction of medical record, a formulary was used, with demographic, clinical, laboratorial, management and outcome data.

This research started after the approval of Ethic and Research Committee (ERC) of Sergipe Federal University, CAAE: 34816620.8.0000.5546. Furthermore, the data collection and the research were in accordance with the Resolutions of the National Research Ethics Commission (NRECA) and the National Health Council (NHS), which determinates the rules to be followed. It is important to say that since this is a study carried out by consulting medical records, researching the data from the Hospital Infection Control Service, the Informed Consent Form (ICF) was dispensed by ERC. In the results, the categoric variables was described trough absolute and relative percentage frequency, and the hypothesis of independence between these variables was tested using Pearson's chi-square or Fisher's exact tests. Continuous variables, on the other hand, were portrayed as means, medians and standard deviations. The hypothesis of adherence of continuous variables and normal distribution was tested using the Shapiro-Wilks test. As not confirmed, the hypothesis of equality of measures of central tendency was tested using the Mann-Whitney T test. The level of significance adopted was 5% and the software used was the R Core Team 2020.

RESULTS

In the hospital where the study was made, which is a strategic unit to the health system in Sergipe and nearby states, 302 patients was consulted as suspicious case of COVID-19 during this study period time. The age median of this patients was 0,87years (II = 0,08-4,00; gap of 1 day and 19 years), and 177 pacients (58,6%) was boys. Fifty-four patients (17,9%) presented one or moresubjacent comorbidities, and the most prevalent was related to respiratory system, as asthma. (Sheet 1).

Sheet 1. Demographic and clinical data of patients with suspected cases of COVID-19 (Aracaju-SE, 2020)

	n	%	Median	II
AGE			0,87	0,08-4,00
SEX				
Feminine	125	41,4		
Masculine	177	58,6		
ORIGIN				
Capital	259	85,8		
Countryside	38	12,6		
Not informed	5	1,7		
COMORBIDITIES	54	17,9		
Cardiovascular Disease	9	3,0		
Malnutrition	2	0,7		
Chromosomal Diseases	2	0,7		
Kidney disease	1	0,3		
Immunosuppression	5	1,7		
Metabolic Disease	2	0,7		
Genetic Syndrome	5	1,7		
Respiratory Disease	26	8,6		
Pregnant in risk	2	0,7		
Laryngomalacia	2	0,7		
Obesity	1	0,3		
Other syndromes	1	0,3		
Postoperative of abdomen obstruction	1	0,3		
Preterm infant	2	0,7		
Tumor	1	0,3		

Legenda: n – absolute frequency. % – percentual of relative frequence. II – Interquartile Interval.
Source: research data, 2020.

Sheet 2. Clinical and laboratory characteristics of patients with suspicious SARS-CoV-2 infection (Aracaju-SE, 2020)

	n	%
Daily Condition	203	67,2
Fever	111	36,8
Cough	142	47,0
Dyspnea	113	37,4
Tiredness	10	3,3
Respiratory Discomfort	56	18,5
Respiratory Insufficiency	1	0,3
Oxygen Saturation <95%	14	4,6
Vomit	21	7,0
Runny nose	13	4,3
Headaches	1	0,3
Nasal congestion	1	0,3
Diarrhea	10	3,3
Sore throat	6	2,0
Abdominal pain	2	0,7
Sepsis	1	0,3
Myalgia	1	0,3
PATIENT CONDITION		
Confirmed	93	30,8
Discarded	207	68,5
Not informed	2	0,7
DIAGNOSIS		
COVID 19	95	31,5
Influenza	5	1,7
Others	202	66,9
RT-PCR		
Detectable	78	25,8
Not Detectable	224	74,2
Clinical bed	225	74,5
Stabilization bed	4	1,3
MECHANICAL VENTILATION		
Yes	31	10,3
No	255	84,4
Not informed	16	5,3
DEATH		
Yes	13	4,3
No	254	84,1
Transference	1	0,3
Not informed	34	11,3

Legenda: n – absolute frequency. % – relative frequency percentual.
Source: data research, 2020.

