

Tale of two Pandemics: Scenarios unfolding with the clash of Type 2 Diabetes mellitus and COVID-19 in the Indian subcontinent

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ABSTRACT

The ongoing pandemic of COVID-19 has a spectrum of presentations ranging from mild (81%) through severe (14%) to critical illness (5%), leading to fatality which has crossed more than 1.3 million deaths globally. Recently published data from the worst affected countries suggests that comorbidities like type 2 diabetes mellitus (DM), hypertension (HTN) and cardiovascular diseases (CVD) are the leading causes of fatality attributed to the pandemic, in addition to old age. Since DM is also a raging global epidemic, it may well have a significant impact on the outcome of burgeoning COVID pandemic, especially in low and middle-income countries like India. The bidirectional relationship of these two pandemics generates a peculiar situation which could lead to a significant loss of lives in the light of limited resources. In a country like India, with a population of 1.4 billion people, out of the 8.7 million affected so far, around 1.2 million would be suffering from diabetes. What is more disturbing is the concern that the health structure of the country is far inferior to that of countries like UK, Italy, Spain and the USA who have demonstrated an overwhelming of their health systems in the face of the current health crisis. If some country specific and innovative strategies beyond lockdown are not implemented urgently, the country will have to face devastating consequences in terms of mortality and stress on the existing health systems. In this review we analyse the background burden of the pandemics, their interaction and required strategies to prevent the repetition of consequences India suffered in Spanish flu pandemic of 1918.

Key words: COVID-19; DM; NCDs, Pandemic; mortality, Asia

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INTRODUCTION

Corona virus, characterized by the presence of spike like structures on its outer surface, first manifested itself in December 2019, as an unidentified pneumonia in Wuhan among patients having a history of exposure to wet markets¹. It belongs to the Corona viridae family which includes three highly pathogenic novel zoonotic viruses with outbreaks reported over the past two decades; Severe Acute Respiratory Syndrome related Corona virus-1 (SARS-COV-1) reported in November 2002, Middle East Respiratory Syndrome related Corona virus (MERS-COV-1) in June 2012 and Severe Acute Respiratory Syndrome related Corona virus -2 (SARS-COV-2) in December 2019². The single stranded RNA (26-32kbs) of SARS-COV-2 shows approximately 80% sequence homology with SARS-COV-1³. SARS-COV-2 (also called as COVID-19) has resulted in a rather severe infectious, highly communicable

and fatal disease to the extent that 216 countries with more than 52.7million people have been affected so far. Therefore, it was declared a 'Pandemic' and '6th Public Health emergency of international concern' by World health organization (WHO) in February 2020⁴.

Cryogenic electron microscopy has revealed that Corona viruses bind to Angiotensin Converting Enzyme-2 (ACE2) receptors on the human epithelial cells via the structural spike (S) glycoprotein on their surface that subsequently gets cleaved into a high affinity receptor binding domainS1 and a membrane fusing S2 domain⁵. Once internalized, the

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infection progresses in three stages including asymptomatic stage with no detectable viral load, mild symptomatic stage and a third stage with severe symptoms leading to respiratory distress characterized by high viral load⁶. Surface and aerosol stability of COVID-19 is similar to that of SARS-CoV-1⁷ under the experimental circumstances tested (3 hours in aerosol, 4 hours on copper, 24 hours on cardboard, 48 hours on stainless steel, and nearly 72 hours on plastics) indicating that differences in the epidemiologic characteristics of these viruses is probably related to other factors including high viral loads in the upper respiratory tract, and ability of asymptomatic persons (super spreaders) to spread the virus^{8,9}. Although, the genome of COVID-19 was quickly sequenced to enable diagnosis, epidemiologic tracking and to develop preventive and therapeutic strategies, there is a constant hunt going on globally to explore effective prophylactic and therapeutic agents for the disease. Therefore, many trials have been initiated to find a safe and effective management of the disease which includes, among other things, finding a vaccine.

