

2 **Viral Aetiology of Severe Acute Respiratory**
3 **Infections in Hospitalised Adult Patients in**
4 **Abidjan, Côte d'Ivoire.**

5
6
7
8 **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

9
10 *Keywords: Pneumonia, Respiratory viruses, adults, real-time multiplex PCR*

11
12
13 **1. INTRODUCTION**

14
15 Acute respiratory infections (ARI) are very common ubiquitous conditions, affecting both adults and children [1]. The
16 infectious etiologies are extremely varied. Among them, **bacteria and viruses are most frequent cause of infection, viruses**
17 **are responsible for most severe form of infection** [1]. Thus, viral respiratory infections are a significant aspect of
18 bronchopulmonary infections [1]. Pneumonia is the most severe form **of all lower respiratory tract infection** [2]. It is a
19 common infectious disease with an estimated incidence of 2 to 11 cases per 1,000 adults in developed countries and a
20 mortality rate of 2% to 14% [3, 4]. **There is a dearth of information on the prevalence of respiratory tract infection caused**
21 **by viruses as they draw attention only when there is a flare up of infection. However, viruses have been reported to be**
22 **responsible for 15-40% of RTI** [5]. **In addition, frequency of viral infection decreases in healthy adults but increases**
23 **significantly in the elderly** [6].

24 Of the 13-50% of diagnosed cases of community -acquired pneumonia, viruses have been reported as the second most
25 frequently isolated cause [7].

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

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

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

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

41 42 **2. MATERIAL AND METHODS**

43 **2.1 Description of the study**

44 This is a prospective experimental study conducted on the basis of the successive recruitment of patients admitted to
45 hospital for severe pulmonary interstitial pneumonitis confirmed by radio or CT scan of the thorax, between February 2016
46 and October 2017. Among all admitted patients in the unit of pneumophtisiology (PPH) of the hospital University, 90
47 patients aged at least 18 years were pre-included. The analysed samples were composed of blood, serum, sputum of
48 patients suspected of having pneumonia. After this biological assessment (Tuberculosis, serology HIV, glycemic,
49 creatinin, transaminase, CRP), 57 patients were excluded at a rate of 63.3% (Figure 1). Inclusion criteria are inpatients, of
50 both sexes, aged 18 years and older with severe febrile alveolo-interstitial pneumonitis confirmed by standard chest
51 radiograph and the negativity of tuberculosis bacilli sputum. The exclusion criteria were the patients detected tuberculous
52 and those refusing to do fibroscopy.

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

57 58 **2.2 Extraction of RNA and DNA**

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

63 64 **2.3 Amplification and molecular detection of viruses by real-time multiplex PCR**

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

70 For viruses with RNA, the amplification conditions consisted of a step of reverse transcription of the RNA into DNA for 30
71 min at 50 ° C followed by an initial denaturation and activation step the Taq polymerase for 2 min at 95 ° C. A second step
72 of the amplification was performed in the same conditions by 45 denaturation cycles at 95 ° C for 15 s, hybridization at 55
73 ° C for 30 s and extension at 55 ° C for 30 s. Finally, a terminal extension at 4°C for 10 min.

74 For viruses with ADN, the amplification conditions consisted of a step of pre-activation of the enzyme for 2 min at 50 ° C,
75 followed by an initial denaturation and activation step the Taq polymerase for 10 min at 95°C. A second step of the
76 amplification was performed in the same conditions by 45 denaturation cycles at 95 ° C for 15 s, hybridization at 60 ° C for
77 1 min and extension at 60°C for 1 min.

78 79 80 **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 distribution by gender

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) Table 2.

3.2 Patient distribution by gender

Based on inclusion criteria, 33/90 patients continued the study. Of the 33 patients suspected of having pneumonia, our series included 16 women or 48.5% of cases and 17 men or 51.5% of cases. The sex ratio H / F was 1.1.

3.3 Period of recruitment of patients according to the seasons

The breakdown of patients included according to the season is as follows: from March to June (45.5%, 15/33) followed by the season from November to February (24.2%, 8/33), then from September to October (24.2%, 8/33) and finally the season from July to August (6.1%, 2/33) Figure 2.

