Original Research Article

Variation in COVID-19 management outcome with progression of pandemic- An observational study of a tertiary covid care centre

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Abstract

Introduction: Uttarakhand reported its first case of SARS-COV-2 on 15th march 2020. This study is a retrospective descriptive analysis of the changing demographic, clinical and case fatality rate of the disease with the progression of pandemic. **Material and methods:** The study is on the data of the admitted patients in a tertiary level facility from March 2020- February 2021. Data was analysed in terms of outcome of the admitted patients and the change in the clinical presentation and demographic profile of disease in the admitted patients with progression of disease over the stipulated time frame. Factors affecting the mortality of the admitted cases were also analysed. **Results:** Symptomatic cases admitted in months of March 2020-July 2020 was 39% while those in month of August 2020-Feburary 2021 formed 90.3% of total admission (p< 0.00001). Case Fatality Rate in age group of >= 60 years was 16% while in <=60 years it was 3.2% (p<0.00001). Comorbidities were associated with 68.8% (n=209) of deaths, of which predominant was diabetes (44%). Out of 139 deaths, 35% were attributed to acute respiratory distress syndrome/Respiratory Failure, 37% were due to Cardiac events while Sepsis with Multiple Organ Dysfunction Syndrome was responsible for 285 mortalities. **Conclusion:** Home Isolation policy of the COVID-19 positive cases with the advancing pandemic had an adverse impact on the clinical profile, demographic profile and the mortality rate of the admitted patients. Early treatment policy of the admitted SARS-COV-2 positive asymptomatic or symptomatic patients did affect the outcome of the admitted patients in the early phase of the pandemic. Ae more than 60 years and also the co-morbidities are an independent risk factor for mortality in COVID-19 and also the co-morbidities.

Key words: COVID-19 Outcome; Clinical Profile; Comorbidities; Early Treatment.

Introduction

SARS CO-V 19 first case was detected in December 2019 in Wuhan city of China. The disease took a global form by march 2020, when it was declared a pandemic by WHO on 11th March 2020. As on date 25th February 2020 more than 113 million cases have been recorded worldwide with 65.3 million recovered and around 2.5 million deaths reported. India alone has recorded more than 11 million cases with 10.7 million cases recovered and 157 thousand's deaths reported. Presently while vaccination for covid-19 has been widely initiated in the country there has been resurge of fresh waves in 10 states. Protective effect of vaccination is still a time taking process and also vaccinating such a massive population size with varied religious, political and health beliefs is a mammoth task. People from every sphere of life have been hit by the pandemic and strict lockdowns, personal hygiene and masks are the only answers to slow down the ongoing spread of pandemic. Researches are going worldwide pertaining to every field of the disease virus and its treatment, but none of the drugs or remedies have proven to be fully effective in treating the disease.

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The infection of SARS-COV-19 have a varied clinical presentation, the clinical spectra spreading from asymptomatic to mild, moderate, severe Covid-19 pneumonia to death.81% cases have been reported to be mild /asymptomatic. The disease in spite of being highly infectious nature has a case fatality rate of 2.3%. As per a number of studies 14%-15% cases of covid need hospitalization and some 3% to 5% may land up in intensive care units [1,2,3]. On the time line, the incubation period of disease varies from 2 to 14 days, with median time of 4-5 days [4], followed by order of symptoms like fever, cough, cold, myalgia, ageusia, anosmia, days fatigue, headache, low backache, diarrhea and joint pains. The Covid -19 symptomatology follows a predictable pattern of fever first, followed by cough and then other symptoms in majority of individuals infected as per one study [5,6]. Beyond 5 days from the first symptoms, starts the stage of dysregulated immune mechanism when the lower respiratory tract gets involved and patients presents with increase cough, persistent or resurge of fever, breathlessness, chest pain, cyanosis, confusion and falling oxygen saturation level. Patients with severe covid-19 develop ARDS around day 8 to day 10 usually. The median time from onset of illness to Intensive Care Unit admission was 9.5-12 days4. This phase continues up to day 14 beyond which either recovery occurs or the stage of complication like sepsis, multiple organ dysfunction syndrome, cardiac, acute respiratory distress syndrome or death ensues. Average time period from day of admission to death has been reported to be around 18 ½ days. The median length of hospital stay for survivors was 10-13 days.

