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Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14 (2020) 1625–1630

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Impact of COVID-19 and comorbidities on health and economics: Focus on developing countries and India

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ARTICLE INFO

Article history:
Received 23 August 2020
Received in revised form
25 August 2020
Accepted 26 August 2020

Keywords:
COVID-19
Comorbidities
Developing countries
Health
Economics

ABSTRACT

Background and aims: Presence of comorbidities in patients with Coronavirus disease 2019 (COVID-19) have often been associated with increased in-hospital complications and mortality. Intriguingly, several developed countries with a higher quality of life have relatively higher mortality with COVID-19, compared to the middle- or low-income countries. Moreover, certain ethnic groups have shown a higher predilection to contract COVID-19, with heightened mortality. We sought to review the available literature with regards to impact of COVID-19 and comorbidities on the health and economics, especially in context to the developing countries including India.

Methods: A Boolean search was carried out in PubMed, MedRxiv and Google Scholar databases up till August 23, 2020 using the specific keywords, to find the prevalence of comorbidities and its outcome in patients with COVID-19.

Results: All available evidence consistently suggests that presence of comorbidities is associated with a poor outcome in patients with COVID-19. Diabetes prevalence is highest in Indian COVID-19 patients, compared to other countries. Majority of the patients with COVID-19 are asymptomatic ranging from 26 to 76%.

Conclusions: Universal masking is the need of hour during unlock period. Low-income countries such as India, Brazil and Africa with less resources and an average socio-economic background, must adopt a strict policy for an affordable testing programs to trace, test, identify and home quarantine of asymptomatic cases. Despite the huge number of COVID-19 patients, India still has low volume research at the moment.

1. Introduction

Since the Coronavirus Disease 2019 (COVID-19) outbreak started in Wuhan in December 2019, it has spread across every corner of the world including low-income countries. Two low-income countries that bear the major brunt and tops the list along with USA with regards to the number of reported cases of COVID-19 include Brazil and India. Brazil has reported nearly 3.5 Million COVID-19 cases with more than 100 thousand deaths, while India has also crossed over 3.0 Million reported cases with more than 50 thousand deaths, as of August 23, 2020. Although both Brazil and India are placed currently at second and third position respectively just after the USA with more than 6.0 Million reported cases, India is currently reporting highest number of new cases of COVID-19 day-wise, globally [1]. Africa has crossed over 1.0 Million reported cases of COVID-19 with more than 27 thousand deaths, as of August 23, 2020 [2]. Emerging data clearly suggests, that associated comorbidities such as hypertension, diabetes, obesity, cardiovascular disease (CVD), cerebrovascular accident (CVA), chronic obstructive pulmonary disease (COPD), asthma, chronic kidney disease (CKD) and malignancy are often associated with increase in severity and or mortality in patients with COVID-19. We aimed to look at the impact of comorbidities in patients with COVID-19 across the world and present a descriptive analysis on health and economics with a special emphasis on low-income countries like India, Brazil and Africa.

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https://doi.org/10.1016/j.dsx.2020.08.032
1871-4021/

2. Methods

A Boolean search was carried out to find the prevalence of comorbidities and its outcome in patients with COVID-19 in PubMed, MedRxiv and Google Scholar databases up till August 23, 2020 using the specific keywords that include "SARS-CoV2" OR "COVID-19", AND "risk", "severity", "mortality", "obesity", "diabetes", "hypertension", "cardiovascular disease", "chronic kidney disease", "cancer", "chronic pulmonary disease", "developing countries". Full text of all the related articles in English language with supplementary appendix were retrieved. We selected the single largest data published from each country for the descriptive analysis that reported the prevalence and outcomes of comorbidities in patients with COVID-19. The descriptive analysis of overall result was also presented whenever meta-analysis included the pooled data of largest study representing each country that studied the prevalence of comorbidities and its outcome. We excluded smaller case series or retrospective cohort studies from the descriptive analysis whenever the largest data was available, in order to avoid overlapping. In addition, we excluded studies that did not report the prevalence of comorbidities and its outcome.