3.4 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).

3.5 Distribution of viruses according to age

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 3).

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

3.6 Classification of viruses by sex

Of the seven viruses, two men were detected positive for viruses: 1 coinfection Parainfluenza-3 (PV-3) + Coronavirus HKUI and 1 Parainfluenza-3 (PV-3). These two men are 40 years old and 27 years old. Four women were detected positive for the following viruses: 1 Coronavirus OC43, 2 Parainfluenza-3 (PV-3) and 1 human Rhinovirus. These women were aged 24, 30, 33 and 42 years old Figure 4.

3.7 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 5). Viral detection has seen a peak in the March-June season.

135 The age distribution of patients detected positive for respiratory viruses was very different between the four seasons.
136 During the March-June season, most of the patients affected were young adults aged 19-30 (PV-3, 28.6%, OC43, 14.3%).
137 In the March-June period, patients aged 30-40 years (PV-3 + HKUI, 14.3%) as well in the period of September-October
138 and November-February, patients aged 40-50 years (rhinovirus , 14.3%) and people aged 30-40 (PV-3, 14.3%) were very
139 little affected respectively.

140 4. DISCUSSION

141 The objective of this study was to determine the viral etiology of pneumonia in Côte d'Ivoire particularly in Abidjan.
142 During the study period (2016-2017), we included patients whose age was greater than or equal to 18 years. Thus, the
143 age between 30-40 years was strongly represented with a rate of 48,5%. This result is contrary to that obtained in the
144 Taqarort study in which the study population aged 30-39 was the least represented with a rate of 9.8% [10]. The age
145 group over 50 represents 18.1% of our study. This rate is close to that published by Taqarort which is 17.1%. This may be
146 due to the fact that age is a risk factor that is independent of the occurrence of pneumonia [10] and that the frequency of
147 hospitalization for severe pneumonia also increases with age, as well as mortality [11] **Table 2**.

148 Moreover in our series, the study showed that 51.5% of men were the most involved in the occurrence of viral pneumonia
149 than women (48.5%). Our results are in agreement with those of the literature which observes a male predominance in
150 other studies, with varying proportions [12]. This could be explained by the fact that risk factors for pneumonia such as
151 smoking and alcoholism are found in men. This male predominance was also observed in the other studies, with varying
152 proportions. Our results are similar to those of Barouhiel [13] who found men proportions of 52% and women 48%. Our
153 results are also consistent with those of Horo et al [14] who found that male dominance is the rule in community-acquired
154 pneumonia [14, 15]. In addition, the determination of the rate of patients recruited for pneumonia in this study revealed a
155 high rate in the month of March to June which amounted to 45,5%. This rate is higher than previous studies reporting that
156 pneumonia occurred mainly in winter and then in autumn with a rate of 39% [16].

157 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
158 June, a short dry season from July to August, a short rainy season from September to October and finally a long dry
159 season from November to February [17]. The high number of patients recruited this season could be due to the fact that
160 during the months of March to June we are in the rainy season and it is very cold. According to the literature, pneumonia
161 can be observed throughout the year with maximum frequency in winter because cold seasons are conducive to
162 respiratory infections [10] **figure 2**. Also, the distribution of viruses according to the age groups according to our study
163 made it possible to detect that the majority of our patients are located in the slice between 30-40 years with a rate of
164 48,5%. In the series of Bouaïti, most of his patients were over 60 years old. Our results are different from those of the
165 Bouaïti study, which detected a low rate of 10.3% in the 30-40 age group [18]. This could be explained in part by the
166 phenomenon of demographic aging, which is becoming more evident in our country than in previous years. Also, this can
167 be explained by the fact that in developing countries like Côte d'Ivoire, the age of predilection of this pathology is between
168 20 and 49 years old with an average age ranging from 35.12 to 42.05 years old [19, 14]. Certainly the large population at
169 a very young age, the precarious living conditions and the HIV infection are the factors that explain this observation [20].
170 On the other hand, our results are similar to those of Dhaimi whose studied population was younger [21]. Also, the oldest
171 patients (> 50 years) in our study are less represented with a rate of 18.1%. This result is approximately similar to other
172 studies in which 60-69 year olds were reached at a rate of 17.1% [10] and 15% according to the Dhaimi study, [21] **figure**
173 **3**.