First case of covid-19 was reported in India on 30th January 2020 in the state of Kerala. Uttarakhand, a hilly state of India reported its first case of covid-19 on 15th march 2020. In the initial days of pandemic state government had adopted the policy of contact tracing, institutional isolation of confirmed cases and quarantine of close contacts of the RT-PCR confirmed cases. With the rise in cases Government of India adopted the policy of dividing the health infrastructure in 3 levels. Category 1 Dedicated Covid Hospital with fully equipped intensive care unit ventilators and beds with assured oxygen supply to cater to the severe covid cases. Category 2 Dedicated Covid Health Centre with separate areas for suspected and confirmed covid-19 cases areas with beds with assured oxygen support and Category 3 Dedicated Covid Care Centre which could be the makeshift facilities with separate areas for suspected and confirmed cases to cater to patients who were very mildly or mildly symptomatic according to the notice issued by Ministry of Health and Family Welfare[6] on 10th may 2020. Government Doon Hospital attached with Government Doon Medical College was selected as DCH by state of Uttarakhand under this policy in May 2020. The admission policy as well as the disease profile of admitted cases in our hospital thus changed with the progression of pandemic. In this study we are presenting the epidemiological trend and health outcome of the admitted patients in a tertiary level care (designated as DCH) from march 2020-february 2021.

Material and Methods

The Centre is a fully equipped 180 bedded hospital attached to a medical institution with 80 beds in I.C.U and 100 beds with oxygen supply with dedicated hospital staff. The data was collected from the record room of the hospital and was analyzed and evaluated retrospectively. The study material comprised of all admitted patient with lab report of confirmed covid-19 infection, in the institution from 15 March 2020 to 28 February 2021. Admitted patients were broadly categorized into 4 categories depending on the clinical presentation at time of admission.

1. Asymptomatic
2. mild- with symptoms of fever, cough, myalgia, muscle pain, joints pain, rhinitis, sore throat, headache, nausea, vomiting and diarrhea, or any other symptom (excluding chest pain, breathlessness and fall in oxygen saturation levels below 95%).
3. Moderate- presenting with Spo2 between 94 % to 91%, with breathlessness and chest pain.
4. Severe/critical- cases with Spo2 less than equal to 90% requiring assisted support in form of HFNM, NIV, or Mechanical ventilation. Patients with moderate disease but with any complication like MODS, MI, CVA and CKD were also placed under same category.

Treatment protocol for each category was set according to the Ministry of Health and Family Welfare guidelines for covid-19 management guidelines and state government guidelines. Asymptomatic patients above age of 18 years were treated with ivermectin 12 mg for 3 days along with hydroxychloroquine 800 mg on day 1 followed by 400 mg daily for next 4 days along with vit c supplementation of 500 mg daily for 10 days. Mildly symptomatic patients were treated as asymptomatic patients along with either azithromycin 500 mg daily / doxycycline 100 mg twice and antiallergics, antipyretics, lozenges as per need. Baseline ECG of high risks patients (which included age more than 45 years, patients with cardiac disease, diabetes, Chronic Kidney Disease, Chronic Lung Disease) started on hydroxychloroquine was taken. Patients with moderate or severe disease were treated with intravenous dexamethasone and remdesivir as per recommended doses by Ministry of Health and Family Welfare guidelines for covid-19 treatment. Besides intravenous antibiotics, tocilizumab and convalescent plasma therapy was used as per the guidelines.

Outcome was evaluated in terms of discharge, death, and referral to other centers for management of covid-19 sequalae and/or on patients request. Deaths were further analyzed in terms of age, comorbidities, time of death post admission and probable cause. The data was used for framing future plans of betterment in covid-19 management and also highlighting the shortcoming in management protocol.

Statistics

Data was evaluated in proportions and percentages and where ever needed z-test of significance between two proportions was calculated using online tool. $P<0.05$ and $p<0.00001$ was considered to be significant.

Results

Total number of patients admitted in stipulated period of time were 3756. The demographic profile of the admitted patients was as given in [table 1]. Total number of females admitted was 1260 (33.5%) and total number of males admitted was 2496 (66.5%) ($p=0<0.05$). Maximum number of patients admitted were in age groups between 18-40 years of age (42%) followed by those in age group of 40 to 60 years (36.1 %) [table 1].