Epidemiological trends of COVID-19

Coronavirus pandemic, currently gripping 216 countries, is displaying staggering and relentlessly galloping statistics with >52.7million people affected and >1.3 million fatalities till date¹⁰. The epidemic is second to that of Spanish flu, also known as the 1918 flu pandemic which was an unusually deadly influenza pandemic lasting from January 1918 to December 1920 that infected 500 million people with fatalities estimated between 17 to 100 million¹¹. United States of America (USA) with a total tally of more

than 11.3 million COVID-19 cases and more than 0.2 million deaths has left behind other countries¹⁰. The natural history reported so far points towards heterogeneous presentations across countries^{2,12} and as per the published reports nearly 81% of cases had mild, 14% severe and 5% suffered from critical illness².

Data¹³ from various countries show variable (0.2% to 7.7%) crude fatality rates (CFRs i.e. total number of deaths divided by total number of confirmed cases), that can be attributed to variety of factors such as employment of non-uniform case definition criteria, variable population susceptibility, reporting bias etc. (Table 1). Reports from Italy^{12,14}, the second largest country with elderly population harbouring co-existing illnesses show higher mortality as compared to the lower rates in countries like Germany, Singapore, South Korea etc. This could be attributed to swift measures such as more liberal testing, vigorous quarantine and social distancing measures etc. Verity R et al¹⁵ assessed the severity of COVID-19 on model based analysis and reported best estimate of CFRs of 1.38% (1.231.53), after adjusting for censoring, demography and under-ascertainment, with substantially higher ratios 0.32% (0.270.38) in patients younger than 60 years vs. 6.4% (5.77.2) among those older than 60 years and up to 13.4% (11.215.9) in those aged 80 years or older. Publications from China, USA and Italy^{2,16,18} suggest that though cases in age group >60 years constitute minor proportion of infected cases, they had higher risk of succumbing to the critical illness.

Besides age, second most important factor predisposing to

Table 1. Summary of studies from various countries showing variable Crude fatality rate (CFR).

Study	Country	Sample size	Characteristics of included subjects	CFR (overall)	CFR (Critically ill)
China CDC weekly [2]	China-	72-314	Confirmed and suspected Covid 19 cases	2.3% -	49%
Livingston E et al. [12]	Italy	27,980	Confirmed Covid 19	7.7%	-
WHO (update)[13]	Germany	4838 (till 16 th march)	Confirmed Covid 19 cases	0.2%	-
Guan et al. [18]	China	1099	Confirmed Covid 19 cases hospitalized	-	-
Chen et al. [16]	China	99	Covid 19 with pneumonia	11%	-
Yang et al. [20]	China	52	Critically ill	-	61.5%

Abbreviations: CDC: Centers for disease control; NEJM: The New England Journal of Medicine; WHO: World Health Organization; CFR=Case fatality rate

worst outcome of COVID-19 was presence of one or more co-existing illness (Table 2) with 38.7% falling in severe and 58.2% in the critical sickness category¹⁸. The common associated illnesses were HTN- 22%, DM- 16% and CVD- 21% with respective CFRs of 6%, 7.3% and 10.55%, as reported by Chinese Centre for Disease Control and Prevention in 72,314 COVID-19 cases². Preliminary estimates of prevalence of co-existing illness by CDC COVID-19 Response Team¹⁹ also reported similar trends, with 37.6% having at least one co-existing illness, with increasing prevalence among hospitalized and ICU admissions (71% and 78% respectively) with DM (10.9%) being most common, followed by CVD (9.0%). Data from other relevant studies[2024] has been tabulated (Table 2).

The Indian scenario

Although, India currently has more than 4,04,539 active infections with more than 1,30,112 deaths till 16th November²⁵, the numbers have risen as more labs have been roped in for testing. According to Ministry of health and family welfare, India²⁶, nearly 47% of cases are <40 years old, 34% cases in 40-59 year of age group, and 19% are >60 years, and most of critically ill are elderly (age>60year) with co-existing illness. Crude case fatality for India is nearly 4% which is likely overestimated because of under testing (Figure 1), further supported by detailed analysis of

severity of COVID-19 infection by Verity R et al¹⁵.