174 The study showed that the detection rate of viruses in women is higher (4/7, 57.1%) than men (3/7, 42.9%). This results
175 are different to those of Barouhiel [13] who found men proportions of 52% and women 48% **Figure 4**.

176 This study revealed a viral etiology in 7 cases (21.2%) of 33 pneumonia patients. These results approximate those of
177 other studies in which viral infection rates in pneumonia patients increased from 23-56% [22, 23, 24]. This difference
178 would probably be due to the different methods chosen and the distinctions of different regions and populations. So this
179 difference could be explained by the difference in climate and season in the countries where the studies would be
180 conducted. In tropical environments, the incidence is highest during the rainy season. Indeed, the incidence of infections
181 varies with the season; the frequency is higher in winter and spring [25]. Viral detection showed a peak in the March-June
182 season (28.6%) because the season from March to June is a cold period **Figure 5**.

183 PCR in this study revealed four types of viruses including OC43 coronavirus, Coronavirus HKUI, human rhinovirus and
184 Para-influenza virus. The most incriminated virus in patients with pneumonia was Parainfluenza-3 (57.1%, 4/7). In fact,
185 according to a study conducted in Lorraine, the PIV-3 subtype was the most frequently found subtype (62.7%) compared
186 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
187 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
188 subtype infections occur in the spring and especially in the summer of each year [28].

All patients with fever aged at least 18 years and diagnosed
with bilateral alveolo-interstitial pneumonia confirmed by
chest x-ray or CT scan from February 2016- October 2017.
N = 90