Table 1: Age wise data of covid positive patients

Month	Total number of admissions	<18years	18-40years	41-59	>=60	Percentage of admissions below 60	Percentage of admissions >=60
March	5	0	4	1	0	100%	0%
April	20	1	16	1	2	90%	10%
May	153	11	94	31	17	88.89%	11.11%
June	324	12	216	77	19	94.14%	5.86%
July	580	21	357	153	49	91.55%	8.45%
August	855	26	383	291	155	81.87%	18.13%
September	870	19	341	319	191	78.05%	21.95%
October	226	4	100	79	43	80.98%	19.02%
November	245	5	65	99	76	66.37%	33.63%
December	311	4	81	129	97	68.81%	31.19%
January	124	3	33	47	41	66.94%	33.06%
February	43	1	19	13	10	76.74%	23.26%
TOTAL	**3756**	**107**	**1709**	**1240**	**700**	**81.36%**	**18.64%**

Elderlies' comprising of 60 and above age groups formed 18.63% of total admissions while children formed 2.85% of total admissions. Of the total cases, 23.24% cases were asymptomatic at time of admission, 29.50% were mildly symptomatic. Cases presenting with moderate disease were 29.39% of total admissions in the stipulated period while 17.86% were the cases of severe covid-19 disease [table 2].

Table 2: Month-wise covid data

month	no. of admission	asymptomatic	mild	moderate	severe	number of deaths	percentage
March	5	5	_	_	_	0	0
April	20	20	_	_	_	0	0
May	153	93	49	2	9	1	0.65
June	324	235	71	1	17	5	1.54
July	580	354	186	1	39	7	1.2
August	855	83	644	30	98	33	3.86
September	870	79	619	81	91	72	8.23
October	226	4	81	93	48	24	10.6
November	245	_	56	133	56	22	8.9
December	311	_	128	138	45	26	8.4
January	124	_	51	32	41	16	12.90
February	43	_	8	25	10	3	6.97
total	3756	873	1893	536	454	209	5.56

Out of total 700 admissions in more than 60 years 27.6% were admitted with severe covid-19, while in less than 60 years age group out of 3056 admission 8.54% were of severe covid pneumonia (p=0<0.05) [table-3].

Table 3: Age wise data of covid positive patients

s.no.	age group	asymptomatic	mild	moderate	severe	total
1	less than 18	54	40	7	6	107
2	between 18-40	590	902	145	72	1709
3	between 40-60	165	676	216	183	1240
4	more than 60	64	275	168	193	700
total		873	1893	536	454	3756

846 patients were treated in intensive care units.1175 (31.3%) patients needed oxygen therapy, 24.7% in form of nasal canula (NC), 4.21% high flow nasal mask (HFNM)/Non-invasive ventilator (NIV), while 2.34% were supported with mechanical ventilation (MV).

Table 4:Oxygen supportive therapy

No supportive oxygen therapy	Oxygen by nasal canula	Oxygen by HFNM/NIV	Mechanical ventilator	Total
2582	928	158	88	2756

Cases referred to higher centers were the ones who needed long oxygen therapy or physical rehabilitation and prolong physiotherapy or who requested to be shifted to other hospitals for further management. These were shifted once only when two repeated nasopharyngeal throat swabs samples for RT-PCR turned negative [table-5, fig. 4].

Table 5: Final outcome of admitted patients

Total admission	discharged	Home isolation	Referred to ccc	Referred to higher centre	Deaths
3756	1393	748	1192	214	209

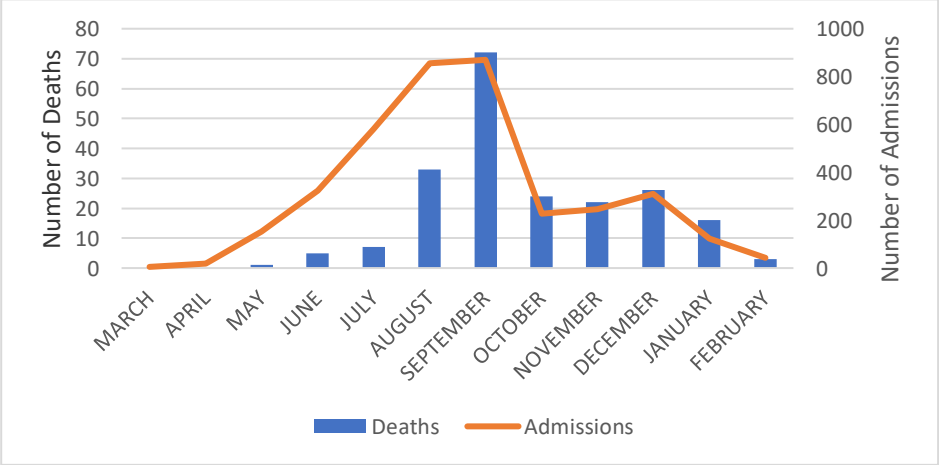

Fig 4: showing increasing mortality with progressive months of pandemic

Covid Care Centers (CCC), was the extended facility of the institution where patients were shifted once undergone baseline investigations and treatment of 3 to 5 days and remaining stable

Total deaths attributed to covid-19 and its complication were 209 of which 145 were males (69.35%) and 64 females (30.65%). 70 deaths have occurred within 48 hours of admission and were not analyzed while ascertaining the probable cause of mortality [table 6].

