

# GLOBAL JOURNAL

OF MEDICAL RESEARCH: K

Interdisciplinary

A pair of hands wearing blue nitrile gloves holds several small brown vials and white labels. The labels contain text such as 'TUDORHEROL, D, ALPHA', 'LUTEIN', 'Grade P', 'Lot: 00020311-050', 'Qty: 50mg', 'Store At: +4C', 'Expiry: 3/2018', 'Lot: 00012453-007303', 'Qty: 100mg', 'Store At: -80C', 'Expiry: 6/2022', and 'For RESEARCH USE ONLY'.

Politics of Science Denial

Spread of COVID-19 in Bangladesh

Highlights

Diagnostic and Educational Tools

Development of Medical Law in Hungary

Discovering Thoughts, Inventing Future



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# Medical Best Practices and the Politics of Science Denial during the COVID-19 Pandemic

By Don Albrecht

**Abstract-** An analysis of data from over 3,000 U.S. counties revealed that during the second year of the COVID-19 pandemic (March 1, 2021 – March 1, 2022) when vaccines were available to adults, the number of deaths per 100,000 residents was 3 times greater in counties where Trump received more than 75 percent of the vote compared to counties where he received 25 percent or less of the vote. It is clear that widespread misinformation and science denial, often politically motivated, had disastrous consequences. Rebuilding trust in science and medical expertise is vital if we hope to benefit from the important medical break throughs that are occurring.

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MEDICALBESTPRACTICESANDTHEPOLITICSOFSCIENCEDENIALDURINGTHECOVID19PANDEMIC

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# Medical Best Practices and the Politics of Science Denial during the COVID-19 Pandemic

Don Albrecht

**Abstract-** An analysis of data from over 3,000 U.S. counties revealed that during the second year of the COVID-19 pandemic (March 1, 2021 – March 1, 2022) when vaccines were available to adults, the number of deaths per 100,000 residents was 3 times greater in counties where Trump received more than 75 percent of the vote compared to counties where he received 25 percent or less of the vote. It is clear that widespread misinformation and science denial, often politically motivated, had disastrous consequences. Rebuilding trust in science and medical expertise is vital if we hope to benefit from the important medical break throughs that are occurring.

## 1. INTRODUCTION

Longstanding concerns about the possible emergence of a new infectious disease for which humans had little or no natural defense (e.g., Hatchett et al. 2007; Lewis 2021; Morens and Fauci 2007; Quammen 2012; Quick and Fryer 2018; Webster et al. 1997) became reality with the appearance of COVID-19. Between late 2019 and March 2022, the disease spread around the world resulting in the deaths of more than 6 million people. Every person on the planet has been impacted in some way by the pandemic. Critically, however, death rates have varied widely from one location to another, making it apparent that non-medical factors have played a prominent role in disease outcomes (Albrecht 2022a).

By recognizing the significance of non-medical factors to the pandemic, two conclusions can be drawn. First, the response of the medical community to the pandemic was remarkable (Wiersinga et al. 2020). Science and health experts quickly understood the nature of the disease and how it spread. This knowledge allowed experts to recommend best practices to keep people safe. Approaches for the care of the severely ill were refined. Most significantly, safe and effective vaccines were developed in record time, and these vaccines saved many thousands of lives (Harris 2021; Gupta et al. 2021; Le et al. 2020; Zuckerman 2021). Among people who followed best practices and were vaccinated as soon as possible, COVID-19 death rates tended to be relatively low.

A second conclusion is that vast numbers of people failed to follow medical best practices and refused vaccination. Rather than listening to and

following the advice of knowledgeable experts, many people denied science and believed the misinformation available on social media and other sources (Brennan et al. 2020; Bursztyn et al. 2020; Calvillo et al. 2020; Latkin et al. 2021; Lewandosky 2021; Priniski and Holyoak 2022). The results were disastrous and many thousands of lives were unnecessarily cut short.

A primary factor in science denial and the spread of misinformation was politics. Political views strongly influenced people's decisions about the severity of the disease and appropriate actions to take in response (van Holm et al. 2020). Understanding the relationship between political views and the acceptance of misinformation and science denial is vital for the medical community moving forward if societies hope to take full advantage of impressive scientific and medical breakthroughs that are occurring and to more effectively address new problems and concerns that will inevitably emerge. This manuscript seeks to improve our understanding of this critical relationship by exploring the link between political views and COVID-19 outcomes as determined by deaths per 100,000 residents across the more than 3,000 U.S. counties.

### a) Science Denial and Misinformation

The impact of science on the lives of everyone is immense. Through an improved understanding of disease, developments in antibiotics, and improved sanitation, science has resulted in our lives being healthier and longer (Doig 2022). In the United States, for example, average life expectancy increased from about 49 years in 1900 to 79 years in 2020. Science has made it possible for food production to increase substantially and made it possible for us to have cleaner and safer water (Walker 2019). Because of science, transportation and communication are faster and more extensive (Isaacson 2014). Because of science, our homes are safer and more comfortable. Science is an engine of prosperity and provides an understanding and explanation of the world around us, greatly reducing fear and uncertainty (Pinker 2012).

Despite tremendous and obvious benefits, science has come under increasing attack in recent decades. On a wide range of issues, scientific evidence has been discounted and often ignored (Lewandosky 2021). Among the issues where a clear scientific consensus has been discounted include the health impacts of tobacco (Bell 2011; Bell and Dennis 2013;

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Bondurant et al. 2001; Brandt 2007), vaccination safety (Albrecht 2022b; Jolly and Douglas 2014; Loomis 2018), and climate change (Berners-Lee 2021; Carmichael and Brulle 2017; Dunlap and McCright 2008; Giddens 2009; Lahsen 2005; McCright and Dunlap 2003; 2011; Oreskes and Conway 2008; 2011; Rahm 2010; Washington and Cook 2011). The reasons for the attacks on science are numerous and varied and are part of a growing trend in which misinformation and conspiracy theories are believed by significant numbers of the general public (Kavanagh and Rich 2018; Lewandowsky et al. 2012). In some cases, attacks on science are made by industries and individuals who may suffer financially (McCright 2007; McCright and Dunlap 2003; Oreskes and Conway 2008); in other cases, persons are troubled as new information raises questions about cherished beliefs (Garvey 2008); some people may fear that lifestyle changes will be required (Bondurant et al. 2001).

The tactics used in science denial are similar across issues. These techniques have become increasingly effective with the Internet, social media, and the proliferation of websites and news services that lack a commitment to facts and truth (Chou et al. 2018; Lazer et al. 2018; Scheufele and Krause 2019). At the heart of denial campaigns are efforts to create doubt about scientists and the scientific process (Lewandowsky et al. 2017; Oreskes and Conway 2011; Powell 2011). A common approach is to create the illusion that there is disagreement among scientists when in fact disagreements are likely limited to processes and details. Typically, denialist “experts” present flawed evidence that sounds truthful but contradicts the broadly accepted scientific consensus. For example, denialists tend to “cherry-pick” evidence. That is, they will mention exceptions to the rule such as Uncle Henry who was a heavy smoker and lived to be 102 casting doubt on the dangers of tobacco, or that some city in the northeast experienced the coldest January in decades seeming to indicate that climate change can’t be real. Additionally, claims have been made by science deniers that scientists are a cabal seeking to deceive the public for personal gain (Oreskes and Conway 2011). Rush Limbaugh, for example, claimed that science is one of the “pillars of deceit” that seeks to mislead the public.

When scientific evidence becomes overwhelming, science deniers often change tactics and claim that addressing the issue is an attack on individual freedom or that the economic costs of change are too great. Many are concerned that addressing the issue will require an expanded role for government (Oreskes and Conway 2011). The end result is that after decades of science denial and misinformation campaigns, high levels of distrust of science have emerged among certain segments of the population, and this distrust contributes to the spread of misinformation and conspiracy theories (Lewandowsky et al. 2012;

Lewandowsky et al. 2017; Oreskes and Conway 2011). Of relevance to this manuscript, these same approaches have been utilized to spread misinformation during the COVID-19 pandemic (Rutjens et al. 2021; van Der Linden et al. 2020).

#### b) *Science Denial, Misinformation and Politics with COVID-19*

From the beginning of the COVID-19 pandemic, science denial and misinformation were prominent (Douglas 2021). Examples include claims that false cures such as gargling with lemon juice or salt water or injecting bleach could kill the virus and that wearing a mask would exacerbate spread of the disease (van Der Linden et al. 2020). Especially harmful was misinformation about COVID-19 vaccinations (Jennings et al. 2021; Loomba et al. 2021). Some argued that the vaccines would alter a person’s DNA, would negatively affect fertility or that microchips were being injected into people so their behavior could be monitored and controlled (Romer and Jamieson 2020).

Acceptance of misinformation and science denial were much more prevalent among some segments of the population than others (Roozenbeek et al. 2020). Throughout the pandemic, Democrats were much more likely to take the threat of the virus seriously and to support efforts to control the virus, while Republicans were more likely to accept misinformation (Bruine de Bruin et al. 2020; Hamilton and Safford 2020). This is consistent with other issues where trust in science is greater among Democrats than Republicans (Dunlap and McCright 2008; Oreskes and Conway 2011; Rutjens et al. 2021). Consequently, state and local governments under Republican control were less likely to implement restrictive policies than those under Democrat control (Hsiehchen et al. 2020). Early research found that counties with a higher share of Trump voters tended to have lower perceptions of the dangers of COVID-19, and these perceptions led to riskier behavior (Barrios and Hochberg 2020; Calvillo et al. 2020). States with more Trump voters were more resistant to stay-at-home orders (Hill et al. 2020a). In more religious states, which tend to be heavily Republican, people were found to be more mobile during the pandemic despite recommendations to stay home (Hill et al. 2020b). Perry et al. (2020) found that Christian nationalism, which has strong ties to the Republican Party, was related to many of the far-right responses to COVID-19, including unfounded conspiracy theories. Thus, it is not surprising that persons more able to distinguish scientific facts from misinformation were more likely to be vaccinated (Montagni et al. 2021).

Science denial relative to COVID-19 started at the top. From the beginning, the severity of the pandemic was downplayed by President Trump. Trump talked about how the virus would magically disappear.

He then claimed that the virus would be eliminated by warmer spring weather. For months, he argued that we were turning the corner and that the disease wasn't that bad anyway. He recommended ways of addressing the disease that lacked scientific merit. Trump held political rallies where thousands of people gathered, most not wearing masks. Reacting to shutdown policies intended to slow disease spread, Trump tweeted messages such as "Liberate Michigan" (Paz 2020).

Beyond the president, other political leaders and media outlets sent divergent messages on COVID-19. Again, Republicans and the right-wing media tended to downplay the threat of the disease and express opposition to steps intended to prevent spread (Allcott et al. 2020; Gadarian et al. 2021). With support from Republican leaders and the right-wing media, protests were held throughout the country in opposition to mask mandates, business and school closures and vaccination mandates. Thus, throughout the pandemic, Republicans have been more likely than Democrats to resist medical best practices. Consequently, in this manuscript, it is expected that in counties where the percent voting for Trump in the 2020 presidential election was greater, the number of COVID-19 deaths per 100,000 residents will be more extensive.

This manuscript explores data for the first two years of the pandemic. It could be argued that the pandemic began impacting the lives of most Americans in March 2020. One year later, in March 2021, vaccines were generally available for most American adults. Thus, during the first year of the pandemic (from March 2020 until March 2021), the tools available for people to protect themselves from the virus were limited and included social distancing and wearing masks. For the second year (March 2021 until March 2022), safe and effective vaccines were available. Consequently, it is expected that the strength of the relationship between political views and COVID-19 deaths will be stronger during the second year of the pandemic relative to the first year. This is because persons who accept medical health expertise and best practices had a more effective tool to protect themselves during the second year.

An additional reason that the relationship is expected to be weaker during the first year of the pandemic is that during the early months of the pandemic, the death rates were much higher in major U.S. cities compared to smaller communities and rural areas. This is because metropolitan areas are home to travelers from around the world who may have brought the disease from elsewhere. In cities people live and work in close proximity to one another and are more dependent upon mass transit, all of which makes social distancing more difficult. These circumstances provide prime conditions for the virus to spread. In contrast, in rural areas there are fewer people, and these people are more widely dispersed, making it easier for people to remain apart slowing virus spread (Albrecht 2021;

Rocklov and Sjoden 2020). This is of relevance to this study because residents of large cities are much less likely to vote Republican and thus cast their ballot for Donald Trump in the 2020 election than small town and rural residents (Goetz et al. 2018; Monnat and Brown 2017).

In exploring the relationship between political views and COVID-19 death rates, it is important to control for other independent variables that could impact this relationship. For this manuscript, three control variables will be considered including percent non-Hispanic white, percent of adults 25 years old and older with a college degree, and percent of households in poverty.

## II. METHODS

The county is the unit of analysis for this study. Counties are relatively small geographic units where data are available for all of the variables utilized in the study. The analysis is based on 3,112 counties for which data are available on all variables used in the analysis. U.S. counties provide an excellent opportunity to test the relationship between political views and COVID-19 outcomes because there are extensive variations on both variables. The dependent variable is the number of COVID-19 deaths per 100,000 residents for each county. To measure the dependent variables, county-level data were obtained from the New York Times COVID-19 dataset. This dataset provides the number of COVID-19 deaths for each county in the U.S. on a daily basis. The data are obtained from state, regional and county sources on a continual basis. New York Times data are virtually identical to COVID-19 data from other sources since they all obtain their information from the same places. The advantage of the New York Times dataset is that data is available to the public and can be easily downloaded. For this study, the cumulative number of COVID-19 deaths for each county were downloaded on two dates, March 1, 2021 and March 1, 2022. The number of COVID-19 deaths per 100,000 residents for the first year is determined by the number of deaths in each county from pandemic beginnings until March 1, 2021. COVID-19 deaths per 100,000 residents for the second year is based on deaths from March 1, 2021 until March 1, 2022. The variable used in the model is based on total COVID-19 deaths divided by the total population of the county based on the 2014-2018 American Community Survey (ACS) and then multiplied by 100,000.

The primary independent variable is political views, measured by the percent of votes in each county in the 2020 presidential election for Donald Trump. County-level voting data were obtained from the New York Times, and determination was made of the percent of voters in each county that cast their ballot for Donald Trump. Again, New York Times data was chosen



because it is easily downloadable. The three other independent variables are obtained from the 2014-2018 American Community Survey conducted by the U.S. Census Bureau. Race/ethnicity is measured by the percent of residents in each county that are non-Hispanic white. Educational attainment is determined by the percentage of persons aged 25 and older with a college degree in each county. The poverty measure is determined by the percent of households in each county living in poverty.

The analysis begins with a bivariate overview of the relationship between political views and the number of COVID-19 deaths for each of the two years of the pandemic. For this analysis, counties are categorized into five groups based on the percent voting for Trump. The categories are (1) counties where Trump received less than 25 percent of the vote; (2) counties where Trump received from 25 percent to less than 45 percent of the vote; (3) counties where Trump received from 45 to less than 55 percent of the vote; (4) counties where Trump received from 55 percent to less than 75 percent of the vote; and (5) counties where Trump received 75 percent or more of the vote. Following the bivariate analysis, regression models are run with COVID-19 deaths per 100,000 residents for each year as the dependent variable, while the independent variables are the percent voting for Trump, race/ethnicity, educational attainment and poverty levels. The regression models are weighted by the total population in the county.

### III. FINDINGS

The data in Table 1 show that during the first year of the pandemic, the relationship between percent voting for Trump and COVID-19 death rates was not especially strong. During the second year, however, the relationship between political views and COVID-19 death rates was very strong. After vaccines were available, the per capita death rate from the disease increased steadily as the percent voting for Trump increased. In counties where Trump received more than 75 percent of the vote, death rates per 100,000 residents was more than 3 times greater (223.4) than in counties where Trump received less than 25 percent of the vote (73.6). Overall, during the first year of the pandemic, more than a half million Americans died (about 153 per 100,000 residents), while during the second year more than 425,000 people died (about 130 per 100,000). In counties where Trump received 55 percent or more of the vote, the death rate during the second year of the pandemic was greater than during the first year. In contrast, in counties where Trump received less than 55 percent of the vote, the death rate during the second year was less than during the first year. In counties where Trump received less than 25 percent of the vote, the death rate during the second year was less than one-half of what it had been during the first year.

Table 1 also presents data on the other independent variables used in the model and their relationship with the percent voting for Trump. It is clear that counties with large shares of Trump voters had high proportions of non-Hispanic white residents, educational attainment levels tended to be low and poverty levels were also relatively low. Thus, counties leaning for Trump in the 2020 presidential election tended to homes of large shares of the white working class.

Table 2 presents the results of regression models for both the first and second years of the pandemic. For the first year, the relationship between the percent voting for Trump and COVID-19 death rates was statistically insignificant. The strongest predictor of death rates during the first year was educational attainment where death rates declined as the percentage of the population with a college degree increased. Also, death rates were lower in counties with large non-Hispanic white populations, and were higher where poverty levels were greater. In total, the independent variables explained about 15 percent of the variation in COVID-19 death rates.

For the second year of the pandemic, results were very different. The best predictor of COVID-19 death rates was the percent voting for Trump. As the proportion of voters for Trump increased, the death rate also increased. Consistent with the first year, as educational attainment increased, death rates declined, and as poverty levels increased, death rates also increased. During the first year of the pandemic, there was an inverse relationship between percent non-Hispanic white and COVID-19 death rates. By the second year of the pandemic, this relationship had switched, with death rates greater in counties with a higher percentage of non-Hispanic white residents. No question, this change can be explained by the fact that counties with large numbers of non-Hispanic white residents tended to vote for Trump, and the death rate increased sharply in these counties. During the second year of the pandemic, the independent variables explained nearly 60 percent of the variation in COVID-19 death rates.

### IV. CONCLUSIONS

Widespread misinformation and science denial with respect to the COVID-19 pandemic have had disastrous consequences. Basing their decision on misinformation often driven by politics, millions of people failed to follow the advice of health professionals and refused to get vaccinated. The result was many thousands of unnecessary deaths. The data presented in this manuscript revealed that during the second year of the pandemic (March 1, 2021 – March 1, 2022) when vaccines were available to adults in the U.S., counties where Trump received 75 percent of the vote or more,

had more than 3 times more COVID-19 deaths per 100,000 residents compared to counties where Trump received less than 25 percent of the vote.

The consequences of the results of this study are profound. With respect to the COVID-19 pandemic, the deaths of thousands of people were completely unnecessary. It is estimated that the average person in the U.S. who died from COVID-19 lost over 16 years of life (Dukhovnov and Barbieri 2021). No question there is far more to consider in developing responses to a pandemic than trying to prevent everyone from getting a dangerous disease. School and business closures and extensive social distancing have severe mental health, economic and educational costs that may take years to fully understand and even longer to address. There is plenty of room for political discussion as we seek to find the best balance between safety and other concerns. This political discussion, however, should be based on facts and accurate information rather than misinformation and science denial. Moving forward, there is no question that the world will face other crises. It is vital that we somehow rebuild trust in science and medical health expertise so that in the future more people base their decisions on the best available information and people are better equipped to recognize and reject misinformation and conspiracy theories.

## REFERENCES RÉFÉRENCES REFERENCIAS

1. Albrecht, Don E. 2021. COVID-19 in Rural America: Impacts of Political Views and Disadvantage." *Rural Sociology*. <https://DOI: 10.1111/ruso.12404>.
2. Albrecht, Don E. 2022a. "Politics and the Spread of COVID-19 in the United States." *Medical Research Archives* 10(2).
3. Albrecht, Don E. 2022b. "Vaccination, Politics and COVID-19 Impacts." *BMC Public Health* 22: 96.
4. Bell, K., 2011. "Legislating Abjection? Secondhand Smoke, Tobacco Control Policy and the Public's Health." *Critical Public Health* 21(1): 49-62.
5. Bell, K. and S. Dennis. 2013. "Toward a Critical Anthropology of Smoking: Exploring the Consequences of Tobacco Control." *Contemporary Drug Problems* 40(1): 3-19.
6. Berners-Lee, M., 2021. *There Is No Planet B: A Handbook for the Make or Break Years Updated Edition*. Cambridge University Press.
7. Bondurant, S., R. Wallace, P. Shetty, and K. Stratton (eds.). 2001. "Clearing the Smoke: Assessing the Science Base for Tobacco Harm Reduction." National Academies Press.
8. Brandt, A.M. 2007. *Cigarette Century: The Rise, Fall and Deadly Persistence of the Product that Defined America*. New York: Basic Books.
9. Brennen, J.S., Simon, F., Howard, P.N. and Nielsen, R.K. 2020. "Types, Sources, and Claims of COVID-19 Misinformation." *Reuters Institute* 7: 1-13.
10. Bursztyn, L., Rao, A., Roth, C.P. and Yanagizawa-Drott, D.H. 2020. "Misinformation during a Pandemic" (No. w27417). National Bureau of Economic Research.
11. Calvillo, D.P., Ross, B.J., Garcia, R.J., Smelter, T.J. and Rutchick, A.M., 2020. "Political Ideology Predicts Perceptions of the Threat of COVID-19 (and Susceptibility to fake news about it)." *Social Psychological and Personality Science* 11(8): 1119-1128.
12. Carmichael, J.T. and Brulle, R.J. 2017. Elite cues, media coverage, and public concern: an integrated path analysis of public opinion on climate change, 2001–2013. *Environmental Politics*, 26(2), 232-252.
13. Chou, W.Y.S., Oh, A. and Klein, W.M., 2018. "Addressing Health-Related Misinformation on Social Media." *Jama* 320(23): 2417-2418.
14. Doig, Andrew. 2022. *The Mortal Coil: A History of Death*. London: Bloomsbury Publishing.
15. Douglas, K.M. 2021. "COVID-19 Conspiracy Theories." *Group Processes & Intergroup Relations* 24(2): 270-275.
16. Dukhovnov, D. and Barbieri, M. 2021. "County-Level Socio-Economic Disparities in COVID-19 Mortality in the USA." *International Journal of Epidemiology* (Dec.)
17. Dunlap, R.E. and A.M. McCright. 2008. "A Widening Gap: Republican and Democratic Views on Climate Change." *Environment* 50: 26-35.
18. Gadarian, S.K., Goodman, S.W. and Pepinsky, T.B. 2021. "Partisanship, Health Behavior, and Policy Attitudes in the Early Stages of the COVID-19 Pandemic." *PlosOne* 16(4): e0249596.
19. Garvey, K.J., 2008. "Denial of Evolution: An Exploration of Cognition, Culture and Affect." *Journal of social, evolutionary, and cultural psychology* 2(4): 209.
20. Giddens, A. 2009. *The Politics of Climate Change*. Malden, MA: Polity Press.
21. Goetz, Stephan J., Meri Davlasheridze, Yicheol Han, and David A. Fleming-Muñoz. 2018a. "Explaining the 2016 Vote for President Trump across U.S. Counties." *Applied Economic Perspectives and Policy*. doi:10.1093/aep/ppy026
22. Gupta, S., Cantor, J., Simon, K.I., Bento, A.I., Wing, C. and Whaley, C.M. Vaccinations Against COVID-19 May Have Averted Up To 140,000 Deaths in The United States: Study Examines Role of COVID-19 Vaccines and Deaths Averted in the United States. *Health Affairs*, 2021; 40(9): 1465-1472.
23. Harris, J.E. "COVID-19 Incidence and Hospitalization Rates are Inversely Related to Vaccination Coverage Among the 112 Most Populous Counties in the United States." *medRxiv*, 2021.
24. Hatchett, Richard J., Carter E. Mecher, and Marc Lipsitch. 2007. "Public Health Interventions and



- Epidemic Intensity During the 1918 Influenza Pandemic." *Proceedings of the National Academy of Sciences* 104(18): 7582-7587.
25. Isaacson, Walter, 2014. *The innovators: How a group of inventors, hackers, geniuses and geeks created the digital revolution*. New York: Simon and Schuster.
26. Jennings, W., Stoker, G., Bunting, H., Valgarðsson, V.O., Gaskell, J., Devine, D., McKay, L. and Mills, M.C. 2021. "Lack of Trust, Conspiracy Beliefs, and Social Media use Predict COVID-19 Vaccine Hesitancy." *Vaccines* 9(6): 593.
27. Jolley, D. and K.M. Douglas. 2014. "The Effects of Anti-Vaccine Conspiracy Theories on Vaccination Intentions." *PloS one* 9(2): e89177.
28. Kavanagh, J. and M.D. Rich. 2018. *Truth decay: An initial exploration of the diminishing role of facts and analysis in American public life*. Rand Corporation.
29. Lahsen, M. 2005. "Technocracy, Democracy, and U.S. Climate Politics." *Science, Technology and Human Values* 30: 137-169.
30. Latkin, C.A., Dayton, L., Moran, M., Strickland, J.C. and Collins, K. 2021. "Behavioral and Psychosocial Factors Associated with COVID-19 Skepticism in the United States." *Current Psychology*: 1-9.
31. Lazer, D.M., Baum, M.A., Benkler, Y., Berinsky, A.J., Greenhill, K.M., Menczer, F., Metzger, M.J., Nyhan, B., Pennycook, G., Rothschild, D. and Schudson, M. 2018. "The Science of Fake News." *Science* 359(6380): 1094-1096.
32. Le, T.T., Andreadakis, Z., Kumar, A., Román, R.G., Tollefsen, S., Saville, M. and Mayhew, S. 2020. "The COVID-19 Vaccine Development Landscape." *Nat Rev Drug Discov* 19(5): 305-306.
33. Lewandowsky, S. 2021. "Liberty and the Pursuit of Science Denial." *Current Opinion in Behavioral Sciences* 42: 65-69.
34. Lewandowsky, S., U.K. Ecker, C.M. Seifert, N. Schwarz, and J. Cook. 2012. "Misinformation and its Correction: Continued Influence and Successful Debiasing." *Psychological Science in the Public Interest* 13(3): 106-131.
35. Lewandowsky, S., U.K. Ecker, and J. Cook. 2017. "Beyond Misinformation: Understanding and Coping with the 'Post-Truth' Era." *Journal of Applied Research in Memory and Cognition* 6(4): 353-369.
36. Lewis, Michael. 2021. *The Premonition*. New York: W.W. Norton.
37. Loomba, S., de Figueiredo, A., Piatek, S.J., de Graaf, K. and Larson, H.J. 2021. "Measuring the Impact of COVID-19 Vaccine Misinformation on Vaccination Intent in the UK and USA." *Nature Human Behaviour* 5(3): 337-348.
38. Loomis, Joshua. 2018. *Epidemics: The Impact of Germs and Their Power over Humanity*. Santa Barbara, CA: Praeger.
39. McCright, A.M. 2007. "Dealing with Climate Change Contrarians." Pp. 200-212 in S.C. Moser and L. Dilling (eds.), *Creating a Climate for Change: Communicating Climate Change and Facilitating Social Change*. New York: Cambridge University Press.
40. McCright, A.M. and R.E. Dunlap. 2011. "The Politicization of Climate Change and Polarization in the American Public's Views of Global Warming, 2001-2010." *The Sociological Quarterly* 52: 155-194.
41. McCright, A.M. and R.E. Dunlap. 2003. "Defeating Kyoto: The Conservative Movement's Impact on U.S. Climate Change Policy." *Social Problems* 50(3): 348-373.
42. Monnat, Shannon M., and David L. Brown. 2017. "More than a Rural Revolt: Landscapes of Despair and the 2016 Presidential Election." *Journal of Rural Studies* 55: 227-236. doi: 10.1016/j.jrurstud. 2017.08.010
43. Montagni, I., Ouazzani-Touhami, K., Mebarki, A., Texier, N., Schück, S., Tzourio, C. and Confins Group. 2021. "Acceptance of a COVID-19 Vaccine is Associated with Ability to Detect Fake News and Health Literacy." *Journal of Public Health* 43(4): 695-702.
44. Morens, David M. and Anthony S. Fauci. 2007. "The 1918 Influenza Pandemic: Insights for the 21<sup>st</sup> Century." *Journal of Infectious Diseases* 195(7): 1018-1028.
45. Oreskes, N. and E.M. Conway. 2008. "Challenging Knowledge: How Climate Science Became a Victim of the Cold War." Pp. 55-89 in R.N. Proctor and L. Schiebinger (eds.), *Agnotology: The Making and Unmaking of Ignorance*. Stanford, CA: Stanford University Press.
46. Oreskes, N. and E.M. Conway. 2011. *Merchants of doubt: How a handful of scientists obscured the truth on issues from tobacco smoke to global warming*. New York: Bloomsbury Publishing.
47. Pinker, Steven. 2012. *The better angels of our nature: Why violence has declined*. New York: Penguin Group USA.
48. Powell, J.L. 2011. *The Inquisition of Climate Science*. New York: Columbia University Press.
49. Priniski, J.H. and Holyoak, K.J. 2022. "A Darkening Spring: How Preexisting Distrust Shaped COVID-19 Skepticism." *PloS one* 17(1): p.e0263191.
50. Quammen, David. 2012. *Spillover: Animal Infections and the Next Human Pandemic*. New York: Norton.
51. Quick, Jonathan D. and Bronwyn Fryer. 2018. *The End of Epidemics*. New York: St. Martins Press.
52. Rahm, D. 2010. *Climate Change Policy in the United States*. Jefferson, NC: McFarland.
53. Rocklöv, J. and H. Sjödin. 2020. "High Population Densities Catalyze the Spread of COVID-19." *Journal of Travel Medicine* 27(3): p.taaa038.

54. Romer, D. and Jamieson, K.H. 2020. "Conspiracy Theories as Barriers to Controlling the Spread of COVID-19 in the US." *Social Science & Medicine* 263: 113356.
55. Roozenbeek, J., Schneider, C.R., Dryhurst, S., Kerr, J., Freeman, A.L., Recchia, G., Van Der Bles, A.M. and Van Der Linden, S. 2020. "Susceptibility to Misinformation about COVID-19 around the World." *Royal Society Open Science* 7(10): 201199.
56. Rutjens, B.T., van der Linden, S. and van der Lee, R. 2021. "Science Skepticism in Times of COVID-19." *Group Processes & Intergroup Relations* 24(2): 276-283.
57. Scheufele, D.A. and Krause, N.M. 2019. "Science Audiences, Misinformation, and Fake News." *Proceedings of the National Academy of Sciences* 116(16): 7662-7669.
58. van Der Linden, S., Roozenbeek, J. and Compton, J. 2020. "Inoculating against Fake News about COVID-19." *Frontiers in Psychology* 11: 2928.
59. van Holm, E.J., Monaghan, J., Shahar, D.C., Messina, J.P. and Surprenant, C. 2020. "The impact of Political Ideology on Concern and Behavior during COVID-19". Available at SSRN 3573224.
60. Walker, K.D., 2019. *The Grand Food Bargain: And the Mindless Drive for More*. Island Press.
61. Washington, H. and J. Cook. 2011. *Climate Change Denial*. Washington, DC: Earthscan.
62. Webster, R.G., K.F. Shortridge, and Y. Kawaoka. 1997. "Influenza: Interspecies Transmission and Emergence of New Pandemics." *Immunology and Medical Microbiology* 18(4): 275-279.
63. Wiersinga, W.J., Rhodes, A., Cheng, A.C., Peacock, S.J. and Prescott, H.C. 2020. "Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): a Review." *Jama* 324(8): 782-793.
64. Zuckerman, Gregory. 2021. *A Shot to Save the World*. New York: Penguin.