3. Results

3.1. Prevalence of comorbidities in COVID-19

Several meta-analyses have reported the prevalence of comorbidities in patients with COVID-19 [3–9]. However, many of them have included studies only from China and notably, several Chinese studies included have apparently overlapped data that can limit any conclusions [10]. In this regard, our recent meta-analysis that included 18 studies (N = 14,558) from China, USA and Italy after carefully excluding the overlapped studies, have reported a prevalence of hypertension in 22.9% (95% confidence interval [CI], 15.8–29.9), diabetes in 11.5% (9.7–13.4), CVD in 9.7% (6.8–12.6), cancer in 3.9% (2.5–5.4), COPD in 3.1% (1.0–5.2), CVA in 3.0% (1.8–4.2) and CKD in 2.4% (1.5–3.2) patients with COVID-19 [11]. A large study from UK alone from the pooled data of 166 hospitals (n = 20,133) reported a prevalence of diabetes in 20.7% (3650/17,599), CVD in 30.9% (5469/17,702), COPD in 17.7% (3128/17,634), CKD in 16.2% (2830/17,506) and asthma in 14.5% (2540/17,535), while 22.5% (4161/18,525) had no documented comorbidities in patients with COVID-19 [12].

Surprisingly, only a few large published studies are currently available with regard to the prevalence of comorbidities in patients with COVID-19 from India, despite having a huge number of COVID-19 patients. A retrospective study of 522 confirmed patients with COVID-19 from a large medical college and hospital of Jaipur, India, reported presence of comorbidities in 14% (95% CI, 11.1–17.2), of which, hypertension (42.5%), diabetes (39.7%), past history of tuberculosis (20.5%), COPD/Asthma (16.4%), CAD and CKD (13.7%) represent the common comorbidities. Table 1 summarizes the prevalence of comorbidities in patients with COVID-19 from the largest reported data from China, USA, UK, Italy, Mexico, Spain, Kuwait and India [13–19]. Unsurprisingly, diabetes prevalence is highest in Indian COVID-19 patients compared to other countries.

Interestingly, as many as 75.7% (95% CI, 73.0–80.2) patients in the study from India were asymptomatic and had no symptoms at the time of diagnosis [13]. A similar finding of disproportionately higher asymptomatic (46.3%) COVID-19 patients were also observed from Kuwait [19]. In contrast, studies from Taiwan [20], USA [21] and China [22] reported around 18–21% of asymptomatic cases, and a Korean study [23] found only 2% of asymptomatic cases of COVID-19. While these discordant findings could be attributed to the mass screening carried out in some studies, it is also likely that some of these so-called asymptomatic cases may have been detected early in the pre-symptomatic stage. To this end, a study from Italy that analyzed and differentiated pre-symptomatic to asymptomatic cases reported a 42.5% (31.5–54.6) prevalence of asymptomatic cases [24]. Collectively, these findings suggest a large proportion of patients with COVID-19 could be asymptomatic and therefore a due care is urgently required to recognize these cases though trace, test and treat (quarantine) approach [25]. Study has clearly shown that universal use of mask effectively reduces the chance of contracting COVID-19 amongst the health workers [26].

3.2. Impact of non-communicable disease on COVID-19

The largest Chinese data found significantly increased case-fatality rate (CFR) in presence of any comorbidity. Although overall CFR was 2.3% for overall population (N = 44,672), the presence of comorbidities such as CVD, diabetes, COPD, hypertension and cancer increases the CFR to 10.5%, 7.3%, 6.3%, 6.0%, and 5.6% respectively [27]. The latest report from CDC, USA found presence of CVD (including hypertension, coronary artery disease, stroke, heart failure and other cardiovascular diseases) in 60.9% (6481/10,647), diabetes in 39.5% (4210/10,647), CKD in 20.8% (2209/10,647), COPD (including asthma, tuberculosis) in 19.2% (2047/10,647) of 10,647 cases of death reported in patients with COVID-19 [28]. Data from Mexico found obesity, diabetes, CKD, COPD and hypertension were associated with an increased risk of death in patients with COVID-19, while obesity exclusively conferred an increased risk of death (Hazard ratio 1.26; 95% CI, 1.11–1.43), compared to non-COVID-19. Interestingly, patients with asthma had no increase in mortality and there was a suggestion of protective effect in the Mexican study [18]. In contrast, presence of asthma was the only comorbidity that was associated with a significant higher risk of death (Odds ratio 4.92; 95% CI, 1.03–23.44), besides smoking and high pro-calcitonin, in patients with COVID-19 from Kuwait [19]. UK data also found chronic cardiac disease, COPD, CKD, obesity and liver disease to be associated with significant increase in mortality, apart from male sex and increasing age [12]. Several meta-analyses have shown a significant increase in severity and mortality in individuals with comorbidities with COVID-19, apart from increasing age [3,4,6,8,9]. Our meta-analysis that pooled the studies from China, USA and Italy found a significant 1.5 to 3-fold increase in severe COVID-19 associated with either hypertension or diabetes or CVD or COPD or CKD and or cancer. Similarly, patients with COVID-19 with CVD or hypertension or diabetes had a significantly 2-fold increase in mortality [11]. In addition, other studies from USA and UK have also found obesity to be associated with a significant increase in mortality [12,29].