Table 6: death distribution according to hospital stay in hours

Duration after admission	Number of deaths	
<= 48 hours	70	33.5%
>48-72 hours	17	8.1%
>72 hours	122	58.4%
total deaths	209	5.56%

Co-morbidities formed 68.9% of total deaths compared to 31.1% of non-comorbid deaths (p=0<0.05). Patients with single comorbidity were 58.3% of total deaths while those with 2 or more than 2 were 44.4% of the deaths with comorbidity

Table 7: Comorbidity-wise mortality distribution

Total Deaths	With Comorbidities	With 2 or more than 2 comorbidities	With single comorbidity	Without Comorbidity
209	144	60	84	65

Diabetes hypertension and coronary artery diseases (63.9%, 43.8%, 36.11% of death with comorbidities respectively [table 8] were important existing risk factors with mortality.

Table 8: Comorbidities and Death

Comorbidity	Number of deaths
Diabetes	92
Hypertension	63
Coronary Artery Disease	52
Others (Chronic Liver Disease, Chronic Kidney Disease, Hypothyroidism, cancer)	38

Age more than 60 years formed 54.07% of all deaths in institution

Table 9: Age wise distribution of death

Age in years	Number of deaths	Percentage
<18	1	0.47%
18-40 years	23	11.00%
41-60 years	72	34.44%
>60 years	113	54.07%

On post covid death audit out of 139 deaths, 35% deaths were attributed to acute respiratory distress syndrome (ARDS) / Respiratory failure, 37% were due to cardiac events while Sepsis with Multiple Organ Dysfunction Syndrome (MODS) was responsible for 28% mortalities [table 10].

Table 10: Probable causes of deaths

Cause	Deaths
ARDS/Respiratory Failure	49
Cardiac	51
Sepsis with MODS	39
Total	209

Discussion

The state of Uttarakhand had initial policy of contact tracing and institutional admission till the month of June when the pandemic was at slow pace but once the cases started rising and the hospitals had admission more than their capacities, home isolation for asymptomatic and mildly symptomatic cases (with limitations of age less than 60 years and no comorbidity) was introduced on patient's choice with close monitoring and follow up by state health machinery. A shift in the clinical profile of admitted patient was detectable as shown by fig 2 after the introduction of home isolation policy for asymptomatic and mildly symptomatic patients came into action.

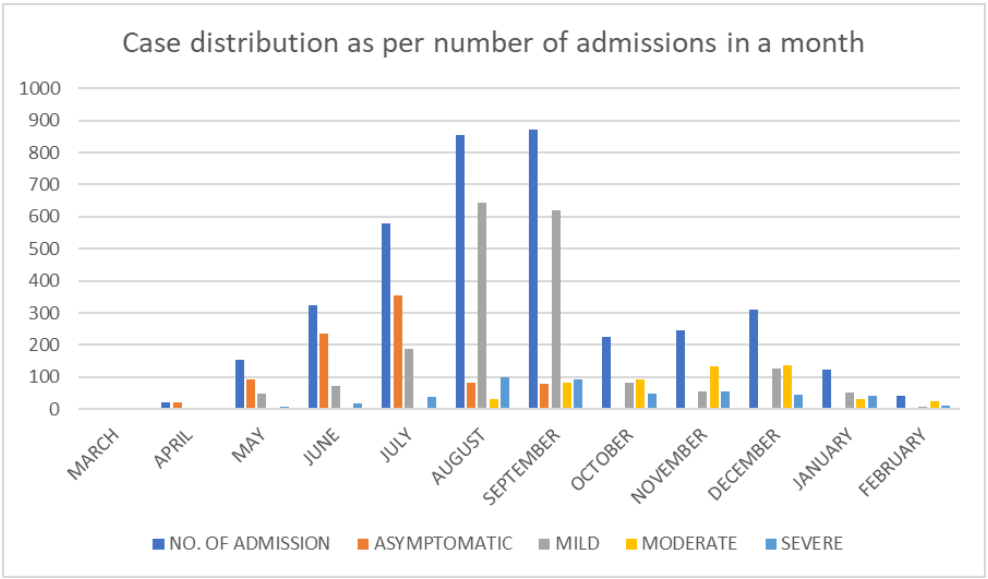

Fig 5: Changing Clinical Profile Trend- showing the changing trend of pandemic clinical profile in admitted patients with advancing months attributed to the change in the home isolation policy for covid -19 positive cases. With advancing months moderate to severe cases admissions increased compared to earlier months of pandemic

