Review Article

The Increased Risk of Elderly Population in India in COVID-19 Pandemic

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ABSTRACT

Increase in life expectancy and decline in mortality rate has resulted in a very fast growth rate of elderly population in India. Poor economic condition, low literacy and poor hygiene make the elderly in India at much higher health risk. Most people above the age of 60 suffer from chronic diseases such as, respiratory diseases, cardiovascular diseases (CVD), diabetes, hypertension, dementia, etc. In addition, impaired Immune system associated with old age makes them more susceptible to various infections. The elderly population in India has been the most vulnerable group in COVID-19 pandemic, contributing to ~ 53% of the reported fatalities due to COVID-19. The SARS-CoV-2 virus interacts with angiotensin-converting enzyme 2 (ACE2) on the host cell surface with its S (spike) glycoprotein and then undergoes endocytosis. Inside the cell, the virus replicates and triggers the release of cytokines which can induce an inflammatory response. Chronic increase in systemic inflammation has been seen in the elderly, which is further aggravated on SARS-CoV-2 virus infection. Patients with chronic respiratory diseases have shown significant increase in ACE-2 expression which may increase viral load in case of COVID-19 infection. COVID-19 patients also show elevation of cardiac troponins (cTnI) which puts CVD predisposed patient at a higher risk. The elderly in our country need extra care to be protected from diseases and proper disease management in case of disease manifestation.

Key words: Elders, COVID-19, ACE2, Immunity, Comorbidity

INTRODUCTION

As old age sets in, people above the age of 60 are considered elders. The elderly population in India has steadily increased and has almost doubled in the past 20 years. (Figure 1). [1] While the overall population of India is projected to grow by 40 per cent from 2006 to 2050, the elderly population is projected to grow by 270 percent. Hence, the aging population is expected to surpass the population of children in another 20 years. [2]
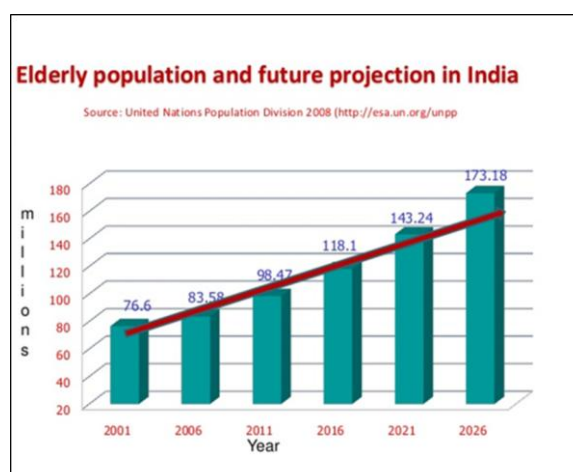

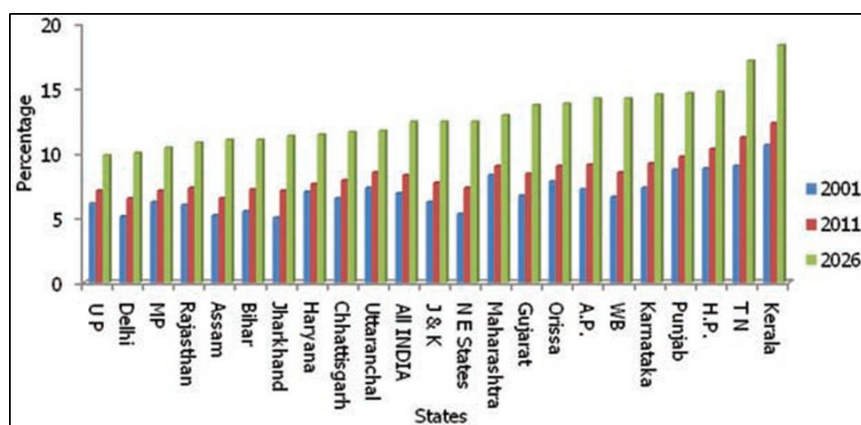Figure 1. Elderly population and future projection in India. [1]

Figure 2: Proportion of elderly in India and its States, 2001, 2011 and 2026.[3]