Sheet 3. Demographic and clinical data of the cases according to the etiological diagnosis (Aracaju-SE, 2020)

	Diagnosis		
	COVID 19	Others	p-value
Age, *Median (II)*	0,33 (0,08-2,00)	1 (0,17-4,00)	0,014 M
SEX, *n (%)*			
Feminine	36 (37,9)	88 (43,6)	0,379 Q
Masculine	59 (62,1)	114 (56,4)	
ORIGIN, *n (%)*			
Capital	81 (86,2)	173 (86,5)	0,136 Q
Countryside	11 (11,7)	27 (13,5)	
Not informed	2 (2,1)	0 (0)	
COMORBIDITIES, *n (%)*	18 (18,9)	36 (17,8)	0,872 F
Cardiovascular Disease, *n (%)*	5 (5,3)	4 (2)	0,151 F
Malnutrition, *n (%)*	1 (1,1)	1 (0,5)	0,538 F
Chromosomal Diseases, *n (%)*	0 (0)	2 (1)	1,000 F
Kidney disease, *n (%)*	0 (0)	1 (0,5)	1,000 F
Immunosuppression, *n (%)*	3 (3,2)	2 (1)	0,332 F
Metabolic Disease, *n (%)*	0 (0)	2 (1)	1,000 F
Genetic Syndrome, *n (%)*	3 (3,2)	2 (1)	0,332 F
Respiratory Disease, *n (%)*	7 (7,4)	19 (9,4)	0,663 F
Pregnant in risk, *n (%)*	0 (0)	2 (1)	1,000 F
Laryngomalacia, *n (%)*	1 (1,1)	1 (0,5)	0,538 F
Obesity, *n (%)*	0 (0)	1 (0,5)	1,000 F
Other syndromes, *n (%)*	1 (1,1)	0 (0)	0,320 F
Postoperative of abdomen obstruction, *n (%)*	0 (0)	1 (0,5)	1,000 F
Preterm infant, *n (%)*	1 (1,1)	1 (0,5)	0,538 F
Tumor, *n (%)*	1 (1,1)	0 (0)	0,320 F

Legenda: n – absolute frequency. % – relative frequency percentual. II – Interquartile Interval. Q – Pearson's Chi-squared test. F – Fisher Test. M – Mann-Whitney Test.
Source: research data, 2020.

Sheet 4. Clinical and laboratory characteristics of patients according to the etiological diagnosis (Aracaju-SE, 2020)

	Diagnosis		
	COVID 19	Others	p-value
Daily Condition, *n (%)*	59 (62,1)	144 (71,3)	0,141 Q
Fever, *n (%)*	31 (32,6)	80 (39,6)	0,304 Q
Cough, *n (%)*	39 (41,1)	103 (51)	0,135 Q
Dyspnea, *n (%)*	36 (37,9)	77 (38,1)	1,000 Q
Tiredness, *n (%)*	4 (4,2)	6 (3)	0,731 F
Respiratory Discomfort, *n (%)*	15 (15,8)	41 (20,3)	0,427 F
Respiratory Insufficiency, *n (%)*	0 (0)	1 (0,5)	1,000 F
O2 saturation <95%, *n (%)*	3 (3,2)	11 (5,4)	0,560 F
Vomit, *n (%)*	6 (6,3)	15 (7,4)	0,813 F
Runny nose, *n (%)*	3 (3,2)	10 (5)	0,561 F
Headaches, *n (%)*	1 (1,1)	0 (0)	0,320 F
Nasal congestion, *n (%)*	1 (1,1)	0 (0)	0,320 F
Diarrhea, *n (%)*	2 (2,1)	8 (4)	0,511 F
Sore throat, *n (%)*	1 (1,1)	5 (2,5)	0,668 F
Abdominal pain, *n (%)*	0 (0)	2 (1)	1,000 F
Sepsis, *n (%)*	1 (1,1)	0 (0)	0,320 F
Myalgia, *n (%)*	0 (0)	1 (0,5)	1,000 F
RT-PCR, *n (%)*			
Detectable	77 (81,1)	1 (0,5)	<0,001 F
Not Detectable	18 (18,9)	201 (99,5)	
Clinical bed, *n (%)*	66 (69,5)	155 (76,7)	0,200 F
Stabilization bed, *n (%)*	2 (2,1)	2 (1)	0,595 F
Mechanical Ventilation, *n (%)*	16 (18,2)	15 (7,8)	0,013 F
Death, *n (%)*	10 (11,8)	3 (1,7)	0,001 F
Time between collect samples and medical discharge, *Median (II)*	6 (3-10)	4 (2-6,25)	0,002 M

Legenda: n - absolute frequency. % - percentage relative frequency. II - Interquartile Interval. Q - Pearson's chi-square test. F - Fisher's exact test. M - Mann-Whitney test.
Source: data research, 2020.

