

Susceptibility of the Bhopal–methyl isocyanate (MIC)–gas–tragedy survivors and their offspring to COVID-19: What we know, what we don't and what we should?

Suscetibilidade dos sobreviventes da tragédia de Bhopal–isocianato de metila (CIM)–gás e seus filhos ao COVID-19: O que sabemos, o que não sabemos e o que devemos?

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Abstract *There is credible evidence that the 1984–Bhopal–methyl isocyanate (MIC)–gas–exposed long-term survivors and their offspring born post-exposure are susceptible to infectious/communicable and non-communicable diseases. Bhopal's COVID-19 fatality rate suggests that the MIC–gas tragedy survivors are at higher risk, owing to a weakened immune system and co-morbidities. This situation emboldened us to ponder over what we know, what we don't, and what we should know about their susceptibility to COVID-19. This article aims at answering these three questions that emerge in the minds of public health officials concerning prevention strategies against COVID-19 and health promotion in the Bhopal MIC-affected population (BMAP). Our views and opinions presented in this article will draw attention to prevent and reduce the consequences of COVID-19 in BMAP. From the perspective of COVID-19 prophylaxis, the high-risk individuals from BMAP with co-morbidities need to be identified through a door-to-door visit to the severely gas-affected regions and advised to maintain good respiratory hygiene, regular intake of immune-boosting diet, and follow healthy lifestyle practices.*

Key words *Bhopal, India, Methyl isocyanate (MIC)–gas–tragedy survivors and their offspring, COVID-19 susceptibility, Preventive measures*

Resumo *Há evidências plausíveis de que os sobreviventes a longo prazo da exposição a gás de 1984 e isocianato de metila (CIM), em Bhopal, e seus filhos nascidos após esse fato estão suscetíveis a doenças infecciosas/transmissíveis e não transmissíveis. A taxa de fatalidade COVID-19 de Bhopal sugere que os sobreviventes da tragédia do gás MIC estão em maior risco, devido a um sistema imunológico enfraquecido e comorbidades. Essa situação nos encorajou a refletir sobre o que sabemos, o que não sabemos e o que devemos saber sobre a suscetibilidade deles ao COVID-19. Este artigo objetiva responder a essas três perguntas que surgem na mente dos funcionários de saúde pública sobre estratégias de prevenção contra o COVID-19 e promoção da saúde na população afetada pelo Bhopal MIC (BMAP). Nossas visões e opiniões apresentadas neste artigo chamam a atenção para prevenir e reduzir as consequências do COVID-19 no BMAP. Da perspectiva da profilaxia com COVID-19, os indivíduos de alto risco do BMAP com condições comórbidas precisam ser identificados por meio de uma visita de porta em porta nas regiões severamente afetadas por gases e aconselhados a manter uma boa higiene respiratória, ingestão regular de dieta que estimule o sistema imunológico e seguir práticas de estilo de vida saudáveis.*

Palavras-chave *Bhopal, Índia, Sobreviventes da tragédia de isocianato de metila (MIC) e seus filhos, Suscetibilidade ao COVID-19, Medidas preventivas*

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Introduction

In December 2019, the fatal outbreak of a novel coronavirus (2019-nCoV) causing febrile respiratory pneumonia-related illness first reported in Wuhan, Hubei Province, the People's Republic of China. In a short period, 2019-nCoV has raised global concern after continued its transmission in 213 nations and territories¹. Later the virus was identified as a kind of Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2) because of its genetic proximity with the CoV, which caused the SARS outbreak of 2003. The highly contagious spread of SARS-CoV-2 to almost every nook and corner of the globe necessitated public health emergency, and the World Health Organization officially named it as coronavirus disease (COVID-19) on January 30, 2020². Since then, the gradual increase of symptomatic and asymptomatic morbidity recorded every day and mortality rate heightened amongst the different age groups of people. However, the COVID-19 dependent mortality rate has been observed associated with age varying from country to country depending on several reasons, including a compromised immune system and co-morbidities. There is currently an ongoing debate about the susceptibility of people of all ages with co-morbidities, and severe underlying medical conditions that might manifest a higher risk for severe illness from COVID-19³. Besides, it is assumed that children and elderly adults aged ≥ 60 years belong to COVID-19 susceptible groups⁴. Undoubtedly, another group who should be in the debate is the life-threatening chemical exposed people surviving with chronic respiratory disorders. Here, we emphasize one such population who faced the World's worst chemical disaster in 1984 in Bhopal (Figure 1), survived the deadly methyl isocyanate (MIC) exposure with multiple complications including cancers⁵⁻⁷, pulmonary function abnormalities⁸, and obstructive lung function⁹. Almost thirty-five years over, the MIC-exposed long-term survivors and their offspring born post-exposure (also referred to as the Bhopal MIC-affected population) and their health status remain controversial. The COVID-19 mortality reports from Bhopal¹⁰ prompted us to ponder over what we know, what we don't, and what we should know about their susceptibility to infectious/communicable diseases. The medical emergency of COVID-19 has impelled us to answer these three specific questions that emerge in the minds of public health officials taking care of the Bho-

