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Flu at a central hospital in the 2018 epidemic peak

Gripe num hospital central no pico epidémico de 2018

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ABSTRACT: *Introduction*: Influenza constitutes a global threat to public health aggravated by increased life expectancy. It is responsible for countless hospitalizations, deaths and expenditures in the health sector every year. *Objectives*: To characterize and determine the analytical profile of the sample diagnosed with influenza in a Central Hospital during the month of January, 2018. The following variables were analyzed: age, gender, discharge diagnosis, hospitalization time and analytical alterations. *Material and methods*: Retrospective observational study with clinical data collection (ALERT and SClinico) and data processing in Microsoft Excel®. A total of 131 patients were selected as a positive Xpert FLU Kit (GeneXpert®) aged ≥18 years. *Results*: 58.8% of the patients were female and the mean age was 67.1 years. 20.6% were type A flu, of which 9% were H1N1 and 79.4% were type B flu. At the analytical level: 63.6% of the patients had no changes in leukocytes at admission (of these 62.8% they had neutrophilia and 65.1% relative lymphopenia) and 46.5% thrombocytopenia. *Discussion*: The present study also allowed to evaluate the diagnostic approach to influenza and establish an analytical profile of the suspicion of the patient with influenza. *Conclusion*: The analytical profile allows, together with the clinic, a suspicious orientation for the management of rapid virological diagnostic resources, important for the initiation of antiviral therapy, implementation of infection control and prevention measures for flu patients. Positivity implied a high number of hospitalizations in isolation that merited reflection on hospital, clinical and economic management.

Keywords: Influenza A virus, H1N1 Subtype; Influenza A virus; Influenza B virus; Epidemics; Portugal/epidemiology.

RESUMO: *Introdução*: A gripe constitui uma ameaça global para a saúde pública agravada pelo aumento da esperança de vida. É responsável por inúmeras hospitalizações, mortes e gastos no setor da saúde todos os anos. *Objetivos*: Caracterizar e determinar o perfil analítico da amostra com diagnóstico de gripe num Hospital Central, durante o mês de janeiro de 2018. Analisaram-se as seguintes variáveis: idade, género, diagnóstico na alta, tempo de internamento e alterações analíticas. *Material e métodos*: Estudo observacional, retrospetivo, com recolha de informação do processo clínico (ALERT e SClinico) e tratamento de dados em Microsoft Excel®. Foram selecionados 131 pacientes como Kit Xpert FLU (GeneXpert®) positivo com idade ≥18 anos. *Resultados*: 58,8% dos pacientes pertenciam ao sexo feminino e a média de idades foi de 67,1 anos. 20.6% eram Gripe do tipo A, destes 9% são H1N1 e 79,4% Gripe do tipo B. A nível analítico: 63,6% dos doentes não apresentavam alterações dos leucócitos na admissão (mas destes 62,8% apresentavam neutrofilia e 65,1% linfopenias relativas) e 46,5% trombocitopenia. *Discussão*: O presente estudo permitiu também avaliar a abordagem diagnóstica da gripe e estabelecer um perfil analítico de suspeição do doente com gripe. *Conclusão*: O perfil analítico permite juntamente com a clínica, uma orientação de suspeição para gestão dos recursos de diagnósticos virológico rápido, importante para o início de terapia antiviral, implementação de medidas de controle de infeção e prevenção para pacientes com gripe. A positividade implicou um elevado número de internamentos em isolamento que merecem reflexão da gestão hospitalar, clínica e económica.

Descritores: Vírus da influenza A Subtipo H1N1; Vírus da influenza A; Vírus da influenza B; Epidemias; Portugal/epidemiologia.

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INTRODUCTION

Influenza is a contagious acute respiratory disease caused by the primary infection caused by the Influenza virus (VI)[1].

The etiological agent of influenza is Myxovirus influenzae, also called Influenza virus and belongs to the family Orthomyxoviridae, genus Influenzavirus[2].

