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Review Article

Immunological Landscape Diversity to Covid-19 Differential Mortality and Response - A Tenable Hypothesis

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Abstract

Consequent to the outbreak of SARS-COV1-2 virus throughout the world since 2020, the mortality or death toll was noticed in all countries. The death due to COVID-19 diseases was attributed to the adverse pathological effects of the virus on the lung alveolar cells and the endothelial cells. The death was also enhanced in morbid patients suffering, diabetic cardiac, B.P, and kidney problems. The excess secretion of inflammatory cytokines and the cytokine storms brought the above overt and covert deaths. Inspite of the potential of the virus's infection from individuals, groups and through ambience and materials the deaths among were differential. The differential mortality and prevalence rate was marked within a single geographical province like Indian peninsular regions and in its southern state (Tamil Nadu). The meta- analysis and epidemiological comparisons of seroprevalence in different populations attribute immunological landscape diversity to the differential mortality and response. Such diversities in immunological profile do exist between individuals, populations and ethnic groups for various diseases like cancer, arthritis and other auto immune diseases. Several intrinsic and extrinsic factors are determinants to such variations, and to the susceptibility of individuals or to their resistance. Taking cue from the polymorphic potential of the SARS virus and their antigenic expressions, the present note elucidates the importance of different preventive strategies to overcome the pandemic and to curtail the exacerbating factors.

Keywords: SARS-COV-2; Immunological Landscape; Seroprevalence; Lung Cells Pathology; Immunization

Introduction

It is known that the immunological landscape and immunological resistance to the infection of microbes in general and for the viruses in particular are differential between individuals, haplogroups populations and ethnic groups. Several intrinsic cum extrinsic factors determine the above differential immunity among populations. The viral load as well as the antibody responses is not finite but stochastic. The different gradations among infected individual may include:

- Asymptomatic healthy survivors and transmitters.
- Asymptotic carriers and non transmitters.
- Symptomatic carriers and transmitters
- Symptomatic non-survivors are known.

The last two categories represent the epicentric mass groups who can spread the pandemic. But recent reports revealed that the first two categories are also as contagious as the latter and may help enhance group immunity among youth populations and thus help getting acquired immunity (active) or they may spread the infections to comorbid populations.

The differential prevalence or incidence and mortality rate due to COVID-19 implies that the high rate of infection and the consequent deaths of individuals in the hot spot countries viz., U.S.A, Italy, Spain, UK, and Germany while the lesser magnitude of infection and death rate in the Indian geographical province with differential states are due to the poor immune response in the former while highly reactive response in the latter respectively. Throughout the world 206 million corona positive cases were reported and the total deaths were 43, 48,193 (i.e. 4.3 million). The higher death incidences were reported in USA (636298) Brazil (566988), UK (130701), Italy (128334) and India (430285). Compared to total positive cases in India Viz., 32117826 the deaths were low only. Incidence and mortality may also be attributed to strains difference in virulence in SARS COV-2.

The Americans and Europeans suffered death because they all may represent the immune compromised individuals constitutively or poor responders immunologically which caused the acute infection of SARS-CoV-2 from the ambience or from the infected individuals or clusters. Their death may be attributed to the immunologically mediated lung/bronchial cells collapse and the consequences follow as sequelae on kidney, heart and B.P. The various immunological reasons that may account for their death are as follows:

- The excess secretion of inflammatory cytokines and the resulting cytokine storm is one. This is plausible in view of the TLRs (Toll Like Receptors) and their interactions with viral receptors to induce the secretion of proinflammatory cytokines.
- The individuals may be poorly immunogenic.
- Their immunological landscape may be defective in the development of adaptive or acquired immunity in terms of cellular and humoral immune response. Such immunological lapses among different ethnic groups leading to more incidences of cancers have been reported [1]. The Comorbid conditions and the habits of smoking and drinking in European population may also be an added cause for their death.

In India, the death or mortality due to COVID-19 was reported to have occurred in aged, comorbid and vitamin-D deficient people. The Meta analysis of the death rate, age wise, could reveal the above. Moreover the immunological landscape of Asians in general and Indians in particular may be efficient in terms of their cellular and humoral responses i.e., in antigen processing and presenting; in the degradation of the macro-molecular proteins of the SARS-CoV-2 and the plasma cells capability to synthesize polyclonal antibodies.

The above responses may not be unexpected in view of the structural profile of the SARS-CoV-2.