Disparities exist if we compare the growth rate of elderly population of different states of India. The rate of growth of elderly population is highest in southern states such as Andhra Pradesh, Karnataka, Kerala, and Tamil Nadu. Amongst the southern states Kerala has the largest growing rate of elder's population. The other Indian states, notably Haryana, Himachal Pradesh, Maharashtra, Orissa, and Punjab are also experiencing a boom in elderly population, largely in rural areas (Figure 2). [3] India would soon make a demographic transition from a young nation to an aging nation with a 20% aging population in the next 20 years. The decline in fertility and mortality rate and increased life expectancy, is resulting in this gradual increase in the number of elderly persons in the population. This demographic shift poses massive challenges to Indian society and policy makers to our progress towards a healthy nation.

The cultural and geographic diversity of our country is reflected in the heterogeneity of our elderly population, majority (80%) of whom reside in the rural areas and a large percentage (30%) of the elderly are below the poverty line. 51% of the elderly population would be women. [4] NSSO, 2006 data shows that a majority of rural (66%) and urban (63%) dwellers are dependent on their children, who are expected to provide financial and social support and personal care. [5] The absence of universal social security and health programs contribute to the dependency of

India's elderly population. 74% of rural and 40% of urban elders lacked formal schooling and education. This has a direct impact on direct access and management of their health care needs. Poor access to health services, poor economic condition, and poor hygiene in rural areas as compared to urban areas is further responsible for poor health and more reported ailments in rural areas as compared to urban areas.

In the urban areas, if dependency has its problems, living alone makes the elderly even more vulnerable. Breakdown of the traditional joint family system and more and more children opting to move out of their homes to bigger cities or other countries in search of better opportunities, the elderly are forced to spend the rest of their lives alone or with their spouses. With the absence of the blanket of family social environment and economic security, the elderly feel even more isolated, lonely and helpless. [6] As a society we have to address these issues to make our elderly more self-independent, self-reliant and well taken care off.

Aging brings along with it many health related issues and challenges. Aging itself is a disease which requires proper management and care. Very few people reach old age completely free of disease .With aging, there is a decline in the normal functioning of the body which results in poor mobility, hearing, vision, inability to eat and digest food properly, a decline in memory, the inability to control certain physiological functions and various other

chronic health problems. Poor metabolism, low BMI, compounded by less physical activity leads to anorexia coupled malnutrition. Malnutrition leads to weight loss, reduced muscle mass, decreased immunity, frailty, deficiency of micro and macro nutrients causing anemia, osteoporosis, electrolyte imbalance and many other complications.

The most common chronic diseases afflicting the elderly are: cardiovascular disease, adult onset diabetes, arthritis, kidney and bladder problems, dementia, Parkinson's disease, eye disease, osteoporosis, enlarged prostate, Alzheimer's disease, and depression. The incidence of chronic diseases would also increase in the elderly with an increase in aging population (Table 1). [7] This would dramatically increase the disease burden and health care requirements. Cardiovascular diseases (CVD; coronary artery, cerebro-vascular, and peripheral vascular diseases) are a leading cause of mortality among the elderly in India. CVD accounts for one third of elder mortality, with 10–12% in urban areas and 4–5% in rural areas. [8] It is well established that conventional

Table 1. Incidence of Chronic Diseases amongst the Elderly (India, 2011–2050). [7]

Major chronic diseases	Prevalence% (2011)	Incidence in million cases				
		2011	2015	2020	2030	2050
Arthritis	29.3	30.4	34.1	40.8	55.9	96.7
Hypertension	21.0	21.8	24.5	29.3	40.1	69.3
Diabetes	10.1	10.5	11.8	14.1	19.3	33.3
Asthma	7.7	8.0	9.0	10.7	14.7	25.4
Heart disease	5.8	6.0	6.8	8.1	11.1	19.1
Depression	1.5	1.6	1.7	2.1	2.9	5.0
Alzheimer's disease	1.4	1.5	1.6	2.0	2.7	4.6
Cerebral stroke	1.0	1.0	1.2	1.4	1.9	3.3
Dementia	0.9	0.9	1.0	1.3	1.7	3.0
Cancer	0.4	0.4	0.5	0.6	0.8	1.3
One or more chronic ailments	64.8	67.3	75.5	90.3	123.6	213.9

risk factors such as, smoking, hypertension, diabetes mellitus, obesity, unhealthy diet, and reduced physical activity together account for more than 95% of risk factors for CVD in urban areas. Changing lifestyles in rural India, modern amenities, and less physical labor are increasing cardiovascular risk factors among elderly in rural India with time.

