

## Ivermectin as Prophylaxis Against COVID-19 Retrospective Cases Evaluation

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**ABSTRACT**

*The current SARS COV2 (COVID 19) pandemic has generated a high number of infections among Health Agents. Around 25% of them have had to leave - temporarily or permanently - their jobs, due to having contracted the disease.*

*Likewise, numerous deaths have been lamented within this group, which acts as the first defense against this and other pathologies that threaten the individual.*

*All this has happened despite Personal Protective Equipments (PPEs), which makes it essential to optimize -from the pharmacological point of view- these elements, in order to reduce the risk of contagion as much as possible.*

*In this sense, Ivermectin has shown its usefulness against SARS COV2, both in treatment and in prophylaxis.*

*Therefore, this work compiles the characteristics of the group of Health Agents (and their close contacts) from a Buenos Aires Hospital specialized in Infectious Diseases, who resorted to it, as well as the results that were obtained.*

**Keywords**

COVID-19, Virus, Ivermectin.

**Introduction**

At the end of December 2019, the incidence of a typical pneumonia of unknown cause was reported in the Chinese city of Wuhan.

This species, initially named nCoV19 and later renamed SARS-CoV-2 due to its structural similarity to the homonymous species, quickly spread. The early association identified between SARS-CoV and SARS-CoV-2 was supported by subsequent analyzes of

protein S (spike) [1].

The only significantly different portion is a furin-binding domain in the SARS-CoV-2 protein S, which has been speculated could expand the tropism or increase virus transmission, compared to SARS-CoV of 2003.

On the other hand, one of the most conserved portions of the protein is the receptor-binding domain (RBD), which has a similar (or reportedly higher) affinity to angiotensin converting enzyme type 2 (ACE2) in comparison with SARSCoV [2].

A second receptor, TMPRSS2, would also be involved in the entry of the virus into the host cell.

To the proteiform manifestations of presentation, must be added those of the comorbidities that accompany the patient, which will negatively affect their prognosis.

The vast majority of patients will present mild forms and / or will be asymptomatic, but the high contagiousness of this viral entity makes a rapid and accurate diagnosis imperative to prevent them from becoming silent disseminators of the pathology in the community (Figure 3).

It has been confirmed that the most severe cases present with an overlap of hyperinflammation and hypercoagulability (Figure 4) [3,4].

The percentage of cases that evolve into critical and / or fatal forms is highly variable and there is no initial form - however slight - that can predict them. Thrombotic risk is significantly affected by age and comorbidities, along with accumulating evidence of the importance of coagulopathy in the pathogenesis of COVID-19, these are findings that increase the intriguing possibility that pulmonary vasculopathy could contribute evolutionary differences in the malignancy of the condition, which highlights the age susceptibility to mortality from COVID -19 (Figures 5 and 6).

If to all these comorbidities and greater age susceptibility we add work performance in the area of greatest risk of contagion (Figures 7 and 8), it can easily be deduced that the most enormous efforts should be applied to avoid the spread of the virus within Health personnel.

## Updated Knowledge About Ivermectin (IVM)

Ivermectin (IVM) is an antiparasitic (endodecticide), with nematocidal and ectoparasiticidal properties [5]. It is a macrocyclic lactone derived from avermectins, a group of highly active endodecticidal antiparasitic agents isolated by fermentation of the soil microorganism *Streptomyces avermitilis*. It was discovered in 1960 in Japan by Satoshi Omura. In 1981, William C. Campbell began the studies that allowed its veterinary use. Both received the Nobel Prize in Physiology and Medicine in 2015.

In 1985, the French proved its usefulness in onchocerciasis in Africa. It was approved in 1997 by the FDA for treatments of: strongyloidiasis and crusted scabies, in patients with AIDS.

In Human Medicine, it has been used in children from 5 years of age onwards, for the management of ecto and enteroparasitosis [6].

Orally, in humans, it does not cross the blood-brain barrier. It is contraindicated in pregnancy.

Recently, its viricidal effects on flaviviruses, dengue, Zika, Chikungunya, among others, have been compiled [7,8].

Ivermectin is an inhibitor of the causative virus (SARS-CoV-2). This activity is due to the dependence of many RNA viruses on  $IMP\alpha / \beta 1$  during infection. Recently, another mechanism of action has been proposed, assuming its role as an ionophore agent. Ionophores have many oxygen atoms internally, and are essential for binding cations and transporting them through phospholipid bilayers (cell membranes; phospholipid capsid of the virus). As a consequence, it determines an ionic imbalance between the external and internal environment, with the consequent osmotic lysis.