Early transmission dynamics in China²⁷ and the optimistic projections proposed by Imperial College London²⁸ suggest that at least 5% Indians are likely to be affected in next 3-4 months. On the basis of these modelling projections, a total of 67 million COVID cases are likely to occur in India with 10 million (15%) having severe and 3.3 million (5%) ending up with critical illness. During the Spanish flu of 1918, India was the country that bore the greatest burden suffering an estimated 18 million casualties, which accounted for about 6 per cent of the country's population at the time. The deaths that time were attributed to malnutrition and monsoons but DM was not prevalent that time¹¹.

Ongoing pandemic of Non-communicable diseases (NCDs)

DM is chronic, heterogeneous, multifaceted NCD which poses a huge burden on health system across the globe owing its barrage of complications. Global estimates on 2.7 million individuals from 199 countries in 2008 showed that 347 million adults were affected with DM and projections were estimated to reach 472 million by 2030. Surprisingly, the galloping epidemic reached 463 million in 2019 only with 27.8% in the age group of >65 years²⁹. The overall prevalence of DM is 8.3% worldwide, with 12.2% in Middle East, followed by 11.3% in South East Asia and

Table 2. Showing comparative description of comorbidities in the published COVID series.

Study	Country	Sample size (n)	Comorbidity (>1)	HT	DM	CVD	Cancer	Respiratory disease	Obesity
Onder et. al. [14]	Italy	355 Critical patients who died	-	-	36%	30%	25%	-	-
Guan et. al. [17]	China	1590	25%	17%	8%	54%	1.1%	1.5%	-
Chow et. al. [19]	USA	7162	38%	-	11%	9%	-	9%	0.2%
Yang et. al. [20]	China	52 Critical patients	40%	-	9%	10%	4%	8%	-
Zhang et. al.[21]	China	140 Critical patients	-	30%	12%	-	-	1.4%	-
ISARIC[22]	Mostly UK	1123	-	-	21%	20%	8%	23%	9%
Yang et. al. [23]	China	46,428	-	17%	8%	5%	-	2.4%	-
Zhou et. al. [24]	China	191	48%	30%	19%	8%	-	-	-

ISARIC: International Severe Acute Respiratory and Emerging infection Consortium; ERJ: European Respiratory Journal; Int J Infect: International journal of infectious disease; EID CDC: Emerging Infectious Disease, Centers for disease control; JAMA: Journal of American Medical Association, .HT: Hypertension; DM: Diabetes mellitus, CVD: Cardiovascular disease.

11.1% in North America. Almost 80% global burden of DM is in low-income and middle-income countries²⁹ with China having maximum burden (116 million) followed by India (77 million). Because of this alarming rise in prevalence of DM worldwide, it was considered as global pandemic in 71st meeting of American Diabetes Association (ADA) held in USA in 2011. Most important attributing factors for this stormy rise in India are population growth, ageing and unfortunate shift towards a western lifestyle of unhealthy diet and lower physical activity. Moreover, the DM population has increased risk of other NCDs (CVDs, HT, obesity, renal dysfunction) because of common predisposing factors or are likely to have any of these as complications of DM. This is further supported by data from DISCOVER study³⁰, a global prospective study on 315,992 patients with DM across 38 countries, that showed high prevalence of vascular complications (CAD:8.2%, heart failure:3.3%, stroke: 2.2% and chronic kidney disease:5%). These associated NCDs and complications have been shown to account for substantial economic burden for treating patients with DM. The worldwide cost of diabetes was estimated to be \$1.31 trillion in 2015, encompassing 1.8% of the global gross domestic product (GDP) and is