Adult onset, type 2 diabetes is a major health problem among the elderly and is on a rise in India. National data of 2004 and 2014 suggest notable increases in prevalence of diabetes among urban elderly (7%−11%), those above 75 years of age (3%−5%) and rural elderly(3%−9%). The number of reported cases and the heterogeneity in clinical presentations appeared to increase higher among the males than females. [9] Diabetes requires long-term medication and management hence puts increased economic burden on the family unit.

Studies show that about 17.93% of elderly men and 26.21% of elderly women in the country experience either mild or severe disability and the burden is increasing substantially with the rising life

expectancy. [10] Arthritis, vision associated disability, Parkinson's disease, and stroke are some of the common causes of disabilities. In absence of access to costly aid instruments such as auto self-regulated wheelchairs, disabilities in India affect the activities of daily living (ADLs) among elderly people in India. With better medical care and management the wealthy elderly people experience a lower prevalence of disability than the poor do. Disability affects wellbeing, the quality of life and increases morbidity.

Mental health is a taboo subject in India, patients rarely seek help regarding their mental health problems until the situation becomes beyond their control. The heterogeneity in clinical presentations and symptoms sometimes makes diagnosis difficult. Dementia is the most common neuropsychiatric illness besides depression which is a major contributor to disability in people above 60 years of age, accounting for one-quarter of all disability affected elderly. Eight large-scale epidemiological studies have indicated that dementia prevalence for the aged who are >85 years in India ranges from 18% to 38% and, in those >90 years, it ranges from 28 % to 44 %. [11] Dementia is a decline in cognitive, intellectual and memory function due to affection of the central nervous system without loss of consciousness. There is slow onset of forgetfulness, loss of interest in day to day activities and impairment in social skills. Other common symptoms include disorientation in time and space, and language impairment. Such people are incapable of taking care of themselves, hence specialized dementia care homes which are conspicuous by their absence in India need to be developed. Impaired immunity makes elder persons more susceptible to infections than younger adults. [12]

Tuberculosis, urinary tract infections, lower respiratory tract infections, skin and soft tissue infections, intra-abdominal infections (cholecystitis, diverticulitis, appendicitis, and abscesses),

bacterial meningitis, and herpes zoster appear to have a special predilection for elderly persons. Poor prognosis in the elderly can be attributed to many factors apart from impaired immunity. These include, delays in diagnosis and therapy, poor tolerance to invasive diagnostic and therapeutic procedures, delayed or poor response to antimicrobial therapy, and higher rates of adverse reactions to drugs, including antibiotics. [13] Physiological changes in the elderly affect the pharmacokinetics and pharmacodynamics of drugs in the elderly. [14]

Corona virus disease (COVID-19)

Coronavirus disease (COVID-19) caused by transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) appeared for the first time in Wuhan, China, at the end of 2019. Spread by human-to-human contact was declared a global pandemic of enormous proportion by WHO, infecting more than 30 million people across 188 countries and resulting in more than 1 million fatalities (Sept, 2020). The disease is ever evolving and spreading unabated. The clinical symptoms range from a common cold, fever, head ache, to more severe manifestation such as bronchitis, pneumonia, severe acute respiratory distress syndrome (ARDS), multi-organ failure, and even death.