In the clinical presentation, the main complaint was cough, related in 142 cases (47,0%), followed by dyspnea, 113 cases (37,4%), and fever, 111 cases (36,8%). It is important to note that other symptoms weremention in less frequency like headaches, runny nose, vomit, and abdominal pain. Besides, 56 patients (18,5%) mentioned respiratory discomfort and 14 (4,6%) presented oxygen saturation< 95%. As from sheet 2, it is visible that the most part of the suspicious COVID-19 cases was discarded, being just 95 cases (31,5%) diagnosed with SARS-CoV-2 infection, and inside this group, 78 cases (82,1%) had confirmed cases through laboratorial criteria (molecular biology test), while 17 (17,9%) through epidemiologic-clinical criteria. The discarded cases, 5 patients (1,7%) had etiologic diagnosis of Influenza virus infection, while 202 cases (66,9%) by other etiologies. About the time range between the sample collect and the hospital discharge, the median was 4 days (II= 2-7). The median age of COVID-19 diagnosed cases was 0,33 years (II= 0,08-2,00), and 59 patients (62,1%) were boys. Apart from it, 18 patients (18,9%) had one or more comorbidities, which respiratory diseases was the most prevalent, followed by cardiovascular diseases. Comparing the SARS-CoV-2 confirmed cases with discarded ones, there is no significative difference in sex, origin, and comorbidities presence (Sheet 3). In sheet 4 its notable that the complains fever, cough and dyspnea was related in a proximal number of cases of the COVID-19 patients, cough being the most prevalent, in 39 cases (41,1%), followed by dyspnea in 36 cases (37,9%) and fever, 31 cases (32,6%). It is important to say that 13 deaths were registered, 10 of these (76,9%) was in confirmed diagnosis patients with SARS-CoV-2 infection. In sheet 4 we can observe that signs and symptoms did not show any significative difference between SARS-CoV-2 infected patients and non-infected, for example, dyspnea (37,9% *vs* 38,1%; $P = 1,000$) and respiratory discomfort (15,8% *vs* 20,3%; $P = 0,427$). Comparing with discarded suspicious cases, the confirmed ones presented less median of age ($P = 0,014$), bigger necessity of using mechanical ventilation (18,2% *vs* 7,8%; $P = 0,013$), evolution to death (11,8% *vs* 1,7%; $P = 0,001$) and a bigger time gap between collect samples and hospital discharges ($P = 0,002$). In addition, the biggest number of reverse transcription tests followed by detectable polymerase chain reaction (RT-PCR) for SARS-CoV-2 (81,1% *vs* 0,5%; $P < 0,001$).

DISCUSSION

In the state of Sergipe, 207,965 suspected cases of COVID-19 were tested and reported until November 28, 2020, which 42.8% (N = 88,999) had confirmatory tests for SARS-CoV-2 infection. It is noted that at Santa Isabel Hospital and Maternity, during the study period, the percentage of suspected cases with confirmed tests in children and teenagers was 35.5% (N = 95), remaining close to what was observed in the state in all age groups(Sergipe, 2020). Through data analysis we observed that there is no signs or symptoms related to COVID-19. This can be justified because there is no clinical, radiological and laboratory specific founds related exclusively to this infection, since this founds can be similar to other prevalent etiological diseases in younger than 19 years, for example, influenza, parainfluenza, rhinovirus, respiratory syncytial virus, and others. The pattern of most agent's incidence coincides with the peak period of SARS-CoV-2 cases (Sociedade Brasileira de Pediatria, 2020).

It is known that the SARS-CoV-2 severity may vary from light to critical, and the severe presentation have dyspnea, hypoxia, or pulmonary implication, while the critical have respiratory insufficiency, shock, or multiorganic disfunction. In this study, 36 (37,9%) patients relateddyspneaand only 3 (3,2%) relatedhypoxia (oxygen saturation <95%), while none of respiratory insufficiency case was mentioned and only 1 (1,1%) from sepsis, characterizing an organic disfunction. In people younger than 19 years old, besides COVID-19 incidence being only 1 to 5% of the total case numbers, the light manifestations happen in a majority way, with a low incidence of severe and critical, as related in Santa Isabel Hospital and Maternity. This can be explained because in pediatrics age, the pulmonary cells express less ACE2 receptors, and maybe explain the lower incidence and severity of COVID-19 in this group[18].The relation can be observed in this study when, for example, 79 (81,8%) childrendid not need the mechanical ventilation and only 2 (2,1%) needed stabilization beds (Brasil, 2020). The patient stabilization with COVID-19 in pediatrics is soften the respiratory difficulty, made with non-invasive mechanical ventilation and continuous positive pressure in airways. When the discomfort persists, with evolution to respiratory discomfort, a nasal canula with high flow can be used

