INTRODUCTION

From the origin of virus in Wuhan, China in December 2019 to declaration of SARS-CoV-2 as pandemic, its variants (most recent “Nu” as variant of concern) and vaccines equity and efficacy has challenged health systems across the globe. Over 262 million cases of confirmed COVID-19 have been detected globally with a mortality exceeding 5 million by the end of November 2021, as per World Health Organization (WHO).1 According to the WHO, the case fatality rate of COVID-19 ranges from 0.1% to 25% in different health settings and regions.2 In India, on 30th January 2020, the first case of COVID-19 was reported, thereafter country has faced two waves with disastrous second wave. A total of about 34 million cases and 4.68 lakh deaths have been reported so far from India. Few studies have reported death rate as 5.7% among COVID-19 patients with at least one co-existing medical condition, as compared to 0.7% in patients without any comorbidity.3

Background: In India, on 30th January 2020, the first case of COVID-19 was reported, thereafter country has faced two waves with disastrous second wave. A total of about 34 million cases and 4.68 lakh deaths have been reported so far from India. Few studies have reported death rate as 5.7% among COVID-19 patients with at least one co-existing medical condition, as compared to 0.7% in patients without any comorbidity. Materials and Methods: This is an observational study from April 2020 to July 2021 which is based on records obtained from death audit reports of a dedicated COVID-19 facility at a tertiary hospital, Agra, Uttar Pradesh. The state authorities introduced a standard “COVID-19 Death Audit Proforma” on a death audit portal to audit all deaths related from COVID-19 (SARS-CoV-2) infection. Statistical analysis used: The data were recorded in Microsoft Excel and analyzed using statistical software, Microsoft Excel (Version 16.49). The results are presented accordingly in form of descriptive statistics. Results: We have reported findings from 467 COVID-19 deaths from our dedicated COVID-19 facility in the present study. Median age of deceased was found to be 57 years with (71.9%) deaths in males, with predominantly 77.1% of patients residing in urban area. 74% of COVID-19 deaths were reported along with one or more comorbid illness at the time of admission with hypertension to be the most common comorbid disease (42.9%) followed by diabetes (34.5%). Median length of hospital stay is reported as 4 days. Conclusion: Our analysis from Uttar Pradesh dedicated COVID-19 facility found that comorbidities were present invariably in 74% of deaths from SAR-CoV-2 infection. Early diagnosis and timely aggressive management is pillar for reducing morbidity and mortality from COVID-19 disease.

Key words: Co-morbidity; COVID-19 deaths; Death audit; Mortality; SARS CoV-2
SARS-CoV-2 and comorbidities have been discussed in parallel in the context of severity and mortality associated with it, as a tale of cascade of immune system dysregualtion. Several studies conducted worldwide showed that the middle-aged and elderly patients with underlying co morbidities, namely, diabetes mellitus, hypertension, and cardiovascular diseases were more likely to have a severe form of COVID-19 disease with a higher mortality rate. Few studies have reported death rate as 5.7% among COVID-19 patients with at least one co-existing medical condition, as compared to 0.7% in patients without any comorbidity.45

A robust data is a key for better analysis of factors contributing to COVID-19 mortality. Therefore, the state authorities in Uttar Pradesh initiated “policy of death audit for the COVID-19 deceased in the state of U.P” for keeping record and tabulation of information in a structured method concerned to all COVID-19 deceased to assess various factors related to the cause of death and other underlying or contributing disease conditions leading to mortality in COVID-19 cases.4 Since the first reported case of COVID-19, from Agra region we have also faced the fiery two waves of COVID-19, and still have many unanswered queries, challenges, and ambiguity about COVID-19. 7

Aims and objectives
The present study aimed to analyze the death audit records to study the demographic characteristics, various comorbidities contributing to the COVID-19 deaths, duration of hospital admission and mortality trends in dedicated COVID-19 facility from Uttar Pradesh.

MATERIALS AND METHODS

This is an observational study from April 2020 to July 2021 which is based on records obtained from death audit reports of a dedicated COVID-19 facility at a tertiary hospital, Agra, Uttar Pradesh. The state authorities introduced a standard “COVID-19 Death Audit Proforma” on a death audit portal to audit all deaths related to COVID-19 (SARS-CoV-2) infection.6 We analyzed the death audit data of 467 COVID-19 death cases considering factors of age, gender, area of residence, cause of death, related comorbidities and relation with duration of hospital stay and presence or absence of comorbidity in COVID-19 death cases.

