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2
3 **Viral etiology of hospitalized adults patients**
4 **with severe acute respiratory infections in**
5 **Abidjan, Côte d'Ivoire**
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10 **ABSTRACT**

Aims: Pneumonia is a leading cause of morbidity and a significant cause of mortality worldwide. Although information is available on pneumonia in children, the incidence in adults in many parts of Africa including Côte d'Ivoire is unknown. Knowledge of local etiologic agents of pneumonia is critical for making reasonable decisions about treatment as differences in etiology may result in poor response to therapy chosen to cover common pathogenic microbes in studies done in high countries of income.

The objective of this study was to identify the viral etiology of pneumonia in adult patients with pneumonia in Abidjan, Côte d'Ivoire.

Study design: This is a prospective experimental study conducted on the basis of the successive recruitment of patients admitted to hospital for severe pulmonary interstitial pneumonitis confirmed by radio or CT scan of the thorax.

Place and Duration of Study: Pneumophtisiology department (PPH) of the University Hospital Center of Cocody (Côte d'Ivoire) and laboratory of Bacteriology- Virology of Pasteur Institut of Côte d'Ivoire, between February 2016 and October 2017.

Methodology: Among all admitted patients in the unit of pneumophtisiology (PPH) of the hospital University, 90 patients aged at least 18 years were pre-included. A total of 33 bronchoalveolar lavage fluid (BAL) samples from adults suspected of pneumonia were analyzed. The viruses were identified by the real-time multiplex reverse polymerase chain reaction (RT-PCR).

Results: Of the 33 BAL samples tested, 18.2% (6/33) viral agents were detected. Parainfluenza-3 PV-3 was the most prevalent virus (57.1%, 4/7), followed by coronavirus OC43 (14.3%, 1/7), coronavirus HKUI (14.3%, 1/7).) and human rhinovirus (14.3%, 1/7).

A virus and virus association was detected, which was PV-3 associated with coronavirus HKUI (14.3%, 1/7).

Conclusion: The viral etiology of pneumonia is not very frequent in Côte d'Ivoire

11
12 *Keywords: Pneumonia, Respiratory viruses, adults, real-time multiplex PCR*
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15 **1. INTRODUCTION**
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17 Acute respiratory infections (ARI) are very common ubiquitous conditions, affecting both adults and children [1]. The
18 infectious etiologies are extremely varied. Among them, bacteria and viruses occupy a prominent place, with respiratory
19 viruses as the leader [1]. Thus, viral respiratory infections are a significant aspect of bronchopulmonary infections [1].
20 Pneumonia is the most severe form of all lower respiratory infections [2]. It is a common infectious disease with an
21 estimated incidence of 2 to 11 cases per 1,000 adults in developed countries and a mortality rate of 2% to 14% [3, 4]. The

prevalence of viruses in respiratory infections is difficult to estimate because they are rarely searched outside of certain epidemic contexts. In fact, respiratory viruses are responsible for 15 to 40% of the known etiologies of respiratory pathologies of infectious etiology [5]. Their frequency decreases in healthy young and adults, but increases significantly in the elderly [6].

Studies of the etiology of community-acquired pneumonia consistently report the presence of viruses as the second most common cause, behind *S. pneumoniae*, ranging from 13 to 50% of diagnosed cases [7].

In addition, the causative agents are in most cases of the viral type with among them: influenza and para-influenza viruses, respiratory syncytial virus, rhinoviruses, coronaviruses, and adenoviruses [8].

Since molecular biology methods have complemented conventional methods such as viral culture and immunoassays; the diagnosis of viral respiratory infections has not only increased in sensitivity, specificity and rapidity but has also made it possible to detect new virus subtypes [9].

Viral diagnostic methods have evolved significantly with the advent of molecular biology techniques and more specifically so-called "multiplex" molecular tests for the simultaneous detection of a large number of infectious agents [1]. Indeed, various techniques derived from the PCR (Polymerase Chain Reaction) have many advantages: the real-time PCR or RT-PCR ("reverse transcription polymerase chain reaction") allows not only specific but also quantitative detection of viral nucleic acids (DNA or RNA) and multiple techniques can co-detect several different viruses in a single reaction in the presence of signs of respiratory infection [9]. This method is therefore ideal for the rapid detection of a viral origin with panels that can include up to more than 12 different viruses and to identify viral co-infections and study their clinical impact [9].

The purpose of this study is to determine infections of viral origins associated with pneumonia in adult patients hospitalized at the University Hospital Center of Cocody Abidjan, Côte d'Ivoire.