The lungs are the most affected organs as SARS-CoV-2 primarily infects ciliated bronchial epithelial cells and type II alveolar cells. It binds to the surface receptor, angiotensin-converting enzyme 2 (ACE2), through S (spike) glycoprotein found on its surface. On binding of S glycoprotein to the ACE2, the cleavage of trimer S protein is triggered by the cell surface-associated transmembrane protease serine 2 (TMPRSS2) and cathepsin. S1 subunit of S determines the host interaction and facilitates viral attachment to the target cells and S2 subunit mediates the fusion of viral and cellular membranes, ensuring viral entry through endocytosis. [15] After the release of the viral genomic RNA into the cytoplasm, the few viral genes are translated

into polyproteins pp1a and pp1ab, which are then cleaved by viral proteases into small non-structural proteins such as RNA-dependent RNA polymerase (RdRP). The viral genomic RNA is then replicated using viral RdRP, and the four structural proteins (S, E, M and N) are translated using host translational machinery. Finally, the genomic RNA and structural proteins are assembled into new viral particles, leading to their release through exocytosis. [16] 2009). (Fig. 4). Each step of the viral life cycle membrane fusion and endocytosis (a target of the antimalarial drug chloroquine and anti-influenza drug umifenovir) and RNA replication by RdRP (a target of the antiviral agents such as favipiravir, remdesivir and ribavirin). [17] The virus also affects other organs of the body such as gastrointestinal organs, heart, arterial and venous endothelial cells, and arterial smooth muscle cells. ACE2 is abundantly expressed in the glandular cells of gastric, duodenal, rectal epithelium, as well as endothelial cells and enterocytes of the small intestine. [18] Acute inflammatory response that ensues triggers release of a series of cytokines which may result in vasoconstriction responses, thrombus formation and chronic damage to the cardiovascular system. [19] (Wadman et.al. 2020). Such severe responses are found in late progression of the disease and are often fatal.

Innate immune response is the first line of antiviral defense and is essential for immunity to viruses. Though our understanding of the specific innate immune response to SARS-CoV-2 is extremely limited, however, the virus-host interactions involving SARS-CoV-2 are likely to be similar to CoVs, due to their shared sequence homology. On entry into the cell via endocytosis, downstream signaling cascades trigger the secretion of cytokines. Among these, type I/III interferons (IFNs) are considered the most important for antiviral defense, but other cytokines, such as proinflammatory tumor necrosis factor alpha (TNF-α), and interleukin-1 (IL-1), IL-6, and IL-18 are also released. [20] As these cytokines represent a major barrier to viral infection, CoVs have evolved several mechanisms to inhibit IFN-I induction and signaling. Efficient adaptive immune response involving T and B cells are also essential for viral control.

COVID-19 impact on the elderly

The elderly population is the most vulnerable group in the present COVID-19 pandemic. According to US based National Bureau of Economic Research (NBER) July data, COVID-19 affects the older people more severely. (Figure 3). The 'case fatality rate' or CFR which is the share of deaths in all confirmed cases is highest in the older age groups. The younger 74% of the population (up to 39 years old) account to only 10% of all COVID-19 related deaths, while the 60+ years age group, making up just 9% of the population has an immensely large share of 53% of all deaths (Figure 3). [21] The 60+ years age group, amount to just 15% of India's confirmed cases but 53% of deaths due to COVID-19.

The patient's ability to control viral load will determine whether a patient will have mild or severe COVID-19 symptoms. To fight the virus, the immune system has to first recognize the viral infection, then effectively induce a response to destroy and eliminate SARS-CoV-2. Each of these mechanisms are known to be dysfunctional and increasingly heterogeneous in older people. [22] During aging, there is a gradual decline in immune function called immunosenescence, which hampers pathogen recognition, alert signaling and clearance. Aging and dysfunctional cells arrest their cell cycle and can become epigenetically locked into a pro-inflammatory state in which they secrete cytokines and chemokines. During aging there is also a chronic increase in systemic inflammation called inflammaging, which arises from an overactive, yet ineffective alert system. [23] Immunosenescence of the innate and adaptive immune system in those over 60 years of age is a major determinant in severity of COVID-19. A decline in