192

193

194

195

196

197

198

199

200

201

202

203

204

205

206

207

208

209

210

211

212

213

214

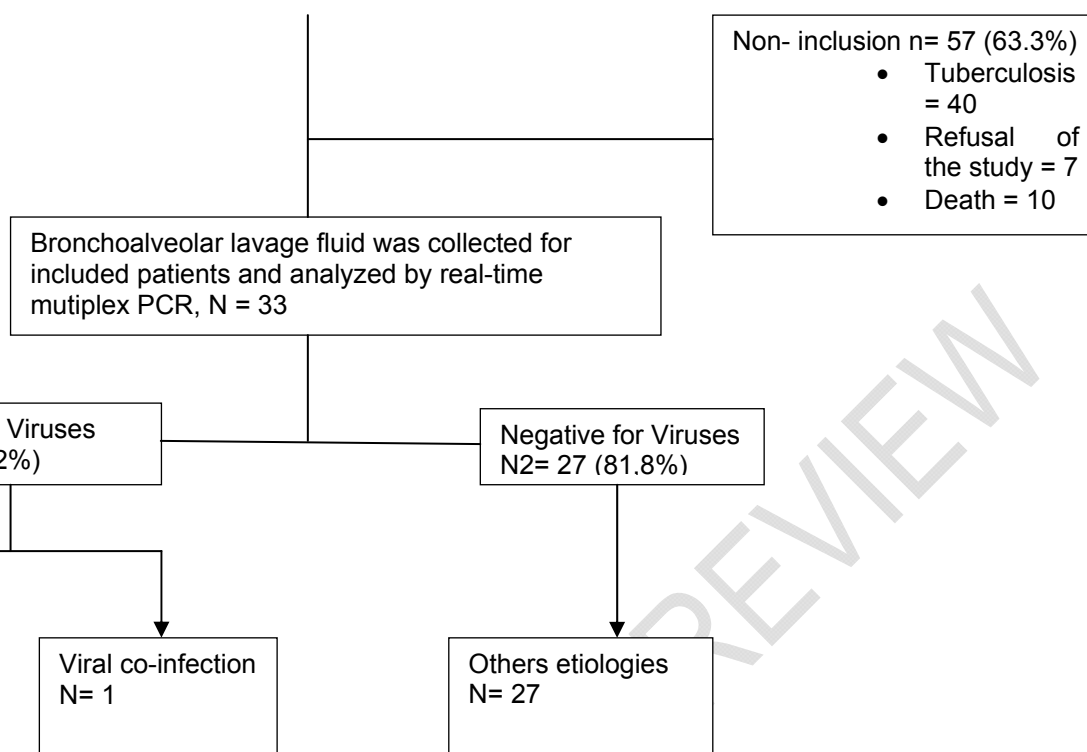


Fig. 1. Recruitment chart of adult pneumonia patients and detection of viral etiology by real-time multiplex PCR

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

Multiplex	Viruses	Sequence (5'- 3')
1	PIV-1	Fwd: GTTGTC AATGTCTTAATTCGATCAATAATT
		Rev: GTAGCCTMCCTTCGGCACCTAA
		Pr: (FAM)-TAGGCCAAAGATTGTTGTGCGAGACTATTCCAA-(TAMRA)
1	PIV-2	Fwd: GCATTTCCAATCTTCAGGACTATGA
		Rev: ACCTCCTGGTATAGCAGTGACTGAAC
		Pr: (CY5)-CCATTTACCTAAGTGATGGAATCAATCGCAA-(BHQ-2)
1	PIV-3	Fwd: TGATGAAAGATCAGATTATGCATATC
		Rev: CCGCGACACCCAGTTGTG
		Pr: (ROX)-TGGACCAGGGATATACTACAAAGGCAAAT-(BHQ-2)
2	COV-OC43	Fwd : CGATGAGGCTATTCCGACTAGGT
		Rev : CCTCCTGAGCCTTAATATAGTAACC
		Pr : (ROX)-TCCGCCTGGCACGGTACTCCCT-(BHQ-2)
2	HRV	Fwd : AGTCCTCCGGCCCCTGAAT
		Rev : ACACGGACACCCAAAGTAGT

		Pr : (CY5)-TGAGCAATTGTGGATGGGA-(BHQ-2)
	FLUB	Fwd : AAATACGGTGGATTAAATAAAGCAA Rev : CCAGCAATAGCTCCGAAGCAA Pr : (JOE)-CACCCATATTGGGCAATTCCTATGGC-(BHQ-1)
	HMPV	Fwd : ATGTCTCTTCAAGGGATTACCT Rev : AMAGYGTTATTTCTTGTGCAATGATGA Pr : (JOE)-CATGCTATATTAAGAGTCTCARTAC-(BHQ-1)
3	VRS	Fwd : GCAAATATGCAAACATACGTGAACA Rev : GCACCCATATTGTWAGTGATGCA Pr : (ROX)-CTTCACGAAGGCTCCACATACACAGCWG-(BHQ-2)
	FLUA	Fwd : CTTCTAACCGAGGTCGAAACG Rev : AGGGCATTGGACAAAKCGTCTA Pr : (FAM)-CCTCAAAGCCGAGATCGCGCA-(BHQ-1)
	COV-229E	Fwd : CAGTCAAATGGGCTGATGCA Rev : AAAGGGCTATAAAGAGAATAAGGTATTCT Pr : (FAM)-CCCTGACGACCACGTTGTGGTTCA-(TAMRA)
4	COV-HKUI	Fwd : CCTTGCGAATGAATGTGCT Rev : TTGCATCACCCTGCTAGTACCAC Pr : (CY5)-TGTGTGGCGTTGCTATTATGTTAAGCCTG-(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)