2. MATERIAL AND METHODS

2.1 Description of the study

This is a prospective experimental study conducted on the basis of the successive recruitment of patients admitted to hospital for severe pulmonary interstitial pneumonitis confirmed by radio or CT scan of the thorax, between February 2016 and October 2017. Among all admitted patients in the unit of pneumophtisiology (PPH) of the hospital University, 90 patients aged at least 18 years were pre-included. The analysed samples were composed of blood, serum, sputum of patients suspected of having pneumonia. After this biological assessment (Tuberculosis, serology HIV, glycemic, creatinin, transaminase, CRP), 57 patients were excluded at a rate of 63.3% (Figure 1).

Only 33 (36.7%) patients were included and underwent fibroscopy to obtain bronchoalveolar lavage fluid (BAL). BAL was performed during fibroscopy by instillation and aspiration of saline into the nasal cavity in sub segmental bronchi. Thirty three LBAs samples were collected in a sterile disposable container and sent to the Bacteriology-Virology laboratory in transport containers containing cold accumulators, within one hour for virus detection.

2.2 Extraction of RNA and DNA

Bronchoalveolar lavage samples were placed in Eppendorf tubes after specimens collection. Thus, total viral nucleic acids (DNA or RNA) were extracted from 140 μ L of each clinical sample of BAL using the QIAamp® viral RNA mini kit, QIAGEN for the extraction of RNA viruses and the QIAamp® DNA mini kit, QIAGEN for that of viruses. The DNA / RNA was eluted with 60 μ L of AVE elution buffer supplied with the kit and stored at -80°C until use.

2.3 Amplification and molecular detection of viruses by real-time multiplex PCR

Samples were analysed using the Super script ®III platinum® One-step qRT-PCR system detection kit (Van Allen Way Carlsbad CA 92008, USA) for simultaneous detection of respiratory viruses. Two DNA viruses (Adenovirus and Bocavirus) and 14 RNA viruses were amplified and detected using a real-time thermal cycler: ABI® 7500 FAST. This kit uses a 5-tube multiplex PCR technique for the simultaneous detection and identification of viruses. The primers and probes used were recorded in Table 1.

For viruses with RNA, the amplification conditions consisted of a step of reverse transcription of the RNA into DNA for 30 min at 50 ° C followed by an initial denaturation and activation step the Taq polymerase for 2 min at 95 ° C. A second step of the amplification was performed in the same conditions by 45 denaturation cycles at 95 ° C for 15 s, hybridization at 55 ° C for 30 s and extension at 55 ° C for 30 s. Finally, a terminal extension at 4°C for 10 min.

For viruses with ADN, the amplification conditions consisted of a step of pre-activation of the enzyme for 2 min at 50 ° C, followed by an initial denaturation and activation step the Taq polymerase for 10 min at 95°C. A second step of the amplification was performed in the same conditions by 45 denaturation cycles at 95 ° C for 15 s, hybridization at 60 ° C for 1 min and extension at 60°C for 1 min.

2.4 Statistical analysis

Data entry and description were performed using Epi-info software version 7.2.0.1. These data were then transcribed into an Excel database making their analysis easier. Statistical tests were interpreted at the significance level corresponding to an alpha risk of 5%. Statistical analyzes were analyzed using the STATA version 15.0 software. Thus, the quantitative variables were expressed as mean and standard deviations of the mean, and the qualitative variables as numbers and percentages. The Chi2 statistical test was used for proportion comparisons with a significance threshold P of 0.05.

3. RESULTS

3.1 Age

The mean age was 40.2 years, the median age of patients was 40 ± 13.7 years with extremes of 18 to 77 years. The age distribution of adult patients was shown in Table 2. In total, 21.1% of patients (19/90) were under 29 years of age, 30% (27/90) were 30 to 39 years old, 28.9% (26/90) were between 40 and 49 years old, 8.9% (8/90) were between 50 to 59 years old and 11.1% (10 / 90) were over 60 years old. The most represented age group in our study was the 30-39 age group with 30% (27/90).

3.2 Sex

In study, we note a female predominance with a sex ratio (M/ F) of 0.9. Of the 90 patients, 46.7% (42/90) of the samples were obtained from male patients and 53.3% (48/90) were obtained from female patients. Patient information has been entered in Table 2.

3.3 Period of recruitment of patients with pneumonia

In 2016, the number of hospitalizations of patients was divided according to the following seasons: March-June (23.3%, 21/90), July-August (10%, 9/90), September-October (11, 1%, 10/90) and November-February (13.3%, 12/90). In 2017, the number of hospitalized patients was according to the following seasons: March-June (22.2%, 20/90), July-August (2.2%, 2/90), September-October (5.6 %, 5/90) and November-February (12.2%, 11/90). The seasonal pattern of recruitment in both years was shown in Figure 2. High recruitment of pneumonia patients was observed in the season from March to June (45%, 41/90) followed by season from November to February (25.6%, 23/90) then from September to October (16.7%, 15/90) and finally the season from July to August (12.2%, 11/90).