- The report that the strain infecting the Asian geography, weak in the native state may be one factor to the lower mortality.
- The climatic conditions like temperature, humidity, pH, and interacting substances could have weakened the strain and its 100 percent infection could have been ruled out.
- The combination of tissue protein with the viral antigen could have induced a high immunogenicity in this Indian haplogroup. This may be expected in view of the fact that the SARS CoV-2 after synthesizing their RNAs and proteins, the latter undergo glycosylation in the host cell golgi complex with such sugars as glucose, manose, glucosamine or galactosamine etc.,

It may also be construed that the plasma B cells could have synthesized in response to SARS-CoV-2 antigen, polyclonal type of circulating antibodies. The positive cases of identification by kits and the plasma antibody therapy trials resulted in curing the patients (Delhi) are also evidences for this. Recently in Tamil Nadu (state), the directorate of public health and preventive medicine (DPH) in its serosurvaey (July 2021) for SARS-COV-2 antibodies with a sample population of 26610 individuals in 888 clusters (revealed 66.2%) seropositivity. The survey also revealed that Erode had the lowest at 37% and virudhunagar and Chennai the highest sero positivity rate of 84% and 82% respectively. It was attributed to natural infection and due immunization. However this may also be attributed to food and supplementary nutrients which afford immunity.

Previous studies on some diseases of autoimmune origin such as arthritis have revealed that the incidence and prevalence rate of arthritis was more in UK and USA as compared to India [2]. The greater incidence of both cancer and arthritis among the western population in contrast to the Indian counterparts has also been attributed to the dietary patterns in these regions [1,3]. Similarly Indira and Ramalingam [4] have revealed the socio-cultural factors behind cancer incidence in individuals. Various prerequisites for effective immune response and survival may be the following:

- Vitamin -D level especially D_3 is crucial for survivors.
- Vitamin -E being the effector and booster of immune system, its optimum level helps fight during flu session.
- An effective immune system keeps the active functioning of viral fighters such as T-lymphocytes, macrophages NK-cells and B cells. These cells especially T lymphocytes will bind to the receptors of the viral infected cells and kill the viruses alongside the infected cells by secretory anti-inflammatory cytokines Viz., IL6, IL10.
- Vitamin -C is already known to afford resistance to the body against viruses. Hence optimal vitamin-C is also required to prevent as well as to fight against the viruses.
- The statistical data have elucidated that the incidence of the autoimmune diseases like arthritis is more in European populations and in USA & UK. In this context reports exist that the titer of mannose binding lectin when reduced, it may induce above disease. Hence the mannose binding lectin (MBL) is also a plasma indicator to either disease resistance or susceptibility. Towards this, viral protein takes up mannose and undergoes glycosylations of interest to mention. So sugar is an important scalar quantity by which the glycosylation of viral proteins may be regulated after their protein synthesis and their transit to golgi complex.

The containment of SARS-CoV-2 should involve not only the extrinsic strategies to break the chain of infection but also needs intrinsic strategies to prevent or arrest the growth and proliferation of the virus inside the host respiratory (organ) cells. The various strategies include:

- By boosting the immune system the person may able to put forward the III and IVth line defense against the virus. For instance an active T-cell or NK cell may able to secrete anti-viral proteins to squash both the host cells and the viruses inside.
- By restricting the supply of sugar and the glycosylation of viral proteins, the full fledged proliferation of the viruses inside the host cells may be hampered or at least delayed to a certain extent.
- Diabetic patients succumbing to death due to COVID-19 is an outstanding evidence that their unstinted supply of blood glucose (Hyperglycemic) may promote the unregulated proliferation of the viruses and the viral load *in vivo*. Hence regulation of blood sugar is a critical factor to contain the disease, through phytochemical substance like phenol, flavones, flavonoids, isoflavones etc.
- Infiltration of SARS-CoV-2 Viruses inside the endothelial cells of lower respiratory organ brings about the collapse of the lung cells. This could be possible in a comorbid individual where these endothelial cells permeability could have become increased due to thinning which could have been in turn enhanced by self habituations like intense smoking, alcohol drinking, lack of aerobic respiratory exercise, intake of excess of sugar of zero (0) calories etc. Towards this, increasing the thickness of the endothelial cells may resist the infiltration of the viruses inside the cells. Though receptors interaction of the cells and the antigenic surface of the viruses pave way to the entry of viruses, several phytochemical compounds like β-carotene can prevent such interactions and viral entry inside. Gopal., *et al*. (2010) in their study on nude mice with cerebral aneurysm revealed that consistent feeding of those mice with β-carotene increased the thickness of the endothelial cells, and weight of the spleen. [5]. Taking cue from the above study it is plausible to bring the enhancement of spleen potential and the endothelial cell thickening by the phytonutrients or compounds derived from the vegetables. Moreover the recent research report also elucidated how chloroquine and Zinc could cause the disruption of virus replication inside the host cells. Zn Combines with ACE receptors and couples with chloroquine and the internalization or endocytosis of Zn and Chloroquine increase the alkalinization and inhibit the virus's replication. Recently Philip., *et al*. [6] have also revealed the importance of Zn and azithrocin in the management in the COVID-19 patients in hospitals [7].

Conclusion

As viral pathogens often takes asylum in the vector animals and remain as inert gene component in human carriers and emerge out recurrently after some years in same form or in mutated form as variants, more than the preventive vaccines which build a short duration immunity *in vivo* and/or in addition to immunization, the preventive phytochemical compounds may build up the natural cellular cum humoural immunity. The latter strategy would go a long way in the fight against the pandemics.

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