The family Orthomyxoviridae is divided into five genera: Influenza A, B, C, Isavirus and Thogotivius viruses[2].

The first global epidemic that fits the description of influenza occurred in 1580. At least four influenza pandemics occurred in the 19th century and three occurred in the 20th century[3,4]. The first pandemic of the 21st century occurred in 2009-2010 by the Influenza A (H1N1) virus (pdm09) which is now a seasonal influenza virus that co-circulates with other seasonal viruses (influenza A (H3N2) and influenza B)[5,6].

In Portugal during the flu season 2016/2017 the number of deaths from "all causes" between week 51 2016 and week 5 2017 was estimated to be 4,467 deaths over expected (rate of 43 deaths per 100,000 inhabitants and a relative excess of 27%)[7].

VI viruses are respiratory viruses with immense mutability, creating new viruses with different genetic material than their origin. Small antigenic mutations (drift) generate new serotypes (strains) which may be responsible for outbreaks[8]. Already antigenic shifts only involve type A. These are rare but deeper processes that give rise to a new subtype that in previous years had not circulated[9].

VI are enveloped negative-stranded single-stranded RNA particles with substantial differences between virus types with respect to genetic organization, protein structure, host, as well as characteristics related to symptomatology and epidemiology. Viruses are subdivided based on antigenic nucleoprotein (NP) and matrix protein (M1) differences in viruses A, B and C, with only viruses A and B having clinical relevance in humans[10-12].

Influenza A Virus (VIA) was isolated in 1933 by Wilson Smith, being a genetically distinct virus and has variables that it shares with several hosts, including poultry, swine and humans. The interspecies presence and intercontinental viral spread make the ecology of VIA more complex. According to the US National Center for Immunization and Respiratory Tract Disease, VIA is classified into subtypes based on two proteins on the virus surface: hemagglutinin (H) and neuraminidase (N). There are 18 different hemagglutinin subtypes (H1-H18) and 11 neuraminidase subtypes (N1-N11)[5,8,13].

Influenza A may be caused by the subtypes: H1N1, H1N2, H2N3, H3N1, and H3N2. Subtypes (H1N1 and H3N2) are the most common strains worldwide[5,8,13].

The 2009 pandemic influenza A (H1N1) virus pdm09 contained a combination of gene segments that had not previously been described in animals or humans. The H1N1 virus haemagglutination (HA) gene evolved from the 1918 avian influenza pandemic H1N1 virus, thought to have infected human and swine populations at the same time, but evolved into distinct strains in pigs and humans[5,13,14].

Influenza B virus (VIB) was isolated in 1939 by Francis, being divided into two strains: Victoria and Yamagata and is known only for infecting humans and seals, which conditions a relative lack of animal models to study HIV infection in contrast to the VIA. The two strains are similar and their hemagglutinin proteins show approximately 96% homology. For the preparation of the inactivated or cold-adapted trivalent vaccine VIB component, a Victoria or Yamagata virus is selected. Viruses from both strains of influenza B virus are antigenically distinct, making it difficult to prepare the vaccine, as viruses from both strains can circulate in a given season, and sometimes even co-circulate in the same outbreak. As well, changes in VIA may also make it difficult to prepare the vaccine[5,15,16].

Influenza C virus (VIC) was isolated by Taylor in 1950, being more stable and therefore less frequently involved in epidemics. Infects humans and pigs, but does not infect birds. There are records of transmissions between pigs and humans in the past. Due to limited host range and lack of genetic diversity in influenza C this form of influenza does not cause pandemics in humans[5,13,14].

In Portugal, the Directorate-General for Health (DGS) reported that since the beginning of October 2017, over 1.3 million free flu vaccines have been administered at the National Health Service (NHS). Thus, 255 thousand more people were vaccinated for free than in 2015/2016 and 170 thousand more people than in 2016/2017[17].

According to the World Health Organization (WHO) recommendation trivalent influenza vaccines for the 2017-2018 season in the Northern Hemisphere include: a viral strain A (H1N1) pdm09 identical to A / Michigan / 45/2015, a viral strain A (H3N2) identical to A / Hong Kong / 4801/2014 and a viral strain B (Victoria strain) identical to B / Brisbane / 60/2008[18].