3.4 Virus detection according to the seasons

In this study, the distribution of viruses according to the seasons revealed the following results: the season of March-June PV-3 (28.6%, 2/7), coronavirus OC43 (14.3%, 1/7) , PV-3 + HKUI (14.3%, 1/7); the July-August season: no virus detected (0%, 0/7); the September-October: human rhinovirus season (14.3%, 1/7) and November-February PV-3 (14.3%, 1/7) (Figure 3). Viral detection has seen a peak in the March-June season.

3.5 Epidemiological characteristics according to the viruses

Based on inclusion criteria, 33/90 patients continued the study. Of the 33 patients suspected of having pneumonia, 16 (48.5%) were contracted by women and 17 (51.5%) by men, an H / F ratio of 1.1.

The age of patients ranges from 19 to 68 years, with an average of 39.6 years.

The incidence of pneumonia according to the age of the patients is as follows: 19-30 years (27.3%, 9/33), 30-40 years (48.5%, 16/33), 40-50 years (6.1%, 2/33) and over 50 years (18.1%, 6/33). Seven viruses were detected in this study. In patients aged between 19-30 years, a total of 3 isolates including 2 types of virus (42.8%, 3/7) were identified. These included the following viruses: parainfluenza-3 PV-3 (28.6%, 2/7) and coronavirus OC43 (14.3%, 1/7); in patients aged between 30-40 years, 2 viruses (28.6%, 2/7), parainfluenza-3 PV-3 (14.3%, 1/7), and viral infection parainfluenza-3 (PV-3) associated with coronavirus HKUI (14.3%, 1/7), in those having 40-50 years, rhinovirus was found (14.3%, 1/7) and finally it has not been detected in adults over the age of 50 with no virus (Figure 4).

There is no significant difference between age and virus detection because the calculated probability is higher ($P = 0.136 > P = 0.05$).

The age distribution of patients detected positive for respiratory viruses was very different between the four seasons. During the March-June season, most of the patients affected were young adults aged 19-30 (PV-3, 28.6%, OC43, 14.3%). In the March-June period, patients aged 30-40 years (PV-3 + HKUI, 14.3%) as well in the period of September-October

and November-February, patients aged 40-50 years (rhinovirus , 14.3%) and people aged 30-40 (PV-3, 14.3%) were very little affected respectively.

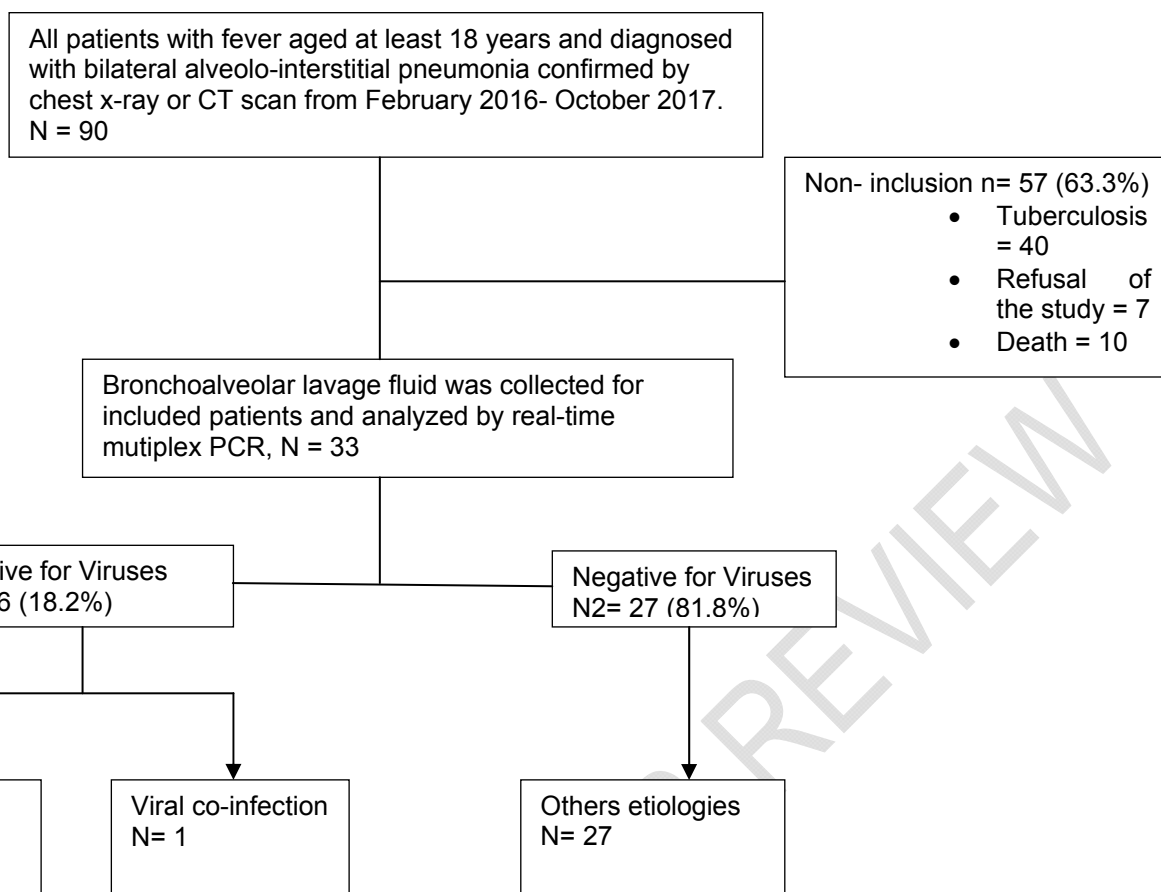
3.6 Detection and identification of respiratory viruses by real-time multiplex PCR