Table 1: COVID-19 and Independent Variables by Percent Voting for Trump (N = 3,112)						
Variable	Percent Voting or Trump					
	Less than 25 Percent (N=54)	25-45 Percent (N=328)	45-55 Percent (N=317)	55-75 Percent (N=1,310)	75 Percent or More (N=1,103)	Total (N=3,112)
March 1, 2021						
Total COVID-19 Deaths Deaths Per 100,000	45,514 152.8	182,121 148.5	97,774 146.4	133,636 156.6	41,841 181.6	500,886 152.9
March 1, 2021 - March 1, 2022						
Total COVID-19 Deaths Deaths Per 100,000	21,918 73.6	124,453 101.6	83,280 124.6	144,074 168.9	51,453 223.4	425,178 129.8
Total Pandemic						
a. Total COVID-19 Deaths	67,432	306,574	181,054	277,710	93,294	926,064
b. Deaths Per 100,000	226.4	250.1	271.0	325.5	405.0	282.7
c. Percent Non-Hispanic White	43.5	56.7	68.4	79.6	85.6	77.6
d. Percent with College Degree	37.3	29.7	25.5	19.7	16.2	20.4
e. Percent in Poverty	21.5	18.4	17.2	16.1	16.6	16.7
Total Population	29,778,394	122,572,218	66,801,292	85,319,109	23,036,379	327,507,892

*Table 2:* Regression Models Showing Relationship Between Independent Variables and COVID-19 Deaths per 100,000 Residents During Two Years of the Pandemic (N=3,112)

Independent Variables	First Year		Second Year	
	Parameter Estimate	Standard Beta	Parameter Estimate	Standard Beta
Percent Voting for Trump	0.000	0.010	0.001*	0.397
Percent Non-Hispanic White	-0.001*	-0.170	0.000*	0.081
Percent with College Degree	-0.002*	-0.277	-0.002*	-0.327
Percent in Poverty	0.001*	0.104	0.003*	0.233
Intercept	0.002*	-	0.001*	-
F-Value	135*	-	1,098*	-
Model R2	0.148*	-	0.586*	-

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# Historical Foundations of the Development of Medical Law in Hungary

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HISTORICAL FOUNDATIONS OF THE DEVELOPMENT OF MEDICAL LAW IN HUNGARY

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# Historical Foundations of the Development of Medical Law in Hungary

Dr. Jur. Zoltán Lomnici PhD

**Abstract-** The study briefly presents the public law-historical foundations of Hungarian medicine; describes the main peculiarities of the early, unchiseled regulation and the fact that the institutional care of the sick and poor was first dealt with by the clergy and the monastic orders. Real development began in the last third of the 19th century, and the first serious steps in public law were the changes at the legislative level of 1871 and 1876. By the 20th century, the pharmaceutical profession had developed, the organization of social security had been established, and after the Second World War the Ministry of Health was established in Hungary.

## THE BEGINNINGS

As a starting point, it should be noted that the early Hungarian regulations were rather unchiseled. It is well known that the institutional care of the sick, the poor was first dealt with by the clergy and monastic orders.<sup>1</sup> The Benedictine order settled by King St. Stephen (ruler 1000-1038) in particular can be highlighted, as they - as a primary healing order - maintained a hospital in Pannonhalma, in the area of the abbey, as early as 1221.<sup>2</sup>

In addition to all this, one of the decrees of King Kalman (ruler 1095-1116) is probably the first piece of health legislation. It clearly states, "Women who have lost their fetuses should atone to the principal."<sup>3</sup>

Despite the lack of legal bases and qualifications, several so-called domus hospitalis (hospital) was built from the 13th century, after the already mentioned Pannonhalma in Sopron (1274), Esztergom (1303), Buda (1439) and Debrecen (1529). However, we must look for the ancestors of real hospitals not in this age, but later, at the time of the appearance of camp hospitals.<sup>4</sup>

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<sup>1</sup> The Second Book of the Decrees of King St. Stephen states, "Know ye all, our brethren, that the priests labor above all."

<sup>2</sup> In addition to them are the Antonites, Johannites, Templars, Paulists, Jesuits, and Cistercians. It is important to note that domus hospitalis cannot yet be considered a real hospital, mainly because their "managers" and nurses did not usually have a medical qualification. See: Gábor Jobbágyi: Personality Rights - Health Contract (in Hungarian), in: Jogtudományi Közöny 1984/1 16. p.

<sup>3</sup> Source: Corpus Iuris Hungarici CD; KJK-KERSZÖV

<sup>4</sup> This was the case on Margaret Island in 1686 and in Buda in 1688. However, Article 30 of King Rudolf's 1596 Decree states: "The faculties and royal orders understood the desire of His Imperial Majesty to care for the wounded and sick soldiers and, for this purpose, to equip hospitals." Cf. Gábor Jobbágyi: New Questions of the Civil Liability of a Doctor in Judicial Practice (in Hungarian), in: Jogtudományi Közöny, 1986/4 15-17. p.

Until 18-19. century, medical concepts and activities were mixed. Doctors (Latin phisicus) were often priests, doctors, and pharmacists at the same time. Contemporary healers have been concentrated in guilds from the beginning to better protect their interests. The first medical specialty was the guild of barber surgeons (Latin chirurgus) from the 16th century.<sup>5</sup>

One of the next stages in the development of the law is a decree of 1714 issued by the city of Debrecen, which required, among other things, a personal presence for the doctor and "humane, gentle, willing treatment of the patient".<sup>6</sup>

There have also been developments in the social approach to patient care: under the provisions of the Royal Decree of 22 August 1721, each village was obliged to provide for its own poor, both in terms of healing and care.<sup>7</sup>

Meanwhile, guilds were constantly established, but they still could not provide a higher standard of medicine. It was rare for such an excellent specialist as Matthias (Mátyás) Lassel, a doctor from Brasov, who practiced between 1760 and 1792. Lassel traveled from town to town, declaring himself an ophthalmologist (German Augenarzt) and performing successful cataract surgeries.<sup>8</sup>

The further tightening of medical activity was brought about by the fact that, from 1751, only persons who had previously been examined "by uninteresting masters" could be admitted to the guild of surgeons.<sup>9</sup>

The first major draft implementing the regulation of public health and medical practice is the "Planum regulationis in re sanitatis" from 1755. The main points of the draft, prepared on the proposal of the health councilor Károly Perbegh, were the following:

- 1) Medical degrees obtained abroad must be presented to the Royal Council of Governors.

<sup>5</sup> For a long time, however, they became "masters" not on the basis of a medical degree but on the basis of a master's examination and the observance of guild requirements (in Hungarian); Cf. Gábor Jobbágyi: JK op cit 17. p. See also: Gyula Magyary-Kossa: Hungarian Medical Memories, Budapest 1940.

<sup>6</sup> See: Gyula Magyari-Kossa: op cit 136-137. p.; See also: Balázs Landi: Issues of Civil Liability of Doctors (in Hungarian). Study 8. p.

<sup>7</sup> See the Explanatory Memorandum to the law Article III of 1875 ("On the coverage of the costs of public patient care").

<sup>8</sup> Cf. Gábor Jobbágyi: JK op cit 17. p.

<sup>9</sup> Gyula Magyary-Kossa: op cit 145. p.

- 2) The authority must keep a "mandatory list" of doctors, the exact definition of which is not given in the draft.
- 3) Pharmacies should be inspected annually for compliance with public health standards.
- 4) "The operation of ophthalmologists, gallstone and hernia cutters and tooth extractors visiting cities should be carefully checked by the authority; it may not allow them to perform other medical functions, such as internal cures, and give them official certificates of surgery only with the utmost care."<sup>10</sup>

Until the 19th century, the shortage of doctors in Hungary was depressing. In 1763, for example, there was no doctor or pharmacy in Békés County. These conditions led the Royal Council of Governors, during 1766, to order centrally that each authority report the doctors, pharmacists, surgeons, and midwives in their district.<sup>11</sup> It was also expected that the reports to be forwarded to the Royal Council of Governors should also indicate which of these individuals met the previously specified examination requirements.

#### *The first signs of development*

Real development began in the last third of the 19th century. Large Hungarian medical figures such as Ignác Semmelweis, Frigyes Korányi, János Balassa and others appeared. By the end of the century, the first serious legislation appeared, and as an institution, first the National Public Health Council (OKT)<sup>12</sup> and then the Forensic Medical Council.

The first significant step in the Hungarian legislation was the enactment of law Article III of 1875 ("On the coverage of the costs of public patient care").<sup>13</sup> In the following, let's review the starting lines for justifying the norm.

The following aspects have guided the drafting of this bill:

1. That the interests of public patient care are adequately protected, while ensuring the survival of hospitals and medical institutions;
2. That the amount hitherto covered by the State Treasury for the cost of medical care be reduced as far as possible;

3. That, by clearly outlining the obligation to reimburse the costs of patient care by whom and in what order, this will allow for faster and more secure recovery of patient care costs'.

Nevertheless, according to Section 7 of the law Article: "every village, in its own bosom, is responsible for the treatment of the wealthless patients competent there and for the care of the incurable". Also, Section 9 provides that "any wealthless person who is cared for and registered as incurable in public hospitals and medical institutions shall be taken over by the municipality of residence for further care and attention". This laid the foundations for healing hospitals.

Ahead of many developed countries, in 1876 the Hungarian parliament passed the law Article XIV of 1876 ("On the Order of Public Health").<sup>14</sup> The law Article consisted of two hundred sections and regulated the most important areas of health care for nearly a century. In the law Article XIV of 1876, we can observe a mixture of administrative and civil law elements. Section 1 states that "the management of public health is the responsibility of the state administration". At the same time, according to Section 47: "A doctor authorized to practice may not be restricted in the application of the treatment, but his operation is under the control of the State and he is responsible for any malfunctions committed by him". In the latter, we can already clearly discover the germs of civil law regulation.

The Preamble to the law Article also emphasizes the importance of the measure. Its opening sentence reads: "A law that would have regulated the issue of public health in Hungary has not existed so far."

It further states that "the task of the health administration is not only to ensure that the troubles which have arisen are to be remedied, but also, and above all, to take measures to prevent such troubles and public health deficiencies and to ensure the well-being of public health; however, in order to solve this task, it is necessary, on the one hand, to determine the powers of the public authorities and, at the same time, to limit the scope of private law, and, on the other hand, to win the interest and participation of the public".

An important innovation of the legislation is the establishment of the aforementioned National Public Health Council (OKT), under the authority of the Minister of the Interior, as a body of the Ministry of the Interior, the history of which dates back to the early 19th century.

At the beginning of the 19th century, the situation of the population of Hungary was miserable. Roughly 90% of the 10 million population had no real estate at all. Due to poor economic conditions, famines were common. There were national and local epidemics, a high number of deaths due to lack of treatment, a large shortage of doctors and surgeons, and a small number of pharmacies. In addition, the number of

<sup>10</sup> Ferenc Linzbauer: Codex sanitario-medicinalis Hungariae I-III. Buda 1852-1861, II.302. See: Balázs Landi op cit 9. p.

<sup>11</sup> The midwives (old women) were essentially midwives. They rarely had a vocational qualification. Incidentally, attempts have been made in several regulations to eliminate their ignorance. The role of midwives has re-evaluated over time. According to Section 27 of the law Article XXXVIII of 1908: "Every town (village) is obliged to keep a qualified midwife." See also Balázs Landi: op cit 11. p.

<sup>12</sup> Based on the suggestions of Balassi and Korányi, among others. See also: Bezerédy-Henz-Zalányi: Centuries of struggle for the health care of Hungary (in Hungarian). K.J.K. Budapest 1967; 24-26. p.

<sup>13</sup> CJH-MTT, Law Article III of 1875 ("On the coverage of the costs of public patient care")

<sup>14</sup> Ibid.

hospitals and hospital beds was alarmingly low, and there was a backlog in the treatment of patients and in hospital hygiene.<sup>15</sup>

After the defeat of the Hungarian Revolution and War of Independence against Austria in 1848-49, Hungary became completely vulnerable. With the Austro-Hungarian Compromise of 1867 (with the creation of a more independent Hungary in addition to Imperial Austria), development began, and this extended to health care.

In response to the changes, a preparatory meeting on the development of the Hungarian public health system was held under the leadership of the Minister of the Interior, Béla Wenckheim, and with the involvement of renowned Hungarian professors. At the meeting, four drafts were presented to the Minister in person: the older one, drafted in 1848, two proposals drawn up at the Wandering Meeting of Doctors and Naturalists in Bratislava and Rimaszombat, and finally the memorandum by Professors Balassa, Korányi, Lumniczner and Markusovszky. Of these, the Minister chose the latter as the basis for negotiation, as it discussed all public health requirements in sufficient detail. This was seen as a finished program of all public health progress.

The draft envisioned the Public Health Council as a Prussian-style advisory body to the portfolio, independent and covering all special professions, for the purpose of giving opinions throughout health care, drafting laws, and preparing instructions and regulations for health officials. This council was tasked with establishing and overseeing examinations of applicable medical personnel, and was the supreme authority for health and forensic medical issues over malpractice, setting medical fees, and proposing pharmaceutical profession. The draft provided an exhaustive and convincing explanation as to why these actions could not be entrusted to officials, the teaching staff, the medical association or the medical college. In April 1868, the king approved the basic structure of the OKT, and in June of that year he appointed János Balassa as chairman, and in addition to the second chairman (Endre Kovács-Sebestény), he also appointed 10 regular and 27 extraordinary members.<sup>16</sup>

As this organization was not effective enough, the law Article XI of 1890 established the Forensic Medical Council with the aim of speeding up criminal sentencing as a body of medical experts. According to the reasoning of the law for the above two bodies: "The compulsion to these bodies, which eliminates slowness and delay, cannot be exercised because they could only

exert greater speed by pushing their ownership responsibilities into the background, which is not only unfair but also wrong. In addition, both bodies will be completely shut down for almost three full months of the year.

This Section states that the council to be set up will be called upon to operate exclusively in the field of the civil service of the judiciary, and is therefore at the disposal of the Minister for Justice."<sup>17</sup>

Meanwhile, the conditions for becoming a doctor have been gradually tightened. According to Section 9 of the law Article I of 1883 ("On the Qualification of Civil Servants"), this is:

"In the Department of Public Health of the Ministry of the Interior, for doctors, a degree in general medicine or a degree in medicine, surgery and obstetrics.

The same is expected of doctors at the metropolitan police station; and from the chief medical officers, district doctors in the capital, and two years of medical practice.

District doctors and doctors from cities with an organized council must have a medical degree and two years of medical practice."<sup>18</sup>

There were special regulations for pharmacists. Pursuant to Decree No. 22.370 / 1883 of the Minister of the Interior, if a pharmacist applies for a permit for the establishment of a new pharmacy, he is obliged to indicate the districts which form part of the turnover of the pharmacy to be newly established. In addition, the following had to be attached to the application:

1. Diploma in pharmacy in original or notarized copy
2. Statement of occupation to date, all certificates in chronological order (...)
3. A moral certificate from the authority of residence<sup>19</sup>

#### *Health legislation of Hungary in the 20th century*

The law Article XXXVIII of 1908 on the Amendment of the Public Health Act classifies the legal relationship between a doctor and a patient as an assignment, namely in connection with the replacement: Pursuant to Section 24, the village (district) doctor may request 3 weeks of leave per year, which is granted to him by the sub-prefect after hearing the district Chief Judge and the county chief medical officer. The latter also arranges, in consultation with the Chief Judge and the district doctor, for replacement in the event of illness of the municipal (district) doctor.

<sup>17</sup> It should be noted that sections 64 and 165 of the law Article XIV of 1876, respectively, place health care under the control of the Ministry of the Interior

<sup>18</sup> The Section 43 of the law Article XIV of 1876 states that only those who have a medical diploma issued by a scientific university in the territory of the country have the right to practice medicine in Hungary

<sup>19</sup> The latter is worth comparing with Section 22 of Act I of 1936 and its critique. See Bezerédyné-Henz-Zalányi, op cit 217. p. Source: Collection of Administrative Legislation, Fővárosi Nyomda Rt., Bp. 1932

<sup>15</sup> Dr. József Honti: The Law XIV of 1876 and antecedents; in: OrvosiHetilap (1997) 16. 1009.-1011. p.

<sup>16</sup> Cf. Lajos Csátary Grósz.: Fifty years of operation of the National Public Health Council (in Hungarian). Budapest, Franklin, 1918. 5-15. p.

The replacement should be entrusted to another local doctor living in the village, or in the absence of such, to a private doctor who lives in the village (district) during the time of the replacement. If this is not the case, or if the latter method of replacement does not prove necessary, the sub-doctor shall replace the replacement with a municipal (district) physician or a private doctor, or, if appropriate, with the division of the medical community into two or more neighboring municipalities (districts).

The municipal (district) doctors are obliged to accept the order and perform the replacement without any separate payment. "

In the 1930s, medical law was essentially in crisis in Hungary. The few monographs that have been born on this subject have only exacerbated the chaos. An example is Béla Szász's Medical Jurisprudence,<sup>20</sup> which examines the relevant provisions through the eyes of a forensic doctor, using criminal and private law aspects.

Although the organization of social security was established in principle, poor health conditions still prevailed in most of Hungary. In addition, the number of medical experimental interventions has increased. In 1935, the publication Rules of Medical Practice reported that a decision had to be made on the so-called On the prohibition of Zeileis treatment<sup>21</sup> because it is unscientific and "could lead to serious harm to some patients". In addition, although local governments for doctors were established, their situation remained unclear vis-à-vis doctors from public and private insurers, so they did not have a serious weight.

The first major change in the field of advocacy was the publication of the law Article I of 1936 ("On Medical Ordinance").

Section 1 (1) of the Act states: "The Medical Chamber is the representation of the interests of doctors. Its task is to guard the patriotic conduct and moral authority of the medical faculty, to enforce the moral and financial interests of doctors in accordance with the public interest, to check the regularity of medical practice, to exercise disciplinary jurisdiction over its members, and to make proposals on medical and public health issues. This task is performed in its territory by the Medical Chamber (hereinafter: the District Chamber), and in the national context by the National Medical Chamber (hereinafter: the National Chamber). "

The second section deals with the question of the examination (approbation): "An activity the performance of which is linked to a medical degree may be pursued only by a member of a district chamber."<sup>22</sup>

The legislation is based on the law Article XXXVIII of 1908, in accordance with the law, classifies

the doctor-patient relationship as a contract type of assignment. According to (3): "Compensation determined by free agreement may be reduced by the court if, as a result of an unforeseen event, the assignment is terminated or the doctor resigns from further activities or does not perform the work for which the amount of remuneration was determined."<sup>23</sup>

Although the law significantly increased the authority of the medical faculty (including doubling the number of members of the upper house that could be elected by the faculty), it was widely criticized, for example, because section 22 of the law tied chamber membership to an impeccable history.<sup>24</sup>

The aforementioned Medical Ordinance Act was repealed in 1945,<sup>25</sup> and after a fourteen-year ex lex status it was enacted under Act VIII of 1959 on Medical Ordinance. In addition, the Law on Pharmacy was enacted between 1945 and 1972,<sup>26</sup> and the Ministry of Health was established in 1950.<sup>27</sup>

<sup>20</sup> See: Béla Szász: Medical Law (in Hungarian). Danubia, Pécs 1925

<sup>21</sup> Read more: Gábor Jobbágyi: JK op cit 17. p.

<sup>22</sup> See also law Article I of 1936 ("On Medical Ordinance")

<sup>23</sup> According to some, this is due to the fact that the civil law literature has so far been unable to break with the theory that there is a contract work between a doctor and a patient.

<sup>24</sup> Read more: Bezerédyné-Henz-Zalányi, op cit 217 p.

<sup>25</sup> 2500/1945. (VI.3) Prime Ministerial Decree

<sup>26</sup> Act XXX of 1948

<sup>27</sup> Act IV of 1950



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# Application of Diagnostic and Educational Tools to Control Childhood Parasitic Infections in the School Environment

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**Abstract- Objective:** To evaluate the frequency of the main intestinal parasitic diseases that affected school-age children in the city of Recife, Pernambuco, between 2008 and 2018. And intervene in the school environment through playful educational practices to raise awareness among students, parents, and employees about preventive measures that could prevent contamination by parasites.

**Methods:** This work is a cross-sectional coproparasitological study, addressing quantitative and qualitative aspects of children aged 12 years or less, who were enrolled in public schools or daycare centers selected for this work and presented the Informed Consent Form (ICF) signed by parents or guardians. The collected samples were submitted to the techniques of Hofmann and modified Kinyoun.

**Keywords:** children; schools; frequency of enteroparasitosis; health education.

**GJMR-K Classification:** NLMC Code: WC 695



APPLICATION OF DIAGNOSTIC AND EDUCATIONAL TOOLS TO CONTROL CHILDHOOD PARASITIC INFECTIONS IN THE SCHOOL ENVIRONMENT

*Strictly as per the compliance and regulations of:*



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# Application of Diagnostic and Educational Tools to Control Childhood Parasitic Infections in the School Environment

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**Abstract- Objective:** To evaluate the frequency of the main intestinal parasitic diseases that affected school-age children in the city of Recife, Pernambuco, between 2008 and 2018. And intervene in the school environment through playful educational practices to raise awareness among students, parents, and employees about preventive measures that could prevent contamination by parasites.

**Methods:** This work is a cross-sectional coproparasitological study, addressing quantitative and qualitative aspects of children aged 12 years or less, who were enrolled in public schools or daycare centers selected for this work and presented the Informed Consent Form (ICF) signed by parents or guardians. The collected samples were submitted to the techniques of Hofmann and modified Kinyoun. Also, lectures were realized for parents, guardians, and employees of Schools or Nurseries and recreational actions for children.

**Results:** A total of 705 samples were collected, of which 340 were positive for 12 different parasite species. *Giardia lamblia* (24.9%), *Cryptosporidium* spp (23.6%), and *Endolimax nana* (21.4%) were the most recurrent among schoolchildren between 2010 and 2018. About applied educational playful practices, they proved to be effective in building knowledge and raising awareness about parasitic endemics, evidencing the need for more practices like these in schools and communities in general.

**Conclusion:** This work presented an expanded view of the parasites' permanence in the school environment and the importance of educational practices aimed at transforming life habits that are harmful to health.

**Keywords:** children; schools; frequency of enteroparasitosis; health education.

## 1. INTRODUCTION

Intestinal parasite infections produced by protozoan and helminths still constitute one of the main global causes of infant morbidity and mortality (1). The prevalence of such infections affects several countries and territories in the world because despite being

cosmopolitan, the transmission of parasites is dependent on the conditions of the host, parasite, and environment (2).

Currently, around 3.5 million people worldwide are affected by one or more species of parasites, representing a relevant public health problem (3). In an analysis of the incidence of intestinal parasite infections of different age groups in children, between 5 and 12 years old, were identified as one of the most affected groups (4). Children are also more likely to generate symptoms and clinical manifestations of parasite infections (cognitive impairment, decreased growth, irritability, and susceptible increase in other pathogen infections), reducing their quality of life (3,5).

One of the biggest causes of children's susceptibility to parasites is due to their immature immune system combined with the precariousness of maintaining personal hygiene (6). Frequent contact with soil and water during recreational activities without guidance can determine the transmission and prevalence of enteroparasitosis in homes and schools (7,8).

In Brazil, the prevalence of parasitic diseases in schoolchildren is directly associated with a low Human Development Index (HDI), ranging from 2% to 36%, reaching 70% in more alarming cases (9). The North and Northeast regions of the country have high prevalence and polyparasitism in several communities, with a high diversity of species involved (10,11). Among the intestinal parasitoses that affect children, the most frequent are those whose means of transmission is the oral-fecal route. Since they are associated with the ingestion of contaminated water or food, as is the case of *Ascaris lumbricoides*, *Entamoeba histolytica*, *Enterobius vermicularis*, *Trichuris trichiura*, and *Giardia lamblia* (12,13).

Prevention is still the best way to avoid enteroparasitosis. In this sense, health education practices in schools and communities improve the knowledge of the population about the risk factors that lead the individual to be infected (14). Because although many individuals assure knowledge about intestinal parasitic diseases, studies reveal that, they have

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misunderstandings regarding the preventive and curative measures of worms (9).

Lack of knowledge about preventive measures, the basic principles of personal hygiene, and care in food handling can contribute to the spread of the disease, facilitate infections and precipitate reinfection in areas considered endemic (15,16,17). Thus, it is necessary to include parents/guardians, teachers, and students in educational activities to make them trained in educational actions (9). The partnership of family and school minimizes the difficulties encountered in the school environment, adding knowledge about the realities experienced (19,20).

This study aimed to evaluate the frequency of intestinal parasites observed in school-age children in the city of Recife, Pernambuco and to determine their main species and intervene in the school environment through playful educational practices to make students, parents, and employees aware of the preventive measures that were took to avoid the contamination of these parasites.

Thus, the present work aimed to identify intestinal parasites, as well as evaluate your frequency in school-age children in the city of Recife, Pernambuco. And intervene in the school environment through educational practices to make students, parents, and employees aware of the preventive measures to avoid the contamination of these parasites.

## II. MATERIAL AND METHODS

### a) Study population

A total of 705 fecal samples did collect from children aged 12 years or less from different public schools or daycare centers located in the city of Recife, PE, between the years 2008 and 2018.

The followed inclusion criteria did consider were the age of the children (aged 12 years or less), public schools and the Informed Consent Form (ICFs) accepted by the parents/guardians.

Regarding the exclusion criteria, children over the age of 12 did not participate in the analysis; private schools and daycare and the absence of parents/guardians that do not agree with their children's participation.

### b) Ethical aspects

The study was approved by the Ethics Committee of the Health Sciences Center (CCS) of the Federal University of Pernambuco (UFPE), presenting the CAAE number: 19640213.0.1001.5208. All children enrolled in this study had the ICF signed by their parents/guardians.

### c) Sample collection

All children or their participating guardians received the ICF and the plastic collecting jars, without preservatives, and received instructions about how to

collect the fecal sample correctly. Two days after, we received the signed ICF and identified collecting pots. All fecal samples were processed and analyzed by expertise personal at the Parasitology Laboratory of the Medical Sciences Center (LP/CCM) by the Federal University of Pernambuco (UFPE).

### d) Analysis and processing of parasitological samples

In the laboratory, fecal material was stored under refrigeration between 4 °C and 8 °C until analysis. First, a macroscopic evaluation of the fecal material was carried out to observe the presence of larvae or helminth proglottids. Samples were processed by the Hoffman/Lutz methods (spontaneous sedimentation) for protozoan cysts, helminth eggs or larvae detections (21) and the modified Kinyoun technique using fuchsin-carbolic, to search for *Cryptosporidium* spp. (22). For each stool collector, two slides were arranged per technique. Enteroparasites were identified by optical microscope under 10 X, 40 X, and/or 100 X objectives. All results were confirmed by a supervisor.

### e) Health education

Awareness about health education was carried out after each stool collection cycle, in schools or daycare centers that are suitable for research, in the year of the study. Through educational activities previously planned by undergraduate students in the health field, together with teachers associated with the LP/CCM/UFPE, parents, guardians, and employees of the Schools were directed to lectures of the type expository-dialog. To bring basic knowledge about parasites, how to identify and the prevention and treatment measures to be taken.

While for children, theatrical plays, competitive and musical games were carried out, to bring knowledge and information playfully about the risks of parasitic infections. Discussing aspects such as signs and symptoms of the disease, modes of transmission, biological cycle of the parasites and reinforcement of prophylaxis measures, both individual and collective. About educational practices aimed at enteroparasitosis, undergraduate students in the health area were mobilized, along with professors from UFPE. Each year, a different school received an interactive lecture with parents or guardians and school staff.

The results of the exams were made available simply and lucidly to the students' guardians. Positive cases of parasite infection were send to treatment at a local Health Center. The education practices about health were carried out after each stool collection cycle in schools or daycare centers that are suitable for this research. First, realized with the parents, guardians, and employees of the Schools. The method employed was an expository-dialog about fundamental knowledge parasites and how to identify them as well as the prevention and treatment.

While for children, theatrical plays, competitive and musical games were carried out, to bring knowledge and information playfully about the risks of parasitic infections. Dialog about aspects such as signs and symptoms of the disease, modes of transmission, the biological cycle of the parasites, and reinforcement of prophylaxis measures, individual and collective. About educational practices aimed at enteroparasitosis, undergraduate students in the health area were mobilized, along with professors from UFPE. Each year, a different school received an interactive lecture with parents or guardians and school staff.

The results of the exams were made available simply and lucidly to the students' guardians. Positive cases of parasite infection sent to treatment at a local Health Center.

#### f) Data analysis

This study comprehends qualitative and quantitative methods (23). A descriptive analysis was performed, using data obtained from coproparasitological exams. Based on the reports, a

spreadsheet survey was performed in Office Excel 365, addressing the number of participating children, the number of samples of fecal material collected, and their respective positivity or negativity.

### III. RESULTS

Between the period of 2008 to 2018, 730 coproparasitological exams were performed on children under 12 years old. These total, 421 samples were negatives, representing 57.67%, and 309 were positive for one or more enteroparasites, with a percentage rate of 42.33%.

Figure 1 shows the relative frequencies of positivity, over the ten years of parasitological analysis of the Daycare and Schools studied. Higher numbers of positive diagnoses for enteroparasitosis were observed in the years 2013 and 2016, with percentage rates of 84.61% (22/26) and 69.38% (68/98), respectively. However, the lowest number of positive parasite reports were observed in 2014 and 2017, with 15.38% (10/65) and 21.91% (16/73), respectively.

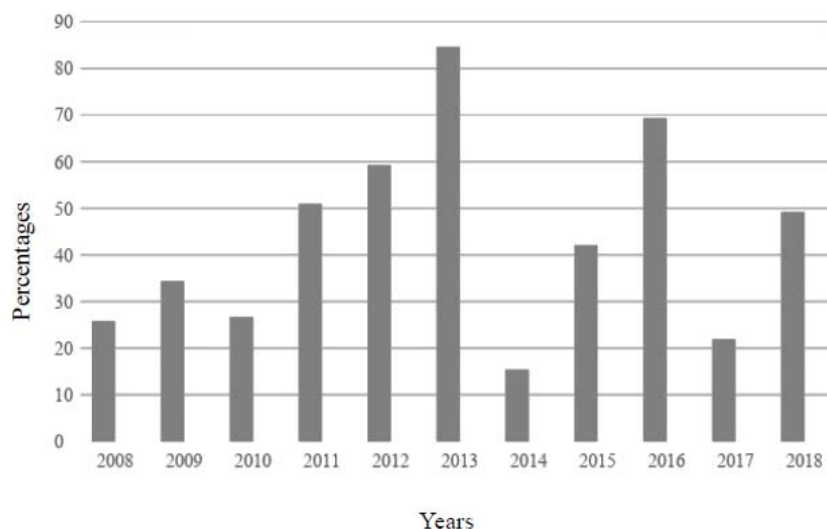


Figure 1: Relative frequency of positive samples for enteroparasites, from 2008 to 2018, in schoolchildren under 12 years old, in the city of Recife-PE.