It is noteworthy that at the present time, the Yamagata strain type B influenza virus was the predominant[19].

The Yamagata circulating strain did not match the strain present in the vaccine for the corresponding time.

CDC guidelines state that when indicated, antiviral treatment should be started as soon as possible after the onset of the disease, ideally within the first 48 hours after the onset of symptoms[20].

The vaccine is the best available strategy for the prevention of influenza and its consequences, providing an indirect impact on reducing work absenteeism and the costs associated with treating secondary infections, hospitalizations and preventable mortality. Annually, during the influenza epidemic period, according to the World

Health Organization (WHO), the annual epidemic results in 1 billion cases of influenza worldwide, and approximately 250,000 to 500,000 deaths[21–23].

The Xpert FLU kit is a next-generation nucleic acid amplification system that provides multiplexed PCR detection of influenza A, influenza A 2009 H1N1, and influenza B viruses in approximately 70 min with minimal use time. The Xpert FLU test has a sensitivity (Se) and specificity (Sp) of respectively 100% for detection of influenza A (influenza A), 98.4% and 100% for detection of H1N1-2009 and 80. 77% and 100% for the detection of influenza type B[24].

In Portugal, the National Surveillance Program of the flu activity has been running since 1990, with clinical and laboratory components. Every week INSA (Ricardo Jorge Institute) publishes a newsletter with relevant information on the subject; It also sends this information to the European Center for Disease Prevention and Control (ECDC), which publishes and disseminates it with other countries. This Portuguese surveillance system is highly regarded among Member States.

OBJETIVES

To characterize and determine the analytical profile of the population diagnosed with influenza in a Central Hospital, from January 1 to 31, 2018.

MATERIAL AND METHODS

Retrospective, observational study with data collection available in the clinical process (ALERT® and SClinico®) and data processing in Microsoft Excel®.

All patients undergoing the Xpert FLU (GeneXpert®) kit were included, and those aged ≥18 years with positive results were selected.

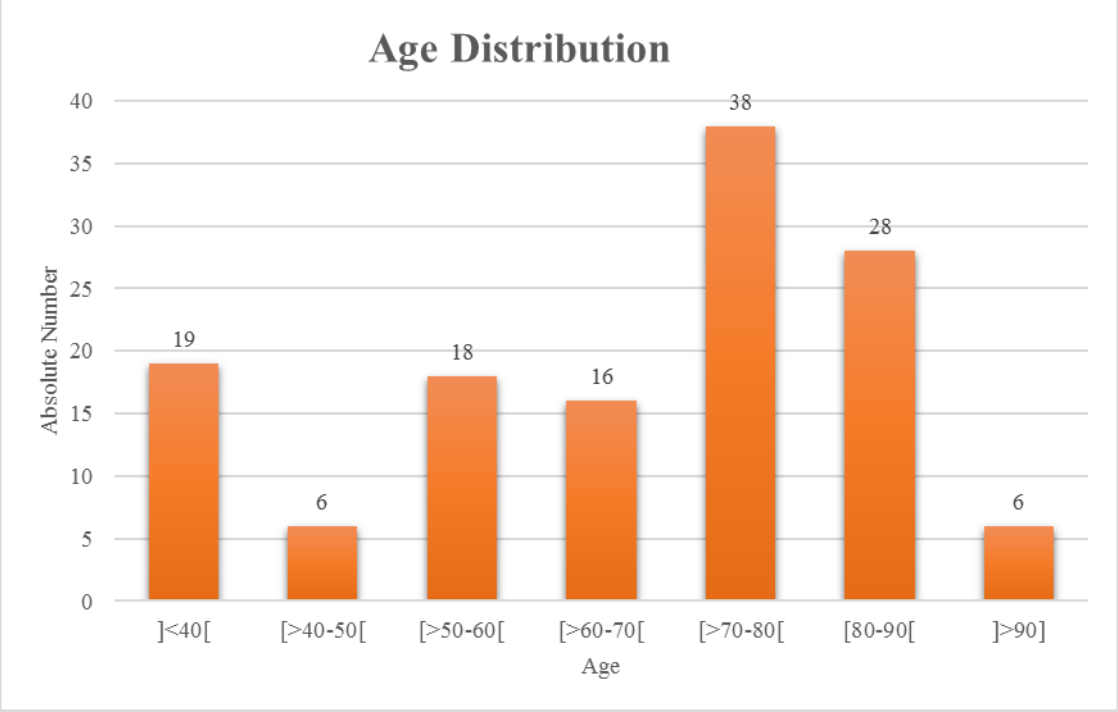
The following variables available in the clinical process were characterized: age, gender, diagnosis at discharge and length of stay in both groups, and in the subpopulation that showed a positive result - pCr).