No large published data is currently available from the developing countries with regard to the association of comorbidities to mortality. Detailed available data of 176 deceased from a total 206 reported cases of deaths as of April 10, 2020 from India found 50.5% of the deceased had one of these preexisting comorbidities, of which diabetes was present in 27.8% (49/176), hypertension in 22.1% (39/176), respiratory disease (COPD and asthma) in 13.6% (24/176) and CVD in 6.2%. Notably, while 13% of the deceased had both diabetes and hypertension, 2.8% had all the three comorbidities (diabetes, hypertension and CVD). Thus, diabetes was the leading comorbidity present in deceased COVID-19 individuals from India [30]. A latest report of July 2, 2020 by the Integrated Disease Surveillance Program, under the Ministry of Health and Family Welfare, India that analyzed the death of 15,962 patients with COVID-19, found presence of any one or more comorbidities in 57% of patients, while 43% had no comorbidities [31]. State-wise data are no different in India. A grey literature report from West Bengal, India on June 8, 2020 found 66% patients had one or more

Table 1
Prevalence (%) of comorbidities in patients with COVID-19 across the world.

First author/group,	Country	Timing of data collection in year 2020	N	Diabetes (%)	HTN (%)	CVD (%)	CKD (%)	COPD/Asthma (%)	Obesity (%)	CVA (%)	Cancer (%)
CCDCP[14]	China	Dec 2019–11 Feb	20,982^	5.3	12.8	4.2	NR	2.4	NR	NR	NR
CDC[15]	USA	12 Feb – 28 March	7162^	10.9	NR	9.0[a]	3.0	9.2	NR	NR	NR
Grasselli[16] et al.	Italy	20 Feb – 18 March	1043^	17.3	48.8	21.4	3.5	4.0	NR	NR	7.8
Docherty[12] et al.	UK	6 Feb – 18 April	20,133	20.7	NR	30.9[a]	16.2	17.7/14.5	10.5	NR	10.0
Prieto-Alhambra[17] et al.	Spain	15 March – 24 April	121,263	9.8	24.3	3.1	5.4	3.3	19.9	2.3	7.4
Bello-Chavolla[18] et al.	Mexico	Up to 18 May	51,633	18.3	21.6	2.7	2.2	2.2/3.1	NR	NR	NR
Almazeedi[19] et al.	Kuwait	24 Feb – 20 April	1096	14.1	16.1	3.7	1.0	0.5/3.9	NR	0.6	NR
Bhandari[13] et al.	India	Last Wk. Feb – 20 April	522	39.7	42.5	13.7	13.7	16.4	NR	NR	NR

[a] Include hypertension, ^ reported comorbidities, CCDCP- Chinese Center for Disease Control and Prevention, CDC- Centre for disease Control, HTN- Hypertension, CVD- Cardiovascular diseases, CKD- Chronic kidney diseases, COPD- Chronic obstructive pulmonary diseases, CVA- Cerebrovascular accident, Wk- Week, NR- Not reported/ retrievable, N - Number.

comorbidities from the 405 deaths analyzed in patients with COVID-19, of which hypertension (27%), diabetes (19%) and cardiac disease (19%) contributed most, along with COPD, cancer and CKD [32]. All patients who died (15/522) with COVID-19 had one or other comorbidities in study by Bhandari et al. from Jaipur, India [13]. Brazil has reported 83% of comorbidities in 17,752 cases of death in patients with COVID-19. Chronic heart disease (35.1%; 5170/14,737) and diabetes (28.7%; 4233/14,737) were the top 2 comorbidities linked to 14,737 deaths reported due to the COVID-19 [33].

3.3. Impact of COVID-19 on population suffering from communicable diseases

While no data (published, unpublished or in grey literature) is yet available with regards to the relation of underlying infectious comorbidities to the outcome in patients with COVID-19, it is reasonable to believe that a large chunk of the 1.3 billion African population is highly susceptibility to severe COVID-19 and would require hospitalization if infected, because of underlying comorbid conditions including the highest prevalence of human immunodeficiency virus (HIV) and tuberculosis (TB) in the world. An analysis conducted in South Africa found that after making an adjustment for other risk factors, HIV increased a COVID-19 patient's death risk by a factor of 2.75, and active TB by a factor of 2.58. Recent estimates from the United Nations Economic Commission for Africa suggested that an unmitigated pandemic could lead to a substantial proportion of the African continent being infected and 23 million severe cases of COVID-19 would require hospitalization [34]. These findings have additional importance in a background of emerging data which suggests blacks (and Asians population) had a higher mortality, irrespective of their socioeconomic or behavioral factors, if they contract COVID-19 [35].