neutrophil activity and migration, depletion of T cells, a condition known as lymphopenia, and less diverse and less responsive B cells are observed with aging.
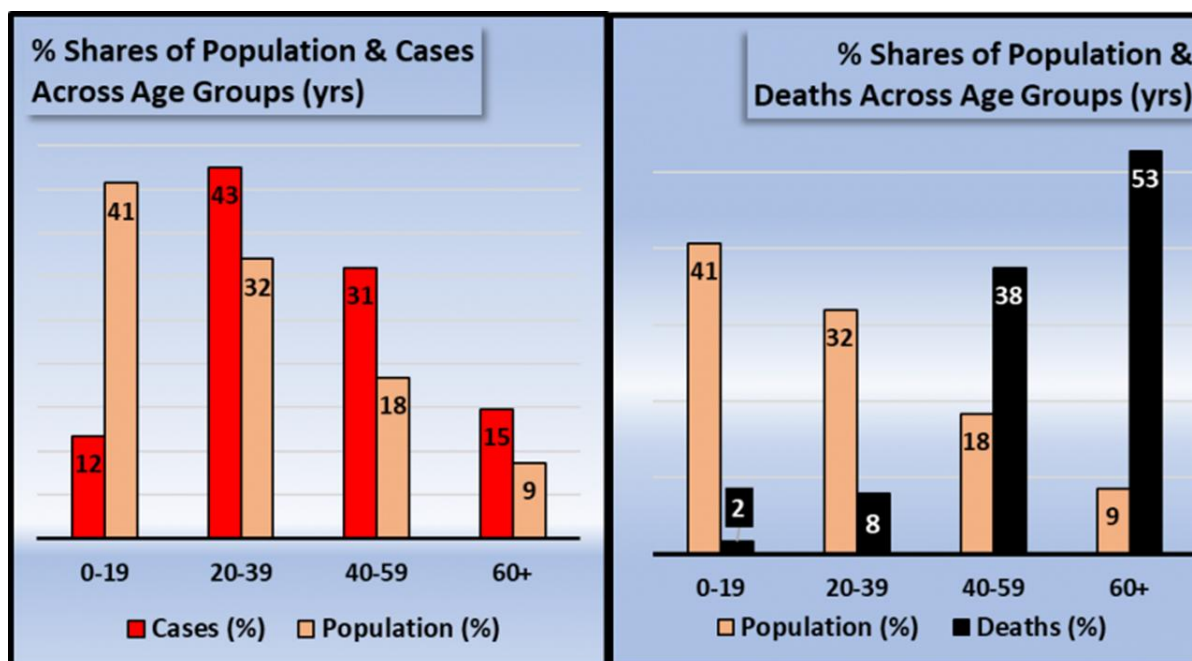

Figure 3. Case fatality rate [CFR] of COVID -19 in India based on National Bureau of Economic Research (NBER) US, July 8 data. [21]

In older patients, the rapid and uncontrolled inflammatory signaling cascade which typically occurs in the later stages of infection, known as a "cytokine storm," triggers inflammation in major tissues such as the lungs, kidneys, heart, liver, blood vessels and brain. The vascular inflammation results in complement-associated microvascular injury and thrombosis in severe COVID-19 cases. All these factors together cause increased risk of bleeding (coagulopathy), hypoxia and finally multi-organ failure. [24]

The situation is further exacerbated in older adults with underlying medical conditions, such as hypertension, diabetes, cancer, kidney disease, cardiovascular disease (CVD) and chronic obstructive pulmonary disease (COPD). Such patients have been linked to more hospitalization and intensive care unit (ICU) admissions and have reported increased morbidity and mortality rates. [25]

Reports from national health centers and hospitals from across the world up to April 2020 have shown that patients with diabetes have a 50% higher risk of dying than those without. In India, the risk is heightened as more than half (57%) of the 77 million diabetes patients in India are unaware that they are diabetic and hence may not monitor their condition or take steps to control it. Of the diagnosed patients, 20% do not seek treatment due to poverty or lack of knowledge. Amongst the patients under treatment, only 60% are able to control and manage their diabetes. [26] An unusually high number of diabetic COVID-19 patients develop diabetic ketoacidosis or hyperglycaemic hyperosmolar syndrome. The virus binds to ACE2 receptors, which are also expressed in pancreatic tissue and β-cells in particular. Therefore, an acute loss of insulin secretory capacity along with a stress condition and the cytokine storm could lead to a rapid metabolic deterioration with development of diabetic ketoacidosis or hyperglycaemic hyperosmolar syndrome. Additionally, hyperglycaemic hyperosmolar syndrome is likely to increase the risk of thrombosis that already characterizes severe COVID-19. The SARS-Cov-2 tropism for the β-cell could cause acute impairment of insulin secretion or destruction of β-cells

which could also result in *de novo* development of diabetes apart from severely impacting diabetic patients. [27]