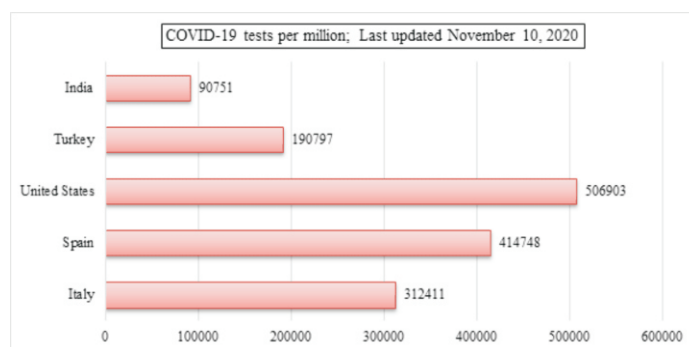
expected to increase to \$2.2 trillion i.e. 2.2% of GDP by 2030³¹

COVID-19 and Diabetes mellitus-a bidirectional relationship

There is a bidirectional relationship of DM with infectious diseases in general and it has taken a peculiar turn in case of COVID-19. Subjects with DM are known to have susceptibility to viral, bacterial, fungal and parasitic infections^{32,34} owing to alteration in neutrophilic, immune and vascular functions. Conversely, infections are known to worsen hyperglycemia and outcomes of various infections are poor in presence of uncontrolled DM³⁵. On the same lines, the emerging data from countries affected with COVID pandemic has shown a bidirectional relationship³⁶ with DM (Figure 2). The data shows that diabetics are at increased risk of getting COVID-19 infection as well as succumb to fatality likely because (a) these patients are usually treated with Angiotensin Converting Enzyme inhibitor (ACEI) or Angiotensin II receptor blocker (ARBs) as for associated complications (like nephropathy) or HTN, leading to up regulation of ACE receptors³⁷. It has been further proposed that use of thiazolidinediones³⁸ in diabetes may also be related to increased risk of COVID-19 infection

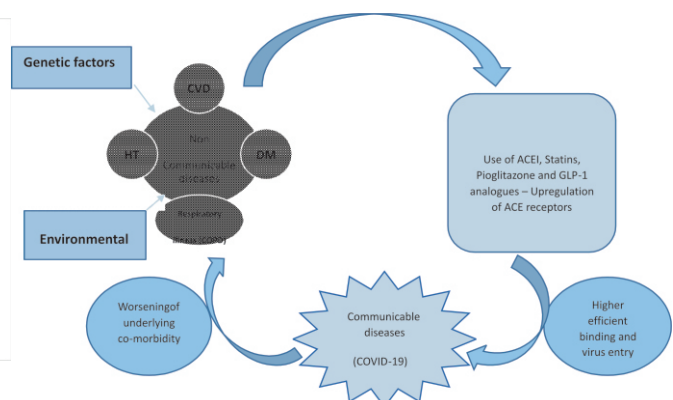
Figure 1: Showing comparison of daily COVID-19 tests per million people across countries:

Total number of COVID-19 tests per million of population done in India is less as compared to other countries complexed with a huge population burden as well as increasing positivity rates mandating a need for ramping up of testing.



Sources: <https://data.worldbank.org/indicator/SP.POP.TOTL> & <https://ourworldindata.org/coronavirus-testing>

Figure 2: Showing possible interacting factors in the bidirectional relationship between DM and COVID-19. Patients with diabetes mellitus are associated with other non-communicable diseases due to common predisposing factors. It has been proposed that pharmacological treatment for these NCDs leads to upregulation of ACE receptors leading to efficient virus binding and entry in human host cells which further leads to worsening of underlying co-morbidity among genetically predisposed individuals.



Abbreviation: HT: Hypertension; DM: Diabetes Mellitus; CVD: Cardiovascular disease, ACE: Angiotensin converting enzyme; GLP- 1 Glucagon like peptide analogue