Detection of respiratory viruses from a total of 33 BAL samples resulted in 7 positive cases (21.2%) and 26 negative cases (78.8%). Real-time PCR performed on 33 BAL samples revealed the presence of the following viruses: coronavirus OC43 (14.3%, 1/7), parainfluenza-3 PV-3 (42.9%, 3/7), rhinovirus human (14.3%, 1/7). A viral coinfection has also been demonstrated in these BAL samples. Parainfluenza-3 (PV-3) was associated with coronavirus HKUI (14.3%, 1/7). The most incriminated virus in this study was the parainfluenza-3 virus (57.1%, 4/7).

4. DISCUSSION

The objective of this study was to determine the viral etiology of pneumonia in Côte d'Ivoire particularly in Abidjan. During the study period (2016-2017), we included patients whose age was greater than or equal to 18 years. Thus, the age between 30-39 years was strongly represented with a rate of 30%. This result is contrary to that obtained in the Taqarort study in which the study population aged 30-39 was the least represented with a rate of 9.8% [10]. The age group over 60 represents 11.1% of our study. This rate is close to that published by Taqarort which is 17.1%. This may be due to the fact that age is a risk factor that is independent of the occurrence of pneumonia [10] and that the frequency of hospitalization for severe pneumonia also increases with age, as well as mortality [11]. Moreover in our series, most patients are women. Our results are contrary to those of the literature, which observes a male predominance in other studies, with varying proportions [12]. This could be explained by the fact that risk factors for pneumonia such as smoking and alcoholism are found more in men than in women. In addition, the determination of the rate of patients recruited for pneumonia in this study revealed a high rate in the month of March to June which amounted to 45%. This rate is higher than previous studies reporting that pneumonia occurred mainly in winter and then in autumn with a rate of 39% [13]. This result could be explained by the fact that in Côte d'Ivoire we have four (4) seasons: a big rainy season from March to June, a short dry season from July to August, a short rainy season from September to October and finally a long dry season from November to February [14]. The high number of patients recruited this season could be due to the fact that during the months of March to June we are in the rainy season and it is very cold. According to the literature, pneumonia can be observed throughout the year with maximum frequency in winter because cold seasons are conducive to respiratory infections [10]. Also, the distribution of viruses according to the age groups according to our study made it possible to detect that the majority of our patients are located in the slice between 30-40 years with a rate of 48,5%. In the series of Bouaïti, most of his patients were over 60 years old. Our results are different from those of the Bouaïti study, which detected a low rate of 10.3% in the 30-40 age group [15]. This could be explained in part by the phenomenon of demographic aging, which is becoming more evident in our country than in previous years. Also, this can be explained by the fact that in developing countries like Côte d'Ivoire, the age of predilection of this pathology is between 20 and 49 years old with an average age ranging from 35.12 to 42.05 years old [16, 17]. Certainly the large population at a very young age, the precarious living conditions and the HIV infection are the factors that explain this observation [18]. On the other hand, our results are similar to those of Dhaimi whose studied population was younger [19]. Also, the oldest patients (> 50 years) in our study are less represented with a rate of 18.1%. This result is approximately similar to other studies in which 60-69 year olds were reached at a rate of 17.1% [10] and 15% according to the Dhaimi study, 1989. The study showed that 51.5% of men were the most involved in the occurrence of viral pneumonia than women (48.5%). This male predominance was also observed in the other studies, with varying proportions. Our results are similar to those of Barouhiel [20] who found men proportions of 52% and women 48%. Our results are also consistent with those of Horo et al [17] who found that male predominance is the rule in community-acquired pneumonia [17, 21]. This study revealed a viral etiology in 7 cases (21.2%) of 33 pneumonia patients. These results approximate those of other studies in which viral infection rates in pneumonia patients increased from 23-56% [22, 23, 24]. This difference would probably be due to the different methods chosen and the distinctions of different regions and populations. So this difference could be explained by the difference in climate and season in the countries where the studies would be conducted. In tropical environments, the incidence is highest during the rainy season. Indeed, the incidence of infections varies with the season; the frequency is higher in winter and spring [25]. PCR in this study revealed four types of viruses including OC43 coronavirus, Coronavirus HKUI, human rhinovirus and Para-influenza virus. The most incriminated virus in patients with pneumonia was Parainfluenza-3 (57.1%, 4/7). In fact, according to a study conducted in Lorraine, the PIV-3 subtype was the most frequently found subtype (62.7%) compared to the other PIV-1 subtypes (25.3%), PIV-2 (7.3%) and PIV-4 (4.6%) [26]. Our results are consistent with those of Thomazelli et al [27] who found a 57.7% positivity rate for parainfluenza-3 virus. This may be due to the fact that PIV-3 subtype infections occur in the spring and especially in the summer of each year [28].