Regarding the main species of parasites found in microscopic evaluations, were identified 12 different species of protozoa and helminths between 2008 and 2018 (Table 1). Related to all identified enteroparasitoses, a higher positivity rate of protozoa, like as *Giardia lamblia* (26.4%), *Endolimax nana* (24.7%), *Cryptosporidium* spp (17.5%) and *Entamoeba coli* (9.9%) when compared to helminths: *Ascaris lumbricoides* (8.2%), *Ascilostoma* spp (2.1%) and *Trichuris trichiura* (0.5%).

In accordance to Table 1, the highest frequency of *Cryptosporidium* spp (75.5%), *G. lamblia* (54.8%), and *E. nana* (40%) occurred in the years 2015, 2017, and 2014, respectively. Whereas no parasite of the species *Blastocystis hominis*, *Ancilostoma* sp, *Iodameba*

*butschlii*, *Balantidium coli*, and *Taenia* sp were detected in the same years.

Among the analyzed years, the largest absolute frequency of positive cases was seen in 2016, highlighting the species *Cryptosporidium* spp 39/68 (57.35%), *Endolimax nana* 11/68 (16.17%), and *Ascaris lumbricoides* 10/68 (14.7%). In the second-highest frequency of enteroparasites, the year 2012 also showed high positivity for *Endolimax nana* 12/48 (25%). Despite the high case number showed in the same year, the relative frequency was no higher due to the total number of samples.

However, unlike in 2016, the species *Giardia lamblia* and *Entamoeba histolytica*/E. *dispar* were the most present species in the stool samples collected in

2012, being responsible for 22.9% and 18.5% of infections.

Another year with a high absolute frequency of parasites was 2015 (N=37). The parasite specie *Cryptosporidium* spp reached 28/37 (75.5%) of students parasitized. While others parasites identified were *E. nana* 9/37 (24.3%), *G. lamblia* 5/37 (13.5%), *E. histolytica/E. dispar* 3/37 (8%), *A. lumbricoides* 3/37 (8%), and *E. coli* 1/37 (2.7%).

Specifically in 2014 occurred the lowest number of parasite positivity (N=10), with *E. nana* 4/10 (40%), *Giardia lamblia* 2/10 (20%) and *Ascaris lumbricoides* 2/10 (20%). Others years, like 2009, 2010 and 2017 presented also a low number of positive samples, showed positivity to *G. lamblia*, varying between 45.5%,

31.3%, and 54.6%, *E. coli* 18.2%, 18.5% and 12.5%, respectively.

In regards to the educational practices, the employees and parents/guardians of the Schools were given lectures focused on parasitic endemics, the signs, and symptoms of enteroparasitosis; how to identify when children are under such infections, and how to prevent their biological cycle (Figure 2A and B). In this practice, limited knowledge on the subject was noted, both by those responsible for the children and school staff. However, throughout the lectures, a great familiarity with the theme was seen when the public stated that friends, relatives, or the parents/guardians themselves had such symptoms or were diagnosed.



Figure 2: A and B: Educational practices for employees and parents/guardians of the Schools.

Children's guardians, however, expressed doubts about some home treatments, passed down through generations. In one of the reports, it was reported that sitting in a basin containing warm water eliminates *Strangyloides stercoralis* and reduces the itching caused by the parasite. Thus, employees intervened in the knowledge of practices like these, demystifying and reporting the best way to follow palliative and curative practices.

About the children, playfully, theaters, competitive games, musicals, and/or more interactive

conversations about parasites were made to attract attention and build knowledge. As a result, great mobilization and interaction were seen, showing interest in the subject and confirming the knowledge received during questioning (Figure 3A and B). When reported on popular names of enteroparasitoses and hygiene habits, a certain prior understanding was evidenced. However, many said they were not adept at such habits that protect from parasitic diseases.



Figure 3A and B: Application of playing educational actions concerning parasitic endemics.



#### IV. DISCUSSION

This work is the first in the State of Pernambuco to use educative strategies to combat enteroparasitosis in public school and daycare through the fecal parasitological examination of the schoolchildren and adoption of health educative measures to aim children and their parents to combat parasite infections. An expanded view of the permanence of parasites in the school environment and the importance of educative practices were able to transform life habits.

All the evaluated daycare and schools showed children with parasite contamination. In this study, between the years 2008 and 2018, were observed high frequencies of commensal protozoa, *Endolimax. nana*, and agents capable of generating human morbidity, as is the case of *Giardia lamblia* and *Cryptosporidium* spp. These three parasites are frequently found in Brazilian children's coproparasitological exams (24-26).

The high frequency of *E. nana* in schoolchildren can be an indicator of hygiene lacking, as demonstrated in the study conducted in Caxias do Sul, with *E. nana* cysts identified in 60% of the analyzed samples (27). Another study in Paracatu (MG) also associates the lack of hygienic care with the occurrence of commensal parasites in nine public schools, with a prevalence of 16.5% for *E. nana* (28). In João Pessoa, Paraíba, a study in children also suggested the same justification for the prevalence of *E. nana* in 40.9% of fecal samples from children (29).

The infection by *E. nana* does not give major symptomatological effects, but promote a greater susceptibility to other parasite infections (30). The major problem of polyparasitism is the clinical manifestations caused for combination by commensal parasites and pathogenic (31). However, it's common a high incidence of polyparasitism like as seen in the study carried out by (32) showed *E. nana* associated in 36.3% of the cases with *Entamoeba coli*, and 9.2% with the species *Ascaris lumbricoides* and *Iodamoeba butschlii*. Similar results were seen in public daycare and preschools from São Sebastião da Gramma, São Paulo State, the *E. nana* and *Blastocystis* spp were combined with the species *G. duodenalis*, *E. coli*, *Entamoeba. histolytic/dispar*, *Strongyloides. stercoralis*, *Taenia* sp., and *I. Butschlii* (33).

The present study also showed a high number of sample positives for *G. lamblia*, an important parasite species responsible for giardiasis that presents diarrhea, abdominal pain, nausea, vomiting, flatulence, anorexia, and fever as symptoms (34). In many cases, diarrheal disease is short-lived and self-limiting. However, some individuals have persistent diarrhea with malabsorption of nutrients, interfering with the quality of life (35).

Similar to our results there are other studies showed enteroparasites contamination of children inside

daycare and school environments (36,37). *Giardia lamblia* was the most common species found in many of these Brazilian studies. In Ribeirão Preto, São Paulo, 50.8% of children infected with parasites obtained positive results for *G. lamblia* (36). In a public school in Cariaca, Espírito Santo revealed a 23% positivity for *G. lamblia* (37). In a philanthropic institution, the habits of hygiene and contact with soil were suggested as one of the causes of the prevalence of *Giardia* spp. (31%), as well as *Cryptosporidium* spp. (62.5%) (38).

For a long time, it believes that cryptosporidiosis affects only immunodeficient individuals. But in recent years, was detected *Cryptosporidium* spp. in immunocompetent people that exhibit watery diarrhea, vomiting, nausea, loss of appetite, weight loss, fatigue, and other symptoms (39). Children under eight years of age were the most affected (38). Despite this, in Brazil, the detection of *Cryptosporidium* spp. and other coccids are not included in routine parasitological examinations, being only investigated with a medical request (40). Thus, the presence of *Cryptosporidium* spp in schools and daycare centers is not properly investigated in the country.

The incidence of infectious and parasitic diseases in preschool children have a relationship with efficient sanitation (41). Also, the lack or low adherence of parents or guardians can underreport the presence of parasites and interfere with the development of parasitological work in schoolchildren (42). This difficulty in adhering to parasitological research is reported by Reuter and collaborators (2015), who received a low number of samples from a daycare center in the Rio Grande do Sul (43). Vargas and Amaral (2016) associate the absence of parental attention to this type of research with the rush of everyday life, which makes it difficult to interact with educational activities (42).

In the present study, the years most affected by low interaction between parents/guardians were 2014 and 2017, with lower absolute and relative frequencies due to the number of stools received. However, these years dispelled parasites such as *G. lamblia*, *E. nana*, *E. histolytica/disparate*, *E. coli*, and *Ascaris lumbricoides*, agents capable of generating morbidity to those infected and being disseminated among children in the school environment (44).

Some strategies to reduce the parasite contamination of schoolchildren can be useful to educate and stimulate the children to repass information about the prevention of parasite diseases to their families and friends. Recreational activities, theatre, musical, and games are educative tolls to transmit knowledge about health and hygiene (14,45). Though these tools like theater, musicals, and games duly adapted to the reality of that parasite affect the children can influence their creativity, motor activity, provide relaxation, and develop socio-cultural abilities, providing

more dynamic and active learning. The construction of children's knowledge about parasites has a positive impact on the change in hygiene behavior, as well as reflected in the rates of geohelminthic infections and other parasites in homes and schools (46).

Educative activities aimed at raising awareness and preventing intestinal parasites are efficient alternatives to fill the process, the gaps found in the content covered in schools (9). Thus, it is essential to plan health education actions to reduce the high rates of morbidity and mortality; and increase health information in the search for the best health status and quality of life (47).

The combination of theory with practice is complementary because the previous knowledge students there are better consolidation of learning during moments of experience (48). Thus, the role of educators and health professionals is to provide knowledge and encourage both parents and students to acquire healthy habits. These actions become essential for the prevention of intestinal parasites (49).

Punctual educative practice will not change the actual situation of high parasite contamination of schoolchildren. However, these actions must be continuous with the insertion and collaboration of parents, which are essential for the change of their children's behavior. Different studies claim that collaboration between the family and the school is important to reduce the difficulties encountered in the school environment since knowledge is constantly experienced (19,20).

Throughout these 10 years of study, the coproparasitological analysis in schoolchildren showed the need for greater attention to enteroparasitosis inside school and daycare environments, since there was parasite positivity in all children evaluated. Thus, some educative actions applied in this study were crucial for building knowledge in the children about forms to detect and prevent parasite contaminations, change bad hygiene and health habits and disseminate learning to other children, their teachers, and members of the family.

## REFERENCES RÉFÉRENCES REFERENCIAS

1. Basualdo JA, Córdoba MA, Luca MMD, Ciarmela ML, Pezzani BC, Grenovero MS, et al. Intestinal parasitoses and environmental factors in a rural population of Argentina, 2002-2003. *Revista do Instituto de Medicina Tropical de São Paulo*. 2007; 49(4): 251-255.
2. Frei F, Juncansen C, Ribeiro-Paes JT. Epidemiological survey of intestinal parasite infections: analytical bias due to prophylactic treatment. *Cadernos de saude publica*. 2008; 24(12): 2919-2925.
3. World Health Organization. Integrating neglected tropical diseases into global health and development: fourth WHO report on neglected tropical diseases. Geneva: World Health Organization; 2017.
4. World Health Organization. *Investing to overcome the global impact of neglected tropical diseases: third WHO report on neglected tropical diseases 2015*. Geneva: World Health Organization; 2015.
5. Belo VS, Oliveira RBD, Fernandes PC, Nascimento BWL, Fernandes FV, Castro CLF, et al. Fatores associados à ocorrência de parasitoses intestinais em uma população de crianças e adolescentes. *Revista Paulista de Pediatria*. 2012; 30(2): 195-201.
6. Zanotto M, Cavagnoli NI, Breda JC, Dalla Santa Spada PKW, Bortolini GV, et al. Prevalence of intestinal parasites and socioeconomic evaluation of a country town in the Serra Gaucha region, Rio Grande do Sul, Brazil. *Revista de Patologia Tropical/Journal of Tropical Pathology*. 2018; 47(1), 19-30.
7. Frei F, Juncansen C, Ribeiro-Paes JT. Levantamento epidemiológico das parasitoses intestinais: viés analítico decorrente do tratamento profilático. *Epidemiological survey of intestinal parasite infections: analytical bias due to prophylactic treatment*. *Cadernos de Saúde Pública*. 2008; 24(12): 2919-25.
8. Filho HBA, Carmo-Rodrigues MS, Mello CS, Melli LCFL, Tahan S, Mauro Batista de Moraes. Parasitoses intestinais se associam a menores índices de peso e estatura em escolares de baixo estrato socioeconômico. *Revista Paulista de Pediatria*. 2011; 29(4): 521-8.
9. Bragagnollo GR, Godoy2 PCG de T, Santos TS dos, Ribeiro V dos S, Morero JAP, Ferreira BR. Intervenção educacional sobre enteroparasitoses: um estudo quase experimental. *Revista Cuidarte*. 2018; 9(1).
10. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Coordenação Geral de Desenvolvimento de Epidemiologia em Serviços. Guia de Vigilância em Saúde [Internet]. 1st ed. Serviços. . Ministério da Saúde. Secretaria de Vigilância em Saúde. Coordenação-Geral de Desenvolvimento da Epidemiologia em, editor. Ministério da Saúde. Brasília; 2016 [cited 2020 Aug 5]. p. 773. Available from: [http://bvsms.saude.gov.br/bvs/publicacoes/guia\\_vigilancia\\_saude\\_1ed\\_atual.pdf](http://bvsms.saude.gov.br/bvs/publicacoes/guia_vigilancia_saude_1ed_atual.pdf)
11. Pernambuco SE da S de. Plano Integrado de Ações para o Enfretamento às Doenças Negligenciadas no Estado de Pernambuco/ SANAR [Internet]. 2nd ed. Secretaria Estadual de Saúde. Secretaria Executiva de Vigilância em Saúde., editor. Vol. 5. Recife: Secretaria Estadual de Saúde. Secretaria Executiva de Vigilância em Saúde.; 2018. 115 p. Available from: <http://portal.saude.pe.gov.br/sites/>

- portal.saude.pe.gov.br/files/plano\_sanar\_2\_edicao\_29.08.17.pdf.
12. Escobar-pardo ML, Paula A, Godoy O De, Machado RS, Rodrigues D, Neto UF, et al. Prevalence of intestinal parasitoses in children at the Xingu Indian Reservation. *Jornal de Pediatria (Rio J)*. 2010; 86(6): 493–6.
13. Camila PC, Silva MC. Fatores de risco das endoparasitoses de escolares públicos da Bahia. *Revista Saúde.Com*. 2014; 10(3): 245–53.
14. Teixeira PA, Fantinatti M, Gonçalves MP, Silva JS da. Parasitoses intestinais e saneamento básico no Brasil: estudo de revisão integrativa. *Brazilian Journal of Development*. 2020; 6(5): 22867–90.
15. Andrade EC De, Cristina I, Leite G, Rodrigues VDO, Cesca MG. Parasitoses intestinais: uma revisão sobre seus aspectos sociais, epidemiológicos, clínicos e terapêuticos. *Revista de APS*. 2010; 13(2): 231–40.
16. Barra M, Bustos L, Ossa X. Desigualdad en la prevalencia de parasitosis intestinal en escolares de una escuela urbana y dos rurales de la comuna de Puerto Montt. *Revista Medica de Chile*. 2016; 144: 886–93.
17. UNA-SUS UA do S, UFMA UF do M. Saúde da criança e a saúde da família: Agravos e Doenças Prevalentes na Infância. Maia EC, Pessoa FS, Soares WL, editors. Universidade Federal do Maranhão. São Luís: Universidade Federal do Maranhão; 2014. 59 p.
18. da Costa Silva AB, Vieira IRS, Firmo WDCA, & dos Santos Aliança AS. Conhecimento acerca da prevenção e ocorrência de parasitoses intestinais em alunos do ensino médio de uma escola estadual do município de Maranhãozinho-MA. *Research, Society and Development*. 2020; 9(7):e190974051-e190974051.
19. Silva SR da, Heller L, Valadares J de C, Cairncross S. O cuidado domiciliar com a água de consumo humano e suas implicações na saúde: percepções de moradores em Vitória ( ES ). *Eng Sanit Ambient*. 2009; 14(4): 521–32.
20. Freitas ADG de, Leite NRP. Linguagem fílmica: uma metáfora de comunicação para a análise dos discursos nas organizações. *Rev Adm [Internet]*. 2015; 50(1): 89–104. Available from: <http://dx.doi.org/10.5700/rausp1186>.
21. Neves DP, Wagner R, Vitor DA. *Parasitologia Humana*. 11th ed. Atheneu; 2010. 494 páginas.
22. González-Ruiz A, Bendall RP. The Use of the Ocular Micrometer in Diagnostic Parasitology Size Matters: *Parasitology Today*. 1995;11(2):83–5.
23. Pereira AS, Shitsuka DM, Parreira FJ, Shitsuka R. Metodologia da pesquisa científica.[e-book]. Santa Maria. Ed (pp. 3-9). UAB/NTE/UFSM.2018. Disponível em: [https://repositorio.ufsm.br/bitstream/handle/1/15824/Lic\\_Computacao\\_Metodologia-Pesquisa-Cientifica](https://repositorio.ufsm.br/bitstream/handle/1/15824/Lic_Computacao_Metodologia-Pesquisa-Cientifica). Pdf.
24. David ÉB, Guimarães S, de Oliveira AP, de Oliveira-Sequeira TCG, Bittencourt GN, Nardi ARM, et al. Molecular characterization of intestinal protozoa in two poor communities in the State of São Paulo, Brazil. *Parasites & vectors*. 2015;8(1): 1–12.
25. Faria CP, Zanini GM, Dias GS, da Silva S, de Freitas MB, Almendra R, et al. Geospatial distribution of intestinal parasitic infections in Rio de Janeiro (Brazil) and its association with social determinants. *PLoS Neglected Tropical Diseases*. 2017; 11(3): e0005445.
26. Mariano A, Santos EN, Santos T, Mota TN, Silva J, Carvalho S, et al. Parasites in south Bahia: focus on giardiasis and ascariasis among preschoolers of Itabuna. *International Journal of Health Sciences*. 2015; 3(1): 61–75.
27. Camello JT, Cavagnoli NI, Dalla Santa Spada PK, Poeta J, Rodrigues AD. Prevalência de parasitoses intestinais e condições de saneamento básico das moradias em escolares da zona urbana de Caxias do Sul, Rio Grande do Sul. *Scientia Medica*. 2016; 26(1): ID21716–ID21716.
28. MG SOP. Prevalência de parasitos e comensais intestinais em crianças de escolas da rede pública municipal de Paracatu (MG). As realizações e os projetos de uma gestão participativa. 2005; 37(4): 209–13.
29. da Silva Monteiro AC, de Araújo Soares D, de Oliveira Ramalho SCP, Cavalcante UMB, Silva AB, de Toledo Vianna RP, et al. Intestinal parasitism and related risk factors for primary school students in João Pessoa, northeast Brazil. *Bioscience Journal*. 2018; 34(4).
30. Poulsen CS, Stensvold CR. *Endolimax nana*. In: Principles and Practice of Pediatric Infectious Diseases. Elsevier; 2018. p. 1309–10.
31. Graczyk TK, Shiff CK, Tamang L, Munsaka F, Beitin AM, Moss WJ. The association of *Blastocystis hominis* and *Endolimax nana* with diarrheal stools in Zambian school-age children. *Parasitology research*. 2005; 98(1): 38–43.
32. da Silva Pereira FR, Pedrotti LA, Zancanaro V. Incidência de parasitoses intestinais em uma escola municipal de educação básica situada no bairro Martello no município de Caçador/SC. *Revista Interdisciplinar de Estudos em Saúde*. 2016;96–105.
33. Rebolla MF, Silva EM, Gomes JF, Falcao AX, Rebolla MVF, Franco RMB. High prevalence of *Blastocystis* spp. infection in children and staff members attending public urban schools in Sao Paulo state, Brazil. *Revista do Instituto de Medicina Tropical de São Paulo*. 2016; 58.
34. Archer J, O'Halloran L, Al-Shehri H, Summers S, Bhattacharyya T, Kabaterine NB, et al. Intestinal schistosomiasis and giardiasis co-infection in sub-



- Saharan Africa: Can a One Health approach improve control of each waterborne parasite simultaneously? *Tropical medicine and infectious disease*. 2020; 5(3): 137.
35. Hossain B, Rashid H, Noor Z, Kabir M, Miah S, Siddique A, et al. A systematic review of human giardiasis in Bangladesh: public health perspective. *Research Square*. 2020; 1-18.
36. da Fonseca REP, Barbosa MCR, Ferreira BR. High prevalence of enteroparasites in children from Ribeirão Preto, São Paulo, Brazil. *Revista brasileira de enfermagem*. 2017; 70(3): 566–71.
37. Lopes IL, Zani T, Borges FV. Prevalência de parasitoses intestinais em crianças de uma escola pública em Cariacica–ES. *Sapientia*. 2013; 50-53.
38. Dias MGPF, Fregonesi BM, Zagui GS, de Abreu Tonani KA, Julião FC, Beda CF, et al. Enteroparasitos em crianças de instituição de ensino filantrópica: ênfase para *Cryptosporidium* spp. e *Giardia* spp. *Arquivos de Ciências da Saúde*. 2018; 25(1): 51–5.
39. Shrivastava AK, Kumar S, Smith WA, Sahu PS. Revisiting the global problem of cryptosporidiosis and recommendations. *Tropical parasitology*. 2017; 7(1): 8.
40. Berne AC, Scaini CJ, Villela MM, Pepe MS, Hauptenthal LE, Gatti F, et al. Presença de coccídios e outros enteroparasitos em uma população de crianças no município de Rio Grande, Rio Grande do Sul, Brasil. *Revista de Patologia Tropical/Journal of Tropical Pathology*. 2012;41(1).
41. Pedraza DF, Queiroz D de, Sales MC. Infectious diseases among Brazilian preschool children attending daycare centers. *Ciencia & Saude Coletiva*. 2014; 19(2): 511–28.
42. de Vargas ÉG, Amaral CP. Estudo da importância da intervenção pedagógica na prevenção de doenças parasitológicas. *Multiciência Online*. 2016; 74-97.
43. Reuter CP, da Silva Furtado LBF, da Silva R, Pasa L, Klinger EI, dos Santos CE, et al. Frequência de parasitoses intestinais: um estudo com crianças de uma creche de Santa Cruz do Sul-RS. *Cinergis*. 2015; 16(2).
44. de Almeida Cardoso L, Cavalcante CS, Moraes KF, dos Santos Medeiros J. Parasitoses intestinais em crianças que frequentam creches. *Journal of Biology & Pharmacy and Agricultural Management*. 2018; 15(1).
45. Arruda AA, de Quadros RM, de Lima Miguel R, Miletto LC, Ramos CJR. Detecção de oocistos de *Cryptosporidium* spp. em crianças atendidas no Laboratório do Hospital Infantil da cidade de Lages, SC. *Revista Brasileira de Higiene e Sanidade Animal*. 2020;14(4): 1–12.
46. Silva ET da, Rocha AB, Silva FA da. Educação em saúde na escola : promovendo a saúde por meio do lúdico, da linguagem artística e da literatura infantil. *Journal of Management & Primary Health Care*. 2016; 7(1): 2016.
47. Lubini VT, Willrich JQ, Emanuel G, Pinheiro W, Prado L, Pickersgill MF. Impacts of Educational Action on Health Indicators: Potentiality and Fragilities. *Revista de Enfermagem UFPE online*. 2018; 12(6).
48. Fernanda M, Figueiredo S, Felício J, Neto R, Reis TC. Modelos Educacionais Não Críticos e Críticos aplicados à Educação em Saúde Educational Models Not Critical and Critical applied to Health Education. *Revista Norte Mineira De Enfermagem*. 2012; 1(1): 79–90.
49. Matos S, Franco A. A Educação Integral. *Pesquisa e Ação*. 2016; 2(1): 57–65.

**Tabela 1:** Relative and absolute frequency of enteroparasitosis identified in children under 12 years old, from 2008 to 2018, in the city of Recife-PE.

Intestinal parasites	2008		2009		2010		2011		2012		2013		2014		2015		2016		2017		2018		Mean	
	N=24	%	N=11	%	N=16	%	N=27	%	N=48	%	N=22	%	N=10	%	N=37	%	N=68	%	N=16	%	N=30	%	%	%
<i>Giardia lamblia</i>	5	20.8	5	45.5	5	31.3	6	22.2	11	22.9	5	22.7	2	20	5	13.5	0	0	9	54.8	11	36.6	26.4	
<i>Endolimax nana</i>	7	29.1	2	18.2	4	25	5	18.5	12	25	6	27.3	4	40	9	24.3	11	15.3	2	12.5	11	36.6	24.7	
<i>Cryptosporidium</i> spp	0	0	0	0	0	0	8	29.6	6	12.5	3	13.6	0	0	28	75.7	39	56.7	1	4	0	0	17.5	
<i>Entamoeba coli</i>	1	4	1	9.1	3	18.8	3	11.1	6	12.5	3	13.6	1	10	1	2.7	0	0	2	14.2	4	13.3	9.9	
<i>E. histolytica/E. dispar</i>	3	13	1	9.1	1	6.25	1	3.7	9	18.8	2	9.09	0	0	3	8	0	0	2	14.2	0	0	7.4	
<i>Ascaris lumbricoides</i>	5	20.8	1	9.1	0	0	2	7.4	2	4.16	0	0	2	20	3	8	10	14.3	0	0	2	6.66	8.2	
<i>Blastocystis hominis</i>	0	0	0	0	2	12.5	1	3.7	0	0	0	0	0	0	0	0	0	0	0	0	1	3.33	1.7	
<i>Ancilostoma</i> sp.	0	0	1	9.1	0	0	1	3.7	0	0	0	0	0	0	0	0	7	10.2	0	0	0	0	2.1	
<i>Iodameba butschlii</i>	0	0	0	0	1	6.25	0	0	0	0	1	4.54	0	0	0	0	0	0	0	0	0	0	0.9	
<i>Balantidium coli</i>	3	13	0	0	0	0	0	0	0	0	2	9.09	0	0	0	0	0	0	0	0	0	0	2	
<i>Trichuris trichiura</i>	0	0	0	0	0	0	0	0	2	4.16	0	0	1	1	0	0	0	0	0	0	0	0	0.5	
<i>Taenia</i> sp	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3.33	0.3	



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# The Close Connection between Opioid use Disorder and Cigarette Smoking: A Narrative Review

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**Abstract-** People with opioid use disorder (OUD) have rates of cigarette smoking approaching 90% and smoking cessation programs are rarely effective. The relationship between long-term opioid exposure and smoking has been epidemiologically observed but not well understood. Nicotine interacts with the nicotinic acetylcholine receptors in the central and peripheral nervous systems, which are involved in anxiety, cognition, sleep, arousal, and pain perception. Cigarette smoking triggers the release of dopamine in the brain. There is equivocal evidence that nicotine may have an analgesic effect, but paradoxically, smokers tend to have higher pain intensity levels than nonsmokers. Pharmacologic treatments for nicotine dependence were often studied in trials that routinely excluded subjects with opioid dependence. Further, the association between smoking and long-term opioid use sometimes includes mental health disorders and/or chronic pain. In fact, smoking may also be comorbid with chronic pain. It has been speculated that smoking, particularly at a young age, may be predictive of OUD.

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THE CLOSE CONNECTION BETWEEN OPIOID USE DISORDER AND CIGARETTE SMOKING: A NARRATIVE REVIEW

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# The Close Connection between Opioid use Disorder and Cigarette Smoking: A Narrative Review

Joseph V. Pergolizzi, Jr., MD <sup>α</sup>, Peter Magnusson, MD, PhD <sup>σ</sup>, Frank Breve, PharmD <sup>ρ</sup>,  
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**Abstract-** People with opioid use disorder (OUD) have rates of cigarette smoking approaching 90% and smoking cessation programs are rarely effective. The relationship between long-term opioid exposure and smoking has been epidemiologically observed but not well understood. Nicotine interacts with the nicotinic acetylcholine receptors in the central and peripheral nervous systems, which are involved in anxiety, cognition, sleep, arousal, and pain perception. Cigarette smoking triggers the release of dopamine in the brain. There is equivocal evidence that nicotine may have an analgesic effect, but paradoxically, smokers tend to have higher pain intensity levels than nonsmokers. Pharmacologic treatments for nicotine dependence were often studied in trials that routinely excluded subjects with opioid dependence. Further, the association between smoking and long-term opioid use sometimes includes mental health disorders and/or chronic pain. In fact, smoking may also be comorbid with chronic pain. It has been speculated that smoking, particularly at a young age, may be predictive of OUD. While smoking is also associated with other forms of substance abuse, the association between OUD and tobacco is particularly intriguing and likely involves common neurobiological pathways.

## I. INTRODUCTION

People in the United States with opioid use disorder (OUD) have a rate of cigarette smoking of 84% to 94%, many times greater than 14% rate of smoking in the general population.<sup>1</sup> These high rates of smoking occur in those taking illicit opioids, those taking prescription opioids as indicated and under medical supervision, recreational and nonmedical opioid users, and those on opioid maintenance therapy (OMT) with buprenorphine or methadone.<sup>2-5</sup> Among adults seeking treatment for a substance use disorder, smoking prevalence is greater among those with OUD than for

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alcohol or other substance use disorder.<sup>1</sup> While many in these populations express an interest in quitting smoking, the success rate for cessation therapy, even with pharmacologic treatment and clinical supervision, remains low.<sup>6,7</sup>

By the same token, OUD occurs more frequently in daily smokers (2.6%) or nondaily but regular smokers (1.5%) than among non-smokers (0.5%) or never-smokers (0.2%). It has been suggested, and challenged, that cigarette smoking might even be a “gateway drug” to opioid use.<sup>8,9</sup> An algorithm of three statistical predictors for adult OUD were developed in the United States: smoking status, mental health disorder, and nonopioid substance use disorder.<sup>10</sup>

The connection between smoking and OUD has long been clinically observed, but studies have been primarily epidemiologic rather than mechanistic or medical. The primary objective of this narrative review was to survey the literature for an understanding of why there is such a strong association between OUD and smoking and how this might help guide future efforts at opioid rehabilitation and smoking cessation.

## II. METHODS

This is a narrative review on the subject of OUD and smoking aimed at better understanding their mutual association. In October 2021, the PubMed database was searched for the terms “smoking AND opioid use disorder OR OUD” with no delimiters as to type of article or date. A total of 1,078 results were retrieved, of which 100 were randomized clinical trials. Google Scholar was also searched as were the bibliographies of many articles retrieved. The authors excluded articles that were not in English or did not explore the specific association between smoking and OUD. A total of 60 articles were used.