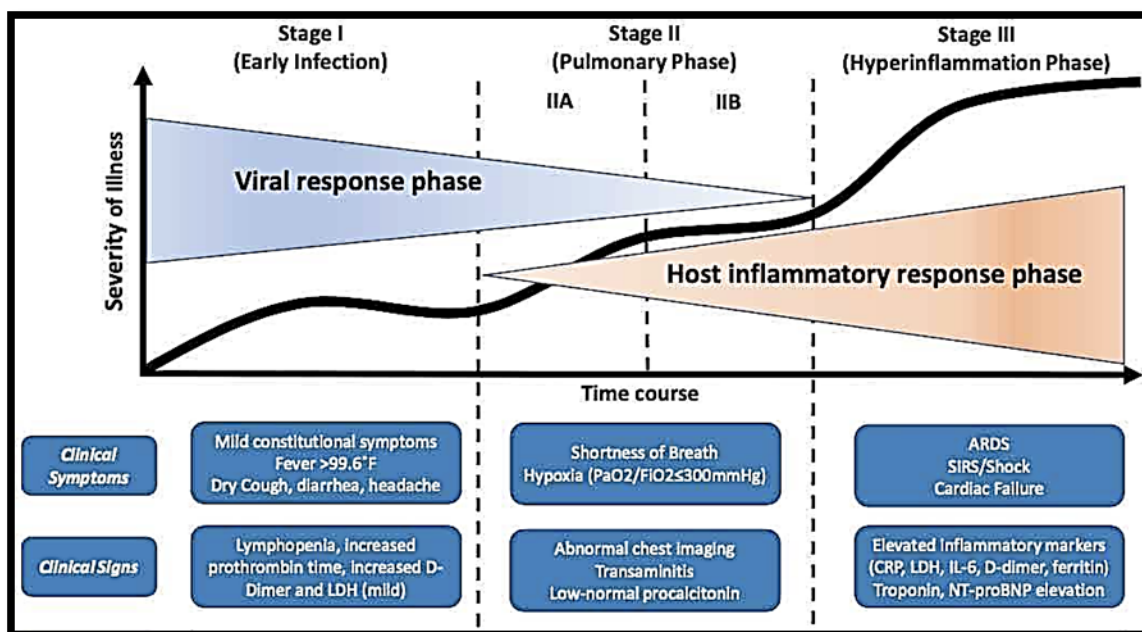


Figure 1: Covid Infection Cycle.