Study subjects
Record analysis of 467 completed death audits of COVID-19 deaths occurring in the COVID-19 facility from April 2020 to July 2021 was included in the study.

Inclusion criteria
Death audit records of all COVID-19 confirmed deaths reported at the COVID-19 dedicated facility of SN Medical College, Agra.

Exclusion criteria
- Any deaths where there is a clear alternative cause of death that cannot be related to COVID-19 disease (e.g. trauma) were not included in the study. (According to ICMR guideline)
- There must not be a period of complete recovery from COVID-19 amid illness and death.
- All deaths reported suspected or probable due to COVID-19 were not included in the study.

Case definition8-10
Death audit
It’s a technique or process of quantitative death record analysis and compiles the information pertaining to the professional activities of the hospital, as well as the quantitative analysis and evaluation of the data so collected.

COVID-19 death case
A COVID-19 death is defined for surveillance purposes as a death resulting from a clinically compatible illness in a probable or confirmed COVID-19 case unless there is a clear alternative cause of death that cannot be related to COVID-19 disease. Confirmed case: A confirmed case is a person with laboratory confirmation of infection with the COVID-19 virus, irrespective of clinical signs and symptoms. Suspected case: A patient with acute respiratory illness (that is, fever and at least one sign or symptom of respiratory disease, for example, cough or shortness of breath) with no other etiology that fully explains the clinical presentation and a history of travel to or residence in a country, area, or territory that has reported local transmission of COVID-19 disease during the 14 days prior to symptom onset. OR a patient with any acute respiratory illness and who has been a contact of a confirmed or probable case of COVID-19 disease during the 14 days prior to the onset of symptoms OR A patient with a severe acute respiratory infection (i.e., fever and at least one sign or symptom of respiratory disease, for example, cough or shortness of breath), who requires hospitalization and who has no other etiology that fully explains the clinical presentation. Probable case: A probable case is a suspected case for which the report from laboratory testing for the COVID-19 virus is inconclusive.8-9

Ethics
The data in this study are the part of the audit and permission to publish the data has been taken from the Institutional ethical committee (SNMC/IEC/2021/49). Anonymity and confidentiality of the data have been
maintained. The data were recorded in Microsoft Excel and analyzed using statistical software, Microsoft Excel (Version 16.49). The results are presented accordingly in form of descriptive statistics.

RESULTS

We have reported findings from 467 COVID-19 deaths from our dedicated COVID-19 facility in the present study. The median age of deceased was found to be 57 years (range from 4 days newborn to 87 years). Youngest COVID-19 death was reported in a female newborn referred from private hospital for premature birth and very low birth weight of 1.5 kg, death caused due to DIC with shock. While 87 years female deceased was the eldest COVID-19 mortality and was without any comorbidity. Majority of COVID-19 deaths occurred in the age group 41–60 years (39.2%) followed by 61–80 years (36.9%), 21–40 years (17.6%), >80 years (3.4%), and least number of deaths (2.9%) was recorded from age group 0–20 years. 60% of COVID-19 deaths in our hospital were in the age group of 0–60 years while 40% were of the elderly age group (above 60 years). In the context of gender-wise distribution, nearly 72% (71.9%) deaths occurred in males, while 28.1% in females. About 77.1% of COVID-19 deaths were reported from patients residing in urban area and 22.9% of patients were from rural area (Figures 1-3).

Among 467 death cases that were analyzed for with or without any pre-existing comorbid disease along with COVID-19 at the time of hospital admission; in 345 cases (74%) of COVID-19 deaths, comorbidities were present while 122 (26%) deaths were without any comorbid disease (Figure 4). Regarding various comorbidities, hypertension was found to be the most common comorbid disease present in 42.9% of deceased followed by diabetes (34.5%). Chronic kidney disease (CKD) was present in 13.9% of death cases. Concurrence of diabetes and hypertension, hypertension and CKD; and of diabetes, hypertension and CKD was recorded from 19.1%, 5.8%, and 3.1% of deceased, respectively. Other comorbidities in COVID-19 deaths were chronic lung disease (6.7%), hypothyroidism (5.5%), cardiovascular disease (3.8%), stroke (3.8%), chronic liver disease (3.2%), and malignancy (3.2%) (Figure 5).