through up regulation of ACE2 receptors (b) DM and chronic hyperglycemia³⁹ are independent risk factors and negatively affect immune function, further increasing morbidity and mortality due to any infection (c) Studies from China¹⁸ found that the use of glucocorticoids was more in those who were already having underlying comorbid condition which might have further aggravated their clinical course such as wide fluctuating levels of glucose in diabetic patients with COVID. These reports are in concordance with study by Casqueiro et al on Influenza A (H1N1) pandemic, in which the presence of diabetes tripled the risk of hospitalization and quadrupled the risk of ICU admissions once hospitalized³⁹. In low and middle-income countries like India, COVID-19 infection among patients with diabetes may lead to high case fatality, as patients with DM are not only at high risk of new infections but they are also at high risk of recurrent infections (post infection sepsis) as a result of microbial persistence and alterations in innate and adaptive immune responses⁴⁰, uncommon life-threatening infections (necrotizing soft tissue infection, emphysematous pyelonephritis) and high prevalence of common drug-resistance phenotypes⁴¹ due to more exposure to antimicrobials than people without diabetes, further complicating the prognosis.

Evaluating the bidirectional nature of COVID-19 and diabetes, Papadokostaki et al. pointed out the possibility of COVID-19-induced new-onset diabetes⁴². Coronavirus causes systemic inflammation and multi organ damage (acute kidney injury or abnormal liver function) resulting in higher ICU admissions, high prevalence of complications including ARDS. To combat this, corticosteroids have been widely used by clinicians to decrease lung inflammation and manage septic shock. Use of corticosteroids, which can alter glucose homeostasis, was found to be highest among patients with newly diagnosed diabetes as compared to known diabetic patients (43). In a retrospective observational study on 85 COVID patients that died, 76.5% received intravenous glucocorticoids (44). Although the exact mechanism is not clear, interaction between corticoid receptors and target genes have been postulated as possible mechanisms by which corticosteroids increase gluconeogenesis in the liver and increase insulin levels. Such patients often develop acute hyperglycemia such as diabetic ketoacidosis⁴⁵ and may also have increased blood pressure resulting from water and sodium retention⁴⁶. These

studies suggest that COVID-19 patients should be screened for blood glucose levels at the time of admission and their glycemic status should be closely monitored. Use of corticosteroids should be carefully planned and alternative anti-inflammatory drugs should be screened for use to reduce disease severity and mortality in COVID-19 patients⁴⁷.

Clash of two pandemics in a population with poor health care infrastructure

As on one side, world is already facing global pandemic of DM with maximum brunt on low- and middle-income countries, it has been now hit harder by another pandemic of COVID-19. Initially, China was the epicentre of COVID-19 which has now shifted to US, both of them sharing one common factor i.e. large vulnerable population with underlying comorbidities like DM, obesity, HT and CAD. Similarly, India, the second populous (1340 million) country in the world, is also the second largest country to have maximum number (77million) of adults with DM^{29,48} after China. Although at present India is having respectable figures in terms of total COVID-19 infected individuals and total deaths as compared to Europe, US and China, the numbers are likely to progress in geometrical progression. The delay in spike of infection giving some breathing space can be due to host of public health measures (repeated awareness about hand washing, respiratory etiquette, and banning large scale public gatherings) using mass media campaigns, contact tracing, quarantine, with the recent countrywide lockdown enforced by Government of India (GOI). Although, these efforts were laudable, the number of cases post lockdown has posed an enormous challenge for the coming times. According to health statistics⁴⁹, there are nearly 6.7 lakh beds in India, with nearly 70,000 ICU beds, and 70,000 ventilators. There are 11.5 lakhs doctors (including 12000 anaesthetics) and 20.48 lakhs nurses in India⁵⁰. Thus, these estimates suggest that health needs created by corona virus pandemic will go beyond health capacity soon in India and it may be the next epicentre of COVID-19 owing to enormous burden of DM and other NCDs).