The chronic obstructive pulmonary disease (COPD) patients appear to suffer worse outcomes upon contracting COVID-19. COPD is a complex disease associated with abnormalities of the airway and/ or alveoli leading to dysfunction of the lung with decrease in airflow. It is predominantly caused by exposure to smoking, noxious gases and particulates over a long period of time. The gene expression profiles from bronchial epithelial cells of COVID-19 patients show that ACE-2 expression is significantly elevated in COPD patients as compared to control subjects. [28] Similar higher levels of ACE-2 expression is also found in smokers as compared to non-smokers. Up-regulation of ACE-2 may predispose such individuals to increased risk of coronavirus infections. In addition, alterations in local/systemic inflammatory response, impaired host immunity, persistent mucus production, and structural damage exacerbates risk of morbidity and mortality in COPD patients when infected with COVID-19.

The prevalence pre-existing cardiovascular disease seems to be linked with worse outcomes and increased risk of death in patients with COVID-19. The COVID-19 infection by itself can also induce myocardial injury, arrhythmia, acute coronary syndrome and venous thromboembolism. The individual case fatality rate of COVID-19 patients with CVD was 10.5% when compared with other comorbidities, such as chronic respiratory disease (6.3%), cancer (5.6%)), diabetes (7.3%) or hypertension (6.0%). [29] Acute myocardial injury is the most commonly described CV complication defined by elevation of different cardiac markers, such as LDH (Lactate dehydrogenase), CK –MB (creatine Kinase-MB), and cardiac troponin I (cTnI) and/or electrocardiographic abnormalities. Significant elevation of cardiac troponins (cTnI), have been observed in COVID-19

patients. It is observed in approximately 8–12% of all patients. A pre-existing CVD condition could worsen the prognosis of the patient. Increased cardiometabolic demand associated with the systemic COVID-19 infection coupled with hypoxia caused by acute respiratory obstruction can impair myocardial oxygen supply and lead to acute myocardial injury. Prothrombotic milieu created by enhanced inflammation increases the risk further. [30]

Hypertension is also reported to have a significantly higher ratio of mortality in patients with COVID-19, especially those who are not on any medication. Several hypotheses have been proposed regarding the net effect of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs), the drugs used for hypertension treatment on COVID-19 infections. It is expected that ACE2 receptor blockade would have beneficial effects by disabling viral entry into the heart and lungs, and an overall decrease in inflammation secondary to ACEI/ARB. It has been observed that elders who have been on long term ACEIs or ARBs treatment show upregulation of ACE2 receptors through a negative feedback mechanism. Hence facilitating the entry of the coronavirus into cells and making people more susceptible to the disease. [31]

The way forward

Aging is a natural process, it cannot be cured, but it can be protected with sensitivity and care. The present corona pandemic has glaringly exposed the vulnerability of our elderly in our society. As an ageing population tends to have a higher prevalence of chronic diseases, physical disabilities, mental illnesses and other comorbidities, preventive health-care and medical needs of the elderly population becomes the joint responsibility of individuals, family, community and the government. The wellbeing of the elderly mandates a multifaceted approach incorporating active collaboration of community, health workers, social workers,

government health-care schemes / programs and welfare schemes for self-independence and sustenance.

To lead a healthy life with dignity, the elderly in our country require: 1. Periodic health checkup for management of chronic diseases and screening for early detection of diseases. 2. Education on the importance of nutrition and healthy eating habits, timely and regular intake of medicine and regular physical activity. 3. Monetary aid to lead independent life with dignity. 4. Insurance plan to cover medical expenses. 5. Availability of affordable physical aids, such as hearing aids, motorized wheelchair etc. 6. Facilities of well-equipped old care homes for elderly with disability or other ailments in absence of family support.

The biggest problem faced by elderly today is Loneliness and anxiety. [32] Cognition Impairment, hearing loss, and various disabilities make the elders more isolated and lonely. India needs to develop a social culture wherein College students should form social groups to volunteer to spend time with the elderly in their homes or in old age care homes. Such voluntary practices are more prevalent in western countries.