## III. RESULTS

Nicotine, the main alkaloid of the tobacco plant, is a botanical insecticide produced in tobacco leaves and making up about 1.5% of the weight of commercial tobacco.<sup>11</sup> About 99% of nicotine in tobacco occurs as the levorotary X-isomer rather than the R-isomer.<sup>11</sup> When tobacco is burned, nicotine is distilled and may be



transported on particulate matter ("tar") which, when inhaled, enters the lungs. Commercial American cigarettes have a pH of around 5.5 to 6.0, which allows ionization of the nicotine so that there is little buccal absorption.<sup>12</sup> More alkaline types of tobacco, such as pipe tobacco (pH $\geq$ 6.5), can be better absorbed in the mouth.<sup>12</sup> When cigarette smoke reaches the tiny airways and alveoli of the lungs, nicotine is rapidly and directly absorbed into the bloodstream and the alkaline content of liquid in the lungs (~ pH 7.4) allows for rapid membrane transmission. In fact, nicotine can reach the brain in about 10 seconds by smoking a cigarette, which is more rapid than by intravenous administration.<sup>13</sup> Cigarette smoking is self-titrating in real time, because smokers can adjust their nicotine intake with depth of inhalation, amount inhaled per puff, and the rate at which they smoke.<sup>14</sup>

Nicotine has an affinity for brain tissue and smokers have enhanced cerebral receptor capacity compared to nonsmokers, which reverses with smoking cessation.<sup>15</sup> While there are numerous nicotine metabolites, about 80% of all nicotine in humans is converted to the cotinine metabolite in a two-step process. First, nicotine is metabolized via the cytochrome-P (CYP) 2A6 enzyme into the nicotine- $\Delta^{1(5)}$ -iminium ion which exists in equilibrium with the 5'-hydroxynicotine. In the next step, this metabolite is catalyzed by the cytoplasmic aldehyde oxidase.<sup>16</sup> Only about 4% to 7% of nicotine metabolites are the nicotine N'-oxide metabolite.<sup>16</sup> About 10% to 15% of cotinine is excreted unchanged in urine.<sup>17</sup> Total clearance of nicotine takes on average 1200 ml/min and is slower in smokers than nonsmokers.<sup>16,18</sup> Nicotine metabolism is often described as the ratio of 3'-hydroxycotinine to cotinine (3HC) which can be readily tested in blood or saliva.<sup>19</sup> The ratio of 3HC to cotinine has been termed the nicotine metabolite ratio (NMR) and as used as a marker for nicotine activity.<sup>20</sup>

As an alkaloid, nicotine interacts with ion channels in the nicotinic acetylcholine receptors (nAChRs), which are distributed in both central and peripheral nervous systems and handle a range of functions including sleep, anxiety, cognition, arousal, and pain perception.<sup>21</sup> There are two types of nAChR with different structures: neuronal and muscle-type. All nicotinic receptors possess five subunits symmetrically arranged around a central pore. These subunits each possess four transmembrane domains with the N- and C-termini outside of the cell. These receptors act as non-selective ligand-gated ion channels, where the central pore can be opened by agonists, such as endogenous acetylcholine or exogenous nicotine.<sup>21</sup>

Nicotine may have analgesic properties at the nAChRs,<sup>22</sup> as demonstrated in preclinical<sup>23</sup> and clinical studies.<sup>24</sup> Paradoxically, smokers tend to have higher pain intensity levels than nonsmokers and are at increased risk for developing certain painful syndromes,

such as low back pain.<sup>25,26</sup> Functional imaging studies suggest that depression and smoking utilize common neurobiological pathways and are both associated with the release of dopamine in the brain.<sup>27</sup>

Nicotine dependence has been found to be more prevalent among people with mental health disorders and/or substance use disorders.<sup>28</sup> In the United States, people with mental health disorders and/or substance use disorders make up 22% of the total population but consumer 44% of all cigarettes.<sup>28</sup> Nicotine is a sympathomimetic drug that releases catecholamines, accelerates heart rate, enhances cardiac contractility, possesses vasoconstrictive properties, and has been associated with transient increases in blood pressure.<sup>29</sup> Prolonged exposure to a combination of nicotine plus opioids can result in binding to the nicotinic receptors of the neurons that contain opioid peptides, resulting in a release of endogenous opioids.<sup>30,31</sup> Chronic nicotine exposure can disrupt the body's endogenous opioid system, which could result in reduced pain thresholds and cross-tolerance to opioid analgesics.<sup>22</sup> A study based on data from the National Survey on Drug Use and Health (n=58,971) found that smokers who were dependent on opioids were more dependent on nicotine than nonsmokers without opioid dependence.<sup>32</sup> This would explain why smokers need higher doses of opioids compared to nonsmokers to obtain equivalent analgesic benefit.<sup>33,34</sup> Furthermore, chronic nicotine exposure may sensitize dopaminergic systems to opioids.<sup>35</sup> The brain's reward and reinforcement systems involved in the perpetuation of opioid dependence may be enhanced by nicotine.<sup>35</sup>

In general, people who take opioids for medical or nonmedical reasons are more likely to smoke and smoke more cigarettes per day than those who do not take opioids.<sup>20</sup> Nicotine metabolism varies among individuals and NMR values have been associated with specific smoking behaviors.<sup>36</sup> For example, rapid metabolizers of nicotine, as measured with the NMR, tend to smoke more cigarettes per day than slow metabolizers. Women are generally faster nicotine metabolizers than men and this metabolic differential increases during pregnancy.<sup>16,37</sup>

It is not entirely clear why smoking and OUD are so closely associated. It has been suggested that the stimulating effects of nicotine might help fight the sensation of drowsiness and somnolence induced by opioids.<sup>38</sup> In people with OUD and chronic pain, it has been speculated that smoking may distract from painful symptoms, alleviate malaise, and serve as a coping mechanism.<sup>39,40</sup> However, nicotine dependence has been associated with more severe chronic pain symptoms,<sup>41</sup> although smoking was not associated with exacerbated pain intensity immediately following certain types of surgery.<sup>42</sup> This analgesic benefit may be short lived. A retrospective chart review of 178 total hip or

knee arthroplasty patients found that those who smoked required an average of 90% more morphine milligram equivalents (MMEs) in the first three months after surgery than nonsmokers.<sup>43</sup> OUD is comorbid with a number of mental health conditions, including depression, and both are linked to higher rates of smoking but this relationship is not well studied.<sup>34</sup>

It can be challenging for any patient population to quit smoking, but successful smoking cessation is rare among individuals with OUD. There are knowledge gaps in pharmacologic treatments for smoking cessation among people with OUD, as clinical trials of these treatments often excluded those with OUD or those taking buprenorphine or methadone for opioid maintenance therapy (OMT).<sup>44</sup> Despite the fact that the vast majority of individuals with OUD are current smokers and that it is well known that smoking increases morbidity and mortality, most opioid treatment centers do not offer smoking cessation programs.<sup>45</sup> It has been argued that people with OUD and their treatment providers foster a pro-smoking culture and most people with OUD have small social circles where smoking is considered normal and accepted.<sup>46</sup> Indeed, for people struggling to with opioid addiction, a chaotic lifestyle, and other difficult issues, smoking may seem to be a relatively a minor problem. Many people trying to navigate issues of addiction, legal problems, ill health, financial instability, broken relationships, disrupted careers, and numerous other difficulties may find smoking an acceptable stress reliever.

It is likely that certain neuroadaptive interactions between opioids and nicotine make it more difficult for a person exposed long-term to opioids to stop smoking.<sup>47</sup> Individuals with any type of substance use disorder have only about 25% the success rate with smoking cessation than others.<sup>32</sup> It has been suggested that OUD may exacerbate the symptoms of nicotine withdrawal, but evidence is not strong.<sup>48</sup> In adults undergoing rehabilitation for OUD (n=22,046) or alcohol use disorder (n=15,251) at 30 days, cigarette smoking had decreased slightly in the alcohol use disorder population but remained the constant for those with OUD.<sup>49</sup>

In a 24-week study of OUD patients taking buprenorphine or extended-release naltrexone for maintenance, naltrexone patients smoked fewer cigarettes per day on average (11.4) than buprenorphine patients (13.3).<sup>2</sup> In a study of patients taking naltrexone for illicit OUD, smoking was reduced by 29% from 14.4 to 9.8 cigarettes per day at one month and decreased further to 8.6 per day at two months.<sup>50</sup> The role of naltrexone as an effective aid in smoking cessation for people with OUD suggests that there may be a pharmacologic interaction between opioids and nicotine. However, a meta-analysis of eight studies (n>1200) could not find strong evidence in support of the use of naltrexone either alone or as an adjuvant agent in a smoking cessation program, but these

studies were for general patient populations rather than those with OUD.<sup>51</sup>

People with OUD may exhibit different patterns of nicotine dependence than those without OUD.<sup>52</sup> At baseline, smokers with OUD had more severe nicotine withdrawal symptoms than smokers without OUD, but after a two-week smoking cessation program, withdrawal patterns were similar for those with or without OUD. Smokers without OUD experienced a flare in withdrawal symptom intensity right after embarking on a quit-smoking program, a pattern not observed among smokers with OUD, who may have mitigated their early withdrawal symptoms with opioid replacement therapy. Cravings for cigarettes occurred in both groups but those with OUD had diminished cravings at the start of the program, while those without OUD had maximal cravings at the outset.<sup>52</sup>

The age at which smoking started may be correlated to OUD. Those who began to smoke before the age of 14, compared to those who started smoking as adults  $\geq 18$  years, were more than twice as likely to report nonmedical opioid use in the past year.<sup>53</sup> The Youth Risk Behavior Survey conducted in the United States in 2018 (n=10,175), surveyed American adolescents between 12 and 17 years and found 13.8% reported having used opioids recreationally.<sup>54</sup> Adolescents who smoked were more likely to have used opioids; among those young people who reported smoking cigarettes, the adjusted odds ratio for recreational opioid use was 2.49.<sup>54</sup> Even parental smoking increased an adolescent's risk for nonmedical opioid use. In a database study of 35,000 parent-child dyads, in children between the age of 12 and 17, nonmedical use of opioids was more likely to occur in children with parents who smoked, regardless of whether the child smoked.<sup>55</sup>

Many people with OUD express an interest in quitting smoking. A cross-sectional study of 68 patients receiving outpatient buprenorphine maintenance for OUD found that 88% were current smokers, 8% former smokers, and 4% had never smoked. Of those who smoked, 83% had tried to quit at least once.<sup>56</sup> Besides putative opioid-nicotine interactions, there are other barriers to smoking cessation for people with OUD including a lack of access to treatment, limited understanding of smoking cessation tools, prioritization of other more pressing medical and social issues, and lack of insurance.<sup>45</sup> Many smoking cessation treatments rely on nicotine delivered via transdermal patches, sprays, gums, lozenges, or inhalers. However, the experience of nicotine consumption using these methods is vastly different from smoking. The nicotine patch, for example, enters the system gradually, is relatively slow to reach the brain, and cannot be regulated by the user as a smoker might do with deeper puffs.<sup>16</sup> Thus, the use of nicotine replacement therapy may not be as satisfying as smoking.

Opioids are indicated for acute and chronic painful conditions and are sometimes street opioids are taken to self-medicate undiagnosed pain. Chronic pain appears to be associated with cigarette smoking and it is unclear how opioid use factors into this association. In a cross-sectional study from a single European multidisciplinary pain center (n=98), the rate of smoking was double that in the general population and 54% of these pain patients took opioids. Smokers in this population used opioids more frequently and at higher doses than former smokers and nonsmokers.<sup>58</sup> A cross-sectional naturalistic study of 798 adults with chronic noncancer pain taking opioid analgesics medically for  $\geq 6$  months found that 216 developed OUD and the odds ratio adjusted for other risk factors was 14.0 for current smokers to develop OUD.<sup>57</sup> Smoking was not the sole risk factor for a smoker to develop OUD: others were younger age, unmarried status, lower socioeconomic status, less education, and the severity of the pain. In that study, 81% of chronic noncancer pain patients who had OUD were smokers compared to 23% of those who had chronic noncancer pain but did not develop OUD.<sup>57</sup> Smoking rates are higher for those who use either illicit or prescribed opioids. Of patients who receive medically supervised long-term opioid treatment to manage pain, smokers outnumber nonsmokers.<sup>59</sup>

Complicating this picture is the association of chronic pain with depressive symptoms.<sup>34</sup> Chronic pain patients who smoke have significantly higher rates of depression and take more MMEs daily than chronic pain patients who do not smoke.<sup>34</sup> In fact, it has been suggested that smoking may be a predictor of depression in chronic pain patients.<sup>34</sup> Likewise, smoking and chronic pain may be comorbid,<sup>39,60</sup> in that smoking is associated with a greater risk for developing chronic pain and the number of cigarettes smoked per day correlates to the increased risk for chronic pain. Smokers with chronic pain report more numerous pain sites, pain of greater intensity, higher degrees of dysfunction, and more long-term disability than nonsmokers.<sup>22</sup> Nicotine dependence is itself associated with more severe symptoms of chronic pain.<sup>41</sup> Smoking in a chronic pain patient has been proposed as a risk factor for substance use disorder, including OUD.<sup>61</sup> Smoking, prolonged opioid exposure, chronic pain, and depressive symptoms frequently occur concurrently but their exact interplay is not elucidated.

#### IV. DISCUSSION

Opioids are associated with powerful neuroadaptive changes in the brain that can help alleviate pain, stimulate reward circuits, produce euphoria or feelings of well-being, and help soothe anxiety. For those with long-term physiologic dependence, taking opioids can restore feelings of "normalcy" and stave off withdrawal symptoms. Thus, it

is perhaps unrealistic to think of opioids as simply pain relievers, because their psychoactive effects may help mitigate symptoms of mental illness, improve coping skills, and provide pleasure while their physiologic effects still cravings, restore a sense of well-being, prevent distressing symptoms, and stimulate the brain's reward circuits. Cigarette smoking exerts powerful effects on the nicotinic receptors, may release dopamine, and enhance the effects of opioids on the brain. The symbiosis between nicotine and opioid dependence has been epidemiologically observed but trivialized as people with OUD or those on long-term opioid therapy have other medical issues which take precedence. Nevertheless, it must be recognized that nearly all people with OUD as well as the majority who take prescription opioids under medical supervision are smokers and have great difficulty giving up cigarettes. Smokers lose 10 years of life compared to those who have never smoked and smoking is associated with numerous comorbid conditions.<sup>62</sup>

An important special population of those with OUD and nicotine dependence are pregnant women. While about 20% of smokers quit as soon as they learn they are pregnant, the majority of smokers smoke over the course of their pregnancy,<sup>63</sup> even though it is well known that smoking is associated with poor pregnancy outcomes.<sup>64</sup> Nicotine metabolism accelerates during pregnancy, making cessation even more difficult.<sup>37</sup> For this special population, alternative interventions to stop smoking are urgently needed.

Actually, the OUD and chronic opioid therapy population has been generally overlooked in the search for smoking cessation strategies. Many clinical trials of pharmacologic treatments excluded those with OUD. While there may be psychological and social reasons that people with OUD continue to smoke or regard smoking as a low-risk acceptable activity, the association between OUD and smoking likely is based on physiologic factors. It is plausible that smoking enhances some of the pleasurable psychoactive or beneficial analgesic effects of opioids. Discontinuing opioid therapy or rehabilitation from OUD is challenging and relapse is common; smoking is another burden on this population. Better pharmacologic treatments and more effective psychosocial interventions are needed to help patients navigate through these dual dependencies.

Our review of OUD and smoking revealed that it was not only OUD and smoking that were so closely related but also depression and chronic pain. The exact interplay of these conditions remains to be elucidated. Like people with OUD, people with mental health disorders have been historically excluded from clinical trials for pharmacologic smoking cessation treatments.<sup>65</sup> Studies of antidepressants such as bupropion have shown promise for smoking cessation, but this agent is also associated with psychiatric adverse events.<sup>66</sup> There

is also evidence in support of varenicline and nortriptyline to aid in smoking cessation but these agents have not been studied in the population regularly exposed to opioids.<sup>67</sup>

Smoking has also been associated with the use of other substances, such as cocaine or alcohol use disorder. The mechanisms behind these associations are likely to be fundamentally different than the connection between opioids and nicotine. While cocaine users are two to four times more likely to smoke cigarettes than the general population, the enhancement of cocaine's psychoactive effects by nicotine are modest.<sup>68,69</sup> While nicotine appears to only slightly potentiate the pleasurable effects of cocaine, both nicotine and cocaine can result in hypertension and tachycardia, making cigarette smoking particularly dangerous for those using cocaine.<sup>68</sup> It has been suggested that the powerful stimulating effects of cocaine can encourage people to smoke or smokers to smoke more.<sup>70</sup> The association between cigarette smoking and polysubstance drug use disorder remains unknown.

## V. CONCLUSION

While long observed in clinical practice, the underpinnings of the association between prolonged opioid exposure and cigarette smoking have not been elucidated. Nicotine may enhance the reward effect of opioid use and may possess some analgesic properties as well. People taking opioids long term can find it difficult to stop smoking and conventional pharmacologic treatments do not appear to be effective in this population. Further, the link between smoking and opioid use may encompass chronic pain and depression in ways that are not yet clear. Since smoking is associated with significant morbidity and mortality, further study is needed, particularly to assist smokers taking opioids who want to quit. This is an urgent unmet medical need for pregnant OUD patients, most of whom are not able to quit smoking during their pregnancy.

### Disclosures

The authors have no relevant disclosures.

## REFERENCES RÉFÉRENCES REFERENCIAS

- Guydish J, Passalacqua E, Pagano A, et al. An international systematic review of smoking prevalence in addiction treatment. *Addiction* (Abingdon, England). 2016; 111(2): 220-230.
- Montgomery L, Winhusen T, Scodes J, et al. Reductions in tobacco use in naltrexone, relative to buprenorphine-maintained individuals with opioid use disorder: Secondary analysis from the National Drug Abuse Treatment Clinical Trials Network. *J Subst Abuse Treat*. 2021; 130: 108489.
- Haas AL, Sorensen JL, Hall SM, et al. Cigarette smoking in opioid-using patients presenting for hospital-based medical services. *Am J Addict*. 2008; 17(1): 65-69.
- Bastian LA, Driscoll MA, Heapy AA, et al. Cigarette Smoking Status and Receipt of an Opioid Prescription Among Veterans of Recent Wars. *Pain medicine* (Malden, Mass). 2017; 18(6): 1089-1097.
- Chapman SL, Wu LT. Associations between cigarette smoking and pain among veterans. *Epidemiol Rev*. 2015; 37(1): 86-102.
- Zirakzadeh A, Shuman C, Stauter E, Hays JT, Ebbert JO. Cigarette smoking in methadone maintained patients: an up-to-date review. *Curr Drug Abuse Rev*. 2013; 6(1): 77-84.
- Miller ME, Sigmon SC. Are Pharmacotherapies Ineffective in Opioid-Dependent Smokers? Reflections on the Scientific Literature and Future Directions. *Nicotine & Tobacco Research*. 2015; 17(8): 955-959.
- Rajabi A, Dehghani M, Shojaei A, Farjam M, Motevalian SA. Association between tobacco smoking and opioid use: A meta-analysis. *Addict Behav*. 2019; 92: 225-235.
- Vanyukov MM. A Gateway That Never Was. *Behav Genet*. 2021.
- Wagner NM, Binswanger IA, Shetterly SM, et al. Development and validation of a prediction model for opioid use disorder among youth. *Drug Alcohol Depend*. 2021; 227: 108980.
- Armstrong DW, Wang X, Ercal N. Enantiomeric composition of nicotine in smokeless tobacco, medicinal products, and commercial reagents. *Chirality*. 1998; 10(7): 587-591.
- Gori GB, Benowitz NL, Lynch CJ. Mouth versus deep airways absorption of nicotine in cigarette smokers. *Pharmacol Biochem Behav*. 1986; 25(6): 1181-1184.
- Benowitz NL. Clinical pharmacology of inhaled drugs of abuse: implications in understanding nicotine dependence. *NIDA Res Monogr*. 1990; 99: 12-29.
- Jarvis MJ, Boreham R, Primatesta P, Feyerabend C, Bryant A. Nicotine yield from machine-smoked cigarettes and nicotine intakes in smokers: evidence from a representative population survey. *J Natl Cancer Inst*. 2001; 93(2): 134-138.
- Breese CR, Marks MJ, Logel J, et al. Effect of smoking history on [3H]nicotine binding in human postmortem brain. *J Pharmacol Exp Ther*. 1997; 282(1): 7-13.
- Benowitz NL, Hukkanen J, Jacob P, 3rd. Nicotine chemistry, metabolism, kinetics and biomarkers. *Handb Exp Pharmacol*. 2009(192): 29-60.
- Benowitz NL, Jacob P, 3rd, Fong I, Gupta S. Nicotine metabolic profile in man: comparison of cigarette smoking and transdermal nicotine. *J Pharmacol Exp Ther*. 1994; 268(1): 296-303.



18. Benowitz NL, Jacob P, 3rd. Nicotine and cotinine elimination pharmacokinetics in smokers and nonsmokers. *Clin Pharmacol Ther.* 1993; 53(3): 316-323.
19. Dempsey D, Tutka P, Jacob P, 3rd, et al. Nicotine metabolite ratio as an index of cytochrome P450 2A6 metabolic activity. *Clin Pharmacol Ther.* 2004; 76(1): 64-72.
20. Oncken C, Mead EL, Dornelas EA, et al. Opioid Use and Rate of Nicotine Metabolism Among Pregnant Smokers. *Nicotine Tob Res.* 2020; 22(6):1046-1050.
21. Taly A, Corringer PJ, Guedin D, Lestage P, Changeux JP. Nicotinic receptors: allosteric transitions and therapeutic targets in the nervous system. *Nat Rev Drug Discov.* 2009;8(9):733-750.
22. Shi Y, Weingarten TN, Mantilla CB, Hooten WM, Warner DO. Smoking and pain: pathophysiology and clinical implications. *Anesthesiology.* 2010; 113(4): 977-992.
23. Tripathi HL, Martin BR, Aceto MD. Nicotine-induced antinociception in rats and mice: correlation with nicotine brain levels. *J Pharmacol Exp Ther.* 1982; 221(1): 91-96.
24. Fertig JB, Pomerleau OF, Sanders B. Nicotine-produced antinociception in minimally deprived smokers and ex-smokers. *Addict Behav.* 1986; 11(3): 239-248.
25. Andersson H, Ejlertsson G, Leden I. Widespread musculoskeletal chronic pain associated with smoking. An epidemiological study in a general rural population. *Scand J Rehabil Med.* 1998; 30(3): 185-191.
26. Mustard CA, Kalcevic C, Frank JW, Boyle M. Childhood and early adult predictors of risk of incident back pain: Ontario Child Health Study 2001 follow-up. *Am J Epidemiol.* 2005; 162(8): 779-786.
27. Brody AL, Olmstead RE, Abrams AL, et al. Effect of a history of major depressive disorder on smoking-induced dopamine release. *Biol Psychiatry.* 2009; 66(9): 898-901.
28. Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: A population-based prevalence study. *Jama.* 2000; 284(20): 2606-2610.
29. Benowitz NL. Cigarette smoking and cardiovascular disease: pathophysiology and implications for treatment. *Prog Cardiovasc Dis.* 2003;46(1):91-111.
30. Hadjiconstantinou M, Neff NH. Nicotine and endogenous opioids: neurochemical and pharmacological evidence. *Neuropharmacology.* 2011; 60(7-8): 1209-1220.
31. D'Souza MS. Neuroscience of nicotine for addiction medicine: novel targets for smoking cessation medications. *Prog Brain Res.* 2016; 223: 191-214.
32. Parker MA, Streck JM, Sigmon SC. Associations between opioid and nicotine dependence in nationally representative samples of United States adult daily smokers. *Drug Alcohol Depend.* 2018; 186: 167-170.
33. Ackerman WE, 3rd, Ahmad M. Effect of cigarette smoking on serum hydrocodone levels in chronic pain patients. *J Ark Med Soc.* 2007; 104(1): 19-21.
34. Hooten MW, Shi Y, Gazelka HM, Warner DO. The effects of depression and smoking on pain severity and opioid use in patients with chronic pain. *Pain.* 2011; 152(1): 223-229.
35. Vihavainen T, Piltonen M, Tuominen RK, Korpi ER, Ahtee L. Morphine-nicotine interaction in conditioned place preference in mice after chronic nicotine exposure. *Eur J Pharmacol.* 2008; 587 (1-3): 169-174.
36. Schnoll RA, George TP, Hawk L, Cinciripini P, Wileyto P, Tyndale RF. The relationship between the nicotine metabolite ratio and three self-report measures of nicotine dependence across sex and race. *Psychopharmacology.* 2014; 231(12): 2515-2523.
37. Kranzler HR, Washio Y, Zindel LR, et al. Pregnant Smokers Receiving Opioid Agonist Therapy Have an Elevated Nicotine Metabolite Ratio: A Replication Study. *Nicotine Tob Res.* 2020; 22(10): 1923-1927.
38. Young-Wolff KC, Klebaner D, Weisner C, Von Korff M, Campbell CI. Smoking Status and Opioid-related Problems and Concerns Among Men and Women on Chronic Opioid Therapy. *Clin J Pain.* 2017; 33(8): 730-737.
39. Ditte JW, Brandon TH, Zale EL, Meagher MM. Pain, nicotine, and smoking: research findings and mechanistic considerations. *Psychol Bull.* 2011; 137(6): 1065-1093.
40. Ditte JW, Zale EL, Kosiba JD, Zvolensky MJ. A pilot study of pain-related anxiety and smoking-dependence motives among persons with chronic pain. *Exp Clin Psychopharmacol.* 2013; 21(6): 443-449.
41. Weingarten TN, Moeschler SM, Ptaszynski AE, Hooten WM, Beebe TJ, Warner DO. An assessment of the association between smoking status, pain intensity, and functional interference in patients with chronic pain. *Pain Physician.* 2008; 11(5): 643-653.
42. Montbriand JJ, Weinrib AZ, Azam MA, et al. Smoking, Pain Intensity, and Opioid Consumption 1-3 Months After Major Surgery: A Retrospective Study in a Hospital-Based Transitional Pain Service. *Nicotine Tob Res.* 2018; 20(9):1144-1151.
43. Cryar KA, Hereford T, Edwards PK, Siegel E, Barnes CL, Mears SC. Preoperative Smoking and Narcotic, Benzodiazepine, and Tramadol Use are Risk Factors for Narcotic Use after Hip and Knee Arthroplasty. *J Arthroplasty.* 2018; 33(9): 2774-2779.
44. Vlad C, Arnsten JH, Nahvi S. Achieving Smoking Cessation Among Persons with Opioid Use Disorder. *CNS drugs.* 2020; 34(4): 367-387.



45. Knudsen HK, Studts JL. Availability of nicotine replacement therapy in substance use disorder treatment: longitudinal patterns of adoption, sustainability, and discontinuation. *Drug Alcohol Depend.* 2011; 118(2-3): 244-250.
46. de Dios MA, Stanton CA, Caviness CM, Niaura R, Stein M. The social support and social network characteristics of smokers in methadone maintenance treatment. *Am J Drug Alcohol Abuse.* 2013; 39(1): 50-56.
47. Martin RA, Rohsenow DJ, Tidey JW. Smokers with opioid use disorder may have worse drug use outcomes after varenicline than nicotine replacement. *J Subst Abuse Treat.* 2019; 104:22-27.
48. Streck JM, Sigmon SC, Priest J, et al. Investigating tobacco withdrawal in response to reduced nicotine cigarettes among smokers with opioid use disorder and other vulnerabilities. *Exp Clin Psychopharmacol.* 2020; 28(6): 714-723.
49. Eastwood B, Clare T, Dockrell MJ, et al. Reciprocal influences of tobacco use on illicit opioid and alcohol use during the first six-months of specialist addiction treatment. *Drug Alcohol Depend.* 2021; 218: 108418.
50. Wang AL, Shi Z, Elman I, Langleben DD. Reduced cigarette smoking during injectable extended-release naltrexone treatment for opioid use disorder. *Am J Drug Alcohol Abuse.* 2020; 46(4): 472-477.
51. David SP, Lancaster T, Stead LF, Evins AE, Prochaska JJ. Opioid antagonists for smoking cessation. *Cochrane Database of Systematic Reviews.* 2013(6).
52. Streck JM, Heil SH, Higgins ST, Bunn JY, Sigmon SC. Tobacco withdrawal among opioid-dependent smokers. *Exp Clin Psychopharmacol.* 2018; 26(2): 119-124.
53. Zale EL, Dorfman ML, Hooten WM, Warner DO, Zvolensky MJ, Ditte JW. Tobacco Smoking, Nicotine Dependence, and Patterns of Prescription Opioid Misuse: Results from a Nationally Representative Sample. *Nicotine Tob Res.* 2015; 17(9): 1096-1103.
54. Barnett TE, Thompson EL, Litt DM, Lewis MA. Correlates of Nonmedical Prescription Opioid Use Among U.S. Adolescents. *Am J Prev Med.* 2019; 57(5):e175-e179.
55. Griesler PC, Hu MC, Wall MM, Kandel DB. Nonmedical Prescription Opioid Use by Parents and Adolescents in the US. *Pediatrics.* 2019; 143(3).
56. Shah PA, Cunningham CO, Brisbane MT, DeLuca JP, Nahvi S. Use of Smoking Cessation Methods Among Patients Receiving Office-based Buprenorphine Maintenance Treatment. *J Addict Med.* 2017; 11(6):494-497.
57. Cheattle MD, Falcone M, Dhingra L, Lerman C. Independent association of tobacco use with opioid use disorder in patients of European ancestry with chronic non-cancer pain. *Drug Alcohol Depend.* 2020; 209: 107901.
58. Plesner K, Jensen HI, Højsted J. Smoking history, nicotine dependence and opioid use in patients with chronic non-malignant pain. *Acta Anaesthesiol Scand.* 2016; 60(7): 988-994.
59. Dobscha SK, Morasco BJ, Duckart JP, Macey T, Deyo RA. Correlates of prescription opioid initiation and long-term opioid use in veterans with persistent pain. *Clin J Pain.* 2013; 29(2):102-108.
60. Zvolensky MJ, McMillan K, Gonzalez A, Asmundson GJ. Chronic pain and cigarette smoking and nicotine dependence among a representative sample of adults. *Nicotine Tob Res.* 2009; 11(12): 1407-1414.
61. Fishbain DA, Cole B, Lewis JE, Gao J. Is smoking associated with alcohol-drug dependence in patients with pain and chronic pain patients? An evidence-based structured review. *Pain medicine (Malden, Mass).* 2012; 13(9): 1212-1226.
62. Jha P, Ramasundarahettige C, Landsman V, et al. 21st-century hazards of smoking and benefits of cessation in the United States. *N Engl J Med.* 2013; 368(4):341-350.
63. Solomon L, Quinn V. Spontaneous quitting: self-initiated smoking cessation in early pregnancy. *Nicotine Tob Res.* 2004; 6 Suppl 2: S203-216.
64. Rogers JM. Tobacco and pregnancy. *Reprod Toxicol.* 2009; 28(2):152-160.
65. Talukder SR, Lappin JM, Boland V, McRobbie H, Courtney RJ. Inequity in smoking cessation clinical trials testing pharmacotherapies: exclusion of smokers with mental health disorders. *Tobacco control.* 2021.
66. Howes S, Hartmann-Boyce J, Livingstone-Banks J, Hong B, Lindson N. Antidepressants for smoking cessation. *Cochrane Database of Systematic Reviews.* 2020(4).
67. Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database of Systematic Reviews.* 2014(1).
68. Brewer AJ, 3rd, Mahoney JJ, 3rd, Nerumalla CS, Newton TF, De La Garza R, 2nd. The influence of smoking cigarettes on the high and desire for cocaine among active cocaine users. *Pharmacology, biochemistry, and behavior.* 2013; 106: 132-136.
69. Kalman D, Morissette SB, George TP. Co-morbidity of smoking in patients with psychiatric and substance use disorders. *Am J Addict.* 2005; 14(2): 106-123.
70. Roll JM, Higgins ST, Tidey J. Cocaine use can increase cigarette smoking: evidence from laboratory and naturalistic settings. *Exp Clin Psychopharmacol.* 1997; 5(3): 263-268.