Strategies to mobilize and organize the efforts against COVID-19

COVID-19, the globally burgeoning pandemic has potential relevance to some nations more than others, in

view of the underlying NCD pandemic. Thus, COVID-19 will act like a second hit to nations already fighting with pandemics of DM and other NCDs. India having largest number of adults with DM and other NCDs, with its weak health infrastructure is likely to be next epicentre for this devastating infection. So, it is need of the hour that health and administrative agencies should intelligently and swiftly strategize by holding brainstorming sessions of experts to have tailor plans for the country by utilizing science and knowledge gained from other countries like prioritizing vulnerable groups, liberal testing etc. In the interest of brevity and at this moment of time following outline for managing the COVID crises in low-middle income countries with special reference to India can be suggested:

A) Making more diagnostic tests available

Government of India declared a complete lockdown (including closure of schools, colleges, transport facilities and all business activities, except those related to health and basic essentials related to daily life). Though, initially India seemed to have better control of the spread as compared to other countries but now there was a rapid surge of positive cases suggesting the beginning of community transmission (stage 3). So, there is need to revise testing guidelines and accelerate testing rate. The current status of testing is 90751 per million⁵¹, a figure still far lower than other nations. Without increasing our diagnostic capacity, we cannot trace the exact status of the outbreak as suggested by countries successful in tackling the pandemic like Singapore that conducted almost 6,93,109 tests per million of its population⁵². In India, this is further supported by success of states like Kerala⁵³ that has been able to contain COVID-19 spread at early stages by accelerating testing rate at community level as compared to Maharashtra. Thus, there is need to use creative ways to mobilize the nation's research laboratories to assist with population screening, create funds through involvement of public and use of alternative and reliable methods (use of rapid diagnostic kits) to identify the scope of epidemic at community level and contain it. In addition to the RTPCR we need use alternative and reliable methods (economical, simplistic, point of care antibody, rapid, antibody based diagnostic kits) to identify the scope of epidemic at community level and contain it. Recovered cases and other people who have tested negative by PCR but show positive antibody test can venture in the society to keep the wheel of economy rolling.

B) Stratification of population by using country specific scale and prioritization of health resources accordingly

Stratification can be done in two major groups:-

1) Cases which can be further divided in three subgroups a) Confirmed cases are those who have been confirmed with RT-PCR. b) Suspected cases include those who are symptomatic with a history of travel or contact with confirmed case but who tested negative. These should be treated as confirmed cases because of poor reliability of diagnostic methods. In an ideal scenario both of these groups require complete isolation and hospitalization under a specialist to observe for warning signs (Dyspnea, RR>30/m, SaO₂<93%) and intensive management if needed. But, in view of limited tertiary care hospitals with proportionately small number of ICU beds and ventilators, we propose patients should be triaged in a very judicious way to super select ones needing intensive care referral and management. This can be done by employing simple screening-cum-assessment tool which we worked on the basis of components from WHO-China joint task force recommendations⁵⁴ and Guan et al.¹⁸ for stratification of COVID risk. This could serve as a guide in classifying into categories as minimal, moderate and high risk individuals for COVID-19 (Table 3) and accordingly suggest the level of care required using a step-care triage system from community through existing healthcare structure chain to tertiary care referral. c) Recovered cases- include those who have recovered from COVID-19 illness, thereby could have developed adequate immunity. Though health care workers are being considered as front-line warriors, the recovered cases could be considered as next to them in this long-term battle against COVID-19. The number of COVID-19 positive persons who recovered till date in India is very high²⁵. Further, they may also be allowed resume their work and also be a part of various voluntary organizations to help needy. Thus, this concerted and determined approach guided by science, can help us to begin and revive businesses of all kinds, to have economic support in long run.

2) High risk groups can be further divided in three sub groups:-

a) Exposed persons- who had travel history or came in direct contact of COVID-19 cases, but are not symptomatic due to variable incubation period and heterogeneous presentation