Time interval between hospital admission and death in COVID-19 case is showcased in Figures 6 and 7. We divided this duration into <5 days and more than 5 days. 32.98% of deaths were found to be within 24 h of hospital admission (1.93% in <6 h while 31.05% in 6 to <24 h). Almost 48.39% of deaths were recorded between day 1 and day 5 (27.62% - between day 1 and 3 and 20.77% - day 3 and 5), 17.77% of deaths occurred (13.7% deaths from day 5 to 10 while 4.07% from day 10 to 15). Only 0.86% of COVID-19 deaths were recorded between days 15 and 25 (0.64% deaths between days 15 and 20, just one death between 20 and 25 days). We did time interval analysis in the context of the presence and absence of comorbidity; in all categories of time intervals, more COVID-19 deaths were with comorbidity. About 77.78% deceased were with
comorbidity within 6 h, 63.45% in 24 h, 69% and 57.82% died between 1 to 3 days and 3 to 5 days had comorbidity. In more than 80% (81.25% - 5–10 days and 84.21% - 10–15 days) of deaths, comorbidity was present in between 10 and 20 days while all deaths (100%) between 15 and 25 days had one or more comorbid condition.

Trend analysis of 467 deaths from April 2020 and July 2021 is shown in Figure 8. Maximum deaths during first wave were recorded in May 2020, second-highest in September (second peak of first wave); during second wave majority deaths were reported in April and May 2021.

**DISCUSSION**

COVID-19 disease and comorbidities are associated with rapid disease progression and poor survival. India is going through an epidemiological transition with a huge burden of non-communicable disease in country and add to this problem is undiagnosed NCDs. The present study describes mortality in COVID-19 patients in the most populous state of Uttar Pradesh in the context of demographic profile
and co-occurrence of comorbidities in the population of Agra. In the context of demographic profile being a second most populated country in the world, India posed major challenges during the COVID-19 pandemic. The age profile in the present study revealed that the majority of deaths occurred in the age group 41–60 years (39.2%) followed by 61–80 years (36.9%). An analysis highlighted, that in early phase of pandemic (till July 2020), 47% of COVID-19 deaths in India were <60 years; a study from Tamil Nadu and Andhra Pradesh (till August 2020) found 54% of deaths under age 65 years.11,12 While early research from Mumbai, suggested increased mortality in age group >40–60 years, study from Pune (both waves analysis) also marked higher age groups (>65 years) with higher mortality, and data from Bihar showed age-based increase in mortality with maximum mortality in the age group 60–74 years.13–15 International studies from Korea, Brazil, and Mexico also conclude mortality to be more in elderly population.16–18 Similarly, in age below 65 years only 5–13% of deaths are reported in 10 European countries and Canada and 8–24% in US states.19 Age group 41–60 years was more severely affected with COVID-19 in India which may be attributed to the fact that Indian population is young budding population with this age group at its maximum exposure of not only contacting COVID-19 disease and also high prevalence of comorbidities such as diabetes and hypertension. Children and adolescents comprised of meager 2.9% of deaths in our study (2.9%) similar to others studies.20,21 A research with comprehensive analysis from the UK on Children COVID cases from March 2020 to February 2021 reported very low risk of death or severe COVID-19 in children. This finding of low mortality in children is also reported from India, even though seroprevalence studies highlighted higher number of children infected with SARS-CoV-2 infection.22,23

Our study reported higher proportion of deaths in male (71.9%) in the ratio of 2.47:1 which was consistent with national and global data.24–27 We found that majority of deaths in admitted patients belong to urban area (77.1%). The lower mortality data among women has been reported in many studies, several explanations were cited; like protection by X chromosome and sex hormones, less risky behavior, and less exposure to outdoors.27 This study concluded that 73.9% of COVID-19 deaths were related with one or other comorbidities. Among comorbidities, hypertension was found common in 42.9% of deaths, followed by 34.5% deaths with diabetes mellitus and 19.1% reported concurrence of hypertension with diabetes. A meta-analysis conducted on around 64000 patient records compared effects of various comorbidities between survivors and non-survivors have reported all comorbid conditions except liver disease to be significantly higher in non-survivors compared to survivors, with hypertension as the highest risk predictor.28