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Fig. 1. Recruitment chart of adult pneumonia patients and detection of viral etiology by real-time multiplex PCR

Table 1: Primers and probes used for the detection of respiratory viruses

Multiplex	Viruses	Sequence (5'- 3')
1	PIV-1	Fwd: GTTGTCAATGTCTTAATTCGATCAATAATT
		Rev: GTAGCCTMCCTTCGGCACCTAA
		Pr: (FAM)-TAGGCCAAAGATTGTTGTGCGAGACTATTCCAA-(TAMRA)
1	PIV-2	Fwd: GCATTTCCAATCTTCAGGACTATGA
		Rev: ACCTCCTGGTATAGCAGTGAAGTGAAC
		Pr: (CY5)-CCATTTACCTAAGTGATGGAATCAATCGCAAA-(BHQ-2)
	PIV-3	Fwd: TGATGAAAGATCAGATTATGCATATC
		Rev: CCGCGACACCCAGTTGTG
		Pr: (ROX)-TGGACCAGGGATATACTACAAAGGCAAAAT-(BHQ-2)
2	COV-OC43	Fwd : CGATGAGGCTATTCCGACTAGGT
		Rev : CCTTCCTGAGCCTTAATATAGTAACC
		Pr : (ROX)-TCCGCCTGGCACGGTACTCCCT-(BHQ-2)
	HRV	Fwd : AGTCCTCCGGCCCCTGAAT

		Rev : ACACGGACACCCAAAGTAGT Pr : (CY5)-TGAGCAATTGTGGATGGGA-(BHQ-2)
	FLUB	Fwd : AAATACGGTGGATTAATAAAAGCAA Rev : CCAGCAATAGCTCCGAAGCAA Pr : (JOE)-CACCCATATTGGGCAATTCCTATGGC-(BHQ-1)
	HMPV	Fwd : ATGTCTCTTCAAGGGATTACCT Rev : AMAGYGTTATTTCTTGTTGCAATGATGA Pr : (JOE)-CATGCTATATTAAGAGTCTCARTAC-(BHQ-1)
3	VRS	Fwd : GCAAATATGCAAACATACGTGAACA Rev : GCACCCATATTGTWAGTGATGCA Pr : (ROX)-CTTCACGAAGGCTCCACATACACAGCWG-(BHQ-2)
	FLUA	Fwd : CTTCTAACCGAGGTCGAAACG Rev : AGGGCATTGTTGGACAAKCGTCTA Pr : (FAM)-CCTCAAAGCCGAGATCGCGCA-(BHQ-1)
	COV- 229E	Fwd : CAGTCAAATGGGCTGATGCA Rev : AAAGGGCTATAAAGAGAATAAGGTATTCT Pr : (FAM)-CCCTGACGACCACGTTGTGGTTCA-(TAMRA)
4	COV- HKUI	Fwd : CCTTGCGAATGAATGTGCT Rev : TTGCATCACCCTGCTAGTACCAC Pr : (CY5)-TGTGTGGCGGTTGCTATTATGTTAAGCCTG-(BHQ-2)
	COV- NL63	Fwd : ACCTAATAAGCCTCTTTCTCAACCC Rev : GACCAAAGCACTGAATAACATTTTCC Pr : (JOE)-AACACGATTCCAACGAGGTTTCTTCAACTGAG-(BHQ-1)
5	ADV	Fwd : GCCACGGTGGGGTTTCTAAACTT Rev : GCCCCAGTGGTCTTACATGCACATC Pr : (FAM)-TGCACCAGACCCGGGCTCAGGTACTIONCGA-(TAMRA)
	BOV	Fwd : GCACAGCCACGTGACGAA Rev : TGGACTCCCTTTTCTTTGTAGGA Pr : (JOE)-TGAGCTCAGGGAATATGAAAGACAAGCATCG-(BHQ-1)

