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Approach to COVID-19 pandemic management in Madrid. Chronic of a year

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ABSTRACT

After more than a year of pandemic, the international medical community has changed the perception of fear to one of respect for SARS-COV-2. This has been the consequence of the integral study of all the dimensions of the disease, from viral recombinant capacity to transmissibility, diagnosis, care and prevention. This document summarizes the main strategic lines of study and approach to the pandemic in Madrid.

Keywords: COVID-19, management, Madrid

The region of Madrid is one of the most populated communities in Spain with a density in 2019 of 834 inhabitants/km^2, 12% higher than the next region in terms of population density, which is Barcelona [1]. It represents the largest labor and logistics node in the country. It is also one of the main immigration destinations and connects with the rest of the country through a developed road network and the largest railway and airport connection in the national territory. Spain is home to the oldest population in Europe and Madrid has the largest number of social-healthcare centers with more than 100 beds [2]. All these are influential elements in the spread of SARS-COV-2 infection.

After the first pandemic impact, all of Spain began to work to adapt to the changes that the pandemic itself generated, mainly related to sociodemographic movements (work, academic or vacation). Since then, the graph of the evolution of the pandemic has been marked by two facts, the development and distribution of vaccines (or lack thereof in some areas of the planet) and the knowledge by massive sequencing of the emergence of viral variants, as a result of the ease of viral recombination and the relaxation of preventive measures in the interaction between people. In Madrid, work was carried out along the four strategic lines described below:

1. Diagnostic development (implementation of diagnostic techniques, development of seroprevalence studies, sequencing for early diagnosis of new variants, etc.) to know the burden of the disease and control of outbreaks.
2. Promotion of prevention measures, implementation of perimetral restriction, people capacity control and sectorization of centers with a higher risk of contagion. Once the vaccine is available, development of distribution and administration circuits.
3. Construction of infrastructures and increase in human resources for diagnosis, treatment and prevention of infection.
4. Search for tools to predict changes in the balance of contagion.

DIAGNOSTIC DEVELOPMENT

Despite the shortage of equipment and consumables at the end of the first wave, an effort was made to increase the diagnostic capacity of the Microbiology Departments of all hospitals, and a special effort was made to implement molecular diagnostic platforms. Overall, diagnostic activity increased to 26,300 PCR tests per day in September, 27,400 at the end of October and more than 28,000 in November 2020. Thus, more than 2 million PCR tests for SARS-CoV-2 were performed from September through December 2020. This figure has already been well exceeded in February 2021 [3,4].

Point-of-care (POC) antigen testing is for WHO [5] particularly useful in the diagnosis of infection if PCR results are not available at short notice, or in case the healthcare system is overwhelmed. They are also recommended in the study of contacts, especially in case of outbreaks or in areas of high community transmission, contexts in which the predictive values are high enough to allow effective infection control, which

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is justified because even in the absence of symptoms the viral load levels are similar to those of symptomatic cases.

Madrid pioneered the implementation of these antigenic tests, developing a document of recommendations on their use, published in this journal and in different care settings (primary care, pediatrics, emergency, social and health centers) [6]. From week 41 to the end of 2020, half of the more than 100,000 SARS-CoV-2 diagnostic tests performed each week in suspected cases were rapid antigen tests. This strategy, implemented in hospital emergency and primary care settings, increased the ability to diagnose COVID-19 cases. Rapid antigen tests were also used in the screening of asymptomatic subjects, achieving a ratio of 250 tests per COVID-19 case detected. All these results demonstrate that the acceptability and simplicity of point-of-care diagnosis of SARS-CoV-2 overcomes the limitations of test sensitivity, including those observed in asymptomatic subjects, and makes antigen testing a valuable tool for monitoring and controlling the pandemic [3]. Four months later, antigen tests can be performed in pharmacies and are even available for sale for self-testing. At present, antigenic tests for clinical use have not lost sensitivity against viral mutational variants [7]. According to data provided by the Ministry of Health to the ECDC, the diagnostic capacity of CM has reached 21 tests (PCR or AT) per case detected by the end of 2020, an average of 2,341 diagnostic tests per 100,000 inhabitants [8].