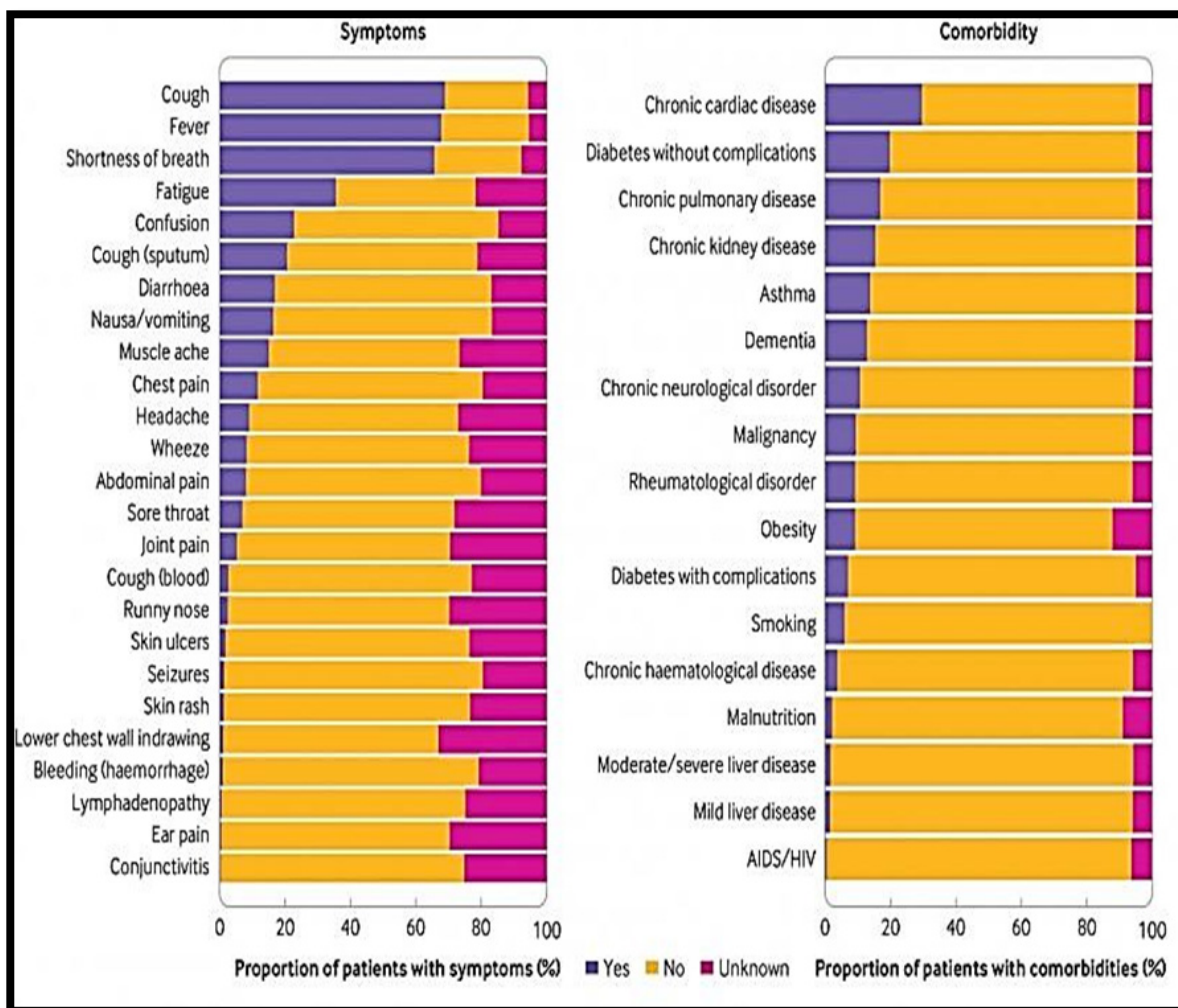


Figure 2: Comorbidities and Symptoms.

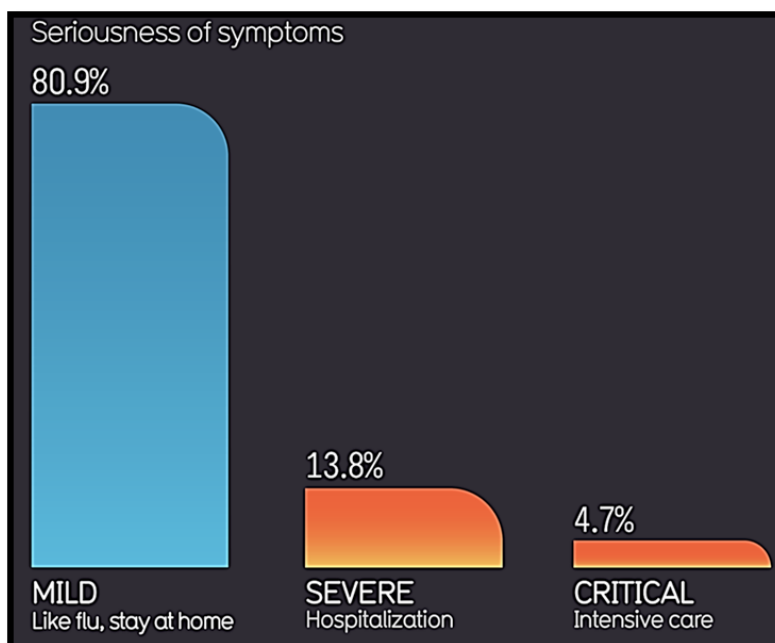


Figure 3: Covid Distribution According To Severity.