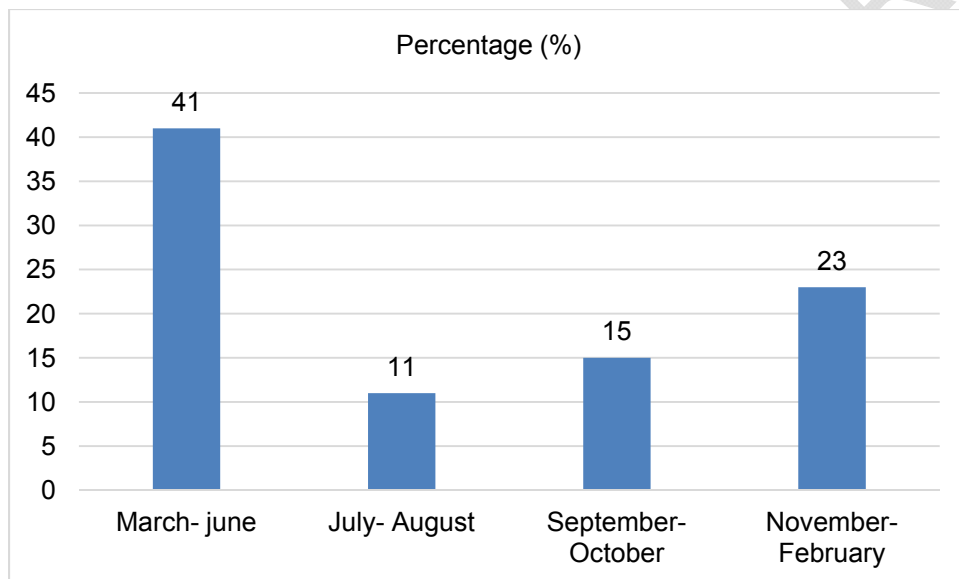
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Table 2: Patient Information

		Numbers	Percentage (%)
Sex	Male	42	46.7
	Female	48	53.3
Age	< 29	19	21.1
	30- 39	27	30
	40- 49	26	28.9
	50- 59	8	8.9
	> 60	10	11.1
Included N= 33			
BAL	Yes	33	36.7
	Non	57	63.3

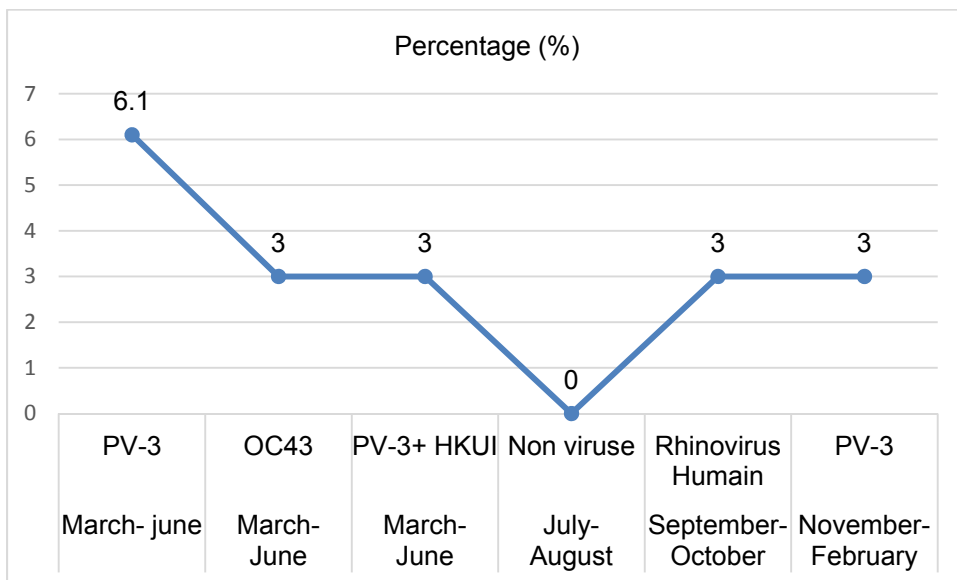
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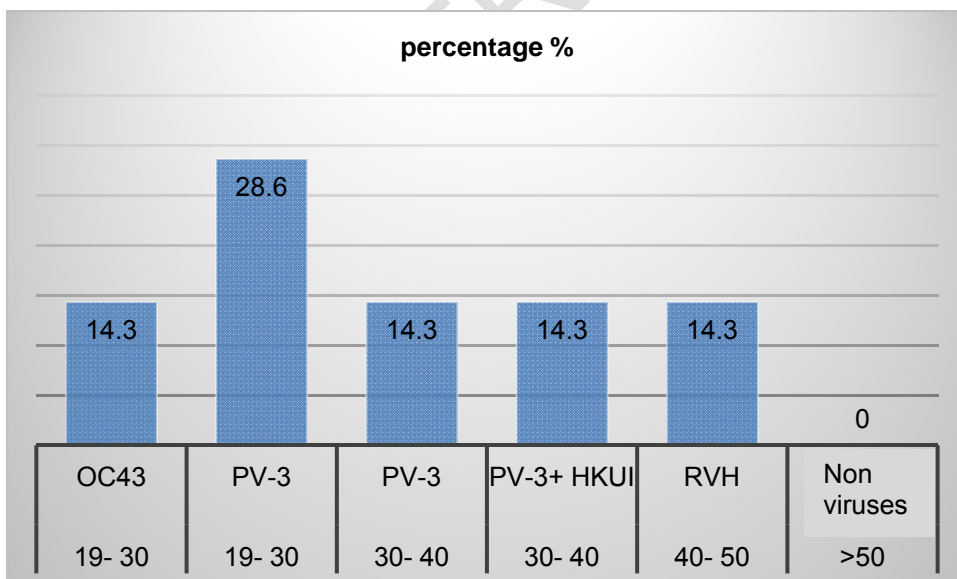
Fig. 2. Number of hospitalizations per season