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# A Practical Approach of Central Monitoring Management System that Ensure Mask Wear to Prevent the Spread of COVID-19 in Bangladesh

By Shaznin Sultana, Raisa Tahsin Taspia, Sadia Afreen, Nafiz Al Asad  
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**Abstract-** The infectious spread of corona-virus disease (COVID-19) has been prevailing in more than two hundred countries and causing millions of deaths worldwide. The pandemic has wreaked havoc in all sectors of life. Since COVID-19, the most common and effective preventive measure to control the transmission has been to wear face masks. With the decline of infectious virus cases in most countries due to vehement vaccination programs, people are now reluctant to wear masks. However, the recent variants of the virus, such as Delta, Omicron, etc., have proven to be resistant to a degree against vaccines. So, there is no alternative to wearing masks to protect ourselves and those around us. The proposed work in this paper implements a full-proof automated system to detect whether a person has worn a mask and warns the person if he has not.

**Keywords:** facemask, COVID-19, consciousness, public health, MAC, hash.

**GJMR-K Classification:** DDC Code: 616.2 LCC Code: RC776.S27



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# A Practical Approach of Central Monitoring Management System that Ensure Mask Wear to Prevent the Spread of COVID-19 in Bangladesh

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**Keywords:** facemask, COVID-19, consciousness, public health, MAC, hash.

## 1. INTRODUCTION

COVID-19 is a highly infectious disease with an extreme morbidity rate. The key reasons behind the recent drop in infection rates is public health awareness by wearing masks, social distancing, country lockdown, travel bans, etc. However, it is impossible for a country with limited resources such as Bangladesh to carry on with extreme preventive measures. Hence, it is strongly recommended to wear masks as it is the easiest and the most effective safety measure for

stopping the spread of the virus. Face masks could be effectively used as a preventive measure in a COVID-19 pandemic [1]. Vaccination percentages have risen; however various strains of the COVID virus continue to spread the disease since people became careless and believed that vaccination might be the only means of protecting themselves [2]. Simultaneously, we must take action to reduce transmission while expanding vaccination coverage. It is accomplished with simple instructions, such as using a well-fitted mask. Right now, the most critical issue is to make sure you do not even get vulnerable to infection. In the proposed system, the person detected without a mask must be notified, which is done securely. The captured photo of the person is sent to the NID database to compare, and the personal information of the said person must be sent back to the system in an authentic way. Consequently, the proposed method generates message authentication codes to encrypt the user's data and verify the data alteration by a virus or a third party. After proper verification, the system notifies the person via email and warns about the further actions to take if they continue to be unwilling to wear masks. Thus, the study proves to be a protected system that ensures the wearing of masks by the public as a safety measure against the COVID-19 pandemic.

### a) Problem Statement

With the frequent detection of more infectious COVID-19 variants, it is vital to wear masks for minimizing COVID-19 expansion effectively. However, citizens are not sufficiently conscious of the risks, and are reluctant to wear masks. Therefore, this research implements a system that ascertains citizens wearing masks by detecting mask-free individuals. It also warns them, followed by penalization if necessary. The system uses authenticated encryption or tag creation approach, thus making the system exceptionally secured.

### b) Rationale of the study

Like the entire world, Bangladesh was able to control corona-virus outbreaks with maintaining lockdowns, medications, and public awareness campaigns. The arrival of the Covid-19 epidemic has inflicted a massive blow on Bangladesh's economy. But lockdown, vaccine activities are not a permanent solution to prevent covid-19.

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<sup>1</sup> The preliminary version of this work has been published into ETSN, SCRIIP [17]

While vaccination can be a viable solution, in this scenario, public perception makes it insufficient. The public's dissatisfaction stems mostly from vaccination side effects, limited efficacy, and unavailability. On the other hand, a prolonged lockdown would be the prudent choice for most governments in these increasingly dire conditions. Because of the lengthy country-wide lockdown, the global economic crisis, and the resulting disruption of demand and supply chains, the economy is likely to experience a prolonged slowdown in recent months. Moreover, people of Bangladesh are not conscious enough about wearing facemasks. Results from unbiased research involving a large number of participants in various Bangladeshi locations show that wearing masks can prevent the spread of Covid-19. Despite the dismal outcome, the studies demonstrate how important face masks are. Face masks have been shown to drastically prevent severe infections in the older population [3]. Other than that, MAC is used to authenticate NID data in this system. The usage of hash functions and symmetric encryption is widespread.

#### c) *Research objectives*

The study's main goal is to raise public awareness of COVID-19 outbreaks in order to reduce outbreaks. As a result, the system's primary goal is to send warnings and fines to the non-mask bearing persons or maintain enough awareness. As vaccination can not provide entire protection. Our primary objective is to slow the alarming progression of COVID cases. However, this technologies might also be used to track and act in other areas. NID data is used to identify individuals and must be kept safe since it contains sensitive information. For authentication, we used MAC, an established way for secure communication. The objective is to maintain NID data security and no erroneous identification during the system application procedure. The motive is to design a system that will be suitable for Bangladesh and other overcrowded countries.

- Limiting the COVID dispersion
- Those who do not use masks are being tracked down and penalized to increase awareness.
- The use of MAC ensures that no personally identifiable information is accessed or manipulated, and that authentication and consent are maintained.

## II. BACKGROUND

This section provides a detailed discussion of related works on COVID-19 dissemination, mask ensuring works were previously done, NID security and MAC in security.

This paper presents an analysis of the current COVID-19 condition in Bangladesh, as well as some recommendations on how the government could address the crisis. Considering its economic position,

Bangladesh is fighting the disease's spread. Almost all country has embraced nontherapeutic methods, but there is a continuous discussion about whether they have been adequately understood and applied. Bangladesh being a low-middle-income country, is subjected to several regulations aiming at minimizing the virus's spreading. This research focused solely on the medical situation in Bangladesh and the constraints in preventing the development of COVID [17]. It depicted the entire COVID condition in Bangladesh, as well as the irresponsibility of people who were not wearing masks. While maintaining the lockdown at all costs with increasingly stringent maintenance, the country is confronted with severe problems. As a result, a new viable approach may be able to reduce the rising COVID problem. Considering the circumstances in Bangladesh, no other model was presented [3].

COVID-19 and other respiratory problems have been studied in the past using a model. In this approach, behaviors like wearing masks and being alone may be measured and interpreted. This model demonstrated a number of things, including how transmission risk and the distance between two linked up people [6].

Their research indicates that broad public usage of face masks could be highly beneficial in reducing communal dissemination and crisis impact. Face masks are estimated to have the most community-wide advantages if used in association with non-pharmaceutical techniques and when adoption is almost uniform, and concordance is strong [7].

In the previous study on NID concerns, the publication "Security Concerns with National ID Cards" introduced three major components of NID. The pros and limitations of a National ID card were covered in the first section, followed by a discussion of its security features and finally a look at prospective threats and their impacts. The threats are detailed in the security analysis section. Many modern technologies, such as ID cards, have faults that need to be considered. Man-in-the-middle attacks, skimming assaults, and authorized personnel have abused the system are all examples of data falsification. Most of the confidential information is disclosed unintentionally - and occasionally intentionally - by the general populace which demonstrates the importance of NID data protection. The purpose of this study is to examine the defining characteristics of national ID cards, the security characteristics of resident ID cards, potential risks, and access controls [5].

Entities from across the world are attempting to grow the maximum cyber security mechanism. The information they convey is usually highly secretive which can be misused. Today, information security is becoming highly significant. To verify the validity of messages, the MAC technique uses a symmetric key cryptography strategy. The MAC approach uses a symmetric key cryptography strategy to check message



correctness. To keep the MAC process running, the sender and receiver exchange a symmetric key  $K$ . A message authentication code (MAC) is a cryptographic checksum created on the core message and sent with it to ensure message legitimacy. [4]. Message authentication and integrity are included in the security characteristics of message transmission. Examples of practical MAC applications include the Internet of Things, where GSM is used for networking, smart meters, and health parameter tracking.

### III. THEORETICAL FRAMEWORK

The implementation of this work is intended for major road crossings [17]. The system's data is arranged into two tables. These are referred to as the Local Server and the NID Server. Even though the system is based on real-time data, the data on the servers is drawn from practical scenarios. The initial function of this system to identify those who are not wearing a mask. The live camera will be looking over everyone's face while they travel along the road. The camera is deliberately placed at a major junction. Individuals without masks will be identified and captured using image processing algorithms. Following that, the image is compared to pictures stored on our local server database to determine personal information of the person. This storage is for the purpose of not accessing the NID server more than once for the same person. So, for instance, suppose that the image does not correspond to anyone in the database. The info is sent to the national identity card server, which keeps track of sensitive personal data for all NID users. Obtained image is compared to the images stored on this server. Name, NID number, and some details of that person are transmitted to the local server which is promptly identified.

A symmetric approach is selected to provide secure communication. The whirlpool method is used in this system to ensure that personal details such as NID numbers, names, contacts, and mailing addresses is not altered with. After that, it will engender an authentication code for the message. When this MAC identifier is combined with the personal information to be communicated, it is delivered to the sender's side, which is our own local server. On the receiving end, the MAC is evaluated to ensure that the data is genuine and allowed. A tag is computed when the information is sent into the tag generation algorithm. Those who possess the secret key are the only ones who can authenticate the tag. The Diffie-Hellman Key Exchange protocol is required for generating this shared secret key. The information received is removed if the tag is not valid; if the tag is legitimate, Personal information is stored on a local server for onward purpose. If an attacker attempts to fake personal information, it will be impossible and will be identified because of the security measures in

place. Following the tag validation, the email address associated with the tag will receive a warning message. For getting caught more than twice, he will receive an email containing a penalty alert. People are charged in this manner. Because of this, they are more conscientious about wearing masks, which is precisely what this approach is designed to do. In addition, the flow diagram of the suggested system is depicted in Figure 2.1: [17]



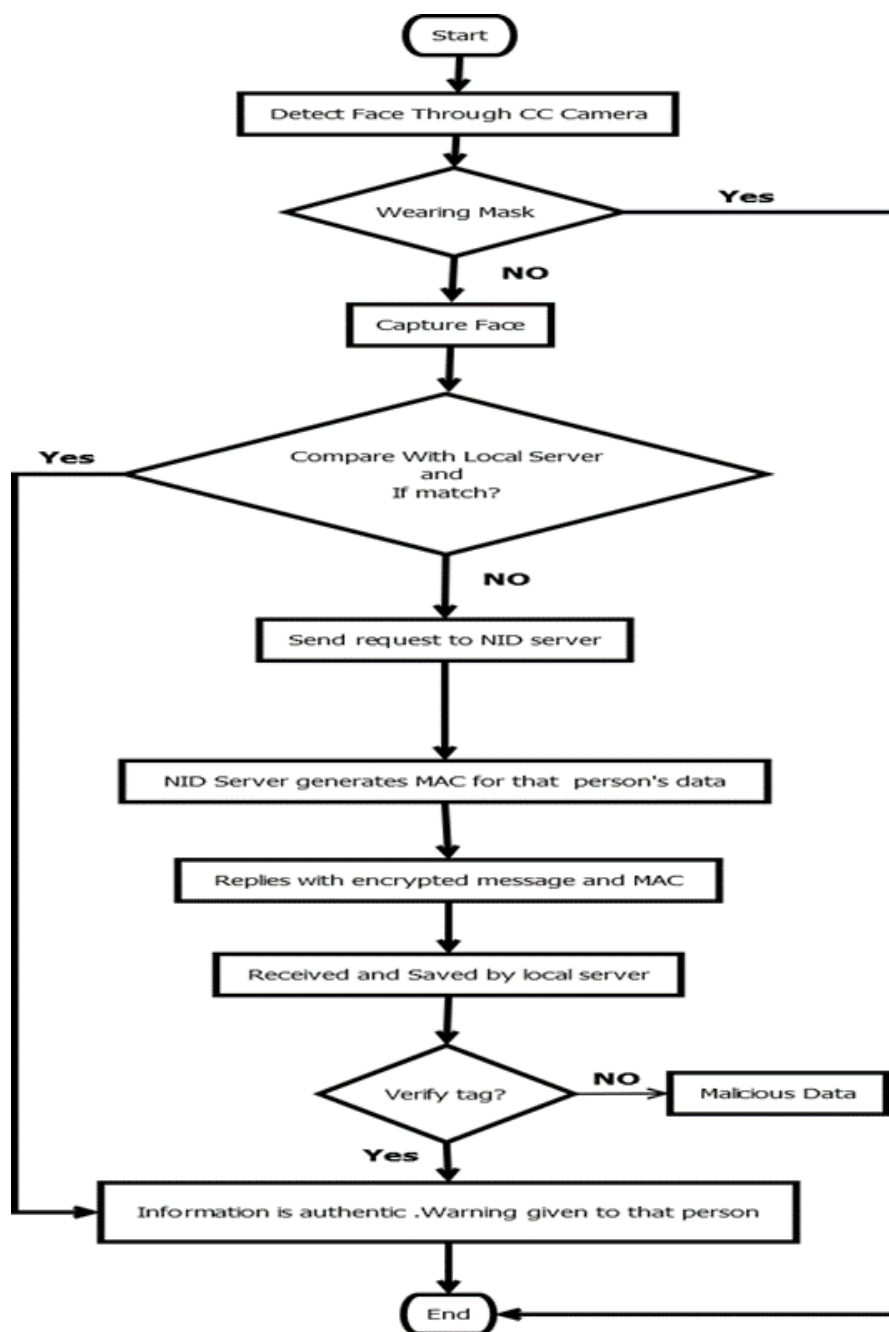


Fig. 2.1: A flow diagram depicting the proposed system's workflow [17]

#### IV. RESEARCH METHODOLOGY

This chapter covers the several approaches utilized in the procedure, data collection, and analysis pertinent to the work. It will incorporate the work sequence, research design, frameworks, data gathering, and security management.

The system implementation has been conducted in a series of steps. A general model diagram depicts the system implementation design (figure 2.2) [17].

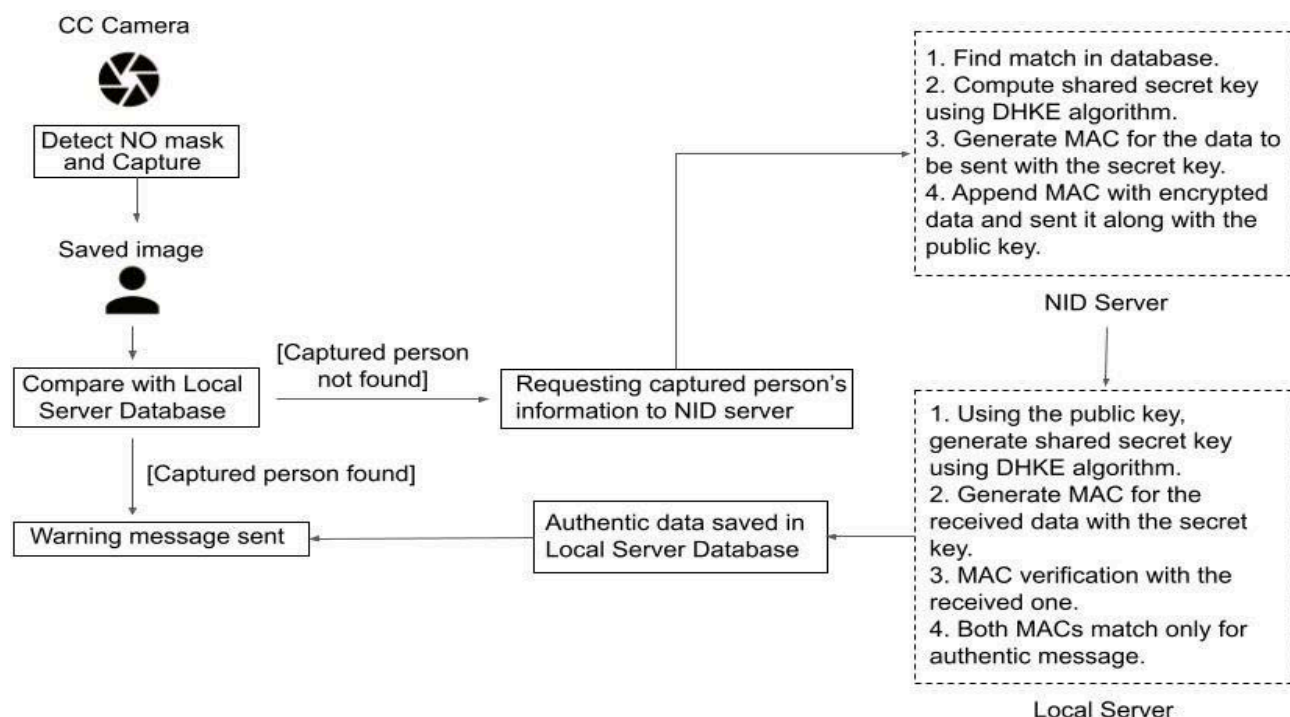


Fig. 2.2: General structure of the system [17]

This section depicts the critical components of a progressive approach. The tasks are conducted via three modules which are described below in detail.

The first step is to capture the individuals without a mask on their faces. To send a notice statement, the photo is matched to its local server for personal details. For subsequent interaction with NID server, a socket connection is made if the image could not be resembled. The person's data is collected by the local server. When they find the necessary details, these are securely sent to the local server using the MAC (Message Authentication Code) and NID details. The MAC is checked at the system's local server on the receiver section. As an outcome, the local server sends an email notification to the guilty.

#### 1) Face Mask Detection

The main functionalities of this module are:

- To recognize individuals who might not be wearing a mask.
- Take a photo of the individual's face.

Using Python, Keras, and OpenCV, a code for face mask identification is constructed within this module. The mask scanner algorithm is being designed to assess whether or not someone is putting a mask. Face detection is intended to evaluate whether any faces are viewable in a photograph or film footage. Face detection finds a face in an image. A face detector locates any uncovered individual recognized by the system, subsequently detected by a facemask recognizer. A face, mask, and other ratios are recognized by this module. Keras is a deep learning

framework with a high-level interface [9]. When there are multiple faces, a bounded rectangle surrounds each one so we know where they are. Captured face image is sent to the server to find out the person's identity.

#### 2) Local Server

The main functionalities of the local server are:

- Comparing the image collected with those in the directory.
- If information isn't available in this database, contact the national id server.
- That person receives a warning notice.
- To validate the message authentication code, construct a shared private key.

Local server is a database containing names, national identity card (NID) numbers, NID images, E-mail addresses of those who have been found guilty of not using masks in the past. The dataset is prepared with XAMP for trial objectives. As soon as the person with no mask is detected and captured through the CC camera, it is matched with the database whether it is already there which is finding out if the person has been caught before. If not, the image is transmitted to the NID server for more information. Socket programming is used to make a link here between NID server and the local server and to convey warning mails. The tag is confirmed after the NID feedback is gathered. The verification algorithm will be applied to the received message to get its corresponding tag and compared to the received tag. The authenticity of the communication is ensured by matching the tags. If not, the data will be erased.

### 3) NID Server

The main functionalities of the NID server are:

- The requested records are securely delivered in response to a request from the local server.
- Compute shared secret key for tag generation.
- Addition to creating a message authentication code and concatenate it to the message to be delivered.

The NID server in this case is a dummy dataset built with XAMP and fifty data records for demonstration reasons, which holds all of the personally identifiable information of national ID holders in the country. A connection is established with the local server for requesting the details of the person in the captured image. It then analyzes the two images and looks for information. As soon as the person is found, their NID number, name, and email address are sent to the local server. A message authentication code (MAC) is generated and appended to the encrypted message to be sent.

## V. RESULT DISCUSSION

The purpose of this chapter is to present an observation of the experimental data obtained using the constructed model. This portion also discusses the outcome of each phase and the method that we employed in our model.

The shared secret key is calculated at first using the Diffie Hellman Key Exchange protocol. This system utilizes Diffie-Hellman Key Exchange to distribute a shared secret key producing the private keys of both the source and the destination. The Whirlpool algorithm is used to encrypt the message and construct the tag. Whirlpool is a block cipher that encrypts data with 512-bit blocks and a 512-bit key. Tags are generated using

this shared secret key. The message is attached with the Message Authentication Code (MAC) and sent to the local server from the NID server. We used a socket connection between the NID server and the local server for requesting and transmission of data. Socket programming is used to establish a connection between two network nodes. The link is connected on both ends [13]. The first steps in socket programming are to import the socket library and create a simple socket. Both endpoints of the link are connected. Warning messages at the last step are also sent via socket programming [14]. The receiver side, which indicates the local server, follows the same approach. The same implementation is used to generate the MAC compared to the MAC obtained from the sender-NID server. As soon as the authentication is completed, the local server verifies the message's authenticity and saves it in the database for later alerting notifications.

The purpose of using MAC is validation of data transmission. A MAC is a hash function that utilizes a secret key as well as the data as input, and the security protection constraint is that estimating the tag value of the data without the key should be operationally challenging [10]. The MAC estimations yield an error in the data if the original message is altered throughout transmission. Message authentication and message integrity are offered as security facilities for communication processes [11]. The tag formation mechanism employed in this system is derived from the PGV compression function [12].

#### a) No mask detection

When someone approaches the machine without wearing a mask, the machine identifies this and snaps a photo of them.

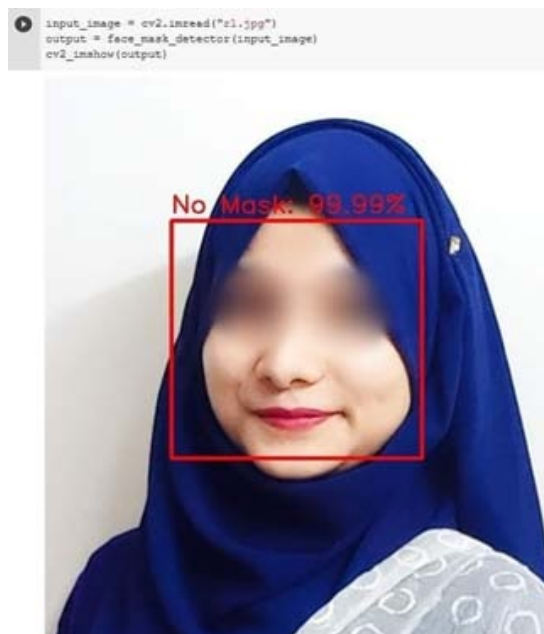


Fig. 3.1: No mask detected

### b) Local Server

A picture that is taken at the start will be compared to the one that is already on its own server. If the picture is found in the database, it email to the

person's email address warning them about the picture and what to do. If the image cannot be found on the local server, then the image will be sent to the NID Server for more information about what it is.

No	Image	Name	NID	MailID	ConcatenateMessage	MacValue
1	[BLOB - 7.3 KIB]	ARSHIA HABIB	7184456708	arshia@gmail.com	ArshiaHabib7184456708arshia@gmail.com	E1x17Vix0...
2	[BLOB - 13.3 KIB]	MD. MUMINUL BARI	6184456708	mumin@gmail.com	MDMuminulBar6184456708mumin@gmail.com	zjrx10[PnDXISDQ...
3	[BLOB - 5.6 KIB]	FOYSAL AL GABID	5151856708	foysal@gmail.com	FoysalAlGabid5151856708foysal@gmail.com	tr_Mix16x07[...
4	[BLOB - 3.6 KIB]	MD. Sujaur Rahman	6454310268	suja@gmail.com	MdSujaurRahman6454310268suja@gmail.com	trix02ID*SBGdP...
5	[BLOB - 105.8 KIB]	Shaznin Sultana	6490576885	shaznin22@gmail.com	ShazninSultana6490576885shaznin22@gmail.com	trixRL*idB*12x...
6	[BLOB - 178.5 KIB]	Sadia Aftreen	5090306855	sadia13@gmail.com	SadiaAftreen5090306855sadia13@gmail.com	trix03Q\$5vPx11...
7	[BLOB - 6.2 KIB]	MD. SAJJAD HOSSAIN SAWRAN	5183456902	sawran@gmail.com	MD.SajjadHossainSawran5183456902sawran@gmail.com	trix00x0e*PWYx...
8	[BLOB - 12.2 KIB]	MEHEDI RIDOY	7403275517	rido06@gmail.com	MehediRido7403275517rido06@gmail.com	trixQV5ix08aW...

Fig. 3.2: Local server

Using socket programming, the NID server connects to the local server.

### c) Socket Successfully Establish

```
c, addr = s.accept()
print ('Got connection from', addr )

# send a thank you message to the client. encoding to send byte type.
c.send(bytes('Thank you for connecting'),'utf-8')
```

Fig. 3.3: Connection setup



Fig. 3.4: Socket establishment

### d) NID Server to Compare Detected Image

Image captures are forwarded to NID if they cannot be found local server. After comparing the NID

image to the captured image, the next step is to proceed to the next step.

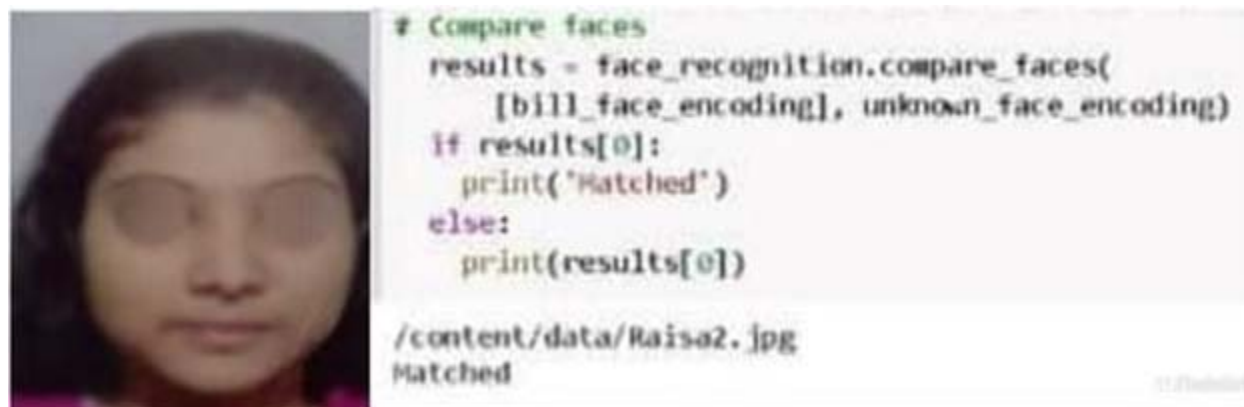


Fig. 3.5: Matched with NID server



The NID server's data is extremely private and crucial. During the system application process, the purpose is to keep NID data secure. A MAC is produced to send the NID data securely to the local server. It is

important to have a common shared key when creating a MAC. Using the Diffie-Hellman key exchange method, a shared key is created.

➡ The Value of P is :999999999989  
The Value of G is :999999937  
The Private Key a for Alice is :999999936  
The Private Key b for Bob is :999999935  
661161930946  
661161930946

Fig. 3.6: Key generated using Diffie-Hellman algorithm

The NID server will send this concatenated information to the local server using the key and whirlpool encrypted message.