Another diagnostic challenge that points to the burden of disease and is crucial for the development of health strategies are seroprevalence studies. These studies, carried out in vulnerable or exposed persons (residents in social and health care centers, people with disabilities, law enforcement officers, prison officers, etc.) and as a complement to the national study [9], have helped to understand the traceability of infections and their modulating factors (cohabitation, transport, groupings, work, etc.). A clear example is the analysis of residents in health care facilities [10], which has made it possible to sectorize the staff, manage opening and visiting hours, the cadence of screening of workers and the tracing of infection flows in outbreaks among residents, etc [11].

The latest diagnostic challenge to date is the implementation of mass sequencing in disease management. The classical nucleic acid sequencing procedure has for years been the Sanger method, designed to generate single amplicon sequences. However, the development of massive whole genome sequencing techniques, based on next-generation sequencing (NGS) methods, allows millions to billions of DNA copies to be sequenced in a single run [12]. Despite its bioinformatics requirements, this methodology is gradually being incorporated into genomic studies in clinical care and epidemiological surveillance at a cost and scale hitherto inaccessible [13]. For the time being, its main application has been the characterization of the successive phenotypically and genotypically different SARS-CoV-2 variants that have emerged in recent months. This characterization has improved knowledge of the spread and severity of the infection. In addition, its use makes it possible to identify cryptic forms of transmission, generating opportunities for health interventions. The main variants of concern include Alpha (B.1.1.7), which emerged in September 2020 in the United Kingdom, Beta (B.1.351; B.1.351-V1), which emerged in South Africa in October 2020, Gamma (P.1, a descendant of B.1.1.28), initially detected in Brazil in December 2020, and Delta (B.1.617), which appeared in India. Among the variants of interest, the most studied are the Epsilon (B.1.429; CAL.20C/B.1.427) identified in California in May 2021 [14]. In Spain the Beta, Gamma and Epsilon variants have circulated very rarely. Alpha has been until recently the majority [15]. Currently, the Delta B.1.617 variant seems to predominate. This variant has recently been subdivided into two: Delta (B.1.617.2) and Kappa (B.1.617.1) [16]. The new variant of interest Lambda, initially distributed in Peru and Chile, has joined this expanding set of strains [17]. A connotation of epidemiological surveillance lies in its obligatory and agile adaptability to changing and unforeseen situations, such as those of the present pandemic. Thus, the integration of molecular epidemiology with traditional epidemiology is a necessity that cannot be postponed. To this end, the creation of multidisciplinary groups for the implementation of consensual practices between microbiologists, bioinformaticians, clinicians, epidemiologists and health authorities represents the best strategy.

PROMOTION OF PREVENTIVE MEASURES

The successive waves of COVID-19 cases currently occurring in European countries, and until vaccination rates achieve the expected herd immunity, are forcing policy makers to make decisions that will impact not only the spread of the pandemic, but also the socio-economic future of their regions. Spain was one of the first and hardest hit by the COVID-19 pandemic in Europe. The rapid spread of the first wave of COVID-19 overwhelmed the healthcare system, leading the government to declare a State of Emergency on March 14, 2020, and to impose one of the tightest closures in Europe, in line with those imposed in Italy and France [18-20]. These restrictions succeeded in reducing the spread of COVID-19, but led to a 17.8% drop in GDP compared to the first quarter of 2020, which placed Spain among the three OECD countries with the largest GDP decline during the second quarter of 2020 [21]. In a mathematical model of confinement-testing, while policies based on increased testing rates would lead to higher healthcare costs, increased mobility restrictions and confinement would be associated with a larger decline in GDP, with differences of up to 4.4% points [22]. Alternative strategies to control the spread of COVID-19 lead to different economic outcomes. Decision makers can use these tools to identify the most appropriate strategy taking into account epidemiological and economic outcomes.