Symptomatic cases admitted in month of July was 39% while those in month of August formed 90.3% of total admission (p<0.00001). Severe cases admitted in months from march-20 to July 20 formed 6.72% of total admissions while in months from August 20-february-21 severe cases were 12.6% of total admission (p<0.00001) [fig.1].

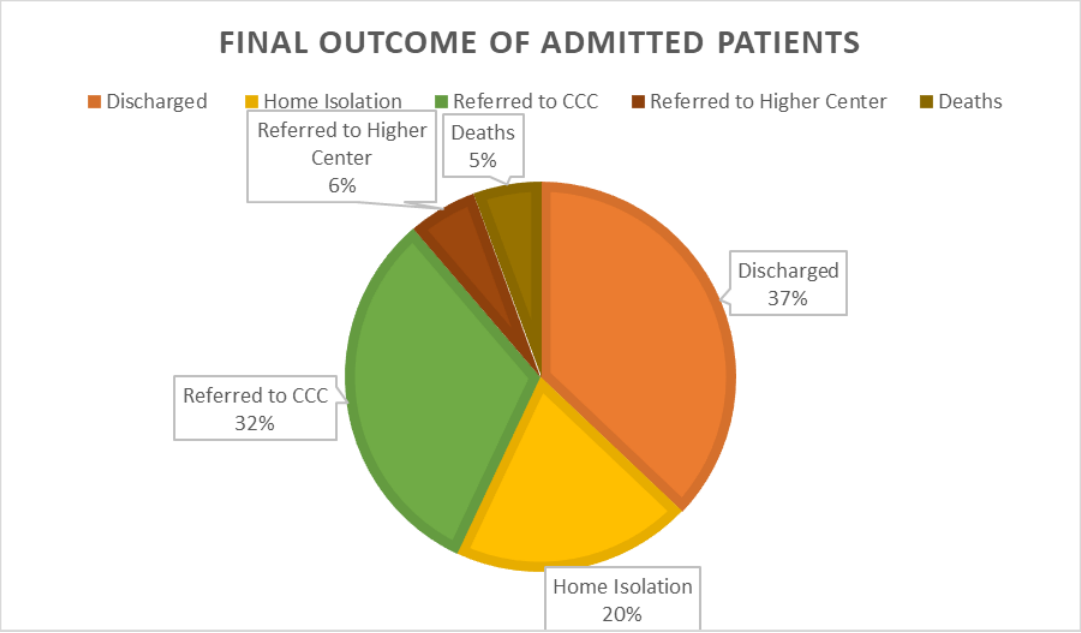

Fig 6: showing final outcome of admitted patients

Our study thus observes that with advancing pandemic, proportion of symptomatic admitted cases increased along with increase in severe covid cases. Contact tracing and mandatory institutional isolation policy of the government may have a role in this change of clinical presentation of admitted patients. Treatment was being advocated to all institution based isolated covid positive patients in initial phase of pandemic. Once the mandatory isolation of positive cases was ceased and permission for home quarantine was given, severe cases came into rise. There are a number of studies indicating that early treatment does lead to better outcome [7-11]. The elderly population comprising of 60 and above formed 8.02% of total admissions in month of March to July while 23% in the latter half of pandemic (p<0.00001) which again reflected the changing trend of the pandemic due to change in the policy of positive cases isolation and the effect of the unlocking of the lockdowns [fig.3].