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Fig. 3. Distribution of viruses by season



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Fig. 4. Distribution of viruses by age

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273 **5. CONCLUSION**
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275 The study of a series of 90 cases of hospitalized pneumonia from 2016 to 2017 at the University Hospital Center of
276 Cocody, Abidjan, Côte d'Ivoire, allowed us to note that this pathology is not frequent enough. The study population was
277 predominantly 30-40 years old, female and of low socio-economic status. Hospital recruitment explains the significant
278 frequency of the disease during cold seasons. The occurrence of acute pneumonia is most commonly seen in individuals
279 with a particular field.

280 Thus, the search for viruses by real-time PCR in the bronchoalveolar lavage fluid gave a low detection rate of 18.2% with
281 four (4) types of virus for a range of ten (10) that we offer the viral detection kit. These are Coronavirus OC43,
282 Parainfluenza-3 PV-3, Human Rhinovirus and Coronavirus HKUI. These respiratory viruses cause seasonal infections in
283 both children and adults, resulting in a wide range of clinical syndromes such as a common cold, laryngitis, bronchiolitis,
284 but also more severe conditions such as pneumonia.

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286 **COMPETING INTERESTS**
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288 The authors state that there are no conflicts of interest.
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291 **CONSENT**
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293 All authors declare that written informed consent was obtained from all the patient for the study.
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295 **ETHICAL APPROVAL**
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297 This study was approved by the national ethics committee according to decision n ° 31 / msls / cnfr-dkn of 23 june 2015
298 All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee
299 and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of
300 Helsinki.

301 **REFERENCES**
302

- 303 1. Dorin J. Etude épidémiologique des infections respiratoires virales des hivers 2009 à 2012 en milieu hospitalier et
304 apport des nouvelles technologies au diagnostic viral. Thèse de Doctorat en Pharmacie, Université de Lorraine, 2012;100.
305 French
- 306 2. Anonymous CMIT. Pneumonies aiguës communautaires. In, E. PILLY. Vivactis Plus Ed, 2008a; 226-35. French
- 307 3. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of
308 America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in
309 adults. Clin Infect Dis. 2007;44:27-2.
- 310 4. Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of
311 community acquired pneumonia in adults: update 2009. Thorax. 2009;64:1-55.
- 312 5. Díaz A, Zaragoza R, Granada R, Salavert M. Acute viral infections in immunocompetent patients. Medicina intensiva /
313 Sociedad Española de Medicina Intensiva y Unidades Coronarias, 2011;35(3):179-85.
- 314 6. Kesson AM. Respiratory virus infections. Paediatric Respiratory Reviews. 2007;8:240-48.
- 315 7. Korppi M, Don M, Valent F, Canciani M. The value of clinical features in differentiating between viral, pneumococcal and
316 atypical bacterial pneumonia in children, Acta Paediatr. 2008;97:943-47.
- 317 8. Guery B, d'Escrivan T, Georges H, Legout L, Leroy O, Viget N, et al. Pneumonie virale sévère de l'immunocompétent.
318 Réa. 2004;13:226-37. French
- 319 9. Cantero VD-L. Infections respiratoires virales chez le patient transplanté pulmonaire: revue et analyse critique des
320 études cliniques. Thèse de doctorat, Université Genève. 2012; 40. French
- 321 10. Taqarort. Profil des pneumonies aiguës communautaires prises en charge au service de pneumologie à l'hôpital Ibn
322 Nafiss entre 2005 et 2009. Thèse de doctorat en médecine. Université Cadi Ayyad, Marrakech. 2011;74:102. French
- 323 11. Mounedji A, Roche N, Rabbate A, Huchon G. Low community respiratory infections in adults (immunosuppression
324 excluded). Encycl Med Chir Pneumology. 2002; 6-003-D-10, 22. French
- 325 12. Jeong-Ok L, Dae-Young K, Joo Han L, Myung-Deock S, Hyeon Gyu Y, Yu Jung K, et al. Risk factors for bacterial
326 pneumonia after cytotoxic chemotherapy in advanced lung cancer patients. Lung Cancer. 2008; 62: 381-84.
- 327 13. Sibari N. Acute lobar pneumonia. Clinical, paraclinical, therapeutic and evolutionary aspects of 51 cases. PhD Thesis
328 Med, Rabat. 1984; 208: 80. French