No	Image	Name	NID	FathersName	MothersName	DateOfBirth	MailID	MacValue
1	[BLOB - 6.2 KiB]	MD. SAJJAD HOSSAIN SAWRAN	5183456902	ABDUL MALEK	SOKINA KHATUN	31-12-1998	sawran@gmail.com	b'1L'w00x0e*PwYv0cGFpX01v03X03P0x...
2	[BLOB - 13.3 KiB]	MD. MUMINUL BARI	6184456708	MANIK MIA	ASIA KHTUN	13-09-1999	mumin@gmail.com	b'z0x10PnDxSDQv06v04R0x05u0eQ0x014X0...
3	[BLOB - 66.8 KiB]	RAISA TAHSIN TASPIA	5276209108	MD. NURUL AFSAR	GULSHAN ARA KHANOM	22-01-1999	raisa@gmail.com	b'cXVx10YIPQAIj0Ux15x11XUx03x01v05Sx03T_...
4	[BLOB - 9.5 KiB]	TARANNUM TORI	8184456708	TAHVIDUL ISLAM	AFROZA KHAN	21-03-1998	Tori123@gmail.com	b'bTEWW0x17qT0x17Y0x0b01x01v03v0x01R0x02...
5	[BLOB - 6.7 KiB]	EMRUL MINHAZ	1844567087	EMDADUL HAQUE	MONI AKTER	19-10-1997	emrul@gmail.com	b'Ux17x11Yx7f0r0Ux1e0x00Yv06x03x01v0...
6	[BLOB - 9.5 KiB]	MAYESHA BINTE MIZAN	5184785670	MD. MOHIUDDIN	MUKTA KHANAM	30-01-1998	mayesha@gmail.com	b'WAjx10P0x07x08v0x16T0R0x0b0x04S0x00x05x...
7	[BLOB - 25.8 KiB]	SHADMAN SHAKIB	5184356808	SOFIUDDIN CHAUDHURY	MOMENA KHANAM	31-12-1998	Shakib123@gmail.com	b'7x00P0x03x0b0x0ePZ0x0bQV5R0x05u06x07v0...
8	[BLOB - 5.6 KiB]	FOYSALAL GABID	5151856708	FORID HOSSAIN	ARUFA AKTER	29-08-1998	foysal@gmail.com	b'#_Mx16x07T0X0x04Q0x08Q0x07v00x03x04e0...
9	[BLOB - 12.1 KiB]	JULIA AFROSE	5190516708	MD. RAHIM	SONIA AKTER	02-12-1999	juliafrose@gmail.com	b'zGZZP0x03KIDTST0x0e0x05x03UQ0x08Zx10...
10	[BLOB - 13.7 KiB]	JAKIR KHAN	5187036708	KAMAL KHAN	NAZIA BEGUM	29-09-1998	jakirhan@gmail.com	b'0x07v0b0x10T0x02v08Q0x05U0x07SZX0QAI...
11	[BLOB - 71.1 KiB]	MIR IMTIAZ TAREK	6220768382	RIDWAN HASAN	NAFISA ISLAM	02-04-1997	imiazmir@gmail.com	b'Yx17x0e0x15x0x07gR0x14PR0x02QVU0x0eP...
12	[BLOB - 10.5 KiB]	JUBIN KHAN	4037265926	MOHAMMAD ALAMIN	SHAHIN PARVIN	16-11-1998	jubin16@gmail.com	b'xLw00ZyT0Ux07v03x02W0x0e0x01j00P_0x13x0...
13	[BLOB - 12.2 KiB]	MEHEDI RIDOY	7403275517	NAHIYAN HOSSAIN	ANTORA ISLAM	16-06-1998	ridoy06@gmail.com	b'0RQV0x08a0W0x0Fv0x04v0b0R0x07v00x06x...
14	[BLOB - 7.3 KiB]	ARSHIA HABIB	7184456708	ASADUZZAMAN KHAN	SAHIDA AKHTER	16-12-1998	arshia@gmail.com	b'E0x170x0b0x0q0U0x01v01R0x02v08x01U0x03...
15	[BLOB - 21.5 KiB]	MOHAIMINUL ISLAM	6305284017	RIDWAN SIDDIKI	ROWZA HOSSAIN	05-04-1996	mohaiminul@gmail.com	b'xZvQZ0x08x0f0v0110J0_w00T0x04v0x05Z0x...
16	[BLOB - 14.9 KiB]	MD. SAKIB	2835028173	AZMAIN IKTIDAR	TANZILA ALAM	20-09-1998	sakib20@gmail.com	b'x05S0x02S0x0b0x03x09v0x07v0Q0x07u0e0x01...
17	[BLOB - 12.3 KiB]	MEHEDI HASAN MISHU	4036492501	TOWSIF HASAN	FARIHA ANIKA	08-07-1999	mishu06@gmail.com	b'W0x04V0x0b0x7Y0Cv03_0x0b0XC0x04v02v0x02x0...
18	[BLOB - 132.5 KiB]	MD. NURUL AFSAR	9381503792	MD. ABU SAYED	ZAKIA KHATUN	31-12-1965	afsar@gmail.com	b'P-AKx11P0SD0U0x01QU0x03T0v05ST0x15W0SIL...
19	[BLOB - 118.8 KiB]	GULSHAN ARA	7401395628	A.B.M ISHAQ	ROKSAN ARA	06-10-1974	gulshanara@gmail.com	b'0x17Ux10Q0V0x14v07x01v0c0x05v07v01v0c0x...
20	[BLOB - 8.6 KiB]	APPEL MAHMUD PRANTO	7401395637	MD. ILIAS MIA	PARUL AKTER	29-12-1999	pranto@gmail.com	b'F0x12J0xP0x0b0x0C0x004x03x0c0x00P0x01RR0...
21	[BLOB - 33.1 KiB]	PRANTA BISWAS	9382504792	SHOILENDRA BISWAS	RINA BISWAS	13-01-1999	pranta13@gmail.com	b'1D0x04u0cMQx11\$0x11v0x16v0x12v0eQ0PW0v0...
22	[BLOB - 9.5 KiB]	K.A.Y Nuruddin Jahangir	1969504792	MD. NURUL HASAN	NILA BEGUM	4-06-1990	nuruddin05@gmail.com	b'0x0v0J0x16Q0x06Z0Y0x07UZ0x02v08P0x03v0x0b...
23	[BLOB - 10.1 KiB]	Mariam Akter	1976504792	MD. MOKBUL HASAN	MIM CHOWDHURY	5-07-1994	konica@gmail.com	b'0x10v0r03v0L0x06v0x04v0b0x02v05v05v06...
24	[BLOB - 229.7 KiB]	MD. Asaduzzaman	1962504792	ABDUL KALAM	AMENA BEGUM	2-02-1993	asaduzzaman@gmail.com	b'U0TBSIM0x18R0x00X0x03x0b0x0b0x04v0x0e0x0T...
25	[BLOB - 312.2 KiB]	Sabeeha Khatun	1970506892	RAHIM KHAN	SALMA AKTER	8-12-1998	sabeeha@gmail.com	b'0x07TPQ_W0x17x10v0x04x0x02v00x00v06YXQ...
26	[BLOB - 274.0 KiB]	Sakib Zaman	6970506892	KARIM HASAN	JANNATUL FERDOUS	6-05-1988	sakib01@gmail.com	b'cWIPU_Q_XZV0x00x00x01R0x00v0x0c0x01x05...
27	[BLOB - 178.5 KiB]	Sadia Aftreen	5090306855	MID NUR UDDHIN	MASHIYAT TASMIN	12-12-1995	sadia13@gmail.com	b'0x03Q0S0v0x11v0x06v0V0V0V0N0SUTP0x16v0x...
28	[BLOB - 105.8 KiB]	Shazrin Sultana	6490576885	RAHMAN CHOWDHURY	DALIA NOUSHIN	23-04-1990	shazrin22@gmail.com	b'0vRL0x0B0x12x04v00W0x04X0x03T0U0x17x0...
29	[BLOB - 199.5 KiB]	Ishrar Mannan	6546776085	ABDUL MANNAN	SINTHIA KABIR	16-10-1994	ishrar@gmail.com	b'zAQOWA0W0x08v03J0x04v0x03x05v06v06P...
30	[BLOB - 3.6 KiB]	MD. Sujar Rahman	6454310268	LUTFUR RAHMAN	AYESHA AYNAZ	25-01-1996	suja@gmail.com	b'0x02ID0SBGDPXW0x06x0c0v01U0x08v03SUZ0x15AX...
31	[BLOB - 194.0 KiB]	MD. Abdul Goni	1962310568	ROHAN KHAN	NAMIRA RAHMAN	27-06-1987	goni@gmail.com	b'Y0x00L0v0eWYQ0x03X0x00W0x05P0x01S0v0e0x0...
32	[BLOB - 260.0 KiB]	Zannatul Ferdous Tunny	6456231446	NAZMUL ISLAM	TANHA ISLAM	20-11-1992	tunny11@gmail.com	b'xQ0c0x0f0x05MM0-PGQ0x0c0x16LVX0S0x01v04x0...

Fig. 3.7: Demo NID server

```

print("The hashed value is")
print(hashed_output)

The hashed value is
19dc821925354fa14632e1df9b5ab14f385d08fc2b450e793519f663fe2bf99c6f75ae31801d06383d36352f162615914de2900080da5eb5d570aaa0deadf984

[9] final_output = sxor(ms,hashed_output).encode('utf-8')
print(final_output)

b'cX\r\x10YfPQA\\JaU\x15\x11XU\x03\x01\x05S\x03T_\x08R\r\x13\x03XG\x07s_X\x05YTH\x00]\x0f'

[10] final_output=str(final_output)
y=str(y)
concat=ms+final_output+y
print(concat)

RaisaTahsinTaspia5276209108raisa@gmail.comb'cX\r\x10YfPQA\\JaU\x15\x11XU\x03\x01\x05S\x03T_\x08R\r\x13\x03XG\x07s_X\x05YTH\x00]\x0f'349949173096

```

Fig. 3.8: Sender will send this concatenate message

After accepting this concatenated message, the receiver will first distinguish between the message and its mac value.

RaisaTahsinTaspia5276209108raisa@gmail.com  
b'cX\r\x10YfPQA\\JaU\x15\x11XU\x03\x01\x05S\x03T\_\x08R\r\x13\x03XG\x07s\_X\x05YTH\x00]\x0f'  
349949173096

Fig. 3.9: Differentiate message & MAC value

Additionally, when a message is received, the receiver generates a MAC value. The message of information is validated if the generated MAC and the received MAC are the same.

```

final_output = sxor(ms,hashed_output).encode('utf-8')
print(final_output)
final_output=str(final_output)
if mac == final_output:
    print("Message is correct!")

b'dwXBWeX[CPZb'
The hashed value is
19dc821925354fa14632e1df9b5ab14f385d08fc2b450e793519f663fe2bf99c6f75ae31801d06383d36352f162615914de2900080da5eb5d570aaa0deadf984
b'cX\r\x10YfPQA\\JaU\x15\x11XU\x03\x01\x05S\x03T_\x08R\r\x13\x03XG\x07s_X\x05YTH\x00]\x0f'
→ Message is correct!

```

Fig. 3.10: Message is authenticated

Following the transmission of authenticated information from the NID server, a warning message will be sent to the individual's email account. It will initially display a prudence notice. If the person makes the same mistake a second time, a penalty will be sent to that person's registered mail.

e) A Warning Message has been sent

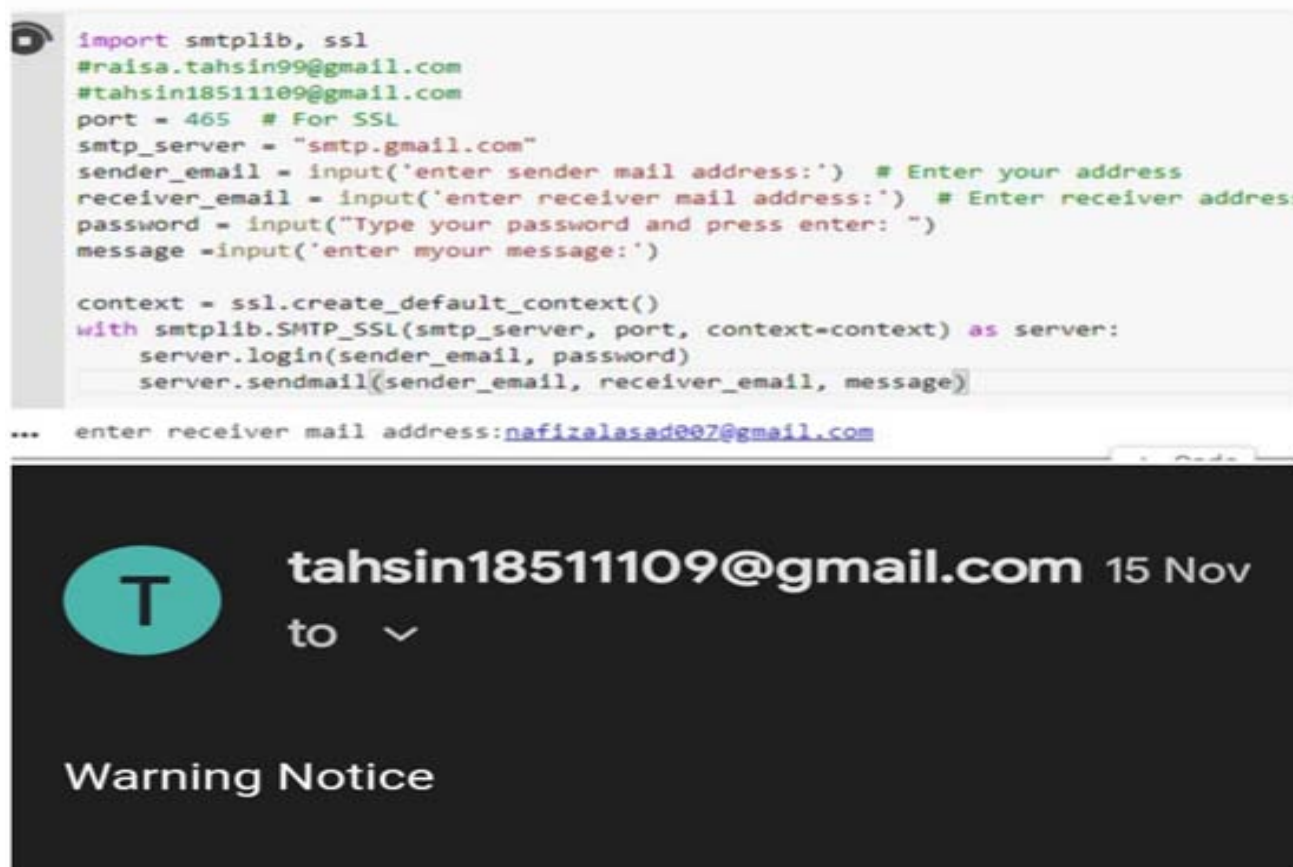


Fig. 3.11: Warning message sent to the specific mail address

## VI. PROPOSED SYSTEM SECURITY DISCUSSION

Security analysis is the process of examining and evaluating a wide range of factors that can impact the overall security of a system. A system intruder or an unauthorized individual will not be able to access any of the system's components or data until and unless the task is completed. In other words, the system will be wholly protected from any acts that could be particularly disastrous. The tag is the primary provider of protection. The whirlpool algorithm is deployed to construct the tag in this context, with a key length of 512 bits and a tag range of 512 bits [16].

Due to a failed tag verification, any forging of the message, whether malicious or unintended because of transmission errors, will be detected by the destination and reported to the source. The MAC considers each element of the message to be critically important. The root of concern is the shared secret key, which is indeed transferred utilizing secure protocol called Diffe-Hellman. An arbitrary large prime figure with a value of at least 1024 bits is used in the system to offer strong security. The whirlpool algorithm, in addition, has a reliable overall structure operating on messages less than in length that is resistant to the

traditional threats directed at block-cipher-based hashes. The collision resistance of this method is. Whirlpool seems to be more robust than most modern hashing algorithms, providing for large-scale component mapping simultaneous execution. Furthermore, it does not necessitate a significant quantity of storage space. As a result, it may be deployed effectively in various applications despite few resources. This could, meanwhile, take advantage of the larger memory space afforded on modern CPUs to gain even greater speed. Because of the hash's increased size, not only would it be more secure towards birthday attacks, yet it allows for a larger inner state for randomness containment, that is required with certain types of pseudo-random number generators [16]. Moreover, the construction adopted from PGV hash functions for generating the MAC is also collision resistant in an extraordinarily powerful way.

## VII. CONCLUSION

The study concludes a secure mechanism against COVID-19 by detecting whether the public is wearing masks [17]. The study adopts MAC to safeguard the personal information of the user against any kind of alteration as it ensures transparency,

security, and immutability. The proposed work is not only a compelling effort to reduce COVID-19 transmission through monitoring an individual's mask use but also an implementation protecting the individual's personal information. This research was inspired by a study conducted in Bangladesh to raise public knowledge about COVID transmission to minimize breakouts while also safeguarding personal information security. Higher authorities can adapt the system to preserve the authenticity of sensitive information, and manage security threats of high priority information such as the NID of citizens used for identification.

#### a) Future Work

The section on future work presents the findings as well as how to improve and extending current project work, methodologies, or assessments. It is equivocal how well it will operate in hardware because it hasn't been tried in the real world. A proposed paradigm has been recently presented [17] and this is an implementation with the local resources where it performs impeccably. However, it is yet to be assessed with a real-time dataset. Depending on the practical use, the system accuracy rate may vary. With key generation and a message authentication code method, we focused primarily on providing security for file sharing. In the future development of this system, maintenance in other sectors, such as face mask detection and person recognition, might be more precise. There are numerous fields in which progress can be made. In the future, the accuracy of mask detection and accurately detecting the person can be increased. Warnings are sent through email to be going on with but for more efficiency, it could be more practical to send alerting messages through a mobile number SMS system. Dataset diversity can enhance a research project. In real-world cryptography applications, message authentication is crucial. Simulations of the more innovative and valuable concepts could be performed and compared to those evaluated. This project has more potential in the future.

### REFERENCES RÉFÉRENCES REFERENCIAS

1. P. Venkatesan, "NICE guideline on long COVID," vol.9, no 2, p.129, 2021.
2. L.S.B.J.P. Janet Green, "Implications of face masks for babies and families during the COVID-19 pandemic: A discussion paper," *Journal of Neonatal Nursing*, vol.27, no. 1, pp. 21-25, 2021.
3. M. N. J. H. Saeed Anwar, "COVID-19 and Bangladesh: Challenges and How to Address Them," 30 April 2020.
4. "Message Authentication," [Online]. Available: [https://www.tutorialspoint.com/cryptography/message\\_authentication.htm](https://www.tutorialspoint.com/cryptography/message_authentication.htm). [Accessed 10 april 2021].
5. Y. Alkhurayyif, "National id cards," *International Journal of Computing Science and Information Technology*, vol. 1 (02), no. ISSN: 2278-9669, pp. 44-48, 2013.
6. C. M. W. Rajat Mittal, "A mathematical framework for estimating risk of airborne transmission of COVID-19 with application to face mask use and social distancing," *Physics of Fluids*, vol. 32(10), 2020.
7. [Online]. Available: <https://docs.opencv.org/>. [Accessed 5 june 2021].
8. "Keras API reference," [Online]. Available: <https://keras.io/api/>. [Accessed 25 july 2021].
9. B. Preneel, "Hash functions and MAC algorithms based on block ciphers," *IMA International Conference on Cryptography and Coding*, vol. 1355, pp. 270-282, 1997.
10. J. P. Christ of Paar, *Understanding cryptography: a textbook for students and practitioners.*, Germany: Springer Science & Business Media, 2009.
11. P. R. T. S. John Black, "Black-box analysis of the block-cipher-based hash-function constructions from pgv," *Annual International Cryptology Conference*, Springer, pp. 320-335, 2002.
12. "Socket Programmingin Python," "Geeks for Geeks," [Online]. Available: <https://www.geeksforgeeks.org/socket-programming-python/>. [Accessed 25 june 2021].
13. "How to Transfer Files in the Network using Sockets in Python," [Online]. Available: <https://www.thepythoncode.com/article/send-receive-files-using-sockets-python>. [Accessed 31 july 2021].
14. "SDLC Waterfall Model," [Online]. Available: [https://www.tutorialspoint.com/tutorial\\_view.htm?cid=sdlc&pid=sdlc\\_waterfall\\_model.htm](https://www.tutorialspoint.com/tutorial_view.htm?cid=sdlc&pid=sdlc_waterfall_model.htm). [Accessed 20 august 2021].
15. W. Stallings, *Cryptography and network security*, India: Pearson Education, 2006.
16. V. R., S. T. S. A., C. N. by Paulo S. L. M. Barreto, "The Whirlpool Hashing Function," In *First open NESSIE*, 2000.
17. Sultana, S., Taspia, R., Hossain, M., Nahiduzzaman, M., Akter, R. and Mazumder, R. (2022) A Secure Model for Preventing the Spread of COVID-19 in Bangladesh. *E-Health Telecommunication Systems and Networks*, 11, 34-46. doi: 10.4236/etsn.2022.111003.



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# Evaluation of Surrogate Risk Factors for Severe Progression of COVID-19 in Tobacco Smoking Sub-Population and its Possible Amelioration by Immune Modulators

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**Study design:** This original research paper is based on population based cohort study.

**Keywords:** COVID-19, smoking, mechanical ventilation, hazard analysis and mycobacterium indicus pranii (MIP).

**GJMR-K Classification:** DDC Code: 616.865 LCC Code: RC567



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**Study design:** This original research paper is based on population based cohort study.

**Methods:** Observational single center retrospective study was conducted in chest disease hospital, Srinagar during March 2020 to March 2021. A total of 883 patients with confirmed COVID-19 were categorized into active smokers (n=69) and those who have never history of smoking (n=814). Patients were characterized on basis of clinical manifestation of disease, serum biochemistry (acute phase proteins, pro-inflammatory cytokines), radiological findings, need for mechanical ventilation and death as primary outcome of COVID-19 disease. Furthermore the present study attempted to evaluate therapeutic role of *Mycobacterium indicus pranii* (MIP) in active smoker (n=47) and non smoker (n=39) subpopulations. These groups were compared on basis of all cause mortality, pro-inflammatory response and acute phase protein response.

**Results:** Clinically and radiologically COVID-19 patients with history of active smoking were having severe manifestation

and wide spectrum of symptoms/findings compared to non smokers. Similarly smokers were having longer duration of hospitalization compared to non smokers. Major highlights of present study were significant lowered levels of acute phase protein response and pro-inflammatory cytokine response in non smokers compared to active smoker population. Similarly we found significantly higher need for mechanical ventilation and higher odds of death in active smoker population compared to non-smoker population. Taking together, in terms of mortality, pro-inflammatory response and acute phase response therapeutically beneficial role of MIP was reported in smoker population compared to therapeutic role in non smoker population.

**Conclusion:** In present study clinical, biochemical and hazard analysis suggests a complex relationship between smoking and outcome of disease in COVID-19 patients. At preliminary stage it seems that smoking has significant effect on all cause mortality as primary outcome in smoking population. Furthermore our results suggest therapeutically more advantage of using MIP in smoker population compared to non smoker population. Though findings are based on single center study, so there is a need of multi centered large cohort study to establish relationship between smoking and COVID-19.

**Keywords:** COVID-19, smoking, mechanical ventilation, hazard analysis and *mycobacterium indicus pranii* (MIP).

## I. INTRODUCTION

World health organization (WHO) has estimated Global count of 1.1 billion active smokers and figures are projected to increase to 1.3 billion in 2025<sup>1</sup>. There are substantial scientific evidences that have revealed the deleterious effect of smoking on respiratory health and smoking is supposed to play pivotal role in wide spectrum of respiratory diseases.<sup>2</sup> In concurrence with this, previous outbreaks caused by Coronaviruses like MERS-CoV has revealed higher case fatality rates in smokers compared to non-smokers.<sup>3</sup> Conflicting findings are reported by authors across the world in the ongoing SARS-CoV-2 disease outbreak; with regard to smoking as risk factor for disease incidence and worse outcome of diseases in COVID-19 patients.<sup>2,4,5,6,7,8,9,10</sup> For instance an earliest study

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published in china concluded smoking as an independent risk factor for severe outcome of disease in COVID-19.<sup>11</sup> Studies have attributed higher rate of mortality in cigarette smokers because of the relative up-regulation of the angiotensin converting enzyme 2 (ACE2) receptor the key receptor used by SARS-CoV-2 to invade the recipient mucous membrane and trigger underlying illness.<sup>4</sup> But subsequent studies have proposed smoking is not associated with severe outcome in COVID-19 disease and in fact smoking prevents severe progression of disease in smokers.<sup>12</sup> Recently some studies have reported decreased expression of ACE-2<sup>13,14</sup> receptors in smoker population which subsequently prevent severe progression of disease in smoker population. However it remains uncertain if the up regulation of the ACE-2 receptor has any impact on mortality in smoker population of COVID-19.<sup>15,16</sup> These studies were widely shared on social media and propaganda was perpetuated by tobacco companies that led World Health Organization (WHO) to issue official statement to condemn beneficial role of tobacco based products against COVID-19 as significant and enough evidences were lacking to support the statement. Furthermore To negate the propaganda European Center for Disease Prevention and Control (ECDC) issued guidelines to avoid identified probable risk factors like smoking and medications that can results in severe outcome in COVID-19 and hence increase burden hospital capacity.<sup>16</sup>

These studies gave conflicting results and were having number of limitations which includes mall cohort size, retrospective design, lack of matching, single centered study, difficulty in establishing smoking status of patients .Owing the established side effects associated with smoking there is an urgent need to study smoking as potential risk factor to accurately predict whether smoking subpopulation are at increased risk of severe outcome and help clinician in rational targeted therapeutic strategies for COVID-19 smoking patients. Therefore, a retrospective observational study on large sample size was performed to assess the clinical characteristics, laboratory findings, radiological findings and clinical outcomes in smoker and never smoker COVID-19 patients. The prime advantages of present study were (1) this is up to this time a large cohort study (n=883) as earlier studies are mostly on limited number of patients. (2). In this study we asked (i) whether inflammatory cytokine response and acute phase proteins can predict severe outcome in smoking COVID-19 patients, in order to study role of cytokines we assayed Interleukins (IL); IL-1, IL-2, IL-6 and TNF- $\alpha$  (Tumor necrotic Factor-Alpha). Similarly for Acute phase response we studied D-Dimer, procalcitonin, Heat Sensitive- C Reactive Protein (Hs-CRP), Ferritin and Lactate dehydrogenase (LDH). (ii) All cause mortality as primary outcome and need for mechanical ventilation as secondary outcome in smoker COVID-19 population.

## II. METHODS

### a) Study Design

Between March 23, 2020 to March 2, 2021, as part of routine clinical treatment, we collected laboratory and health details from 883 patients who were hospitalized with confirmed SARS-CoV-2 infection. Patients included in present retrospective single center cohort study included Adult patients (aged 18 and over) from Chest Disease Hospital Srinagar, Jammu and Kashmir, India. The study was approved by institutional Ethical Committee of Chest Disease Hospital Srinagar (CDSCO U/P No: EC/NEW/INST/2020/7452/01A.). Patients (n=883) confirmed for COVID-19 by RT-PCR of nasopharyngeal swab were categorized as patients with chronic history of smoking (n=69) and those without ever history of smoking (n=814). Record of all COVID-19 patients was retrieved from central repository of hospital. Number of deaths from all cause mortality was recorded on weekly basis for patients infected with COVID-19. A disease severity scale was utilized to classify patients in different grades of disease severity as per previous study<sup>(17,18,19)</sup> and clinical practice of clinician present in Chest disease hospital Srinagar. In both groups COVID-19 disease was categorized as mild/moderate COVID-19 (patients with pyrexia, abnormal CT findings without need for ventilation), Severe COVID-19 (patients which underwent for ventilation and require intensive care) and critically severe COVID-19.

### b) Sample collection

In majority of patients samples were collected once usually after hospitalization (median- 1.53 Days; IQR-1.98 Days). In subset of Patient population were sampling was performed more than once, only those samples were used in current study which were collected immediately after hospitalization. Samples for RT-PCR were obtained from nasopharyngeal/oropharyngeal swab while for biochemical analysis blood samples were collected by venipuncture.

### c) Identification of surrogate markers of smoking

In present study we conducted univariate analyses to evaluate pro-inflammatory cytokine response in patients with associated co-morbidities. Univariate analysis revealed inflammatory cytokines (IL-1, IL-2, IL-6 and TNF- $\alpha$ ) were significantly elevated in patients with history of hypertension, kidney disease (CKD), congestive heart failure, diabetes mellitus and chronic obstructive pulmonary disease. No significant difference was observed in levels of pro-inflammatory cytokine levels between male and female subpopulation when body mass index (BMI) and sex were considered as risk for exaggerated cytokine response. Although with increasing age of patients cytokine response was found to be enhanced which indicates dysregulation in inflammatory pathway with increase in age. Based on

these findings we matched patients with respect to comorbidities and demographic factors in subsequent analysis. Following this we attempted to identify surrogate variables of smoking for that we tested whether smoking was associated with enhanced cytokine response and we evaluated correlation of these pro-inflammatory cytokine with well known inflammatory/acute phase markers identified as an independent risk factors (Hs-CRP, D-dimer, ferritin, procalcitonin and LDH). Following this we evaluated association of surrogate variables of smoking as variable with additional series of well established biochemical parameters for their role in survival in present cohort. We found levels of white blood cells; creatinine, platelet count, neutrophils, LDH, and oxygen saturation were closely associated with surrogate markers of smoking identified. Next we conducted univariate Kaplan–Meier analyses to determine factors affecting survival of COVID-19 patients regardless of the whether patients who died were smokers or non smokers. Finally we quantified four inflammatory cytokines and acute phase protein response known to lead pathogenic inflammation and evaluated their association with disease intensity and survival. Following this survival model was adopted for our analysis of 883 patients tested positive for SARS-CoV-2 with variables which included pro-inflammatory cytokines, acute phase protein response and other laboratory parameters.

d) *MIP treatment Outcomes in smoker and non-smoker population*

A Prospective Interventional cohort study was conducted on smoker/non smoker patients treated with Mycobacterium indicus pranii (MIP) and were compared with Comparator groups for smoker and non smokers respectively. To ensure strict control on baseline characteristics, MIP/smoker recipients were propensity-score matched to comparator patients MIP/non-smoker. After establishing matching, patients were retrospectively chart reviewed by team of experts who were unaware of patient information. Patients whose baseline characteristics were not available in system database were retrieved manually. Patients in MIP groups received Mycobacterium indicus pranii (MIP) at dosage of 0.1 ml intramuscular three times a day at three different sites for three consecutive days in addition to standard treatment used and approved at chest disease hospital Srinagar, Jammu and Kashmir India. While patients in comparator groups received standard/symptomatic therapy which included steroids and remdesvir with symptomatic therapy for comorbidities if any. Primary end point outcome in study population was estimated as all cause mortality observed during time of hospitalization caused by primary COVID-19 disease or underlying secondary disease. While as secondary outcome was estimated on basis of hospital stay, severe manifestation of disease,

pro-inflammatory cytokine response, acute phase protein response and need for mechanical ventilation.

e) *Statistical analysis*

We summarized patient demographic and clinic-biochemical characteristics using standard statistical tools. Continuous variables were expressed as Mean±S.E; IQR (Interquartile Range) while as categorical variables were expressed as count/percentage with OR (Odds Ratio) as randomization was not conducted in present study all statistics were deemed as descriptive. We used Kaplan Meier plots to assessed differences in survival probabilities between smoker and non-smoker population across time of hospitalization in which death was event of interest and discharge from hospital was competing event. Hazard Ratios (HRs) with 95% CIs (confidence intervals) predicted survival probability. Comparison for continuous variables was estimated by Mann-Whitney U test and categorical data was compared by chi square test. Association studies was conducted by using univariate analyses, we assessed association of pro-inflammatory cytokine response with patient clinic-biochemical characteristics by using Mann-Whitney U test, Kruskal–Wallis test and Spearman's rank correlation test as appropriate and spearman's correlation was used for correlation studies. P value of less than 0.05 was considered Statistical significant and statistics was performed with IBM SPSS Statistics, version 20.

### III. RESULTS

a) *Clinical manifestations:* Severe spectrum and severe intensity of clinical signs were observed in COVID-19 smoker population compared to spectrum/intensity of signs in non-smoker COVID-19 population (Table 1). Clinically diseases in smoker compared to non-smoker was presented as Cough (27.27% v/s 55.07%; p-0.01), Sputum (2.2% v/s 17.39 %; OR-5.82; p-0.01), Sore throat (5.7% v/s 21.73%; OR-3.00; p-0.01), Fever (28.99% v/s 39.13%; p-0.47), Anorexia (2.2% v/s 43.47%; OR-5.37; p-0.001), Rhinitis(1.9 % v/s 12.9%; OR-2.38; p-0.01), Insomnia (1.3% v/s 6.4%; p-0.07), hemoptysis (2.0% v/s 4.2%; OR-1.76; p-0.09), dysguesia (3.4% v/s 7.2%; OR-3.15; p-0.03), Nausea (0.8% v/s 23.18%; OR-11.79; p-0.001), Diarrhea (1.3% v/s 6.4%; OR-1.11; p-0.001), Myalgia (7.1% v/s 17.39%; OR-2.09; p-0.05), Fatigue (4.05% v/s 10.14%; OR-2.85; p-0.01), Headache (2.2% v/s 20.28%; OR-2.87; p-0.01) and Nasal Congestion (0.3% v/s 15.94%; OR-4.15; p-0.003). From these results it is seems that smoker population has more severe presentation of disease compared to comparator group of non-smokers. Of the clinical importance, parameters which were significantly elevated in smoker population compared to non-smoker were



productive cough, sore throat, anorexia, nausea, myalgia, fatigue, oro-pharyngeal congestion and conjunctivitis.