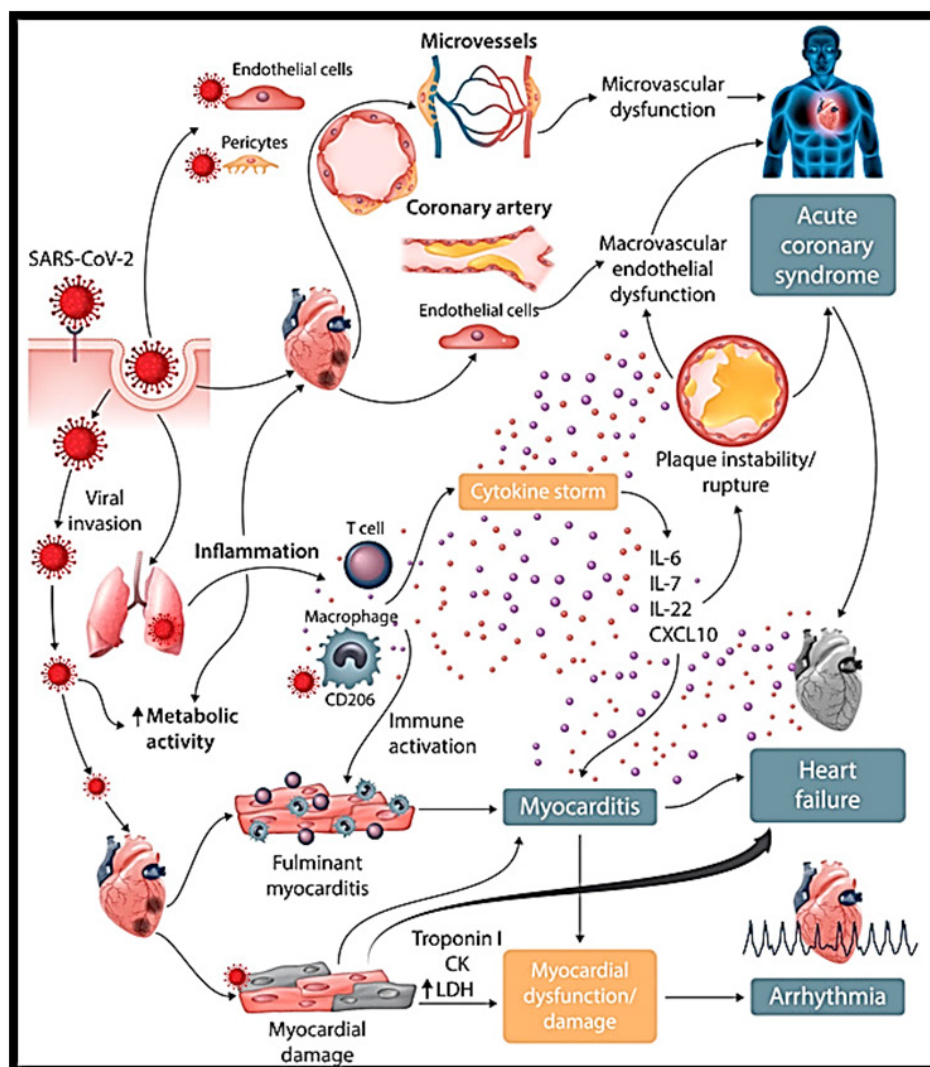


Figure 4: Hypercoagulability and Hyperinflammation Related To Covid.