RESULTS

From a total of 406 patients undergoing the Xpert FLU (GeneXpert®) kit, 301 aged ≥18 years were selected, of which 131 were positive.

In the sample with positive Xpert FLU kits (n= 31), 58.8% (n=77) of the patients were female and had a mean age of 67.1 years (± 18.5) (Graph 1).

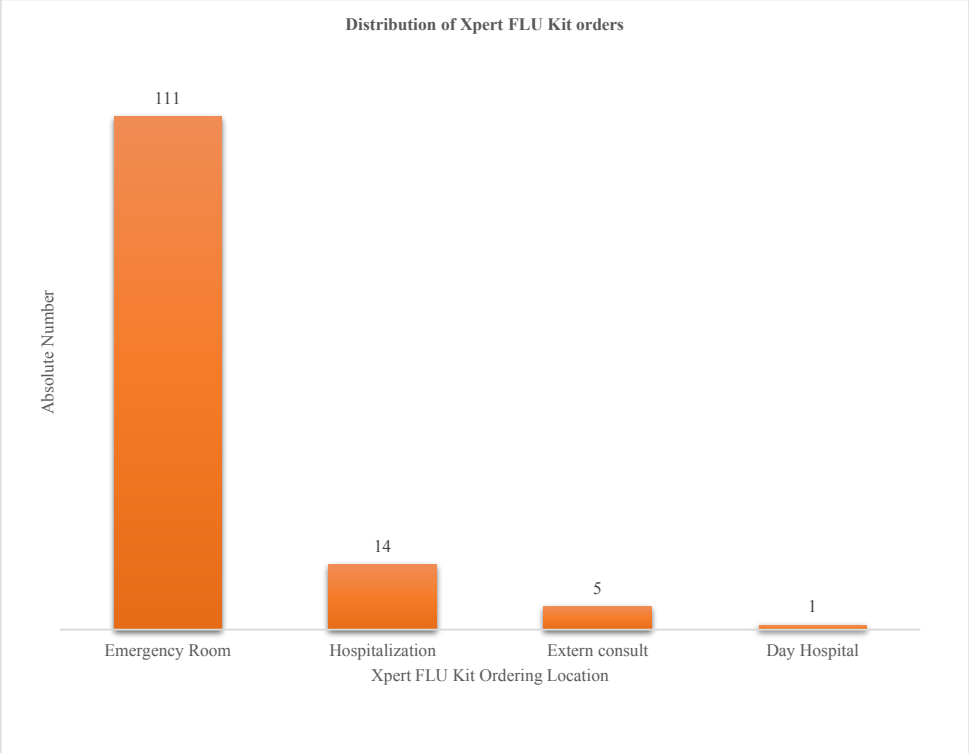
Graph 1 - Age distribution of the sample with positive Xpert FLU kits (n = 131)