Fortunately, the share of the population at increased risk of severe COVID-19 is generally lower in Africa than elsewhere, as most of the population is young, like in India. Moreover, emerging evidence also links a protective role of Bacillus Calmette-Guerin (BCG) vaccination on the COVID-19 mortality outcomes. A strong correlation to the degree of universal BCG vaccination in a country (BCG index) with COVID-19 mortality has recently been observed in different European countries. It is believed that every 10% increase in the BCG index had a 10.4% reduction in mortality due to COVID-19 [36]. Interestingly, the countries such as USA, Italy, France, Germany and Spain, where there is no national universal BCG vaccination program and vaccination is limited only to the individuals at a high risk, have shown a higher mortality despite a better quality of life. India, Russia, China, and Africa where there is a mandatory national universal BCG vaccination have fortunately reported a lower death percentage from the COVID-19, despite an average or poor quality of life [36,37]. Notwithstanding, the consistent association between BCG vaccination and reduced severity of COVID-19 observed in epidemiological explorations, there is still insufficient evidence to establish causality between BCG vaccination and protection from severe COVID-19. To this end, two randomized placebo-controlled clinical trials are currently ongoing with BCG vaccine in health workers in Holland and Australia that will determine to what extent BCG vaccination in adults can confer protection from the COVID-19 [38,39]. Meanwhile, it appears that the "Trained immunity" gained over the years, defined as an enhancement of innate immune response due to repeated exposure to the subsequent repeated infection (viral, malarial, bacterial infections in developing countries) which is achieved through a metabolic programming of immune cells as well as epigenetic factors, along with the universal BCG vaccination that has provided cellular immunity, both combined together, might be offering some role in having less severe COVID-19, as well as lesser mortality in developing countries including India [36,40].

3.4. Impact of ethnicity on COVID-19

The national surveillance agencies of two countries USA (Centers for Disease Control and Prevention) and UK (Public Health England) have assessed the outcomes of COVID-19 based on ethnicity. While a systematic review from initial pre-print studies from both USA and UK found that the risk of infection, hospitalization, severe COVID-19 were higher in Blacks and Minority Ethnic (BAME) groups, the risk of mortality was also higher in BAME population in UK and in particular in Blacks in USA [41]. In addition, several recent cross-sectional, prospective-observational and retrospective studies from UK have also consistently found a significant greater mortality in BAME groups including the South Asians (Bangladeshi > Pakistani > Indians) [42–47]. It should be recalled that migrant South Asians have been found to have a several fold increase in obesity, diabetes, heightened cardiovascular risk, associated complications and mortality from non-communicable diseases. Moreover, the latest Morbidity and Mortality Weekly Report (MMWR) from CDC (July 17, 2020) also found that non-white and black populations are more affected with COVID-19, especially in <65 years of age [28]. While several hypothetical reasons for the heightened rate of infection and mortality with COVID-19 in the BAME group has been hypothesized by the researchers [48,49], one potential contributing factor that could be the most likely explanation seems to be a higher percentage of BAME population engaged in certain occupations such as service industry or essential activities or paramedical or frontline staffs that may preclude physical distancing. Future research is further

required for understanding the mechanism and further steps are needed to prevent devastating outcomes in the minor ethnic community.