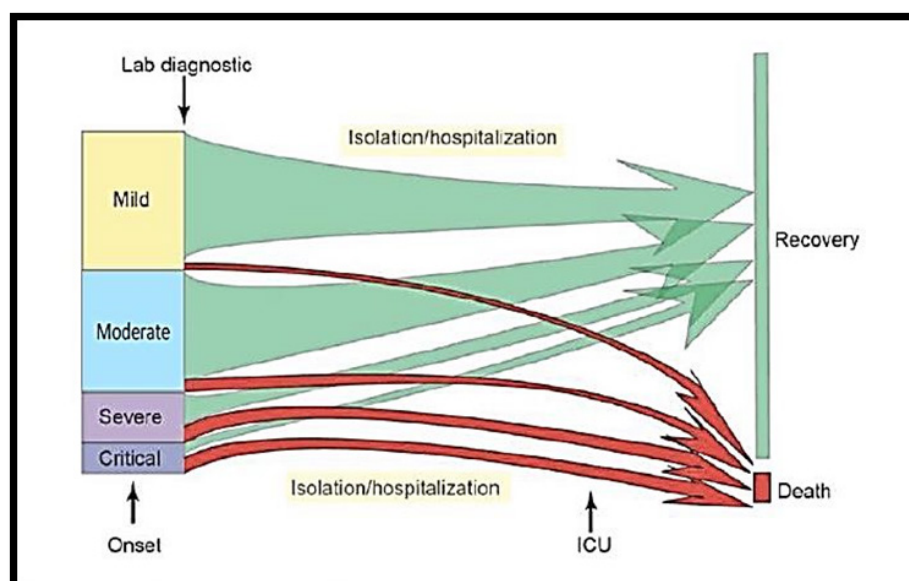
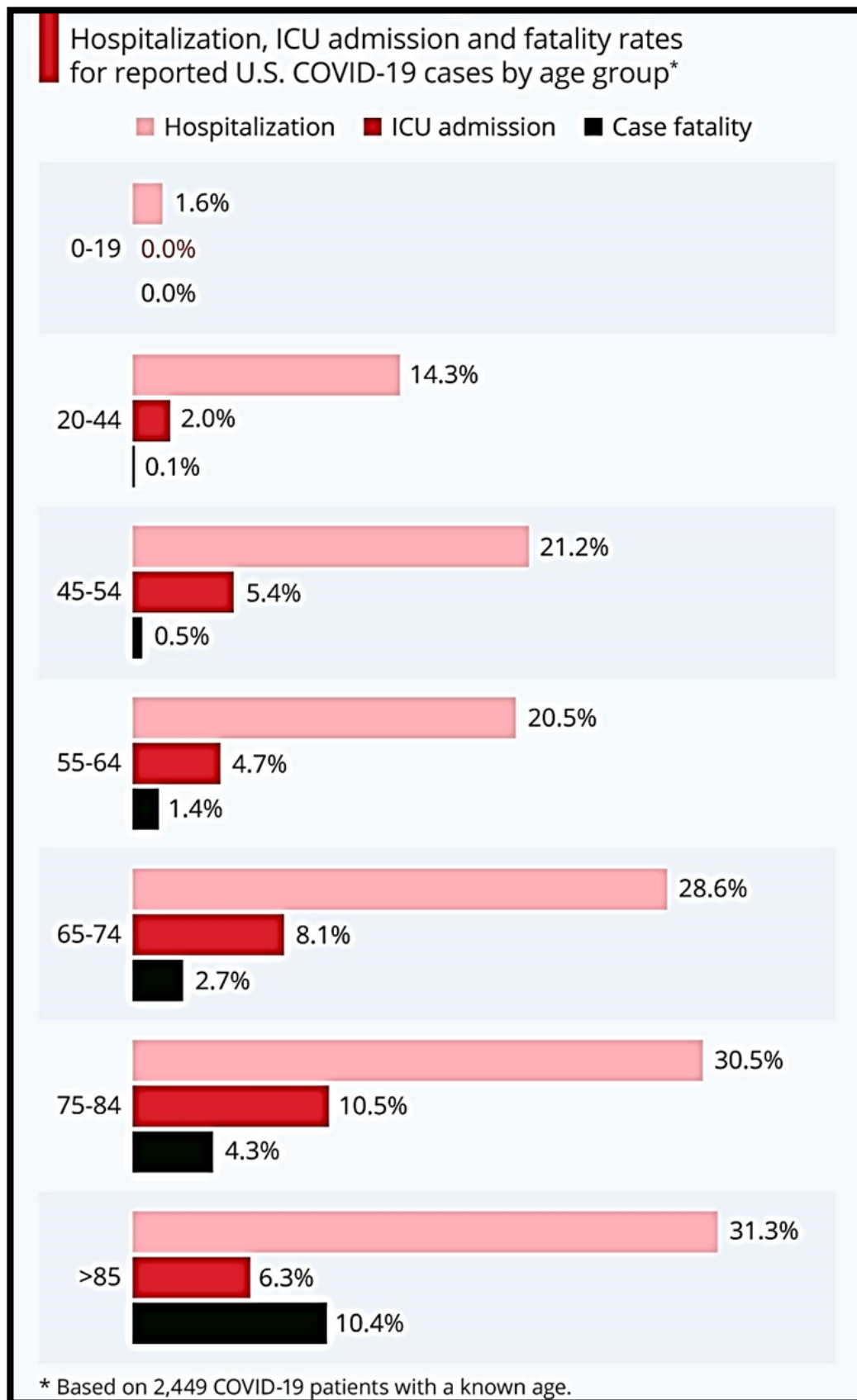


Figure 5: Average Evolution of All Symptomatic Cases.