(Green; *et al*., 2020). To symptomatic newborns, the patient must be isolated in Intensive Care Unit (ICU), with rooms of negative pressure, in closed incubators (Yu *et al*., 2018). In the severe cases of acute respiratory distress syndrome (ARDS), the use of pulmonary surfactants is recommended and inhaled nitric oxide (Lu *et al*., 2020). In the case of newborn reanimation, the pattern of Newborn Reanimation Program must be followed, with all professionals wearing personal protective equipment (PPE) demanded for COVID-19 (Lu *et al*., 2020; Wang *et al*., 2020; Sociedade Brasileira de Enfermeiros Pediatras, 2020). Although there is a lack in relates with long term management, usually, the symptomatic newborns with COVID-19 recover in 2 weeks maximum, without after-effects (Kyle *et al*., 2020). In the published studies, is observed that the feeding method changes to milk formula, and social distancing is necessary between the mom and the newborn, when the newborn tests positive for COVID-19. However, this is controversial between the authors that suggests direct breastfeeding after the breast hygiene associated with the use of mask (Kyle; *et al*., 2020; Breslin *et al*., 2020;Dumitriu; *et al*., 2020). Regarding deaths in pediatrics, SARS-CoV-2 infection cannot be given an exclusive character since the description in the literature of this outcome is always associated with preterm infant or comorbidities [23]. Some studies have also evaluated the association among the deaths of newborns with COVID-19 who had mothers who were also infected and who needed intubation (Hantoushzadeh *et al*., 2020; Yan; *et al*., 2020). In a study conducted in hospitals in Espírito Santo state, until May 2020, of the 889 patients with COVID-19 confirmed diagnosis, 220 (24.4%) had Death as an outcome, whereas in our study, of the 95 patients diagnosed with COVID-19, only 10 (11.8%) had death as an outcome (Maciel;*et al*., 2020). These data show that the pediatric age group evolution to death is less susceptible.

It is essential to emphasize that although the COVID-19 pandemic caused a critical moment in society, the other acute respiratory infections should not be underestimated, especially in pediatrics, where it is observed a relevant prevalence. In this scenario, it is urgent that, as new studies for SARS-CoV-2 infection in this age group are being published, some conducts should be rethought, such as the avoid of breastfeeding, the isolation between the mother and the newborn and the immediate bath after birth, which can bring a lot of biological and psychological damages to these newborns (Ip *et al*., 2007; Sociedade Brasileira de Enfermeiros Pediatras, 2020). Finally, it is noteworthy that several studies have had negative results in the search for SARS-CoV-2 in amniotic fluid, breast milk, placenta and vaginal secretions (Yan; *et al*., 2020; Wang *et al*., 2020). It is worth noting that the data collected in this study between March and September, there are the presence of two seasonal peaks of acute respiratory infections (April and July), which are included as COVID-19 differential diagnosis. Since, as mentioned above, there is a similarity in the clinical presentation among these diseases, with a predominance of respiratory symptoms, such as Cough and Dyspnea, in addition to the non-specific symptoms, of which Fever stands out, mainly, and Headaches. Otherwise, this common transmission route, through the emission of droplets, makes easier the spread of both SARS-CoV-2 and the viruses responsible for acute respiratory infections. This entire context is reflected in the result obtained in the sample of this research, given that, of the 302 cases classified as suspect for COVID-19, only 95 cases (31.5%) had, in fact, a confirmed diagnosis.

Final Considerations

The similarity in the clinical presentation between virus SARS-CoV-2 infection and the acute respiratory infections in pediatrics makes it hard the differential diagnosis between them, being necessary the use of laboratory tests. Besides that, there is a high number of COVID-19 suspicious cases, due to this similarity. In result, COVID-19 was evidenced, due to its pathophysiology, that it can manifest with diverse unspecific symptoms and risk factors, besides being a recent disease that still lack of studies about the clinical aspects, especially in pediatrics.

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