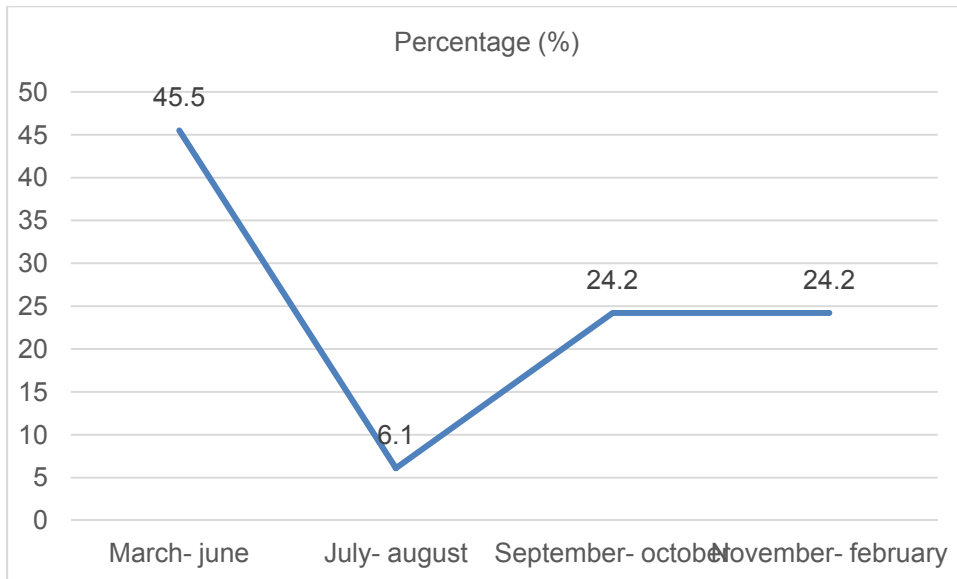
215
216
217
218
219

Table 2: Distribution of pneumonia cases by age

Age (year)	n	%
19- 30	9	27,3
30- 40	16	48,5
40- 50	2	6,1
>50	6	18,1
Total	33	100

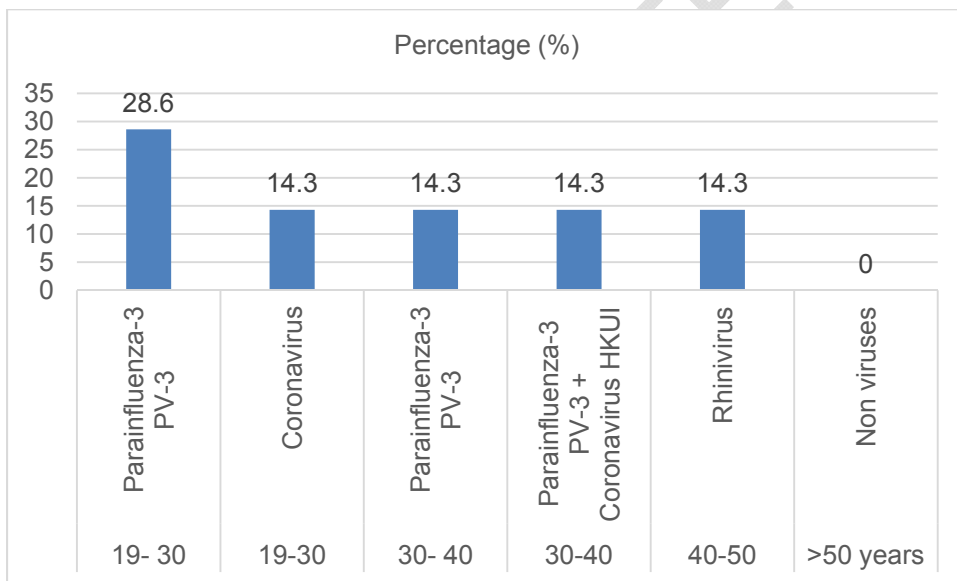
220
221

222
223



224
225
226
227
228
229
230
231
232

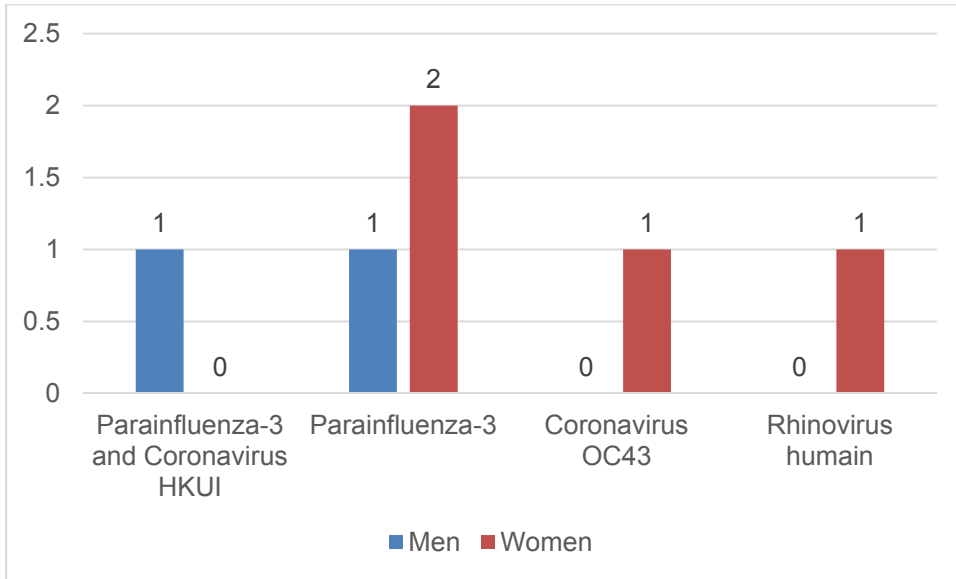
Fig. 2. Recruitment of patient according to the seasons



233
234
235
236
237
238
239
240
241
242

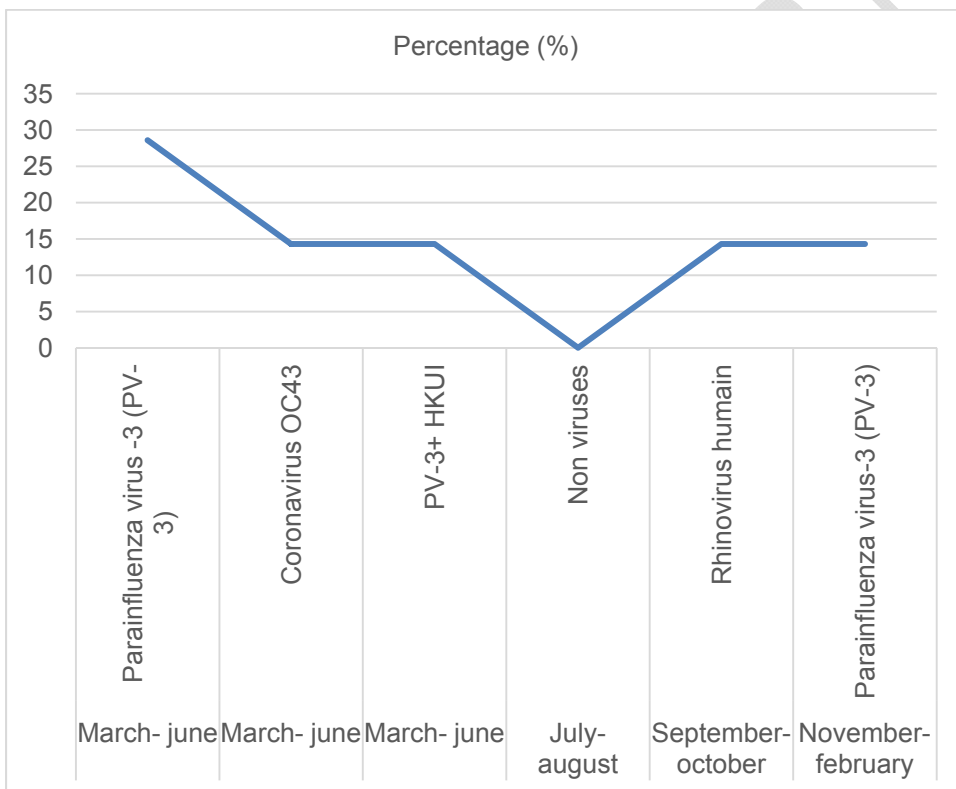
Fig. 3. Distribution of viruses by season

243
244



245
246
247
248
249
250

Fig. 4. Distribution of viruses by gender



251
252
253
254
255

Fig. 5. Classification of viruses according to the seasons

256 5. CONCLUSION

257
258 The study of a series of 33 cases of hospitalized pneumonia from 2016 to 2017 at the University Hospital Center of
259 Cocody, Abidjan, Côte d'Ivoire, allowed us to note that this pathology is not frequent enough. The study population was
260 predominantly 19-30 years old, male and of low socio-economic status. Hospital recruitment explains the significant
261 frequency of the disease during cold seasons. The occurrence of acute pneumonia is most commonly seen in individuals
262 with a particular field.