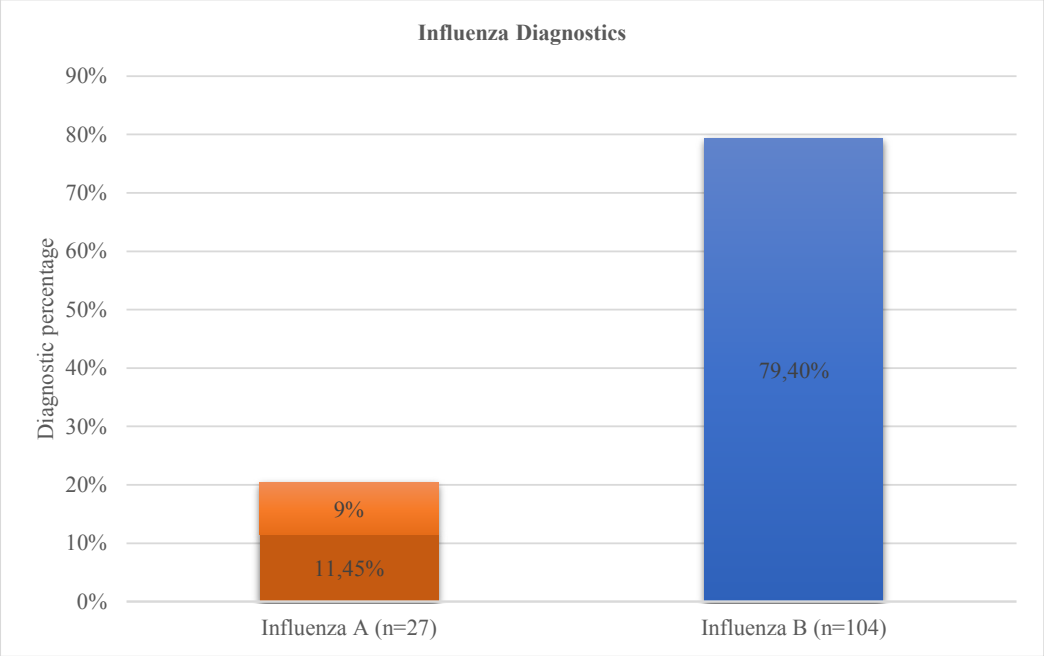
Most of the positive Xpert FLU kits in the sample with were performed in an emergency setting (84.7%) (Graph 2).

Of the sample with influenza (n=131): 20.6% influenza type A (n=27), of these 9% are H1N1 (n=12) and 79.4% influenza type B (n=104) (Graph 3).

Graph 2 - Location of Xpert FLU Kit Orders (Positive (n = 131))