Instead of maintaining strict containment with complete mobility restrictions, a strategy of perimeter containment by basic health zones was implemented in CM. The CM has 286 Basic Health Zones (ZBS) with a median of 21875 inhabitants (IQR 11083) per area. From September 21, 2020 until spring 2021 when confinements were suspended, half of all of them

were confined. This type of confinement, by districts or small municipalities, only in those areas with the highest density of occurrence, minimized the social and economic impact of the closure of commercial activity. The perimeter restriction not only acts on the mobility of citizens, in fact, it includes many other associated measures such as limiting the capacity and opening hours of commercial activity, capacity control or diagnostic-monitoring campaigns as the main interventions. In any case, the measures applied in the CM to confined areas caused a more pronounced decrease in the incidence of cases in the perimeter areas than in those where these restrictions were not applied.

On December 2, 2020, the Technical Working Group on COVID-19 Vaccination of the Vaccination Program and Registry of the Ministry of Health published the Strategy for vaccination against COVID-19 in Spain [23]. After the arrival of the first doses of the vaccine developed by Pfizer-BioNTech pharmaceuticals, the Community of Madrid began, between December 2020 and February 2021, vaccination in health centers in the region. An enormous effort was deployed to vaccinate both the institutionalized population in their residences and the non-institutionalized elderly dependents in their homes. On February 25, vaccination against COVID-19 began in health centers for people over 80 years of age. The different age and comorbidity risk groups were progressively vaccinated, following national and international bioethical criteria for efficacy and safety. After vaccinating the most at-risk patients, vaccination of the rest of the population began. Three mass vaccination centers were opened (HEEIZ, Wizink Center and the Wanda Metropolitano soccer stadium), where, by means of a prior self-appointment request via internet, vaccination could be carried out, first during daytime hours and from July 2021, 24 hours a day [24]. The vaccination process began with mRNA vaccines (mainly Pfizer and to a lesser extent Moderna), to which the AstraZeneca vaccine was added at the end of February and the Janssen vaccine in April. Due to international reports of thrombotic side effects with the use of these last two vaccines, at present, practically all vaccination is being carried out with mRNA vaccines. By August 23, 2021, of the 8,800,000 doses delivered, more than 7 million will have been with mRNA vaccines. On this date, the vaccination percentage of the population is 67%.

INFRASTRUCTURE AND HUMAN RESOURCES

Already in the first week of March 2020, the hospitals had created Covid-No Covid care circuits to guarantee the safety of healthcare workers and patients. From the third week onwards, the healthcare capacity of the Community of Madrid was exceeded and these care circuits were insufficient. It was necessary to set up medicalized infrastructures to support a growing demand for patients. The most effective model for a temporary hospital was the reconversion of an existing structure with the capacity to accommodate crowds, the IFEMA fairgrounds [25]. Fairgrounds are usually built in large, well-connected areas for patient transport and clinical logistics. They have ample spaces that include administration areas, restrooms, air conditioning, pre-installations to incorporate portable equipment, telephony, and wired and Wi-Fi Internet connection. They usually have high ceilings to better control air recirculation and spaces can be set up for patient, bed and trolley passage areas, as well as for dirty waste disposal circuits. In addition, areas can be set aside for patients to walk around, reducing the risk of thromboembolic disease, and where they can control desaturation themselves. All this deployment is quick and easy to set up. The main need in COVID-19 patient care was the high need for oxygen, to ensure optimal ventilatory therapy for all admitted patients. To ensure ventilatory support, more than 25 km of soldered copper tubing circuit was installed and connected to external oxygen towers. This operation was completed in 72 hours. During the period in which the IFEMA hospital was open (March-May 2020), 3,817 patients were hospitalized with mild to moderate grade, with Charlson Comorbidity Score scores between 0 and 3. 91% had a diagnosis of pneumonia (53% were bilateral) and an oxygen saturation of less than 91% [25].

