Variations in hemoglobin levels before and after the isolation associated with the mandatory use of facemasks due to COVID-19
A laboratory data analysis

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Abstract

Introduction: the isolation associated with the SARS-CoV2 coronavirus (COVID-19) pandemic called for multiple measures to reduce the impact of the disease, with one of the main ones being the use of facemasks. The use of facemasks is believed to potentially decrease the fraction of inspired oxygen and therefore stimulate the production of erythropoietin, thus causing hemoglobin variations.

Materials and method: a retrospective observational study was conducted based on an anonymized database to determine if there were variations in hemoglobin levels associated with the use of facemasks.

Results: a total of 224,415 complete blood counts drawn between January 2018 and March 2022 were included. The average hemoglobin in all the samples was 13.72 (95%CI 13.72-13.73); the average hemoglobin prior to May 2020 was 13.73 gr/dL and 13.72 after this date, with a statistically significant variation of 0.1 gr/dL (p:0.002).

Conclusion: there were significant hemoglobin level variations associated with the use of facemasks during the SARS-CoV2 pandemic isolation. By the same token, these differences are not thought to be clinically relevant today. **(Acta Med Colomb 2024; 49. DOI: https://doi.org/10.36104/amc.2024.2967).**

Keywords: *hemoglobin, respiratory protective equipment, mask, quarantine, COVID-19, SARS-CoV2.*

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Introduction

The lockdown associated with the SARS-CoV-2 (COVID-19) pandemic had a large financial, physical and emotional impact. In the medical field, the disease caused by SARS-CoV-2 has had many repercussions for both physical and emotional health. This is due not only to the direct effects of the virus on the body, but also to the measures implemented to reduce the impact of the disease. Among the measures used to mitigate the morbidity and mortality associated with the virus we should highlight the use of face masks, whose use prior to the pandemic was restricted to special work settings (1).

One of the main overall drawbacks of using face masks was the feeling of discomfort and concern about inadequate gas exchange. This latter aspect has aroused the curiosity of some investigators, and opinions on the subject are debated. Although some studies, with a limited number of patients (fewer than 50), have shown that wearing cloth/surgical masks is not significantly associated with episodes of hypoxemia or hypercarbia (2, 3), other studies state that the fraction of inspired oxygen (FiO_2) was lower when oxygen was administered through surgical masks than when patients did not use them (4).

Considering that mask use may affect the FiO_2 (4), it is important to keep in mind that this could lead to reduced oxygen in the alveoli and thus produce hypoxia (5). Red blood cell production is known to be a classic physiological response to systemic hypoxia. Hypoxia-inducible factors (HIFs) coordinate this response by inducing changes in specific cellular gene expression, resulting in increased erythropoietin (EPO) production in the kidney and liver (6). Keeping this in mind, we propose the possibility that the massive use of face masks during the SARS-CoV-2 pandemic may have caused changes in population hemoglobin levels in response to hypoxia.

Materials and method

This was a retrospective observational study based on an anonymized database. All the complete blood counts (CBCs) performed in the outpatient department of a referral laboratory in Bucaramanga, Santander, from January 2018 to March 2022 were included. Complete blood counts with significant abnormalities in any cell lines, including hemoglobin, were excluded. This study had prior approval from the ethics committee.

The main objective of this study was to determine if there were changes in hemoglobin levels associated with wearing face masks. To do this, hemoglobin levels before and after lockdown were compared, dividing the time period as follows: from January 2018 to May 2020, and from June 2020 on.

The data used in the analysis were extracted from anonymous institutional electronic records stored in a validated electronic database. Demographic variables (age and sex) and CBC values were collected.

Measures of central tendency and dispersion were calculated for the quantitative variables, according to their distribution (Shapiro-Wilk test). Qualitative variables were presented as absolute and relative frequencies with their confidence intervals. The Kruskal-Wallis test was used to estimate the difference in means or medians, and Chi square, with an alpha of 0.05, was used for qualitative variables. The data were analyzed using Stata v. 15 statistical software.

Results

A total of 224,415 CBCs drawn from January 2018 to March 2022 were included. Regarding the sociodemographic characteristics of the study participants, most were women (64.9%), and the average age was 53.83 years (95%CI 53.75-53.91). The average hemoglobin in all samples was 13.72 (95%CI 13.72-13.73).