Graphic 3 - Flu Diagnoses

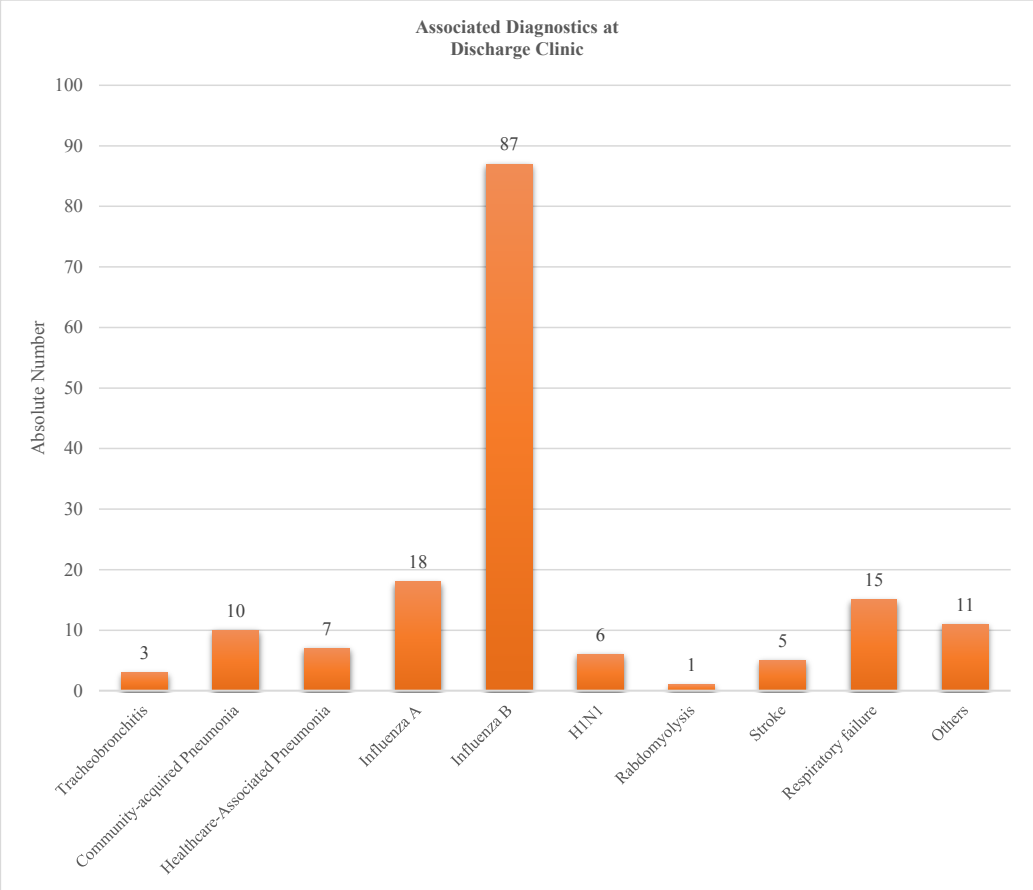


The associated diagnoses in the sample with positive Xpert FLU kits were heart failure (n=15) and community-acquired pneumonia (n=10) (Graph 4).

The average length of stay in the sample diagnosed with influenza was 7.1 days.

In the sample with influenza their analytical profile was analyzed at admission.

Graph 4 - Associated diagnoses at discharge (n=131)



The absolute number of leukocytes (n=129) was normal at admission at 63.6% (n=82), with leukocytosis 8.5% (n= 1) and leukopenia 27.9% (n=36).

At the neutrophil level (n=129) 62.8% had neutrophilia (n = 81), 29.4% had no neutrophil changes (n= 8) and 7.8% relative neutropenia (n=10).

At lymphocyte level (n=129) 65.1% had lymphopenia (n = 84), 31% had no lymphocyte changes (n = 40) and 3.9% relative lymphocytosis (n=5).

Platelets had a mean absolute number of 165.8 x10 ^ 9 / L, 51.2% had a normal platelet count (n=66), 46.5% thrombocytopenia (n=60) and 2.3% thrombocytosis (n=3). But if we establish the lower limit of normal the absolute platelet count lower than 200 x10 ^ 9 / L, we find that 77.5% had thrombocytopenia (n= 00).

Procalcitonin (n = 50) was negative in 82% (n = 41).

pCr (n=128) had a mean value of 15.1 mg / dl. CRP was elevated by 90.6% (≥0.5 mg / dl) (n=116), 65.5% (> 2 mg / dl) and 39.5% (> 5 mg / dl).

Note that in the group with positive Xpert FLU kits, 68.7% (n = 90) of the patients required hospitalization in isolated conditions.

The mortality rate in the group with positive Xpert FLU kits was 0.0024% (n=4).

DISCUSSION

IV is one of the major threats to global public health and could lead to the deaths of nearly half a million people worldwide each year. WHO carries out global influenza surveillance annually, and forecasts several representative types of viruses that may be the most common during the flu season[8,25].

Rapid virological diagnosis is important for early case identification, initiation of antiviral therapy, and implementation of infection control measures for influenza patients[26].

In our series, the majority of cases occurred in older people (> 70 years) who presented with analytical changes (lymphocytosis, neutropenia and thrombocytopenia).

Reaching an older age group warns of the importance of vaccination on this age group in primary care.

Previously published studies have analyzed the characteristics, changes in the leukocyte series and lymphocyte subpopulations of patients with pandemic influenza virus (H1N1) infection and found that the leukocyte count in mild cases has decreased significantly, but in severe cases there has been no reduction. significant. In the latter subgroup, neutrophils increased significantly in

the acute phase; similar to VIA infection (without H1N1)[27].