- b) *Computer tomographic (CT) findings:* The typical findings of chest CT images in smoker COVID-19 v/s non-smoker COVID-19 included GGO'S (10.14 % v/s 3.07%; p-0.001), Local Patchy Shadow (2.89% v/s 0.61%; p-0.03), B/L Patchy Shadow (8.69% v/s 1.1%; p-0.01), SC (10.14% v/s 8.23%; p-0.99), Effusion (2.89% v/s 0.98%; p-0.04), GGO (U/B (24.64% v/s 9.3%; p-0.001), Nodules (4.34% v/s 1.8%; p-0.03), Consolidation (17.39 % v/s 4.42%; p-0.01) and Pleural Effusion (18.84% v/s 1.7%; p-0.01) (Table 2). Taken together present study found increased incidence of overall CT abnormalities in smoker population (24.63 %) compared to non-smoker population (7.86%) with p value of 0.01 (Figure 1A and 1B). An expected finding of present study was higher prevalence of COPD in smoker group compared to comparator group (Table 3). At the time of admission 53.62% smoker population and 16.83% non smoker population were having severe illness of COVID-19 disease. In concurrence with this similarly 52.17% smoker population and 16.83% in comparator population needed mechanical ventilation which further supports severe pathology of lung parenchyma in smoker COVID-19 population compared to non-smoker COVID-19 population.
- c) *Biochemical findings:* At the time of admission LDH ( $423.87 \pm 24.48$ : IQR-204 v/s  $261.44 \pm 21.98$ : IQR-154, p-0.01), heart rate ( $87.05 \pm 0.53$ : IQR-18 v/s  $68.15 \pm 2.16$ : IQR-20, p-0.73), Platelet count ( $159.88 \pm 5.86$ : IQR-232.44 v/s  $79.13 \pm 16.31$ : IQR-167.55, p-0.001), and Bilirubin ( $1.07 \pm 0.26$ : IQR-0.4 v/s  $0.99 \pm 0.14$ : IQR-0.6, p-0.02) levels were significantly elevated in smoker COVID-19 population compared to non-smoker (Table 5). Similarly in present study we found SPO<sub>2</sub> significantly reduced in smoker compared to non-smoker ( $91.14 \pm 0.29$ : IQR-8 v/s  $80.33 \pm 0.98$ : IQR-8, p-0.04) COVID-19 population. Other parameters which did not showed any abnormality between COVID-19 smoker population compared to non-smoker COVID-19 population included temperature ( $95.28 \pm 1.39$ : IQR-4 v/s  $93.20 \pm 6.17$ : IQR-5, p-0.90), White Blood Cell ( $6029.22 \pm 171.97$ : IQR-3700 v/s  $5813.55 \pm 500.77$ : IQR-3900, p-0.56), Lymphocyte Count ( $1517.60 \pm 42.89$ : IQR-900 v/s  $1502.09 \pm 90.59$ : IQR-650, p-0.79), Creatinine, Blood Sugar, SGOT, SGPT, ALP, Protein and CPK levels (Table 5).
- d) *Surrogate endpoints:* Present study identified cytokines and other surrogate endpoints for severe manifestation of diseases in smoker population. In present study distributions of majority of surrogate

endpoints were significantly different between smoker and non-smoker population. In present study we found IL-2 IL-6 and TNF- $\alpha$  levels being closely correlated with lung imaging, need for mechanical ventilator support and fever. Contrarily IL-1 could not presented any significant correlation with body temperature, lung imaging and need for mechanical ventilator support. Based on univariate analysis and correlation studies it can be postulated that IL-2, IL-6 and TNF- $\alpha$  can be used as surrogate endpoints for patient outcomes for severity of diseases and mortality (Figure 2).

- e) *Cytokine and Acute Phase Response:* It is worth mentioning that despite adjustment for the other covariates which include co-morbidities, disease severity, body mass index (BMI) and demographic characteristics in both classes of patient subpopulations, cytokine levels in smoker patients were significantly higher compared to non smoker population. In present study we found IL-2 ( $p \leq 0.001$ ), IL-6 ( $p \leq 0.001$ ) and TNF- $\alpha$  ( $P \leq 0.05$ ) were significantly elevated in smoking COVID-19 serum compared to non smoking COVID-19 serum (Figure 3). Cytokines assessed in present study indicated varied response in smoker population compared to non smoker population, with IL-1 and IL-6 having most dynamic profile followed by TNF- $\alpha$ . While IL-2 was not significantly different between two study populations. From present study it can be postulated that majority of smoker population were having exaggerated cytokine response. Similarly in present study serum ferritin ( $p \leq 0.01$ ), LDH ( $p \leq 0.001$ ) and Hs-CRP ( $p \leq 0.001$ ) levels were significantly elevated in smoker sub-population compared to non smoker COVID-19 sub population. These results further indicate elevated acute phase response in smoker population which might be possible reason for severe outcome of clinical manifestation of disease in smoker population infected with COVID-19 (Figure 2).
- f) *Clinical endpoints:* At the end of study we observed 15 (21.73%) deaths in smoker sub population and 30 (3.68%) deaths in non-smoker COVID-19 population with Hazard analysis-1.724; CI 95% 1.037-2.866; p-0.033. The median time from hospitalization to discharge in smoker group and non-smoker COVID-19 group was  $29.96 \pm 0.17$  and  $32.52 \pm 0.70$  days respectively.
- g) *Effects of MIP inclusion in therapeutic regimen on risk factors identified:* We attempted to evaluate the effect of immune-modulator (MIP) on cytokines and estimated surrogate endpoints, as potential ameliorative strategy should these identified surrogate endpoints be involved in pathogenic pathway of severe manifestation of disease and death. Following these hypothesis results of present



study showed smoker patients treated with MIP had significantly reduced levels of cytokine response, with more pronounced reduction observed in IL-2 and IL-6 while as TNF- $\alpha$  levels decreased gradually after treatment. Pronounced decrease in these surrogate markers were observed in smoker MIP treatment group while as in non smoker subset of patients who received MIP drug in their therapeutic regimen showed less dramatic reduction in pro-inflammatory cytokine levels. These findings indicate beneficial role of MIP inclusion in therapeutic regimen potentially supporting clinical benefits of MIP in smoker population affected with COVID-19. On 7<sup>th</sup> day of treatment no significant difference was observed in post treatment values of ferritin, LDH and Hs-CRP in non-smoker subpopulation treated with MIP compared to pretreatment values, while as significant difference was observed in post-treatment values of these variables in smoker group (p-0.21). Similarly we observed significant reduction in levels of CPK on 7<sup>th</sup> day post-treatment in both smoker and non-smoker (p-0.05) sub-populations, with more pronounced reduction observed in smoker population (p-0.001). In concurrence with above findings significant improvement was observed in SPO<sub>2</sub> in both groups of patients. These results indicate MIP therapy has superior role in dampening of acute phase protein response henceforth normalization of pulmonary function (Figure 3 and 4).

*Effects of MIP on outcome of disease in smoker v/s non-smoker population:* outcomes considered in present study included hospitalization time, Need for high flow Mechanical Ventilation, (comparison performed on 7<sup>th</sup> day of treatment) and all cause mortality on 35 days, Negative conversion of SARS-Cov-2 on basis of RT-PCR on 7<sup>th</sup> day and 14<sup>th</sup> day of treatment, Retrogression to moderate diseases. Results of present study indicates negative conversion of SARS-Cov-2 on basis of RT-PCR on 7<sup>th</sup> day were 46.15% in smoker subpopulation v/s 27.65% non smoker population with p-0.05. While as on 15<sup>th</sup>, 78.48 % in smoker v/s 68.08 % in non smoker population with p-0.19 reverted to negative result of SARS-Cov-2 on basis of RT-PCR. Similarly retrogression to moderate diseases was almost similar in smoker MIP group and non-smoker MIP group. In present study hospitalization time (deaths excluded) was significantly lower in smoker MIP group compared to non-smoker MIP group (25.93 $\pm$ 10.14 v/s 32.45 $\pm$ 7.16 p-0.02). In smoker MIP group 4 (10.25%) and in non-smoker MIP group 5 (10.63%) deaths with p-0.78 were observed during 35 days of hospitalization (Table 5). On 7<sup>th</sup> day post treatment most of the clinical parameters considered remained comparable in patients during this time interval in both groups. The clinical outcomes which showed early resolution in smoker population

included resolution of shortness of breath (p-0.02) (Table 6; Figure 3 and 4).

#### IV. DISCUSSION

In present study an attempt was made to investigate association between smoking and mortality from all causes as outcome of COVID-19 illness. In present study we found significant difference in odds of death between actively smokers compared to never smoker population. These findings are in concurrence with earlier studies they reported current smokers were at higher risk of more severe disease than never smokers. But there was no significant difference between former and never smokers (RR: 1.51; 95% CI, 0.82- 2.80).<sup>10</sup> However findings of present study are contrarily to recently Meta analysis study conducted in 11,590, COVID-19 patients, among then 30% were ever smokers and 18% were never smoking population. They found no significant difference between these two groups in terms of severity and outcome of COVID-19.<sup>20</sup> Similarly in meta-analytic study,<sup>5</sup> and one clinical study<sup>16</sup> support significant correlation between COVID-19 severity and active smoking, while four clinical studies could not appreciate any relation between active smoking and disease severity in COVID-19 patients.<sup>12,13,14,15</sup>

Smoking damages airway passage and predispose patients having history of active smoking towards severe outcome during respiratory infections<sup>23</sup>, so it can be expected that smoking worsen outcome in COVID-19. In March 2020, study was published from china which concluded smoking as risk factor for severe progression of COVID-19.<sup>4</sup> Subsequently a study proposed smoking is not associated with severity outcome in COVID-19 disease which was refuted widely by scientific community.<sup>5</sup> In present study we found severe clinical manifestation of COVID-19 in active smokers compared to non-smoker. A small cohort study identified smoking history as risk factor for severe progression of SARS-CoV-2 led pneumonia.<sup>18</sup> Information gathered from various Meta-analytic and cohorts studies attributes severe outcome of COVID-19 in smokers to increased expression of ACE-2 receptors in pulmonary epithelial tissue<sup>3</sup>, as these receptors act as primary docking sites for Spike proteins of SARS-CoV-2 for internalization into cellular framework.<sup>24</sup> This might increase susceptibility of active smoking population to get infected with SARS-CoV-2. In addition in present study we report increased hospital stay of active smoker compared to non-smokers. These findings are partially supported and partially contracting with findings that found earlier discharge of active smoking patients and lower risk of progressing towards need of mechanical ventilation.<sup>25</sup> Majorities of clinical findings in present study of biochemical parameters did showed increased manifestation of abnormality in COVID-19 smoker

populations compared to non-smoker COVID-19 population. Furthermore we found significantly increased (1.724; CI 95% 1.037-2.866; p=0.033) need of mechanical ventilation in active smokers compared to those who have never smoking history. These findings are in concurrence with the study which observed OR (Odds Ratio) of 1.69 (95% CI, 0.41-6.42) in COVID-19 patients with history of active smoking.<sup>26</sup> These findings may be attributed to over-expression of ACE-2 receptors as they provide effective micro environmental mechanism for severe progression of diseases which are hypothesized to be over expressed in actively smoking population.<sup>27</sup> However some experimental studies have attributed protective action of ACE-2 to catalytic product angiotensin 1-7 (Ang1-7) generated from action of ACE-2 on angiotensin II (Ang II) as these Degradation products like Ang1-7 possess anti-oxidant, anti-inflammatory and vasodilatory activity<sup>5</sup>.

In present study clinical biochemical and hazard analysis suggests a complex relationship between smoking and outcome of disease in COVID-19 patients, so at preliminary levels drawing conclusion may be misleading. Discrepancies in earlier studies may be attributed to categorization of individual data using different criteria, limited number of smokers which ranged between two to five, different response variables in different studies, frequency of tobacco use was not considered, chronicity of tobacco use since those with chronic and frequent use of tobacco might exhibit morphological and pathological modifications in pulmonary tissue. These indirect evidences are further established in studies using recombinant ACE2 (rhACE2) in severe COVID-19 patients where they reported decreased levels of Ang- II and IL-6 after use of rhACE2 thus ameliorating cytokine storm which is commonly associated with severe outcome in COVID-19. To further support this hypothesis an experimental study shows rhACE2 not only lowers risk of severe progression of COVID-19 but also decreases viral load by factor of 1000-5000.<sup>28</sup>

Furthermore in current study an attempt was made to understand role of smoking on pro-inflammatory cytokines henceforth clinical course and outcome of COVID-19. IL-1, IL-2, IL-6 and TNF-alpha levels were significantly elevated in smoker population compared to non-smokers population at the time of hospitalization. Studying 883 patients during span of 12 months, results of present study support smoking as an important predictive risk factor for severe outcome of disease and mortality as these pro-inflammatory cytokines are involved in activation and recruitment of neutrophils<sup>29</sup>. Furthermore after adjustment of demographics and co-morbidities we found among the acute phase proteins considered in present study Hs-CRP, Ferritin, and D-Dimer levels were significantly associated with IL-1 and IL-6. Hence from these results it can be postulated that IL-1, IL-6, Hs-CRP, Ferritin, and

D-Dimer can serve as an early biomarkers for survival and severe manifestation of disease in COVID-19 patients. These parameters were independently associated with need for mechanical ventilation, SPO<sub>2</sub> levels and day of hospitalization, which indicates validity of these markers in stratification of patients according to severity of disease and henceforth their role in prognosis of disease when these parameters were tested along with other clinic-biochemical parameters. Taken together these results suggest possibility of ameliorative role of anti-cytokine treatments in smoker population to retard severe progression of disease and reduction of mortality. This proposition is further supported by results of single centered observational clinical trial which used IL-6 blocking drugs and they proposed clinical benefits in study population<sup>30</sup>. In contrast results from randomized double blinded placebo controlled clinical trial which used anti-IL-6 receptor antibody (sarilumab) reported benefits of this drug in severe diseases and no benefit was observed in mild and moderate disease<sup>31</sup>.

In present study we used cytokine profiling as an inclusion criteria for evaluation of clinical benefits of MIP in smoker sub population, we observed smoker sub-population with significantly elevated levels of pro-inflammatory cytokines were benefited most by inclusion of MIP in therapeutic regimen which might be attributed to immunomodulatory role of MIP in COVID-19 patients with elevated levels of pro-inflammatory cytokines. To support this statement use of immune modulators was observed to result in reduction of IL-6 in critically ill COVID-19 patients and the study has observed correlation between reduced levels of IL-6 and clinical recovery in study population<sup>32,33</sup>. Although some studies have recognized IL-6, IL-1 and TNF-alpha as an independent risk factors for severe outcome of disease in COVID-19 patients<sup>34,35,36</sup>. Present study observed reduction in TNF-alpha and IL-1, IL-6 levels after treatment with MIP in COVID-19 patients having levels of these pro-inflammatory cytokines above threshold which indicates added clinical efficacy of inclusion of MIP in therapeutic regimen. Cytokine levels measured at the time of hospitalization can be used as prognostic markers for clinical outcome of smoker COVID-19 population and using them in treatment decisions. Henceforth cytokine levels can be helpful in prioritization of smoker COVID-19 patients which are at higher risk of progression to severe outcome and mortality.

In conclusion the preliminary results on Kashmiri COVID-19 patients suggest that active smoking has significant association with risk of mechanical ventilation and there is significant relation between smoking and all cause mortality in COVID-19. There are well established deleterious effects associated with smoking. So there is a need of large cohort study to establish relationship between smoking and COVID-19. Although focus of present study was to establish association of chronic smoking and pro-

inflammatory cytokine response in smoking COVID-19 population, which indicates from present study the prognostic value of IL-1, IL-6 and TNF-alpha in smoker COVID-19 population. Additional pro-inflammatory cytokine and acute phase proteins having known role in immune cum inflammatory pathogenic pathways will be useful in standardization of treatment in smoker COVID-19 patients.

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**Ethical approval:** This work did not require ethical approval as it's just a retrospective observational study.

## REFERENCES RÉFÉRENCES REFERENCIAS

- Mattiuzzi C, Lippi G. Which lessons shall we learn from the 2019 novel coronavirus outbreak? *Ann Transl Med* 2020; 8:48.
- Tonnesen P, Marott JL, Nordestgaard B, Bojesen SE, Lange P. Secular trends in smoking in relation to prevalent and incident smoking-related disease: A prospective population-based study. *Tob Induc Dis* 2019;17:72, <https://doi.org/10.18332/tid/112459>
- Vardavas CI, Nikitara K. COVID-19 and smoking: a systematic review of the evidence. *Tob Induc Dis* 2020; 18: 20, <http://dx.doi.org/10.18332/tid/119324>
- Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from wuhan: an analysis based on decade-long structural studies of sars. *J Virol* 2020 Jan 29. <https://doi.org/10.1128/JVI.00127-20>. pii: JVI.00127-20[Epub ahead of print].
- Oakes JM, Fuchs RM, Gardner JD, Lazartigues E, Yue X. Nicotine and the reninangiotensin system. *Am J Physiol Regul Integr Comp Physiol* 2018; 315(5): R895–906.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in china. *N Engl J Med* 2020 Feb 28. <https://doi.org/10.1056/NEJMoa2002032>. [Epub ahead of print].
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in wuhan. China. *Lancet* 2020; 395: 497–506.
- Liu W, Tao Z-W, Lei W, Ming-Li Y, Kui L, Ling Z, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chin Med J February* 2020. <https://doi.org/10.1097/CM9.0000000000000775>.
- Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in wuhan, China: a single-centered, retrospective, observational study. *The Lancet Respiratory Medicine* 2020; 0(0). [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
- Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected by SARS-CoV-2 in wuhan, China. *Allergy* 2020 Feb 19. <https://doi.org/10.1111/all.14238>. [Epub ahead of print].
- Leung JM, Yang CX, Tam A, Shaipanich T, Hackett TL, Singhera GK, et al. ACE-2 expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19. *Eur Respir J* 2020; 55(5): 2000688, <https://doi.org/10.1183/13993003.00688-2020>.
- Gorini G, Clancy L, Fernandez E, Gallus S. Smoking history is an important risk factor for severe COVID-19. *Blog Tob Control*. 2020; <https://blogs.bmj.co.020/04/05/smoking-history-is-an-important-risk-factor-forsevere-COVID-19/>.
- Lippi G, Henry BM. Active smoking is not associated with severity of coronavirus disease 2019 (COVID-19). *Eur J Int Med* 2020; 75: 107-108, <https://doi.org/10.1016/j.ejim.2020.03.014>.
- Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor recognition by novel coronavirus from wuhan: an analysis based on decade-long structural studies of sars. *J Virol* 2020; 94(7): e00127-20, <https://doi.org/10.1128/JVI.00127-20>.
- Oakes JM, Fuchs RM, Gardner JD, Lazartigues E, Yue X. Nicotine and the reninangiotensin system. *Am J Physiol Regul Integr Comp Physiol* 2018; 315(5): 895–906, <https://doi.org/10.1152/ajpregu.00099.2018>.
- WHO. <https://www.who.int/news-room/detail/11-05-2020-WHO-statement-tobacco-use-and-covid-19>, 2020. Date accessed: May 22, 2020.
- Control ECfDPa. Rapid risk assessment: Coronavirus disease 2019 (COVID-19) pandemic: increased transmission in the EU/EEA and the UK – seventh update. European Centre for Disease Prevention and Control 2020.
- Brake SJ BK, Lu W, McAlinden KD, Eapen MS, Sohal SS. Smoking Upregulates Angiotensin-Converting Enzyme-2 Receptor: A Potential Adhesion Site for Novel Coronavirus SARS-CoV-2 (Covid-19). *J Clin Med* 2020; 9: 841, <https://doi.org/10.3390/jcm9030841>.
- Kai, Hisashi, and Mamiko Kai. Interactions of coronaviruses with ACE2, angiotensin II, and RAS inhibitors-lessons from available evidence and insights into COVID-19. *Hypertens Res* 2020; 43: 648-654, <https://doi.org/10.1038/s41440-020-0455-8>
- Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with

- SARS-CoV-2 pneumonia in wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020; 8: 475-481, [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
21. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected by SARS-CoV-2 in Wuhan, China. *Allergy* 2020; 75(7):1730-1741, <https://doi.org/10.1111/all.14238>.
22. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in china. *N Engl J Med* 2020; 382(18):1708-1720, <https://doi.org/10.1056/NEJMoa2002032>.
23. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in wuhan. China. *Lancet* 2020; 395: 497–506, [https://doi.org/10.1016/S0140-6736\(20\)30183-5](https://doi.org/10.1016/S0140-6736(20)30183-5).
24. Liu W, Tao Z-W, Lei W, Ming-Li Y, Kui L, Ling Z, et al. Analysis of factors associated with disease outcomes in hospitalized patients with 2019 novel coronavirus disease. *Chin Med J* 2020; 133(9):1032-1038, <https://doi.org/10.1097/CM9.0000000000000775>.
25. Carmona-Bayonas A, Jiménez-Fonseca P, Echaburu JV, Antonio M, Font C, Biosca M, et al. Prediction of serious complications in patients with seemingly stable febrile neutropenia: validation of the clinical index of stable febrile neutropenia in a prospective cohort of patients from the finite study. *J Clin Oncol Am Soc Clin Oncol* 2015; 10; 33(5): 465-71, <https://doi.org/10.1200/JCO.2014.57.2347>.
26. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020; 8(5): 475–81, [https://doi.org/10.1016/S2213-2600\(20\)30079-5](https://doi.org/10.1016/S2213-2600(20)30079-5).
27. Smith JC, Sheltzer JM. Cigarette smoke triggers the expansion of a subpopulation of respiratory epithelial cells that express the SARS-CoV-2 receptor ACE2. *BioRxiv* 2020, <https://doi.org/10.1101/2020.03.28.013672>.
28. Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell LF, Chernyak Y. et al. Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City. *MedRxiv* 2020, <https://doi.org/10.1101/2020.04.08.20057794>.
29. Sanchis-Gomar F, Lavie CJ, Perez-Quilis C, Henry BM, Lippi G. Angiotensin-converting enzyme 2 and antihypertensives (angiotensin receptor blockers and angiotensin- converting enzyme inhibitors) in coronavirus disease 2019. *Mayo Clin Proc* 2020; 95(6): 1222–1230., <https://doi.org/10.1016/j.mayocp.2020.03.026>.
30. Monteil V, Kwon H, Prado P, Hagelkrüys A, Wimmer RA, Stahl M, et al. Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2. *Cell* 2020; 81(4): 905-913.e7, <https://doi.org/10.1016/j.cell.2020.04.004>.
31. Patanavanich R, Glantz SA. Smoking is associated with COVID-19 progression: a meta-analysis. *Nicotine Tob Res* 2020; 22(9): 1653-1656, <https://doi.org/10.1093/ntr/ntaa082>.
32. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (NCPERET). The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19)—China. 2020. *China CDC Wkly* 2020; 2:113–22, <https://doi.org/10.46234/ccdcw2020.032>.
33. Parascandola M, Xiao L. Tobacco and the lung cancer epidemic in China. *Transl Lung Cancer Res* 2019; 8: S21–30, <https://doi.org/10.21037/tlcr.2019.03.12>.
34. Xu, X. et al. Effective treatment of severe COVID-19 patients with tocilizumab. *Proc. Natl Acad. Sci. USA* 117, 10970–10975 (2020).
35. Liu, J. et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBioMedicine* 55, 102763 (2020).
36. Gritti, G. et al. Use of siltuximab in patients with COVID-19 pneumonia requiring ventilatory support. Preprint at <https://doi.org/10.1101/2020.04.01.20048561> (2020).
37. Ledford, H. Coronavirus breakthrough: dexamethasone is first drug shown to save lives. *Nature* 582, 469 (2020).



**Table 1:** Baseline Clinical Characteristics of COVID-19 infected smokers and non-smoker patients

Parameters n (%)	Group 1 (n=814)	Group II (n=69)	P-value	OR
Cough	222(27.27)	38(55.07)	0.01	7.98
Sputum	28 (2.2)	12 (17.39)	0.01	5.82
Sore throat	47(5.7)	15(21.73)	0.01	3.00
Fever	236(28.99)	27(39.13)	0.47	-
Anorexia	18(2.2)	30 (43.47)	0.001	5.37
Rhinitis	16(1.9)	9(12.9)	0.01	2.38
Insomnia	10(1.2)	6(6.4)	0.06	-
hemoptysis	17(2.0)	3(4.2)	0.09	1.76
dysgeusia	28(3.4)	5 (7.2)	0.03	3.15
Nausea	7(0.8)	16(23.18)	0.001	11.79
Diarrhea	11(1.3)	6 (6.4)	0.07	1.11
Myalgia	58(7.1)	12(17.39)	0.05	2.09
Fatigue	33(4.05)	7(10.14)	0.01	2.85
Headache	18(2.2)	14(20.28)	0.01	2.87
Nasal Congestion	3(0.3)	11(15.94)	0.003	4.15
Lymph Node inflammation	3(0.3)	1(1.4)	0.06	-
Oropharyngeal Congestion	15(1.8)	5(7.24)	0.01	-
Conjunctivitis	12(1.4)	1(1.40)	0.91	-

**Table 2:** Co morbidities of COVID-19 infected smokers and non-smoker patients

Parameters n (%)	Group 1 (n=814)	Group II (n=69)	P-value	OR
COPD	19(2)	6(8.69)	0.01	4.26
DM	72(8.84)	6(8.69)	0.67	-
Cancer	13(1.5)	1(1.4)	0.95	0.94
CLD	8 (0.98)	1(1.4)	0.41	-
CVD	24 (2.85)	2(2.89)	0.81	6.34
Hypertension	157(19.28)	19(27.53)	0.34	1.49
Thyriod	40(4.91)	5(7.24)	0.61	-
Anemia	169(20.76)	19(27.53)	0.22	-

COPD: Chronic Obstructive Pulmonary Disease; DM: Diabetes Mellitus; CLD: Chronic Liver Disease; CVD: Cardiovascular Disease



**Table 3:** Radiographic findings of COVID-19 infected smokers and non-smoker patients

Parameters n (%)	Group 1 (n=814)	Group II (n=69)	P-value
GGO'S	25(3.07)	7(10.14)	0.001
Local Patchy Shadow	5(0.61)	2(2.89)	0.03
B/L Patchy Shadow	9(1.1)	6(8.69)	0.01
Effusion	8(0.98)	2(2.89)	0.04
GGO(U/B)	76(9.3)	17(24.64)	0.001
Nodules	15(1.8)	3(4.34)	0.03
Consolidation	36(4.42)	12(17.39)	0.01
Pleural Effusion	14(1.7)	13(18.84)	0.01
Overall CT Scan Abnormally	64(7.86)	17(24.63)	0.01

GGO'S: Ground-glass opacification/opacity's; B/L: Bilateral

**Table 4:** Treatment protocols and clinical outcome in of COVID-19 infected smokers and non-smoker patients

Parameters n (%)	Group 1 (n=814)	Group II (n=69)	P-value	OR
Azithromysin	696(85.50)	58(84.05)	0.33	-
Hydroxyquinone	570(70.63)	61(88.40)	0.23	1.87
Ivermectin	629(77.30)	62(89.85)	0.44	0.37
Doxycycline	251(30.87)	11(15.95)	0.01	0.41
Plasma	57(7.00)	4(5.7)	0.44	0.98
High flow nasal canula/NIV/Mechanical ventilation	233(28.62)	36 (52.17)	0.40	0.77
Severe Illness	137(16.83)	37(53.62)	0.68	-
Death	30(3.68)	15(21.73)	0.12	2.15

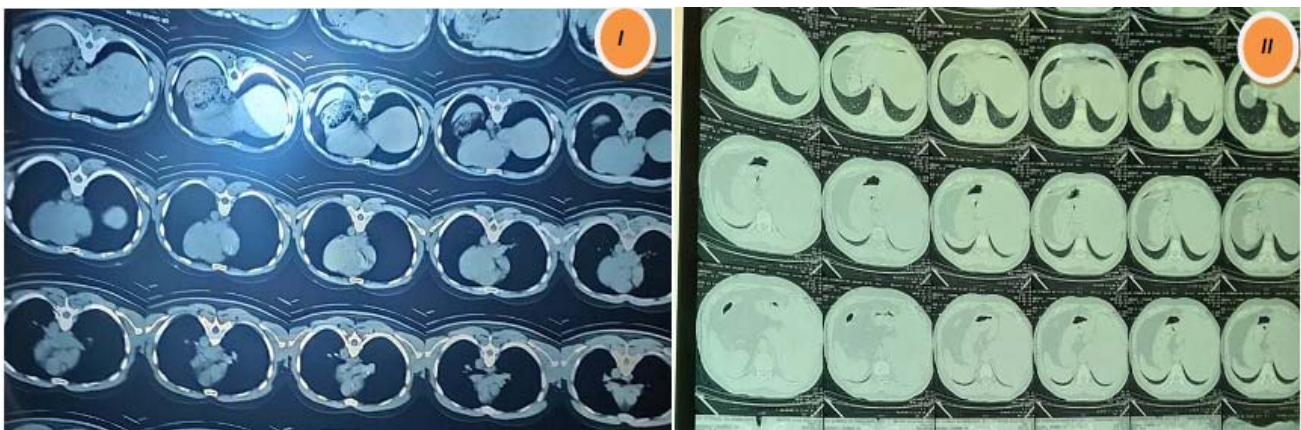
**Table 5:** Laboratory findings of COVID-19 infected smokers and non-smoker patients