The government of India has also launched a number of schemes for the benefit of the senior citizens in the country. These include 1. National Programme for the Health Care of Elderly (NPHCE), launched in 2010,to address the health issues faced by seniors, it provides free or highly subsidized facilities in district hospitals, community health centres (CHC), primary health centres (PHC), and sub-centres (SC) levels through State Health Society. 2. Varistha Mediclaim Policy, designed for senior citizens between the age of 60 and 80 years, it covers the cost of medicines, blood, ambulance charges, and other diagnosis related charges. 3. Rashtriya Vayoshri Yojana, a scheme that provides physical aids and assisted-living devices for older adults above 60 years of age that belong to the BPL (below the poverty line)

category. 5. Senior Citizens' Welfare Fund which aims to make seniors financially stable for their overall welfare and health care. 6. Pradhan Mantri Jan Arogya Yojana, scheme launched in 2018 by the Ministry of Health and Family Welfare aims to cover up to 10 crore people belonging to poor and vulnerable families. All these schemes look good on paper but it remains to be seen how well they are implemented and how many people avail of these schemes and benefit from them.

A caring society, quality assured health-care services and well-meaning and sensitive government will go a long way in addressing the problems faced by elders in our society.

REFERENCES

1. United Nations (2015). World Population Prospects: The 2015 Revision. United Nations Department of Economic and Social Affairs Population Division. Geneva.
2. Raju S. Ageing in India in the 21st Century: A Research Agenda. Mumbai: The Harmony Initiative. 2006 Available from: http://harmonyindia.org /hdownloads/Monograph_FINAL.pdf
3. Alam M, Karan A. Elderly Health in India: Dimensions, Differentials, and Over Time Changes. New Delhi: United Nations Population Fund; Building Knowledge Base on Ageing in India: A series of Programmatic and Research Studies. (2010)
4. Mathur P, Mascarenhas L. Lifestyle diseases: Keeping fit for a better tomorrow. Indian J Med Res. 2019; 149(Suppl 1): S129–S135.
5. NSSO, 2006 (National Sample Survey Organization. (1996). The aged in India: A socio-economic profile – 52nd round. New Delhi, India: Government of India.
6. Mane AB. Ageing in India: Some Social Challenges to Elderly Care. J Gerontol Geriatr Res. 2016; 5. Available from: e136. doi: 10.4172/2167-7182.1000e136
7. United Nations Population Fund 2017. 'Caring for Our Elders: Early Responses' - India Ageing Report – 2017. UNFPA, New Delhi, India.
8. Annual report to the people on Health. Ministry of Health and Family Welfare, Government of India. 2011

9. Kutty VR, Dilip TR, Archana AR, Gopinathan S, Ramanathan M. Shifting pattern of diabetes among the elderly in India: Evidence from the national sample survey organization's data, 2004–2014. Int J Non-Commun Dis. 2018; 3: 67-74

10. Saikia N., Bora JK, Jasilionis D, Shkolnikov VM. Disability Divides in India: Evidence from the 2011 Census. Kokubo Y, editor. PLoS One. 2016;11:e0159809

11. Das SK, Pal S, Ghosal MK. Dementia: Indian scenario. Neurol India 2012; 60: 618-24.

12. Beeson PB. Alleged susceptibility of the elderly to infection, Yale J Biol Med. 1985; 58: 71-7.

13. Yoshikawa TT, Powers DC, Morley JE, Coe RM. Infectious diseases, immunity and aging: perspectives and prospects, Aging, immunity and infection. New York Springer. 1994: 1-11.

14. Schwartz JB, Hazzard WR, Blass JP, Ettinger WH. Jr, et al. Clinical pharmacology, Principles of geriatric medicine and gerontology. 4th ed.New YorkMcGraw-Hill. 1999: 303-31.

15. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens TS, Herrler G, Wu N-H, Nitsche A, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020; 181: 271–280.e8.