Although many studies from different parts of India showed a high prevalence of one or more comorbidities in COVID-19 deceased diabetes being reported to be more commonly associated tailored by hypertension alone or in concurrence with diabetes and coronary artery disease.14,15,26,29 Different studies from varying regions of the world reported patients with any one of the comorbidity more likely type 2 diabetes to have increased severe form of COVID-19 causing around 70% of deaths.30,31 One international study has reported arterial hypertension as the most prevalent chronic condition in the decedents (65.4%), followed by obesity (38.5%).32 Research from the US till December 2020, showcased that odds ratio of mortality with cardiovascular disease and hypertension was 40 times higher than without comorbidity.33 In 14% of cases, CKDs was found alone and in concurrence with other diseases, which is similar to studies from different parts of India reporting variation of its concurrence from 3.12% to 22%.34,35 Similarly study done by The Centers for Disease Control and Prevention reported 12 times higher deaths among patients with underlying conditions compared with those without underlying conditions.35 Comorbidities was also reported linked with 70–90% of deaths found in studies from china, South Korea and Brazil.34,36

Around 26.2% of deceased in our study reported having other comorbidities such as COPD, chronic liver diseases including hepatitis, cardiovascular diseases, hypothyroidism, stroke, or any malignancy; however, the presence of these as independent comorbidity was found to be very low. This is a little higher in other studies from India, but individually there is an only minor variation from our stud.35,36 The early onset, poor management, and huge burden of undiagnosed non-communicable diseases such as hypertension and diabetes demands major reforms in health policy and interventions. In ongoing pandemic, population with comorbid conditions especially DM needs to be prioritized at all levels of health care, as these patients might be predisposed to develop severe form of COVID-19 disease, leading to the worst consequences and death. This has been explained by the weak immune system in diabetic individuals, more commonly observed in those with poor glyemic control.24

As estimation of time interval from onset of symptoms was a little difficult due to increased biased information, we opted for the time interval from the day of hospital admission to death to gain knowledge about the relation between the patient hospital stay and comorbidity. From our time interval analysis in the context of presence and absence of comorbidity, we concluded that in all categories...
of time intervals, more COVID-19 deaths were with comorbidity 73.9%, 81.4% deaths were seen in time interval <5 days, of which 71.8% were seen with one or more comorbidities, but we observed a relatively higher mortality within a day of hospital admission as 31.04% compared to studies from south India which reports One-fourth of (24.2%) deaths within a day of hospital admission.26

Study from Tamil Nadu7 reported the median time interval between hospital admission and death as 4 days which is quite similar to median hospital stay in our current study as 4 days but shorter than few studies from India which reported the median length of hospital stay of COVID-19 patients as 6–7 days.25,26 Other countries reported a slightly higher, but a wider range of 5–16 days of time interval between hospital admission and death which indicates a better access of the population of these countries to health interventions in comparison to us.38,39

We have reported month-wise trend analysis of 467 deaths from April 2020 and July 2021; the first wave of pandemic in Agra faced two peaks in the month of May and September respectively and one peak during second wave in April and May 2021. The September peak in first wave and the April–May peaks in second wave also coincide with the COVID-19 positive patient load admitted during that phase in Agra. The first peak in May during first wave can be attributed to the unpreparedness phase during onset of pandemic, our centre being a tertiary hospital and catering all the severe cases of this region along with being the epicenter of COVID-19 in Uttar Pradesh in the early phase in 2020. A study on both waves from Pune reported that the sharp decline of COVID-19 mortality during the first wave also appears to coincide with the availability of more information and revised national guidelines on clinical management such as optimal use of corticosteroid, antivirals, and appropriate early supportive treatment following hospitalization of moderate and severe COVID-19.14

Limitations of the study
Our study is limited to COVID-19 mortality from one tertiary care centre. We missed the co-morbidities like obesity which seems to impact mortality in COVID-19 patients We have also not included relation between duaration of co-morbidities and COVID-19 mortality.

CONCLUSION
Our analysis from dedicated COVID-19 facility found that comorbid condition was present invariably in about 74% of deaths from SARS-CoV-2 infection. As world has seen more than 5 million deaths and news of omicron hanging over health systems, high-risk groups should be identified and protected to prevent excess mortality. Early diagnosis timely and aggressive management is pillar for reducing morbidity and mortality from COVID-19 disease. In ongoing pandemic and huge burden of NCDs in our country, strategic guidelines need to be framed to tackle this dual burden.

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