pal MIC-affected population (BMAP). We aim at discussing these issues in this article.

What we know?

Long-term effects in the BMAP

Following exposure to the toxic MIC-gas, many succumbed to death instantly, and those who survived yet suffer from agonizing prolonged health issues. Since then, the long-term effects of the exposed survivors and transgenerational repercussions in their offspring born post-exposure remain contentious¹¹⁻¹³. For the past three decades, the government and non-government organizations have been striving to understand the MIC-induced late effects in the BMAP. A large body of peer-reviewed epidemiological, clinical, and experimental evidence accumulated from case-only, case-control, and cohort studies have substantiated the MIC-induced late effects. Several clinical studies show respiratory complications in the MIC-exposed survivors. A retrospective observation of spirometry indicates the relative risk of pulmonary function anomalies amongst young survivors of the disaster. Smoking habits appeared to accentuate obstructive pattern in spirometry of the survivors⁸. Yet another study involving annual changes in spirometric parameters showed an accelerated decline in the pulmonary function of the exposed survivors with chronic respiratory symptoms. They were suggested to be at higher risk of developing obstructive lung function⁹.

In line with this, we have done a considerable amount of groundwork to understand the MIC-induced late effects of BMAP through bio-monitoring study supported by the Council of Scientific and Industrial Research (CSIR), Government of India. Data analyzed from five years descriptive cross-sectional epidemiologic study revealed increased site-specific cancer incidence, particularly of breast cancer in females and lung cancers in males in the case-only cohorts⁵. Subsequently, a prospective cohort study monitored the immune system and cancer susceptibility of MIC-exposed healthy long-term survivors and their offspring *vis-à-vis* gender-age-group-matched unexposed healthy controls from Bhopal and various other regions of India, after rigorously incorporating several lifestyle attributes and dietary habits demonstrated the high occurrence of atypical lymphocytes¹². It was almost a regular observation in the exposed females (EF)¹⁴.



Figure. Memorial carving of a mother running with her kids to save their life from the deadly MIC gas (Established in remembrance of the Bhopal gas disaster victims those lost their lives on 1984 December 03).

An increase in the frequency of micronucleus suggested cytogenetic damage in the EF and female offspring of the MIC-exposed substantiated transgenerational effect of MIC¹³. This evidence demonstrated MIC appears to afflict offspring born post-exposure of the survivors, particularly from the standpoint of an anomaly in the cytogenetic status. Our novel findings on alterations in the humoral immune function, genetic surveillance of Glutathione S-transferase *M1* (*GSTM1*) and *T1* (*GSTT1*) deletion polymorphism, and hypoxanthine-guanine phosphoribosyltransferase (*HPRT*) mutation frequencies suggests genetic susceptibility and other risks are yet to be published. Findings from the biomonitoring study have paved the way for a better understanding of MIC-induced late effects in the BMAP and their susceptibility.

What we don't know?

Is BMAP vulnerable to infectious/communicable diseases?

Our studies with immunological parameters showed a negligible long-term effect of MIC on cell-mediated immunity in BMAP¹⁴. In contrast, significant alterations in the circulating proteins, particularly the suppression of α_1 -globulin corresponding to α_1 -antitrypsin (a key inflammatory regulator in the human airway) deficiency, which in turn may contribute to chronic airway obstruction suggests a long-term depreciatory effect of MIC on the humoral immunity of BMAP (Unpublished data). However, our understanding of the MIC-induced-airway obstruction in BMAP is limited, at present, and it may be worthwhile to investigate the genes involved in thiol-redox homeostasis in the airways in the context of long-term effects of MIC-exposure on the respiratory function. These observations commensurate with earlier published data on the MIC-exposed survivors^{8,9}, tend to suggest their decreased responsiveness and increased susceptibility to infectious diseases.