Table 3: Proposed country specific tool for calculating COVID risk Score to stratify and judiciously allocate resources			
Symptom/History: Do you have any of the following?			COVID-19 Risk Score points
Fever with or without chills			5
Cough			5
Sputum			4
Fatigue			4
Myalgia/Arthralgia			2
Sore throat			1
Nasal congestion (runny nose)			1
Headache			1
Nausea or vomiting			1
Diarrhoea			1
Travel outside state/country in the past 14 days			10
History of contact with COVID positive patient			10
History of any of the following risk factors? Hypertension, Diabetes mellitus, Cancer, Liver or Kidney disease, Asthma, Chronic lung disease			10
Interpretation			
≤ 9	Minimal risk	Subject has minimal or no symptoms suggestive of COVID-19 infection	No need to be tested for COVID-19. Maintain hygiene, Social distancing.
10 – 20	Moderate risk	Subjects has chances of COVID-19 infection	Maintain home quarantine. Monitor closely for evolution of sign/symptoms. May or may not be tested for COVID-19.
20-30	High risk	High risk subjects may have risk of progression to critical illness RR>30/mt, Heart rate >120/mt and SpO2 sat <90%	Refer to COVID designated facility with ICU setup. CXR/ CT Should be put on O2 therapy/ Non-invasive Ventilation, if chest findings s/o COVID Need to be tested for COVID 19.
≥30	Urgency	RR ≥ 30 or Pulse rate ≥ 120 SpO2 < 90% on O2 or NIV and oxygen	Refer to ICU/Tertiary care Assessment for invasive ventilation

Note : Scoring is based on WHO-China joint task force recommendations [48] and Guan et al [18]

of COVID-19, need testing and even if negative, should be advised isolation for at least 14 days.

b) Person with co-morbidities or elderly(age >60 years)- Though they may not have any travel history or contact with cases but are at high risk of developing severe disease if infected as suggested by data from China and Italy^{2,12,18}. In India, though people age >60 years contribute to only 17% of positive cases but most of who succumbed to the disease were elderly with an associated co-morbidity²⁶. So, it is necessary to direct our health measures to this group. This can be done by:

(I) Optimization of management of co-existing illness^{12,55} with proper supply of medicines especially during complete lockdown period, involvement of voluntary organizations, self-monitoring of blood pressure and blood glucose, adopting healthy life style (exercises, healthy diet, personal hygiene) and enforcement of same by using social media,

issue of sick day guidelines⁵⁶. The healthcare provider team could be contacted by telephone, email or video conference in case of possible symptoms of COVID-19 infection in order to seek advice to avoid risk of deterioration of diabetes control or associated comorbidity, to discuss the possibility to be referred to another specialist or emergency services of the referral hospital in order to prevent serious systemic complication of the viral infection itself.

(II) Their complete isolation and social distancing even during partial lockdown period. Social distancing of elderly may be a social health concern⁵⁷, as it may further increase risk of mental health and cardiovascular problems, interventions like more frequent contact with family members and friends, involvement of geriatric support groups and community outreach projects and use of online cognitive behaviour therapies should be encouraged⁵⁸.

c) Health care workers-They are considered to be the

backbone of health infrastructure and at the same time, are also at risk of getting COVID-19 infection and developing severe illness. So, it is the responsibility of health planners to safeguard them by liberalization of testing for all health workers if they come in contact of positive cases, and prioritization of health resources⁵⁹ such as ensuring adequate supply of N95 masks, PPE and intensive care management if needed..

CONCLUSION

India has well-acted in time in accordance with WHO consensus report, “the experience in affected areas has shown that the transmission can be prevented by adherence to basic public health measures, including rapid case detection, case isolation, contact tracing and good infection control, including hand washing and the use of personal protective equipment” . Lockdown, case and contact tracing, mass quarantines, stratifying risk zones etc. have been critical steps to prevent the community-wide spread, delay exponential growth, reducing the number of cases and spread the demand over a longer period of time to match the capacity of hospitals and other healthcare settings but concerns still remain.

There is ample proof from the historical work that early and sustained implementation measures with the help of mathematical modelling significantly reduced mortality rates in the United States⁶⁰. In view of the COVID infodemic it is possible that these statistics may further fuel the panic among general public but this review is aimed to sensitize policy planners, healthcare providers, decision-makers and other stakeholders to join the tirade of finding means to mitigate this pandemic. The current review is not an institutional or governmental position but is published with constructive intent as responsible doctors having best interests of society in mind. Therefore, it is aimed to foster discussion among the healthcare stakeholders to help plan and implement country and population specific pathways to minimize the impact of the COVID-19 epidemic.

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