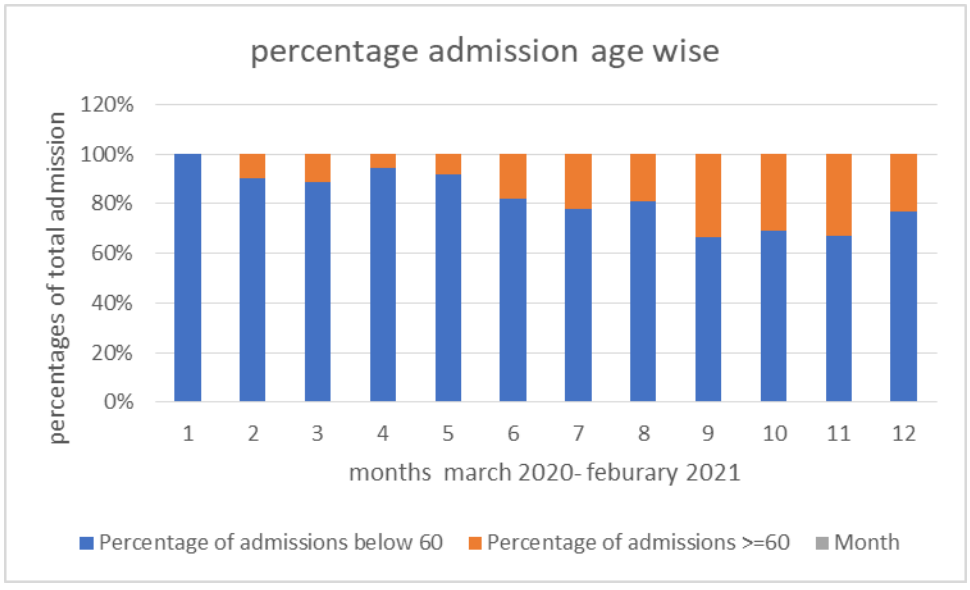

Fig 7: showing the change in admitted age profile with progressive months of pandemic

The rise in mortality can be explained with the changing profile of the admitted patients in form of increasing moderate to severe cases and also the people above the age of 60 years which has been proven to be a vulnerable group for covid infections in a number of studies globally [15-17]. Overall case fatality rate in our institution was 5.44% compared to 1.4% to that of India (p=0<0.05) [18]. Higher mortality rate of covid in our institution in reference to national statistics is because of the denominator comprising of large number of moderate to severe cases admitted in the institution and lesser number of mild cases or asymptomatic cases which were not being admitted in later part of pandemic as state covid management policy**.** High mortality was seen in age group of more than 60 years (54.07% of total deaths) while in age group of 40 to 60 years it was 34.44% comparable to national data as reported by Union Health Ministry. Case Fatality Rate in age group of more than equal to 60 years 16% while in less than 60 years it was 3.2% (p<0.00001). We also observed that as the pandemic progressed, with the increase in the admissions of the old age people (>60 years), the case fatality rate of institution also increased, thus highlighting the old age as an independent risk factor for covid mortality [fig 5].

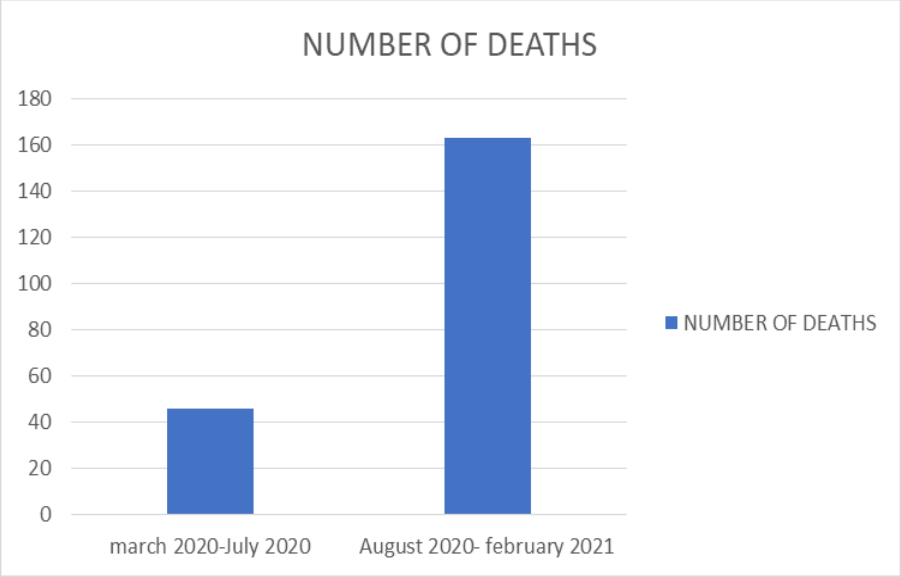

Fig 8: showing the cumulative in the two halves of pandemic

Comorbidities were associated with 68.8 % (n=209) of deaths, of which predominant was diabetes (44%).60 deaths of these were of individuals with 2 or more than 2 comorbidities (29%, p<0.00001) [fig 6,7,8,9].