3.5. Impact of lockdown and subsequent wave of COVID-19 in patients with non-communicable diseases

The latest estimates of International diabetes federation (IDF), Diabetes Atlas 9th edition, 2019, suggests that worldwide nearly 463 million adults in the age of 20–79 year have diabetes, of which nearly 80% of them live in low- or middle-income countries and nearly 60% of them are Asians. The estimates also found, 1 in 11 adults have diabetes and 1 in 5 of the people with diabetes in the world come from South-East Asia, and 1 in 6 adults with diabetes in the world come from India [50]. These large numbers pose a major challenge in managing diabetes during the COVID-19 pandemic. Expectedly, a large chunk of patients with diabetes have increased snacking/carbohydrate intake and decreased physical activity during the lockdown period that have resulted in weight gain and destabilize the glucose control which might results in a likely increase in diabetes-related complications [51]. Moreover, as per one estimate, weight gain during lockdown may increase the diabetes risk by 7% [52]. A simulation model analysis predicted a significant >2% increase in HbA1c and 0.5–14% increased risk of macro- and microvascular complications of diabetes, at the end of 30 days of lockdown [53]. In contrast, a real-world study that examined the effect of lockdown on HbA1c change in 205 individuals with diabetes, found a significant reduction (Δ −0.5%, $p < 0.001$) attributed to an increased use of telecommunication and self-monitoring of blood glucose [54]. Undoubtedly, while smartphone-based teleconsultation has been widely used during the lockdown period, countries with poor resources have also faced technical and bandwidth glitch, besides the poor quality of audio and video that limits the adequate and satisfactory advices with regards to diabetes education, proper counselling and insulin techniques etc. [55]. Moreover, majority of rural population in developing countries including India still lacks a proper tele-communication system and household availability of smartphones which will further increase the burden of non-communicable diseases and its related complication. Another issue that has been recently forecasted is the effect of an expected second wave of COVID-19 on the metabolic control and its outcomes. It is estimated that COVID-19 related mortality may have two peaks such as now, and possible another peak although smaller in quantum sometime in 2021 [56]. Therefore, one should remain prepared for a compounding effect of both, hospitalizations related to the diabetes-associated acute and chronic care disruptions, and the second wave of COVID-19 [57,58].

In this context, it is necessary to identify high risk cases who are likely to progress to severe COVID-19 and in-hospital death. A recent study has proposed a risk-based scoring criteria after conducting a binary multivariable regression analysis using 52 variables and found age of patient (<60 year: 0 score, 60–75: 1 score, >75 year: 2 score), presence (1 score) or absence (0 score) of coronary artery disease (CAD), percentage of lymphocytes (<8%: 1 score, > 8%: 0 score), levels of procalcitonin (>0.15 ng/ml: 2 score), and D-dimer (>0.5 mcg/ml: 1 score), can differentiate in identifying high risk (>2 point score) versus low risk (≤2 points score) cases with a reasonable accuracy [59].

3.6. Impact of COVID-19 on economics

Indian economy, already affected by a slow growth in the previous fiscal year, is going to be severely affected by the lockdown and COVID-19 pandemic. Severe economic losses have been predicted during the lock down and subsequently, it is estimated that economy may contract further by 10–20% [60]. Interruption of medical care and supervision during this time may be deleterious for patients with diabetes, CAD and other chronic non-communicable diseases, which may add to further economic losses in future due to the increase in disease burden and complication loads. It is estimated that health and nutrition indices will suffer due to the worsening socio-economic inequalities resulting from pandemic [61,62]. Moreover, syndemic of tuberculosis with diabetes may worsen, adding further to the morbidity and mortality burden and thus economic losses [63].

4. Conclusion

All available evidence clearly hints that presence of comorbidities is associated with a poor outcome in patients with COVID-19. Diabetes prevalence is highest in Indian COVID-19 patients, compared to other countries. However, there are comparatively less published research on prevalence of comorbidities and associated outcomes from India, despite being third in ranking across the world with regards to the number of COVID-19 patients. Considering that the majority (ranging from 26 to 76%) of patients with COVID-19 could be asymptomatic, as observed in some of the studies reported from China, Italy, Kuwait and India, it is advisable that low-income countries such as India, Brazil and Africa with an overwhelmed medical infrastructure with less resources and an average socio-economic background, must adopt a strict policy for making an affordable testing programs to trace, test, identify and home quarantine of asymptomatic cases. Emerging data also finds that universal masking is associated with a significantly lower rate of contracting COVID-19. This clearly emphasizes the importance of social distancing and mandatory use of mask during the unlock period, as most of these countries are already in this phase now. Since majority of patients with mild COVID-19 recover without any major interventions, there should be no mandatory rule to admit every case of confirmed COVID-19. With regard to identifying the high-risk cases, those who are prone to progress to severe COVID-19 and are at a heightened risk of death, a risk-based scoring could be applied as an admission criterion to the hospital, in order to minimize the burden of already overwhelmed health infrastructure.

Funding

No funding.

Authorship

All authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship and take responsibility for the integrity of the work.

Authors contribution

AKS and AM conceptualized. AKS searched the database, wrote first draft. AKS and AM revised the manuscript. Both decided to submit the manuscript.

Declaration of competing interest

Nothing to disclose.

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