The major healthcare challenge is the construction of new structures designed specifically for the treatment of infectious diseases. Examples are centers such as Huoshenshan or Leishenshan in Wuhan, built in 10 days and with a capacity for more than 2,000 people, the one in Zhengzhou with a capacity for 800 or other smaller ones such as Fuqing or Weihai with less than 400 [26]. The design of these hospitals contemplates the sectorization by wards and Halls of the care areas, the access circuits and the pre-installation of any clinical equipment, beyond those necessary for patient care. This allows the reuse of the facility for other public health purposes, from vaccination, rehabilitation or radiological screening centers to the installation of hybrid operating rooms to alleviate the surgical waiting list. This versatility has been developed in the Hospital de Emergencias Enfermera Isabel Zendal (HEEIZ) in Madrid, completed at the end of the second wave, with 1,056 beds, 20 of them for critical care and another 30 for convertible semi-critical care. It has a laboratory, radiology area, heliport and easy road access [27]. From December 2020 to April 2021, more than 5,500 patients with bilateral pneumonia and respiratory failure have been treated. A total of 16.4% required admission to semi-critical care and 4.1% to ICU (data not published). At present, it is a COVID monographic center, which offers excellent performance in ventilatory support, however, it is designed for multipurpose functions and represents the paradigm of adaptability in healthcare and an investment in public health.

The Regional Public Health Laboratory (LRSP) is a service dependent on the General Directorate of Public Health (DGSP) and its mission is to provide analytical and technical support to the Public Health Programs in the field of public health protection and surveillance. For more than 20 years it has been carrying out this activity through microbiological and physicochemical analyses of water and food, as well as clinical samples related to epidemiological surveillance. The pandemic situation forced to increase the performance of the Clinical Microbiology section, to carry out seroprevalence studies

in Sociosanitary centers and other fragile populations, for the microbiological diagnosis and control of outbreaks in the out-of-hospital context and for the implementation of novel diagnostic techniques that could modulate the evolution of the pandemic. The number of technicians and the number of work shifts were increased, but soon the capacity of the facilities was exceeded, and a new headquarters had to be built to meet the growing need for microbiological results and the other functions of the LRSP. For this purpose, the project for the construction of a new headquarters was undertaken, on an area of 2,400 m^2 included in the HEEIZ complex, which was also completed within 100 days.

Human resources are as important as material resources, both for patient treatment and epidemiological control. Between September and December 2020, 11,324 new positions were created in the CM to strengthen the fight against COVID (1,067 medical staff, 5,063 nursing staff, 3,274 auxiliary staff and 1,247 non-health professionals) [28]. In addition, screening activity was boosted in September with 456 new tracers, so that by the end of the year the number of these positions, primary care, Army, and call-centers, amounted to 1,590 (approximately 1 per 4,264 inhabitants).

SEARCH FOR PREDICTIVE TOOLS FOR CHANGES IN THE BALANCE OF CONTAGION

As a complement to the analysis of data from diagnostic tests and confinement, it is necessary to have some predictive tool for changes in incidence, to establish public health strategies and to optimize health care resources in case of a reoccurrence of cases.

Since April 2020, Canal de Isabel II launched an intensive wastewater analysis initiative to monitor the presence and evolution of SARS-CoV-2 in the Community of Madrid, as an early ecological indicator to monitor behavioral changes in the ecosystem. A total of 289 wells of the water network were analyzed to represent the entire population. Each week, samples were taken from all sampling points and analyzed for SARS-CoV-2 concentration (gc/L, genome copies per liter) and physicochemical parameters are also analyzed to validate or rule out what in principle could be an unusual presence of the virus in two different laboratories. The presence and evolution of SARS-CoV-2 in wastewater correlated significantly with 14-day incidence rates and COVID-19 hospitalizations. This information is shared daily with health authorities for advice and decision making [29]. Similarly, other parameters continue to be explored as predictors of changes in disease incidence and its impact on the healthcare system. The threshold cycle of detection of SARS COV 2 on PCR could be one of them. It has been suggested that it could be related on admission to the clinical course and prognosis of the patient with COVID-19 [30]. Its role as a predictor of admission is yet to be confirmed.

Despite all the material and human efforts, the incidence peaks and the onset of new waves continue to be experienced. Demographic movements and the relaxation of prevention measures, especially during holiday periods, in a population already in need of mobility, favor recombination and the development of viral variants. The most direct consequence is the overload of care, especially in primary care. Therefore, it is so important to achieve herd immunity and to carry out epidemiological surveillance of variants by sequencing.

CONFLICTS OF INTEREST

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