- 329 14. Kouassi AM, Kouamé KF, Koffi YB, Je KB, Paturel JE, Oulare S. Analysis of climatic variability and its influences on
330 seasonal rainfall patterns in West Africa: case of the N'zi catchment (Bandama) in Ivory Coast. 2010. French
331 DOI: 10.4000 / cyberge.23388.
- 332 15. Bouaïti E. Evaluation of the management of community-acquired pneumonia in emergencies: Interest of the
333 classification of Fine and review of literature. Thesis Doctorate Medicine Rabat. 2001; 234: 138. French
- 334 16. N'Guessan O, Adonis L. Contribution to the study of acute bacterial pneumopathies hospitalized in the service of PPH
335 of the cocody CHU. PhD thesis in medicine, Abidjan. 2002; 3276: 130. French
- 336 17. Horo K, Koffi N, Kouassi B, N'gom AS, Kenmogné K, Ahui BJ, et al. Factors of death by acute community pneumonia
337 in the African environment in Abidjan. Rev Pneumol Trop. 2004; 1: 10-3. French
- 338 18. Tchouasseu NL. Prognostic value of HIV-adapted CURB65 and CRB-65 scores in HIV-associated bacterial-
339 associated community-acquired pneumonia. Doctoral Thesis in Medicine, University of Bamako. 2008; 119. French.
- 340 19. Dhaimi M. Pneumonia in a specialized department from 1982 to 1987 concerning 162 cases. Thesis Doctorate
341 Medicine, Casablanca, 1989; 133: 77. French
- 342 20. Barouhiel C. Management of acute community acquired pneumonia in a Parisian hospital: retrospective study of 58
343 cases of hospitalized patients and comparison of medical practices with the recommendations of ANAES 2001. Thesis
344 Doctorat Médecine, University Paris. 2006; 176: 113. French
- 345 1. 21. Koffi N, N'gom A, Kouassi B, Aka-Danguy E, Tchamran MM. Les pneumopathies bactériennes à germes banals
346 au cours de l'infection par le VIH chez l'adulte africain hospitalisé à Abidjan, Cote d'Ivoire. Bull Soc Path Ex.
347 1997;90(5): 370-72.
- 348 2. 22. Voiriot G, Visseaux B, Cohen J, Nguyen LBL, Neuville M, Morbieu C et al. Viral-bacterial coinfection affects the
349 presentation and alters the prognosis of severe community-acquired pneumonia. Crit Care. 2016;20:375.
- 350 3. DOI 10.1186/s13054-016-1517-9
- 351 4. 23. Gadsby NJ, Russell CD, McHugh MP, Mark H, Morris AC, Laurenson IF, et al. Comprehensive Molecular Testing
352 for Respiratory Pathogens in Community-Acquired Pneumonia. Clin Infect Dis. 2016;62:817-23.
- 353 5. 24. Das D, Le Floch H, Houhou N, Epelboin L, Hausfater P, Khalil A et al. Viruses detected by systematic multiplex
354 polymerase chain reaction in adults with suspected community-acquired pneumonia attending emergency
355 departments in France. Clin Microbiol Infect. 2015;21(608):1-8.
- 356 6. 25. Saïdani M. Streptococcus pneumoniae: Rappels bactériologiques et état actuel de la sensibilité aux antibiotiques.
357 Laboratoire de Microbiologie-Hôpital Charles Nicolle de Tunis. 2010;1-39. French
- 358 7. 26. Freymuth F, Vabret A, Dina J, Cuvillon- Nimal D, Lubin C, Vaudecrane A, et al. Bronchiolitis viruses. Arch Pédiatr,
359 2010;17(8):119-01.
- 360 8. 27. Thomazelli LM, Vieira S, Leal AL, Oliveira DB, Souza TS, Golono MA, et al. Surveillance of eight respiratory
361 viruses in clinical samples of pediatric patients in southeast Brazil. J Pediatr (RioJ). 2007;83:422-8
- 362 28. Hall CB. Respiratory Syncytial Virus and Parainfluenza Virus. New England J Med. 2001; 344(25):1917-928.

364 DEFINITIONS, ACRONYMS, ABBREVIATIONS

366 **ARI:** Acute respiratory infections

367 **BAL:** Bronchoalveolar lavage fluid