16. Du L, He Y, Zhou Y, Liu S, Zheng BJ, Jiang S. The spike protein of SARS-CoV--a target for vaccine and therapeutic development. Nat Rev Microbiol. 2009 Mar;7(3):226-36. doi: 10.1038/nrmicro2090. Epub 2009 Feb 9. PMID: 19198616; PMCID: PMC2750777.

17. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): a review. JAMA 2020. Available from: https://doi.org/10.1001/jama.2020.6019.

18. Gu J, Han B, Wang J. "COVID-19: Gastrointestinal Manifestations and Potential Fecal-Oral Transmission". Gastroenterology. 2020; 158 (6): 1518–1519.

19. Wadman M. "How does coronavirus kill? Clinicians trace a ferocious rampage through the body, from brain to toes". Science. 2020. Available from: doi:10.1126/science.abc3208.

20. Channappanavar R, Fehr AR, Zheng J, Wohlford-Lenane C, Abrahante JE, Mack M, Sompallae R, McCray Jr. PB, Meyerholz DK, Perlman S. IFN-I response timing relative to virus replication determines MERS coronavirus infection outcomes. J Clin Invest. 2019; 130: 3625-3639.

21. Philip M, Ray D, Subramanian S. Decoding India's Low Covid-19 Case Fatality rate NBER Working Paper No. 27696, August 2020, JEL No. J10,J11,O10,O57

22. Liu Y, Yan LM, Wan L, Xiang TX, Le A, Liu JM, Peiris M, Poon LLM, Zhang W. Viral dynamics in mild and severe cases of COVID-19. Lancet Infect Dis. 2020. [Epub ahead of print]. Available from: 10.1016/S1473-3099(20)30232-2.

23. Mueller AL, McNamara MS, Sinclair DA. Why does COVID-19 disproportionately affect older people? Aging. 2020; 12(10): 9959–9981. Available from: https://doi.org/10.18632/aging.103344

24. Weaver LK, Behrens EM. Weathering the storm: improving therapeutic interventions for cytokine storm syndromes by targeting disease pathogenesis. Curr Treatm Opt Rheumatol. 2017; 3:33–48.

25. Sanyaolu A, Okorie C, Marinkovic A, Patidar R, Younis K, Desai P, Hosein Z, Padda I, Mangat J, and Altaf M. Comorbidity and its Impact on Patients with COVID-19. SN comprehensive clinical medicine. 2020: 1–8. Advance online publication. Available from: https://doi.org/10.1007/s42399-020-00363-4

26. Singh AK, Gupta R, Ghosh A, Misra A. Diabetes in COVID-19: prevalence, pathophysiology, prognosis, and practical considerations. Diabetes Metab Syndr Clin Res Rev. 2020; 14(4): 303–10

27. Apicella M, Campopiano MC, Mantuano M, Mazoni L, Coppelli A, and Del Prato S. COVID-19 in people with diabetes: understanding the reasons for worse outcomes The Lancet Diab Endocrin. 2020; 8(9): 782-792. Available from: DOI: 10.1016/S2213-8587(20)30238-2

28. Leung JM, Yang CX, Tam A, et al. ACE-2 Expression in the small airway epithelia of smokers and COPD patients: implications for COVID-19. Eur Respir J. 2020; 55: 2000688. Available from: doi:10.1183/13993003.00688-2020

29. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team.

Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) - China, 2020. China CDC Wkly 2, 113–122 (2020)

30. Bansal M. Cardiovascular disease and COVID-19. Diabetes & metabolic syndrome. 2020; 14(3), 247–250. Available from: https://doi.org/10.1016/j.dsx.2020.03.013

31. Mancia G, Rea F, Ludergnani M, Apolone G, Corrao G. Renin-Angiotensin-Aldosterone System Blockers and the Risk of Covid-19. N Engl J Med. 2020 Jun 18;382(25):2431-2440. Available from: doi: 10.1056/NEJMoa2006923. Epub 2020 May

1. PMID: 32356627; PMCID: PMC7206933.

32. Gerst-Emerson K, Jayawardhana J. Loneliness as a public health issue: the impact of loneliness on health care utilization among older adults. Am J Public Health. 2015; 105(5): 1013-1019. Available from: https://doi.org/10.2105/AJPH.2014.302427

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