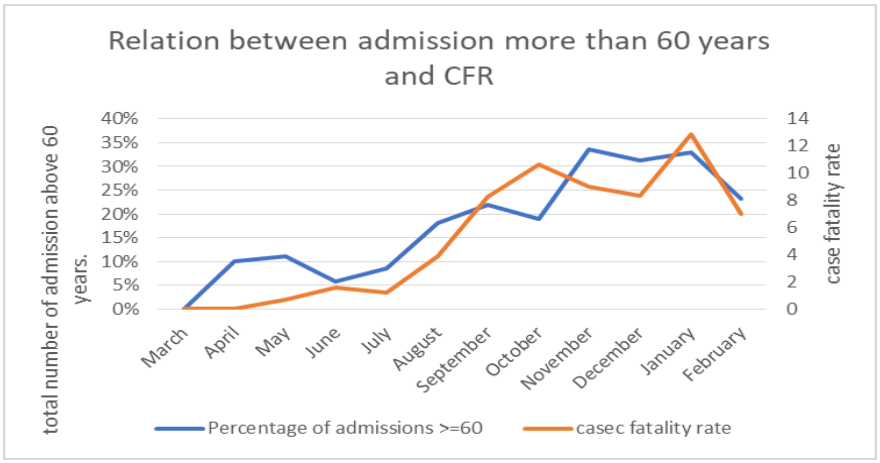

Fig 9: graph showing increase in CFR with relation to increase in > 60 years admission.