263 Thus, the search for viruses by real-time PCR in the bronchoalveolar lavage fluid gave a low detection rate of 18.2% with
264 four (4) types of virus for a range of ten (10) that we offer the viral detection kit. These are Coronavirus OC43,
265 Parainfluenza-3 PV-3, Human Rhinovirus and Coronavirus HKU1. These respiratory viruses cause seasonal infections in
266 both children and adults, resulting in a wide range of clinical syndromes such as a common cold, laryngitis, bronchiolitis,
267 but also more severe conditions such as pneumonia.

270 COMPETING INTERESTS

271
272 The authors state that there are no conflicts of interest.

275 CONSENT

276 All authors declare that written informed consent was obtained from all the patient for the study.

278 ETHICAL APPROVAL

279 This study was approved by the national ethics committee according to decision n° 31 / msls / cnfr-dkn of 23 june 2015
280 All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee
281 and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of
282 Helsinki.

284 REFERENCES

- 285 1. Dorin J. Epidemiological study of viral respiratory infections from winter 2009 to 2012 in hospitals and new technologies
286 to viral diagnosis. PhD Thesis in Pharmacy, University of Lorraine, 2012;100.
- 287 2. Anonymous CMIT. Acute community pneumonia. In, E. PILLY. Vivactis Plus Ed, 2008a; 226-235. French
- 288 3. Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of
289 America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in
290 adults. *Clin Infect Dis*. 2007;44:27-32.
- 291 4. Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I, et al. BTS guidelines for the management of
292 community acquired pneumonia in adults: update 2009. *Thorax*. 2009;64:1-55.
- 293 5. Díaz A, Zaragoza R, Granada R, Salavert M. Acute viral infections in immunocompetent patients. *Medicina intensiva /*
294 *Sociedad Española de Medicina Intensiva y Unidades Coronarias*, 2011;35(3):179-185.
- 295 6. Kesson AM. Respiratory virus infections. *Paediatric Respiratory Reviews*. 2007;8:240-248.
- 296 7. Korppi M, Don M, Valent F, Canciani M. The value of clinical features in differentiating between viral, pneumococcal and
297 atypical bacterial pneumonia in children, *Acta Paediatr*. 2008;97:943-947.
- 298 8. Guery B, d'Escrivan T, Georges H, Legout L, Leroy O, Viget N, et al. Pneumonie virale sévère de l'immunocompétent.
299 *Réa*. 2004;13:226-237. French
- 300 9. Cantero VD-L. Viral respiratory infections in the lung transplant patient: review and critical analysis of clinical studies.
301 PhD Thesis, Geneva University. 2012;40.
- 302 10. Taqarort. Profile of acute community-acquired pneumonia in the pneumology department at Ibn Nafiss hospital
303 between 2005 and 2009. Doctoral thesis in medicine. Cadi Ayyad University, Marrakech. 2011;74:102.
- 304 11. Mounedji A, Roche N, Rabbate A, Huchon G. Low community respiratory infections in adults (immunosuppression
305 excluded). *Encycl Med Chir Pneumology*. 2002; 6-003-D-10, 22.
- 306 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
307 pneumonia after cytotoxic chemotherapy in advanced lung cancer patients. *Lung Cancer*. 2008; 62: 381-384.
- 308 13. Barouhiel C. Management of acute community acquired pneumonia in a Parisian hospital: retrospective study of 58
309 cases of hospitalized patients and comparison of medical practices with the recommendations of ANAES 2001. Thesis
310 Doctorat Médecine, University Paris. 2006;176: 113.
- 311 14. Horo K, Koffi N, Kouassi B, N'gom AS, Kenmogné K, Ahui BJ, et al. Factors of death by acute community pneumonia
312 in the African environment in Abidjan. *Rev Pneumol Trop*. 2004;1:10-13.
- 313