**Figure 6:** Evolution According To Patients Age.



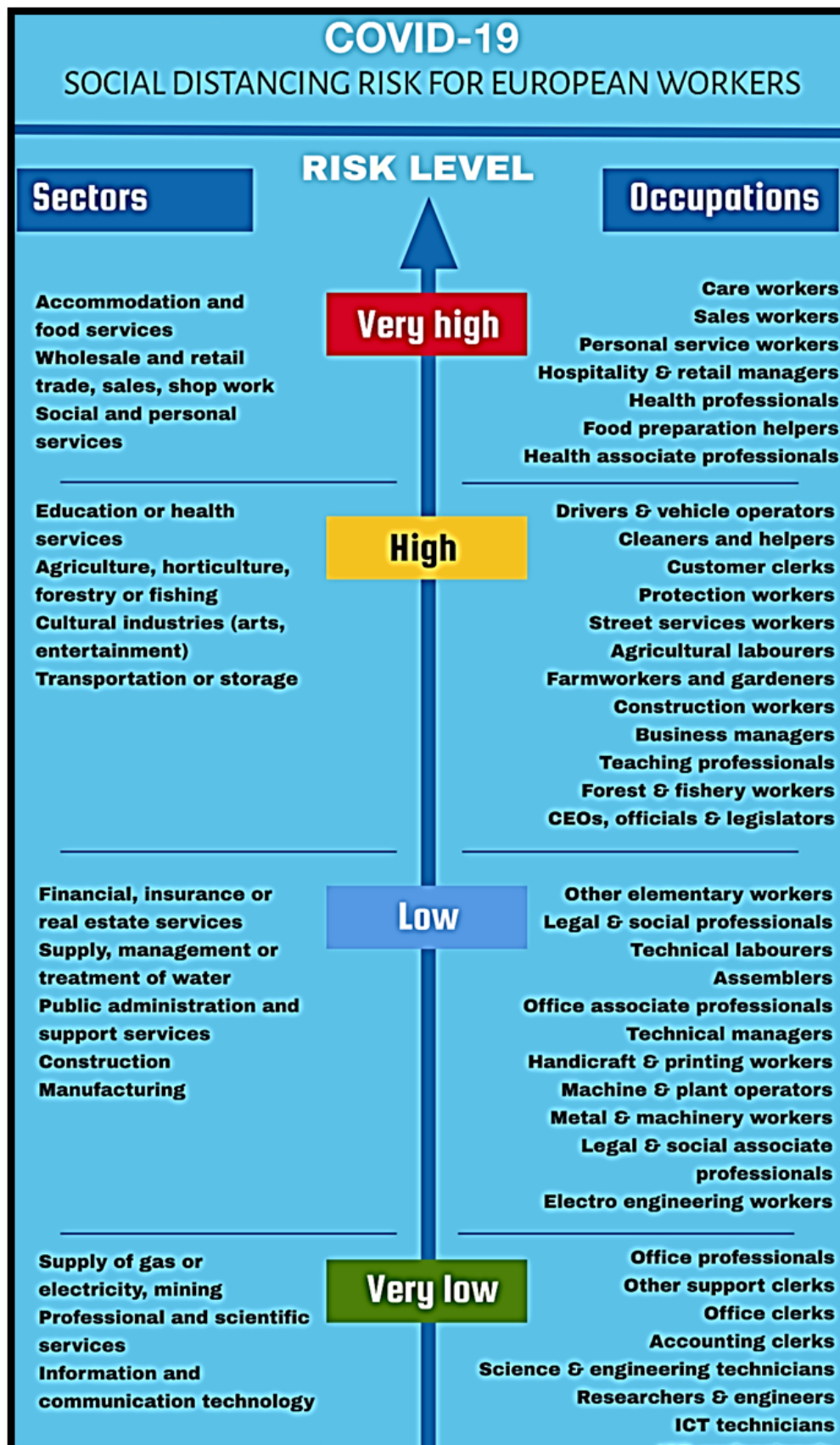
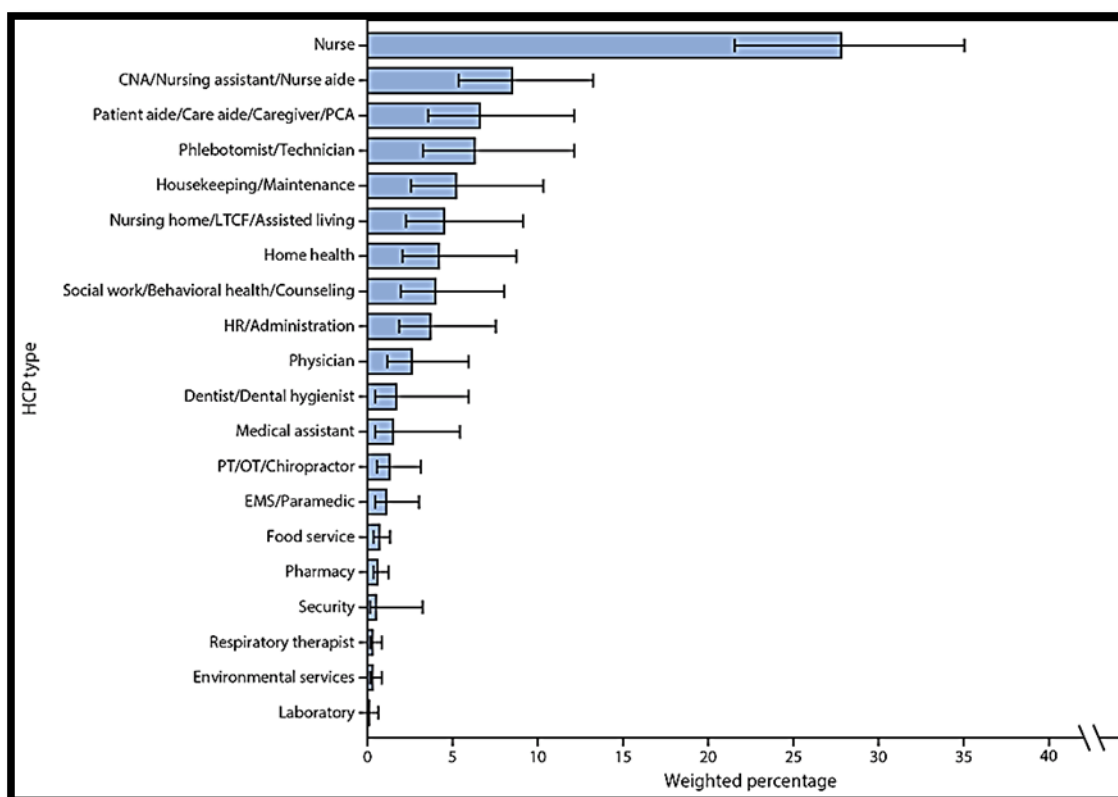