Regarding the change in average hemoglobin according to age (over or under the age of 50), there was a statistically significant difference in the group of patients under the age of 30 (Table 1). As far as the change in average hemoglobin according to sex, there was a statistically significant difference in the group of women (Table 2).

An analysis of the average hemoglobin by year (2018-2022) only showed a significant increase when comparing the 2020 and 2021 levels (0.1 gr p<0.01) (Table 3). Finally, a general analysis of the change in hemoglobin before and after lockdown showed that the average hemoglobin prior to May 2020 was 13.73 gr/dL and after this date was 13.72, thus showing a statistically significant change of 0.1 gr/dL (p:0.002).

Discussion

Medical (or surgical) masks tend to be used as a personal protection measure to protect people from the flu and other respiratory infections in healthcare settings, by providing a physical barrier against potentially infectious droplets (7). In its guidelines published on June 5, 2020, the World Health Organization (WHO) recommended that, in areas with community transmission of COVID-19 at that time, governments should encourage the general population to use masks in specific situations and settings, as part of a comprehensive effort to suppress COVID-19 transmission (8).

Although meta-analyses have shown moderate effectiveness in reducing SARS-CoV-2 transmission (9), there has been a global scientific controversy regarding the benefits and risks of wearing masks in public spaces. This is because wearing face masks has become a new social look in the

Table 1. *Average hemoglobin by age sub-group.*

	Prior to lockdown (prior to May 2020)	After lockdown (after May 2020)	P value
<50 years	13.79 (95%CI 13.78-13.81)	13.76 (95% CI 13.75-13.77)	p<0.001
>50 years	13.7 (95%CI 13.69-13.71)	13.69 (95%CI 13.68-13.7)	p 0.52

Table 2. *Average hemoglobin by sub-group (sex).*

	Prior to lockdown (prior to May 2020)	After lockdown (after May 2020)	P value
Male	14.59 (95%CI 14.57-14.60)	14.58 (95%CI 14.57-14.59)	p 0.64
Female	13.36 (95%CI 13.36-13.37)	13.34 (95%CI 13.33-13.34)	p<0.001

Table 3. *Average hemoglobin by year (2018-2022).*

2018	2019	2020	2021	2022
13.71 (95%CI 13.69-13.73)	13.74 (95%CI 13.73-13.75)	13.63 (95%CI 13.61-13.65)	13.73 (95%CI 13.73-13.74)	13.70 (95%CI 13.68-13.72)

daily life of many countries, simultaneously (10). A review of the literature revealed a study in 2005 showing that wearing surgical masks led to measurable physical effects, with elevated transcutaneous carbon dioxide levels after 30 minutes, which was thought to possibly be related to the fact that face masks expand the natural dead space (nose, throat, trachea, bronchi) outward and beyond the mouth and nose (11), and this carbon dioxide effect was later found in other studies (12-14). Another effect of face masks that has often been shown experimentally is a statistically significant reduction in blood oxygen saturation, a fall in the partial pressure of oxygen in the blood (PaO_2), with the effect of simultaneously elevating the frequency and increasing the respiratory rate (11, 15–17).

Since wearing face masks has been shown to cause blood gas changes, with hypercapnia (blood carbon dioxide/CO_2 levels) and hypoxemia (decreased blood oxygen/O_2 levels), as mentioned previously, this study looked for changes in the hemoglobin levels as a consequence of hypoxia, finding a statistically significant change of 0.1 gr/dL. In addition, the sub-group analysis showed significant changes in those under the age of 50 and in women.

It has been well established that hypoxia, or a low partial pressure of oxygen, triggers the release of EPO, a glycoprotein that stimulates the production of red blood cells to increase the oxygen carrying capacity. Exposure to hypoxia stabilizes hypoxia-inducible factor 1α (HIF-1α) within a few minutes, resulting in transcription and production of the EPO gene. In addition, continuous exposure to hypoxia for 84 to 120 minutes consistently elevates serum EPO levels (18). Considering this, the results of this study, while significant, were the opposite of what was expected according to the physiological associations previously described. It is also worth noting that, as the study was based on a database, the results are subject to limitations with regard to the accuracy and completeness of the data collected.

Conclusions

There were significant changes in the hemoglobin levels associated with wearing face masks during the SARS-CoV-2 pandemic lockdown. At the same time, these results were the opposite of what was expected according to the physiological associations underlying the study. Therefore, we do not consider that these changes are clinically relevant today.

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