- 314 15. Koffi N, N'gom A, Kouassi B, Aka-Danguy E, Tchamran MM. Bacterial pneumopathies with common germs during HIV
315 infection in African adults hospitalized in Abidjan, Côte d'Ivoire. Bull Soc Path Ex. 1997;90(5):370-372.
- 316 16. Sibari N. Acute lobar pneumonia. Clinical, paraclinical, therapeutic and evolutionary aspects of 51 cases. Thesis
317 doctorate Medecine, Rabat. 1984;208:80. French
- 318 17. Kouassi AM, Kouamé KF, Koffi YB, Je KB, Paturol JE, Oulare S. Analysis of climatic variability and its influences on
319 seasonal rainfall patterns in West Africa: case of the N'zi catchment (Bandama) in Côte d'Ivoire. 2010. DOI: 10.4000 /
320 cyberge0.23388.
- 321 18. Bouaïti E. Evaluation of the management of community-acquired pneumonia in emergencies: Interest of the
322 classification of Fine and review of literature. Thesis Doctorate Medicine Rabat. 2001;234:138.
- 323 19. N'Guessan O, Adonis L. Contribution to the study of acute bacterial pneumopathies hospitalized in the service of PPH
324 of the cocody CHU. PhD thesis in medicine, Abidjan. 2002; 3276:130.
- 325 20. Tchouasseu NL. Prognostic value of HIV-adapted CURB65 and CRB-65 scores in HIV-associated bacterial-
326 associated community-acquired pneumonia. Doctoral Thesis in Medicine, University of Bamako. 2008; 119. French.
- 327 21. Dhaimi M. Pneumonia in a specialized department from 1982 to 1987 concerning 162 cases. Thesis Doctorate
328 Medicine, Casablanca, 1989;133: 77.
- 329 22. Voiriot G, Visseaux B, Cohen J, Nguyen LBL, Neuville M, Morbieu C et al. Viral-bacterial coinfection affects the
330 presentation and alters the prognosis of severe community-acquired pneumonia. Crit Care. 2016;20:375.
331 DOI 10.1186/s13054-016-1517-9
- 332 23. Gadsby NJ, Russell CD, McHugh MP, Mark H, Morris AC, Laurenson IF, et al. Comprehensive Molecular Testing for
333 Respiratory Pathogens in Community-Acquired Pneumonia. Clin Infect Dis. 2016;62:817-823.
- 334 24. Das D, Le Floch H, Houhou N, Epelboin L, Hausfater P, Khalil A et al. Viruses detected by systematic multiplex
335 polymerase chain reaction in adults with suspected community-acquired pneumonia attending emergency departments in
336 France. Clin Microbiol Infect. 2015;21(608):1-8.
- 337 25. Saïdani M. Streptococcus pneumoniae: Bacteriological Reminders and Current State of Antibiotic Sensitivity.
338 Laboratory of Microbiology-Hospital Charles Nicolle of Tunis. 2010;1-39.
- 339 26. Freymuth F, Vabret A, Dina J, Cu villon- Nimal D, Lubin C, Vaudecrane A, et al. Bronchiolitis viruses. Arch Pédiatr,
340 2010;17(8):119-201.
- 341 27. Thomazelli LM, Vieira S, Leal AL, Oliveira DB, Souza TS, Golono MA, et al. Surveillance of eight respiratory viruses in
342 clinical samples of pediatric patients in south east Brazil. J Pediatr (RioJ). 2007;83:422-428
- 343 28. Hall CB. Respiratory Syncytial Virus and Parainfluenza Virus. New England J Med. 2001;344(25):1917-1928.

345 DEFINITIONS, ACRONYMS, ABBREVIATIONS

346 **ARI:** Acute respiratory infections

347 **BAL:** Bronchoalveolar lavage fluid

348