Thrombocytopenia is a common analytical disorder and sometimes poses an increased risk of prognostic deterioration in patients with VI, which seems to indicate that platelets may play a significant role during virus infection. The mechanism underlying thrombocytopenia appears to be related to platelet phagocytosis of VI and may be a means of virus clearance during infection[28].

Several studies conducted during the 2009 pandemic approached procalcitonin or pCr values as discriminated levels between the Influenza A H1N1 virus and community-acquired pneumonia of bacterial origin. Procalcitonin and pCr admission levels were compared among hospitalized patients, and procalcitonin measurement potentially helps to discriminate between severe bacterial and H1N1 lower respiratory tract infections of 2009, although less effective than pCr. Low values, particularly when combined with low levels of pCr, suggested that bacterial infection, either alone or in combination with influenza, was unlikely[29,30].

The present study also made it possible to evaluate the diagnostic approach to influenza and to establish a profile of the possible influenza patient in conjunction with clinical symptomatology and the appropriate use of this PCR diagnostic examination from both the clinical and economic point of view.

Chart 1 - Flu patient profile in the sample with positive Xpert FLU kits (n = 131)

Flu Patient Profile		
Leukocytes (Absolute)	Normal	63,6%
Neutrophils (Relative)	Neutrophilia	62,8%
Lymphocytes (Relative)	Lymphopenia	65,1%
Platelets (<200 x10^9)	Thrombocytopenia	77,5%
Procalcitonin	Negative	82%
pCr	>2 mg/dl	65,5%

According to INSA (Ricardo Jorge Institute) on week 8 of 2018 was detected first decrease in the number of influenza viruses. The Yamagata type B influenza virus has been predominantly detected since the beginning of the influenza era. These data show that January was an increasing period of influenza with the peak of influenza reaching February 2018, which may account for the percentage of negative Xpert FLU kits in January.

It should be noted that type B influenza was the most prevalent in the study sample, which is in line with DGS data showing that the Yamagata strain type B influenza virus was predominant in this epidemic period[19]. This strain is not included in the annual influenza vaccine[18]. As the vaccine is the best prevention method, it should be considered the universal vaccine that became available for influenza in the 2018-2019 season[31].

The positivity in 43.5% of the sample (n=301) of the tests performed implied a high number of hospitalizations (n=90) in isolation conditions.

Hospital isolation is a preventive practice and a measure of communicable disease control, and is of great importance given the large number of patients infected with influenza during the epidemic within a hospital unit. Early isolation of these patients can minimize the spread of the virus, reducing infected patients and related costs.

These measures paradoxically generate difficulties in nursing management reducing the turnover of hospital beds.

CONCLUSION

The analytical profile of the influenza patient allows, along with the clinic, suspicious guidance for managing rapid virological diagnostic resources, important for initiating antiviral therapy, implementing infection control measures and prevention for influenza patients.

Primary prevention through providing information and clarifying the sample is a key component in addressing possible epidemics. Public cooperation during a global epidemic is essential to minimize the spread of the disease, ensure compliance and support for hygiene and social remediation measures and vaccination efforts, and avoid unnecessary burdens on the health system. As an epidemic progresses, strategies may need to be modified according to the changing context[21–23].

According to the World Health Organization (WHO) recommendation trivalent influenza vaccines in the Northern Hemisphere 2018-2019 include: a viral strain A (H1N1) pdm09 identical to A / Michigan / 45/2015; a viral strain A (H3N2) pdm09 identical to A / Singapore / INFIMH-16-0019 / 2016 and a viral strain B (Victoria strain) identical to B / Colorado / 06/2017. The quadrivalent vaccine also includes: a viral strain B (Yamagata strain) identical to B / Phuket / 3073/2013.

The positivity implied a high number of hospitalizations in isolation that deserve reflection of hospital, clinical and economic management.

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