Is BMAP at risk attributable to COVID-19?

There is a growing consensus from Bhopal that suggests the exposed survivors with co-morbidities are at higher risk due to COVID-19. The fatality rate appears to be higher because of chronic obstructive pulmonary disease (COPD) coupled with COVID-19¹⁵⁻¹⁸. A recent study of Leung et al. found that people with active cigarette smoking habit and COPD have increased airway expression of angiotensin-converting enzyme II (ACE-2) that facilitates the entry of SARS-CoV-2 and causes COVID-19⁹. A recent meta-analysis by Wang et al. also observed COPD as the chief risk factor for patients with COVID-19²⁰. These shreds of evidence support the plausibility that the MIC-affected people and those with smoking habit and COPD run a higher risk of COVID-19.

What should we know?

How to protect the BMAP from COVID-19?

The substantial scientific evidence emphasizes that the MIC-affected, especially the survivors with COPD, are highly susceptible to COVID-19 owing to their existing pulmonary

complications. Therefore, it is of utmost importance that the affected people become aware of their risk to COVID-19 and its timely prophylactic measures. Health policy-makers need to strengthen the action plans to protect the BMAP from COVID-19. Endeavors should be made to visit door-to-door in the gas-affected zones for preventive screening, raising awareness of preventive hygienic practices, and routine health check-ups of the affected population. Door-to-door visits by public health officials and health care workers may assess the individual-level risk factors and recognize the COVID-19 vulnerable cases and the high-risk families in the affected population. Raising awareness about good respiratory hygiene, proper caring for co-morbid illnesses, counseling on smoking and smokeless tobacco cessation, alcohol avoidance, and intake of immune-boosting diets may effectively minimize the COVID-19 risk among the vulnerable subjects. Regular health monitoring, preventive hygiene and healthy lifestyle practices are mandatory prophylactic measures that help to protect the vulnerable from COVID-19. Door-to-door pamphlet circulation and continuing health awareness-raising programs in the mainstream media, newspapers, and magazines may strengthen awareness among the BMAP. Most importantly, some of the gas-affected areas are congested, and many survivors residing in the narrow untidy lanes with poor ventilation are at high risk. Above all, regular environmental sanitation, waste management, and access to safe drinking water may fortify hygienic measures and prevent disease transmission in these areas.

What are the long-term possible self-care measures for BMAP?

Along with tremendous efforts by the central and state governments to stop the spread of COVID-19 in Bhopal, community participation

is crucial in guaranteeing success. The BMAP needs to adopt several long-term self-care measures, such as the routine practice of good respiratory hygiene with face masks, frequent hand sanitation, maintenance of safe physical distance, travel restrictions to the over-crowded area, safe potable water, consumption of fully cooked fresh home-prepared meals, intake of immune-boosting diet, regular health check-ups for co-morbid illnesses, and healthy lifestyle to prevent COVID-19. The MIC-affected individuals must refrain from smoking and smokeless forms of tobacco and excessive consumption of alcoholic beverages and take supplements along with sound sleep to fortify the immune system. The survivors with COPD and other co-morbidities need to follow rigorous self-care practices. Also, routine sanitation and disinfection of surfaces and living environment can promote their hygiene. There are numerous remedies from the complementary and alternative medicine systems proposed to manage the symptomatic-illnesses of COVID-19²¹. However, non-prescription use or misuse of these remedies in co-morbid conditions may potentially lead to severe complications, especially in elderly people²². Herbal remedies may cause drug interactions and poses risks when taken by themselves for long-term in combination with other substances or alone in excessive doses²³⁻²⁵. Preemptively seeking the medical advice of physicians may help to manage existing co-morbid illnesses and reduce the COVID-19 risk. Briefly, preventive and health promotion strategies must be adopted to safeguard the BMAP from COVID-19.

Disclosure

The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any institute or government.

Collaborations

CS Senthilkumar: Conceptualization/ Data curation/ Formal Analysis/ Writing – original draft / Writing – review & editing – Lead and first author. TM Malla: Writing – review & editing. S Akhter: Writing – review & editing/assistance. NK Sah and N Ganesh: Conceptualization/supervision.

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