Parameters (at)	Group I (n=814)			Group II (n=69)			P-Values
	95% confidence interval Lower Bound –Upper Bound	Mean ± SE	IQR	95% confidence interval Lower Bound –Upper Bound	Mean ± SE	IQR	
BMI	(21.45-23.13)	22.29 ± 0.42	5	(22.43-25.37)	23.90 ± 0.68		0.13
Temp	(92.55-98.01)	95.28 ± 1.39	4	(90.53-95.88)	93.20 ± 6.17		0.90
Heart Rate	(86.00-88.10)	67.05 ± 0.53	18	(83.78-92.53)	88.15 ± 2.16		0.73
White Blood Cell Count	(5691.40- 6367.03)	6029.22 ± 171.97	3700	(4806.67-6820.43)	5813.55 ± 500.77	3900	0.56
Lymphocyt Count	(1433.33- 1601.88)	1517.60 ± 42.89	900	(1319.38-1684.80)	1502.09 ± 90.59	650	0.79
Platelet Count	(148.3672-171.3992)	159.88 ± 5.86	232.44	(46.3153-111.9618)	79.13 ± 16.31	167.55	0.00
Creatinine	(1.073-1.170)	1.12 ± 0.02	0.4	(0.996-1.235)	1.11 ± 0.05	0.5	0.90
Blood Sugar	(103.64-116.30)	109.97 ± 3.21	36	(93.26-116.81)	105.03 ± 5.75	16	0.41
Bilirubin	(0.560-1.595)	1.07 ± 0.26	0.5	(0.687-1.309)	0.99 ± 0.14	0.5	0.02
SGOT	(58.89-74.99)	66.94 ± 4.09	40	(40.83-59.58)	50.21 ± 4.63	35	0.08
SGPT	(62.68-85.33)	74.01 ± 5.75	51	(48.93-74.86)	61.90 ± 6.40	42	0.99
ALP	(119.16-144.26)	131.71 ± 6.36	82	(115.05-166.17)	140.61 ± 12.61	147	0.69
Protein	(6.070-11.928)	8.99 ± 1.48	1.0	(7.440-8.378)	7.90 ± 0.23	1.3	0.08

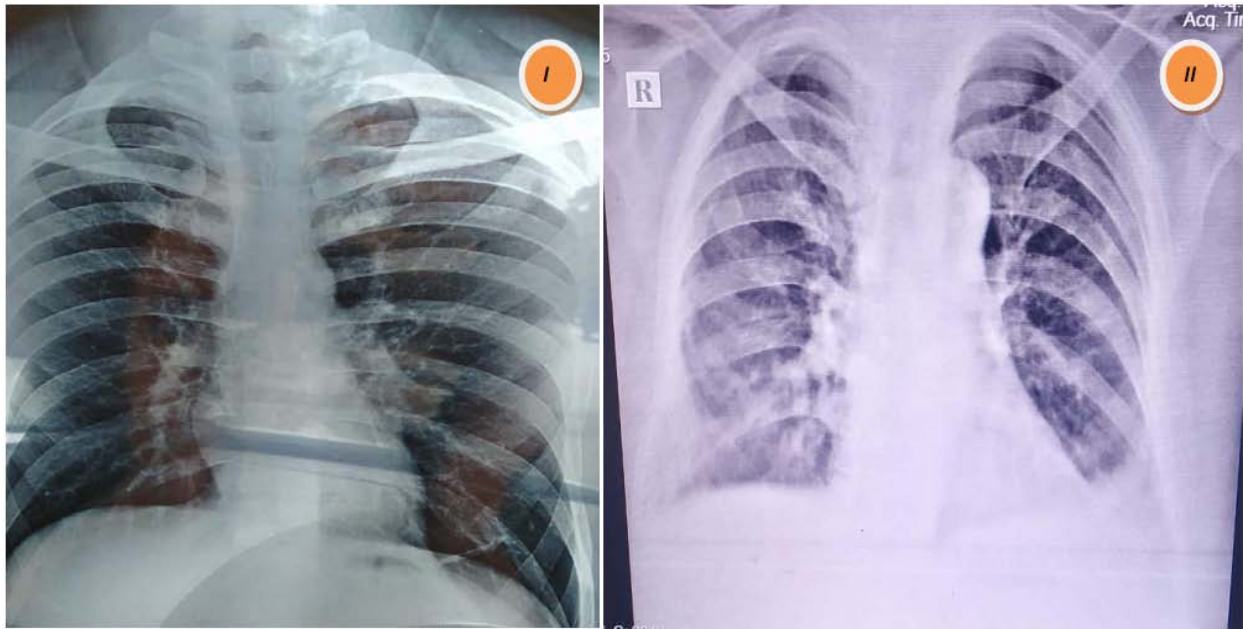
SGOT= Serum Glutamic Oxaloacetic Transaminase; SGPT=Serum Glutamic Pyruvic Transaminase; ALP=Alkaline phosphatase;

**Table 6:** Comparison of outcome in smoker v/s non smoker population treated with MIP

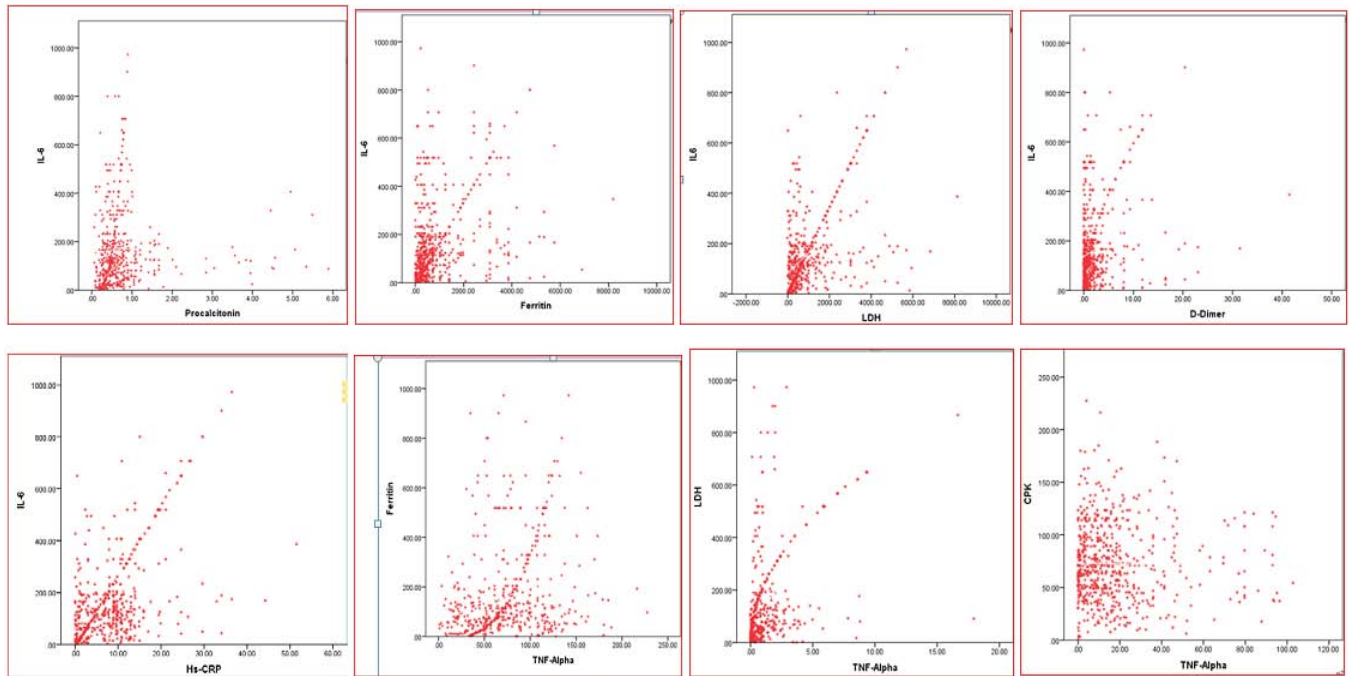
	<i>Smoker (39)</i>			<i>Non-Smoker (47)</i>		
<i>Characteristics</i>	<i>Pre MIP</i>	<i>Post MIP</i>	<i>P value</i>	<i>Pre MIP</i>	<i>Post MIP</i>	<i>P value</i>
Need for high flow Mechanical Ventilation	32 (82.05%)	21 (53.84)	0.01	27 (57.44)	16 (34.04)	0.05
Hospitalization (Days)	25.93±10.14			32.45±7.16		0.02
All cause mortality at 35 days	4 (10.25)			5 (10.63)		0.78
Negative conversion of SARS-Cov-2 on basis of RT-PCR on 7 <sup>th</sup> day	18 (46.15)			13 (27.65)		0.05
Negative conversion of SARS-Cov-2 on basis of RT-PCR on 14 <sup>th</sup> day	31 (78.48)			32 (68.08)		0.19
Retrogression to moderate diseases	33 (84.61)			39 (82.97)		0.34
Resolution of cough on 7 <sup>th</sup> day; n (%).			23 (58.97%)	22 (46.80%)		0.06
Resolution of fever on 7 <sup>th</sup> day; n (%).			33 (84.61%)	24 (51.06%)		0.62
Resolution of myalgia on 7 <sup>th</sup> day; n (%).			33 (84.61%)	19 (40.42%)		0.45
Resolution of sore throat on 7 <sup>th</sup> day; n (%).			31 (79.48%)	31 (65.95%)		0.77
Resolution of shortness of breath on 7 <sup>th</sup> day; n (%).			35 (89.74%)	37 (78.72%)		0.02



**Figure 1A:** CT scan findings in smoker (I) v/s non-smoker (II) COVID-19 patients' on 7<sup>th</sup> day of confirmation based on RT-PCR from nasopharyngeal swab. Patients were of similar age group and both were males.



**Figure 1B:** Radiographic (x ray) scan findings in smoker (I) v/s non-smoker (II) COVID-19 patients on 7<sup>th</sup> day of confirmation based on RT-PCR from nasopharyngeal swab. Patients were of similar age group and both were males.



**Figure 2:** Correlations of acute phase protein markers with pro-inflammatory cytokines.

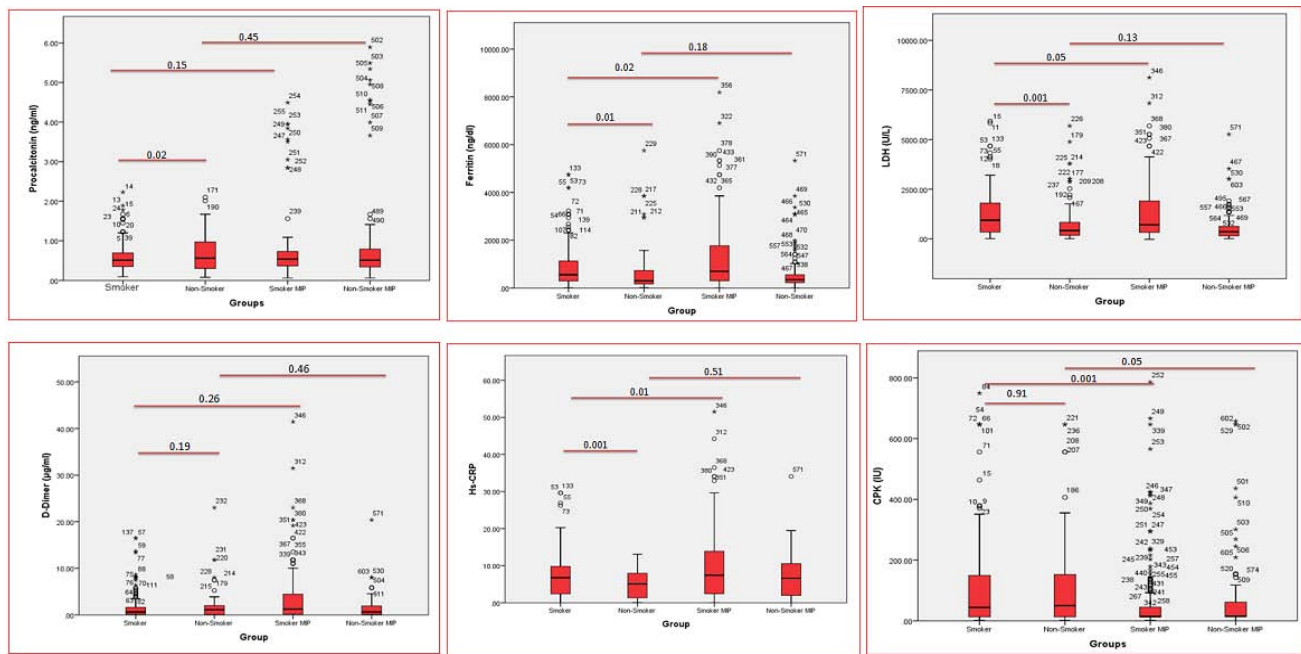


Figure 3: Dynamic Changes of acute phase protein response During Hospitalization in smoker and non smoker COVID-19 population treated with MIP with horizontal lines representing the median value in each group.

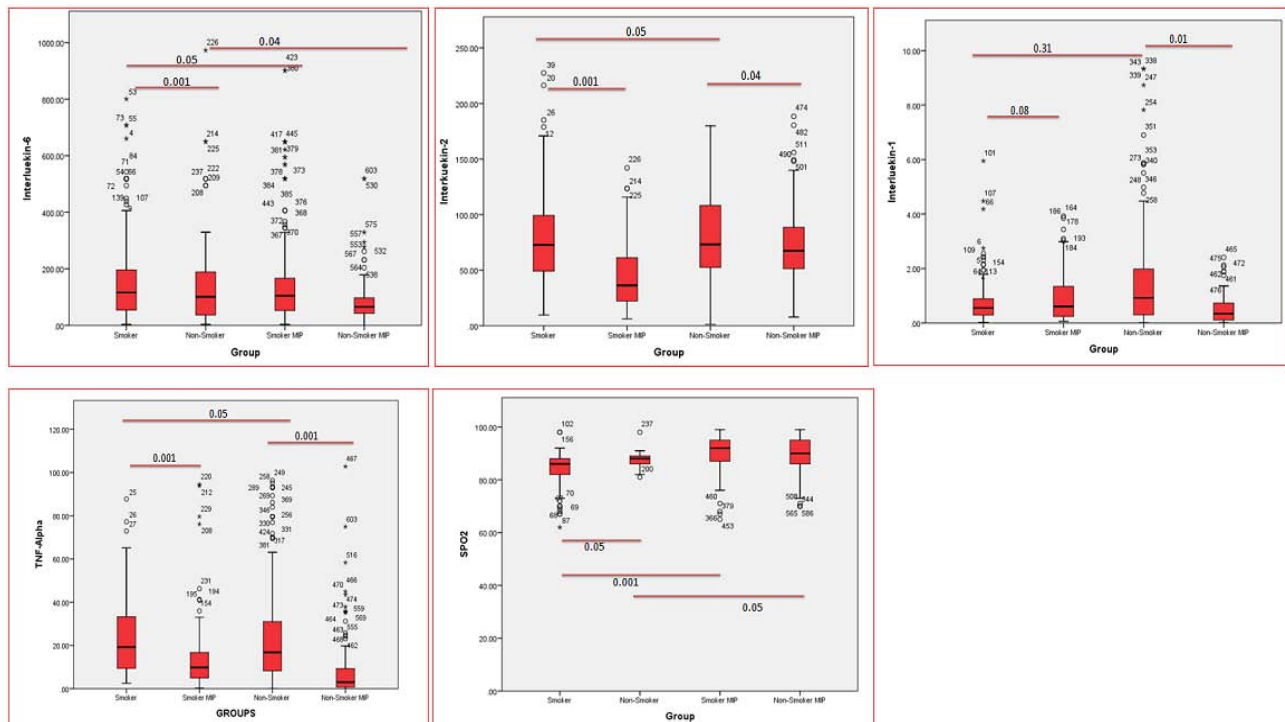


Figure 4: Dynamic Changes of pro-inflammatory response and SPO<sub>2</sub> levels during Hospitalization in smoker and non smoker COVID-19 population treated with MIP where horizontal lines representing the median value in each group.

# GLOBAL JOURNALS GUIDELINES HANDBOOK 2022

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- Paper title should be in one column of font size 24.
- Author name in font size of 11 in one column.
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- Two columns with equal column width of 3.38 and spacing of 0.2.
- First character must be three lines drop-capped.
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- Large images must be in one column.
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The recommended size of an original research paper is under 15,000 words and review papers under 7,000 words. Research articles should be less than 10,000 words. Research papers are usually longer than review papers. Review papers are reports of significant research (typically less than 7,000 words, including tables, figures, and references)

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**4. Use of computer is recommended:** As you are doing research in the field of medical research then this point is quite obvious. Use right software: Always use good quality software packages. If you are not capable of judging good software, then you can lose the quality of your paper unknowingly. There are various programs available to help you which you can get through the internet.

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**7. Revise what you wrote:** When you write anything, always read it, summarize it, and then finalize it.

**8. Make every effort:** Make every effort to mention what you are going to write in your paper. That means always have a good start. Try to mention everything in the introduction—what is the need for a particular research paper. Polish your work with good writing skills and always give an evaluator what he wants. Make backups: When you are going to do any important thing like making a research paper, you should always have backup copies of it either on your computer or on paper. This protects you from losing any portion of your important data.

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**10. Use proper verb tense:** Use proper verb tenses in your paper. Use past tense to present those events that have happened. Use present tense to indicate events that are going on. Use future tense to indicate events that will happen in the future. Use of wrong tenses will confuse the evaluator. Avoid sentences that are incomplete.

**11. Pick a good study spot:** Always try to pick a spot for your research which is quiet. Not every spot is good for studying.

**12. Know what you know:** Always try to know what you know by making objectives, otherwise you will be confused and unable to achieve your target.

**13. Use good grammar:** Always use good grammar and words that will have a positive impact on the evaluator; use of good vocabulary does not mean using tough words which the evaluator has to find in a dictionary. Do not fragment sentences. Eliminate one-word sentences. Do not ever use a big word when a smaller one would suffice.

Verbs have to be in agreement with their subjects. In a research paper, do not start sentences with conjunctions or finish them with prepositions. When writing formally, it is advisable to never split an infinitive because someone will (wrongly) complain. Avoid clichés like a disease. Always shun irritating alliteration. Use language which is simple and straightforward. Put together a neat summary.

**14. Arrangement of information:** Each section of the main body should start with an opening sentence, and there should be a changeover at the end of the section. Give only valid and powerful arguments for your topic. You may also maintain your arguments with records.

**15. Never start at the last minute:** Always allow enough time for research work. Leaving everything to the last minute will degrade your paper and spoil your work.

**16. Multitasking in research is not good:** Doing several things at the same time is a bad habit in the case of research activity. Research is an area where everything has a particular time slot. Divide your research work into parts, and do a particular part in a particular time slot.

**17. Never copy others' work:** Never copy others' work and give it your name because if the evaluator has seen it anywhere, you will be in trouble. Take proper rest and food: No matter how many hours you spend on your research activity, if you are not taking care of your health, then all your efforts will have been in vain. For quality research, take proper rest and food.

**18. Go to seminars:** Attend seminars if the topic is relevant to your research area. Utilize all your resources.

**19. Refresh your mind after intervals:** Try to give your mind a rest by listening to soft music or sleeping in intervals. This will also improve your memory. Acquire colleagues: Always try to acquire colleagues. No matter how sharp you are, if you acquire colleagues, they can give you ideas which will be helpful to your research.





**20. Think technically:** Always think technically. If anything happens, search for its reasons, benefits, and demerits. Think and then print: When you go to print your paper, check that tables are not split, headings are not detached from their descriptions, and page sequence is maintained.

**21. Adding unnecessary information:** Do not add unnecessary information like "I have used MS Excel to draw graphs." Irrelevant and inappropriate material is superfluous. Foreign terminology and phrases are not apropos. One should never take a broad view. Analogy is like feathers on a snake. Use words properly, regardless of how others use them. Remove quotations. Puns are for kids, not grunt readers. Never oversimplify: When adding material to your research paper, never go for oversimplification; this will definitely irritate the evaluator. Be specific. Never use rhythmic redundancies. Contractions shouldn't be used in a research paper. Comparisons are as terrible as clichés. Give up ampersands, abbreviations, and so on. Remove commas that are not necessary. Parenthetical words should be between brackets or commas. Understatement is always the best way to put forward earth-shaking thoughts. Give a detailed literary review.

**22. Report concluded results:** Use concluded results. From raw data, filter the results, and then conclude your studies based on measurements and observations taken. An appropriate number of decimal places should be used. Parenthetical remarks are prohibited here. Proofread carefully at the final stage. At the end, give an outline to your arguments. Spot perspectives of further study of the subject. Justify your conclusion at the bottom sufficiently, which will probably include examples.

**23. Upon conclusion:** Once you have concluded your research, the next most important step is to present your findings. Presentation is extremely important as it is the definite medium through which your research is going to be in print for the rest of the crowd. Care should be taken to categorize your thoughts well and present them in a logical and neat manner. A good quality research paper format is essential because it serves to highlight your research paper and bring to light all necessary aspects of your research.

## INFORMAL GUIDELINES OF RESEARCH PAPER WRITING

### Key points to remember:

- Submit all work in its final form.
- Write your paper in the form which is presented in the guidelines using the template.
- Please note the criteria peer reviewers will use for grading the final paper.

### Final points:

One purpose of organizing a research paper is to let people interpret your efforts selectively. The journal requires the following sections, submitted in the order listed, with each section starting on a new page:

*The introduction:* This will be compiled from reference matter and reflect the design processes or outline of basis that directed you to make a study. As you carry out the process of study, the method and process section will be constructed like that. The results segment will show related statistics in nearly sequential order and direct reviewers to similar intellectual paths throughout the data that you gathered to carry out your study.

### The discussion section:

This will provide understanding of the data and projections as to the implications of the results. The use of good quality references throughout the paper will give the effort trustworthiness by representing an alertness to prior workings.

Writing a research paper is not an easy job, no matter how trouble-free the actual research or concept. Practice, excellent preparation, and controlled record-keeping are the only means to make straightforward progression.

### General style:

Specific editorial column necessities for compliance of a manuscript will always take over from directions in these general guidelines.

**To make a paper clear:** Adhere to recommended page limits.



### *Mistakes to avoid:*

- Insertion of a title at the foot of a page with subsequent text on the next page.
- Separating a table, chart, or figure—confine each to a single page.
- Submitting a manuscript with pages out of sequence.
- In every section of your document, use standard writing style, including articles ("a" and "the").
- Keep paying attention to the topic of the paper.
- Use paragraphs to split each significant point (excluding the abstract).
- Align the primary line of each section.
- Present your points in sound order.
- Use present tense to report well-accepted matters.
- Use past tense to describe specific results.
- Do not use familiar wording; don't address the reviewer directly. Don't use slang or superlatives.
- Avoid use of extra pictures—include only those figures essential to presenting results.

### **Title page:**

Choose a revealing title. It should be short and include the name(s) and address(es) of all authors. It should not have acronyms or abbreviations or exceed two printed lines.

**Abstract:** This summary should be two hundred words or less. It should clearly and briefly explain the key findings reported in the manuscript and must have precise statistics. It should not have acronyms or abbreviations. It should be logical in itself. Do not cite references at this point.

An abstract is a brief, distinct paragraph summary of finished work or work in development. In a minute or less, a reviewer can be taught the foundation behind the study, common approaches to the problem, relevant results, and significant conclusions or new questions.

Write your summary when your paper is completed because how can you write the summary of anything which is not yet written? Wealth of terminology is very essential in abstract. Use comprehensive sentences, and do not sacrifice readability for brevity; you can maintain it succinctly by phrasing sentences so that they provide more than a lone rationale. The author can at this moment go straight to shortening the outcome. Sum up the study with the subsequent elements in any summary. Try to limit the initial two items to no more than one line each.

*Reason for writing the article—theory, overall issue, purpose.*

- Fundamental goal.
- To-the-point depiction of the research.
- Consequences, including definite statistics—if the consequences are quantitative in nature, account for this; results of any numerical analysis should be reported. Significant conclusions or questions that emerge from the research.

### **Approach:**

- Single section and succinct.
- An outline of the job done is always written in past tense.
- Concentrate on shortening results—limit background information to a verdict or two.
- Exact spelling, clarity of sentences and phrases, and appropriate reporting of quantities (proper units, important statistics) are just as significant in an abstract as they are anywhere else.

### **Introduction:**

The introduction should "introduce" the manuscript. The reviewer should be presented with sufficient background information to be capable of comprehending and calculating the purpose of your study without having to refer to other works. The basis for the study should be offered. Give the most important references, but avoid making a comprehensive appraisal of the topic. Describe the problem visibly. If the problem is not acknowledged in a logical, reasonable way, the reviewer will give no attention to your results. Speak in common terms about techniques used to explain the problem, if needed, but do not present any particulars about the protocols here.



*The following approach can create a valuable beginning:*

- Explain the value (significance) of the study.
- Defend the model—why did you employ this particular system or method? What is its compensation? Remark upon its appropriateness from an abstract point of view as well as pointing out sensible reasons for using it.
- Present a justification. State your particular theory(-ies) or aim(s), and describe the logic that led you to choose them.
- Briefly explain the study's tentative purpose and how it meets the declared objectives.

#### **Approach:**

Use past tense except for when referring to recognized facts. After all, the manuscript will be submitted after the entire job is done. Sort out your thoughts; manufacture one key point for every section. If you make the four points listed above, you will need at least four paragraphs. Present surrounding information only when it is necessary to support a situation. The reviewer does not desire to read everything you know about a topic. Shape the theory specifically—do not take a broad view.

As always, give awareness to spelling, simplicity, and correctness of sentences and phrases.

#### **Procedures (methods and materials):**

This part is supposed to be the easiest to carve if you have good skills. A soundly written procedures segment allows a capable scientist to replicate your results. Present precise information about your supplies. The suppliers and clarity of reagents can be helpful bits of information. Present methods in sequential order, but linked methodologies can be grouped as a segment. Be concise when relating the protocols. Attempt to give the least amount of information that would permit another capable scientist to replicate your outcome, but be cautious that vital information is integrated. The use of subheadings is suggested and ought to be synchronized with the results section.

When a technique is used that has been well-described in another section, mention the specific item describing the way, but draw the basic principle while stating the situation. The purpose is to show all particular resources and broad procedures so that another person may use some or all of the methods in one more study or referee the scientific value of your work. It is not to be a step-by-step report of the whole thing you did, nor is a methods section a set of orders.

#### **Materials:**

*Materials may be reported in part of a section or else they may be recognized along with your measures.*

#### **Methods:**

- Report the method and not the particulars of each process that engaged the same methodology.
- Describe the method entirely.
- To be succinct, present methods under headings dedicated to specific dealings or groups of measures.
- Simplify—detail how procedures were completed, not how they were performed on a particular day.
- If well-known procedures were used, account for the procedure by name, possibly with a reference, and that's all.

#### **Approach:**

It is embarrassing to use vigorous voice when documenting methods without using first person, which would focus the reviewer's interest on the researcher rather than the job. As a result, when writing up the methods, most authors use third person passive voice.

Use standard style in this and every other part of the paper—avoid familiar lists, and use full sentences.

#### **What to keep away from:**

- Resources and methods are not a set of information.
- Skip all descriptive information and surroundings—save it for the argument.
- Leave out information that is immaterial to a third party.



**Results:**

The principle of a results segment is to present and demonstrate your conclusion. Create this part as entirely objective details of the outcome, and save all understanding for the discussion.

The page length of this segment is set by the sum and types of data to be reported. Use statistics and tables, if suitable, to present consequences most efficiently.

You must clearly differentiate material which would usually be incorporated in a study editorial from any unprocessed data or additional appendix matter that would not be available. In fact, such matters should not be submitted at all except if requested by the instructor.

**Content:**

- Sum up your conclusions in text and demonstrate them, if suitable, with figures and tables.
- In the manuscript, explain each of your consequences, and point the reader to remarks that are most appropriate.
- Present a background, such as by describing the question that was addressed by creation of an exacting study.
- Explain results of control experiments and give remarks that are not accessible in a prescribed figure or table, if appropriate.
- Examine your data, then prepare the analyzed (transformed) data in the form of a figure (graph), table, or manuscript.

**What to stay away from:**

- Do not discuss or infer your outcome, report surrounding information, or try to explain anything.
- Do not include raw data or intermediate calculations in a research manuscript.
- Do not present similar data more than once.
- A manuscript should complement any figures or tables, not duplicate information.
- Never confuse figures with tables—there is a difference.

**Approach:**

As always, use past tense when you submit your results, and put the whole thing in a reasonable order.

Put figures and tables, appropriately numbered, in order at the end of the report.

If you desire, you may place your figures and tables properly within the text of your results section.

**Figures and tables:**

If you put figures and tables at the end of some details, make certain that they are visibly distinguished from any attached appendix materials, such as raw facts. Whatever the position, each table must be titled, numbered one after the other, and include a heading. All figures and tables must be divided from the text.

**Discussion:**

The discussion is expected to be the trickiest segment to write. A lot of papers submitted to the journal are discarded based on problems with the discussion. There is no rule for how long an argument should be.

Position your understanding of the outcome visibly to lead the reviewer through your conclusions, and then finish the paper with a summing up of the implications of the study. The purpose here is to offer an understanding of your results and support all of your conclusions, using facts from your research and generally accepted information, if suitable. The implication of results should be fully described.

Infer your data in the conversation in suitable depth. This means that when you clarify an observable fact, you must explain mechanisms that may account for the observation. If your results vary from your prospect, make clear why that may have happened. If your results agree, then explain the theory that the proof supported. It is never suitable to just state that the data approved the prospect, and let it drop at that. Make a decision as to whether each premise is supported or discarded or if you cannot make a conclusion with assurance. Do not just dismiss a study or part of a study as "uncertain."



Research papers are not acknowledged if the work is imperfect. Draw what conclusions you can based upon the results that you have, and take care of the study as a finished work.

- You may propose future guidelines, such as how an experiment might be personalized to accomplish a new idea.
- Give details of all of your remarks as much as possible, focusing on mechanisms.
- Make a decision as to whether the tentative design sufficiently addressed the theory and whether or not it was correctly restricted. Try to present substitute explanations if they are sensible alternatives.
- One piece of research will not counter an overall question, so maintain the large picture in mind. Where do you go next? The best studies unlock new avenues of study. What questions remain?
- Recommendations for detailed papers will offer supplementary suggestions.

#### **Approach:**

When you refer to information, differentiate data generated by your own studies from other available information. Present work done by specific persons (including you) in past tense.

Describe generally acknowledged facts and main beliefs in present tense.

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Topics	Grades		
	A-B	C-D	E-F
<i>Abstract</i>	Clear and concise with appropriate content, Correct format. 200 words or below	Unclear summary and no specific data, Incorrect form Above 200 words	No specific data with ambiguous information Above 250 words
<i>Introduction</i>	Containing all background details with clear goal and appropriate details, flow specification, no grammar and spelling mistake, well organized sentence and paragraph, reference cited	Unclear and confusing data, appropriate format, grammar and spelling errors with unorganized matter	Out of place depth and content, hazy format
<i>Methods and Procedures</i>	Clear and to the point with well arranged paragraph, precision and accuracy of facts and figures, well organized subheads	Difficult to comprehend with embarrassed text, too much explanation but completed	Incorrect and unorganized structure with hazy meaning
<i>Result</i>	Well organized, Clear and specific, Correct units with precision, correct data, well structuring of paragraph, no grammar and spelling mistake	Complete and embarrassed text, difficult to comprehend	Irregular format with wrong facts and figures
<i>Discussion</i>	Well organized, meaningful specification, sound conclusion, logical and concise explanation, highly structured paragraph reference cited	Wordy, unclear conclusion, spurious	Conclusion is not cited, unorganized, difficult to comprehend
<i>References</i>	Complete and correct format, well organized	Beside the point, Incomplete	Wrong format and structuring



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