Figure 7: Activity-Related Risk.

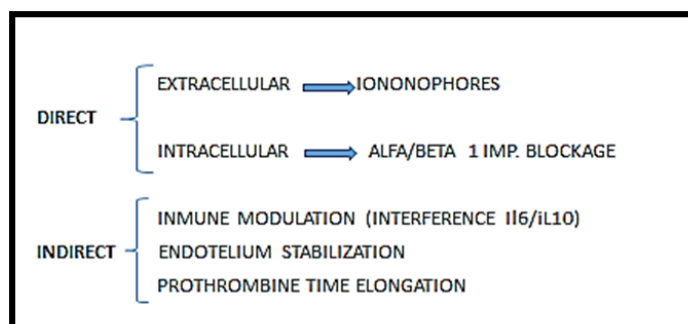


**Figure 8:** Risk According To Health-Care Occupation.

These results, as a whole, demonstrated that ivermectin possesses antiviral action against SARS-CoV-2 in vitro, with a single dose capable of controlling viral replication in 24-48 hours, and the possibility of repeating it periodically.

Research has been added on other forms of action of IVM in the face of COVID disease, not directly on the causative agent, but on the pathophysiological mechanisms through which its deleterious activity develops (hyperinflammation and hypercoagulability).

All of the above is summarized in Figure 9 [9-12].



**Figure 9:** Ivm Mechanisms of Action Against Covid.

## Material and Method

In the period between June 1 and December 15, 2020, and in the absence of prophylactic pharmacological measures against SARS

COV2, a high number of Health Agents from a Metropolitan Infectious Hospital used -of their own free will- Ivermectin (IVM) to alleviate this deficiency.

In all cases, this drug was used at a rate of 0.2 mg per kilogram of weight, in a weekly dose, for eight weeks, followed by an interval of 4 (four) months of rest.

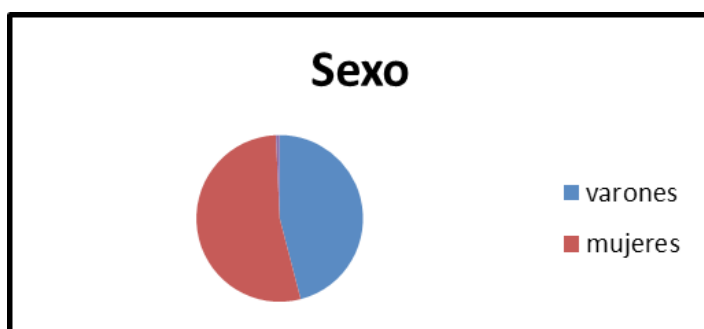
This prophylaxis was extended to the close contacts of the Health Agents, taking into account that the eventual contagion can occur in the workplace or anywhere else, with the home being a conflictive and vulnerable point at the same time.

In the above period, 163 (one hundred sixty-three) people received prophylaxis.

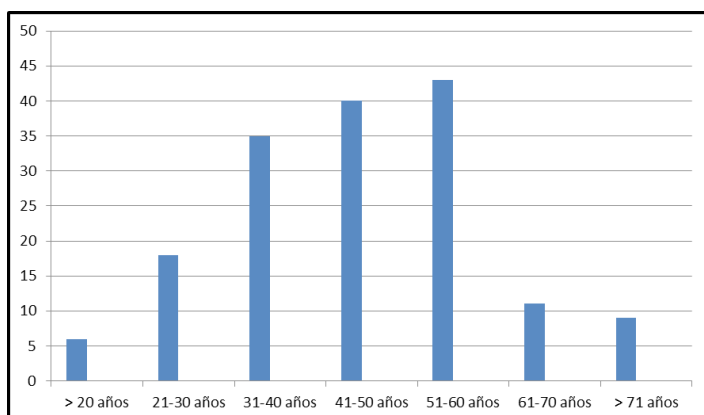
One of them (Health Agent) resigned from her position so it was impossible to follow up on her evolution. With that desertion, 162 people remained in self-evaluation.

The distribution by sex was: 75 men (46.01%), and 87 women (53.98%) (Figure 10).

The average age was 51.6 years, plus / minus 11 years (2 standard deviations), with a dispersion between 10 and 85 years (Figure 11).



**Figure 10:** Sex Distribution.



**Figure 11:** Age Distribution.

To date, 105 (one hundred five) people have completed the first series (8 weeks of prophylaxis and 16 of rest), while 57 (fifty-seven) people have already entered the second series (of them, 17 have completed the 8 weeks of IVM).

No infections were recorded among the 162 subjects during the period mentioned at the beginning.

## Conclusion

The world literature, registered during this pandemic, refers not less than 25% of infections among Health Agents dedicated to the care of Infectious Areas in general, and of COVID in particular [13]. This implies that –throughout the six-monthly follow-up of the subjects included in this collection, no less than 35-45 infections should have been registered, an event that did not occur.

From the data included in this compilation, it appears that Ivermectin has been an excellent adjuvant method for Personal Protective Equipment, for the prophylaxis of SARS Cov 2 in health personnel and their contacts [14].

As such, it is not only recommended to extend it to all Health Agents, but also to all vulnerable population groups (geriatric and psychiatric institutes, orphanages, prisons, etc.).

## References

1. Alfonso J Rodriguez-Morales , Jaime A Cardona-Ospina , Estefanía Gutiérrez-Ocampo, et al. Latin American Network of Coronavirus Disease 2019 Research (LANCOVID 19). Clinical, Laboratory and Imaging Features of COVID-19. A Systematic Review and Meta-Analysis. 2020; 52: 369-372.
2. Hamming I, Timens W, Bulthuis MLC, et al. Tissue Distribution of ACE2 Protein, the Functional Receptor for SARS Coronavirus. A First Step in Understanding SARS Pathogenesis. J Pathol. 2004; 203: 631-637.
3. Hao Xu, Liang Zhong, Jiaxin Deng, et al. High Expression of ACE2 Receptor of 2019-nCoV on the Epithelial Cells of Oral Mucosa. Int J Oral Sci. 2020; 12: 8.
4. Quan-Xin Long, Xiao-Jun Tang, Qiu-Lin Shi, et al. Clinical and Immunological Assessment of Asymptomatic SARS-CoV-2 Infections. Nat Med. 2020.
5. Baraka OZ, Mahmoud BM, Marschke CK, et al. Ivermectin Distribution in the Plasma and Tissues of Patients Infected With Onchocerca Volvulus. Eur J Clin Pharmacol. 1996; 50: 407-410.
6. Leonardo Elías Ordóñez, Esther Sofia Angulo. Efficacy of Ivermectin in the Treatment of Children Parasitized by Strongyloides Stercoralis. Biomedica. 2004; 24: 33-41.
7. Sharun K, Dhama K, Patel SK, et al. Ivermectin, a new candidate therapeutic against SARS-CoV-2/COVID-19. Version 2. Ann Clin Microbiol Antimicrob. 2020; 19: 23.
8. Heidary F, Gharebaghi R. Ivermectin: a systematic review from antiviral effects to COVID-19 complementary regimen. J Antibiot (Tokyo). 2020; 12: 1-10.
9. Hector E Carvallo, Roberto R Hirsch. Ivermectin and Herd Immunity in SARS COV2 Pandemic; from Local Experience to Broader Possibility. Clin Immunol Res. 2020; 4: 1-2.
10. Carvallo Héctor, Hirsch Roberto, Alkis Psaltis, et al. Study of the Efficacy and Safety of Topical Ivermectin + IotaCarrageenan in the Prophylaxis against COVID-19 in Health Personnel. Journal of Biomedical Research and Clinical Investigation. 2020; 2.
11. Hirsch Roberto R, Carvallo Hector E. Covid 19 and Ivermectin Prevention and Treatment Update. Inf Dis Trav Med. 2020; 4: 1-4.
12. Roberto Hirsch, Héctor Carvallo. Covid 19: Children should be Treated Even in Absence of Symptoms. J Clin Toxicol. 2020; 10: 457.
13. Carvallo Héctor, Hirsch Roberto, Farinella María Eugenia. Safety and efficacy of the combined use of ivermectin, dexamethasone, enoxaparin and aspirin against covid 19. medRxiv preprint. 2020.
14. Carvallo Héctor E, Contreras Verónica Y. Estudio de la eficacia y seguridad del uso de ivermectina + iota-carragenina tópicas en la profilaxis de la enfermedad COVID 19 en el personal de salud. 2020; 16: 106-112.