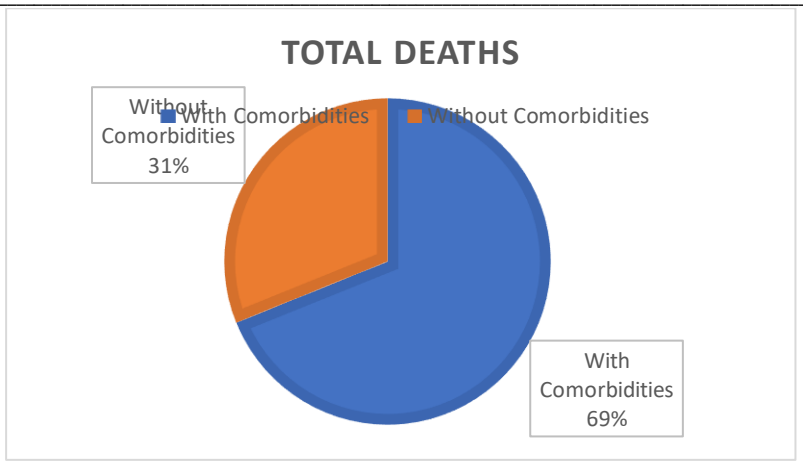

Fig 10: showing death with comorbidity

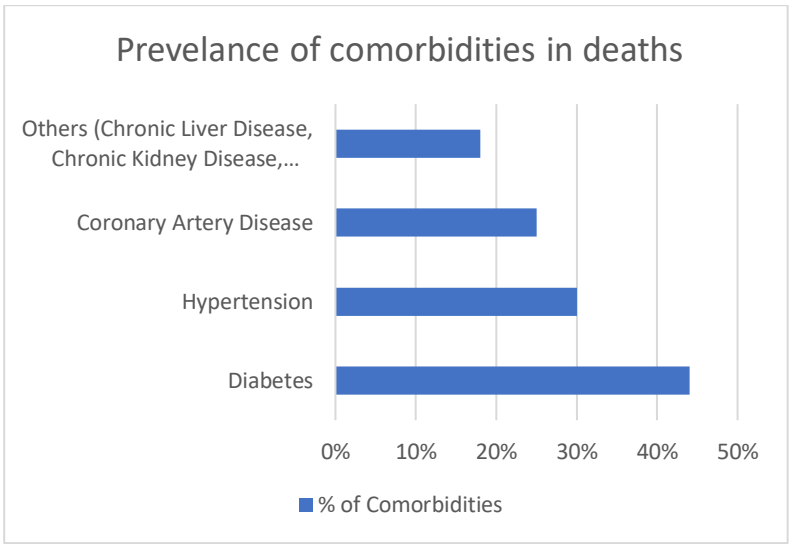

Fig 11: prevalence of comorbidities in deaths

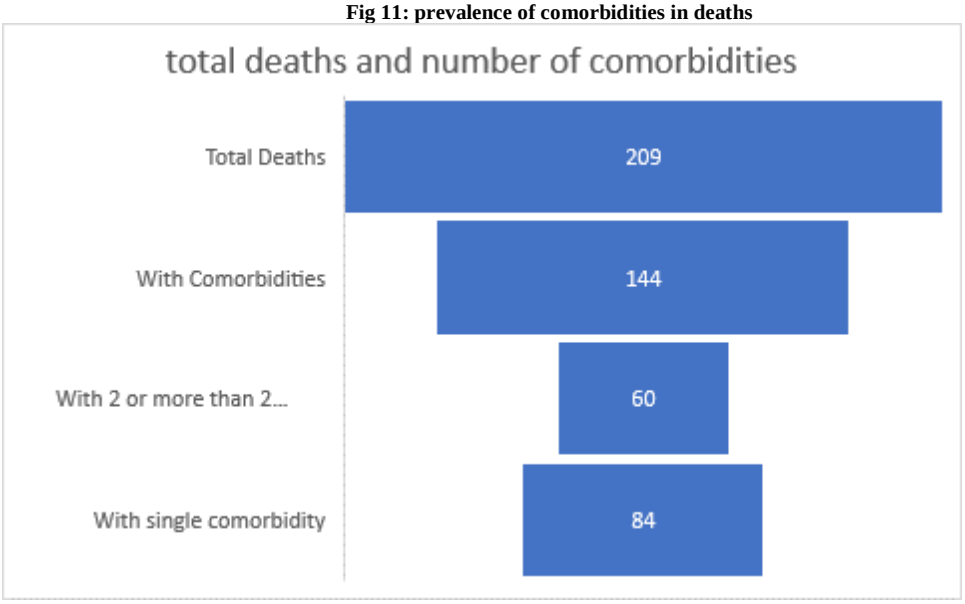

Fig 12: showing mortality in covid-19 patients in relation to number of comorbidities

Other comorbidities associated with death were Chronic Kidney Disease, Chronic Lung disease, Carcinoma which is comparable to the published data till date [15,16,17,19]. Acute respiratory distress syndrome /Respiratory failure, Cardiac events, and Sepsis emerged as the most important cause of deaths in hospitalized patients which is comparable to the published data till date. Cardiac events were the leading cause in the elders above 60 years while respiratory failure/ acute respiratory distress (ARDS) was an important cause of mortality in less than 45 years. Sepsis was an important cause of delayed deaths in hospital settings.

Conclusion

Our study reaffirms the existing studies finding, that mortalities are high in individuals with comorbidities and is directly corelated with the number of comorbidities coexisting**.** Age >60 years came out an independent risk factor for severe form of covid disease and also for high mortality. Our study did not support male gender as an independent risk factor for high mortality though it was observed that the covid infection rate was higher in males than female as ratio of males admitted was higher than females. Case Fatality is associated with the disease severity at presentation as evident by high mortality rate in the latter half of pandemic with increase in admissions with severe form of covid-19. Sepsis has emerged as an important cause of mortality in our study in prolong hospital stay cases. The study exhibits the favorable outcome in days of lockdown and institutional isolation probably due to easy contact tracing, early detection and early treatment. Home isolation policy of the covid positive cases with the advancing pandemic over the months had an impact on the clinical profile, demographic profile and the mortality rate of the admitted patients. The weakness of the study is its' observational retrospective nature with no control group. It is a descriptive study and biasedness while analyzing the data cannot be ruled out though all efforts have been made to minimize this problem. The strength of study is its large sample size, and data collection from single site which was reporting to the health authorities.

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References

1. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) – China 2020 external icon. *CDC weekly*. 17 February 2020. 10.46234/ccdcw2020.032.
2. Stokes EK, Zambrano LD, Anderson KN, et al. Coronavirus Disease 2019 Case Surveillance — United States, January 22– MMWR Morb Mortal Wkly Rep 2020;69: 759–765.
3. Chen, J., Lu, H., Melino, G. et al. COVID-19 infection: the China and Italy perspectives. Cell Death Dis 2020:9
4. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) – China 2020external icon. *CDC weekly*. 17 February 2020. 10.46234/ccdcw2020.032.
5. CDC clinical care guidance updated 16th February 2021
6. Larsen J,Martin J.D, Kuhn P, Hicks J.B. Modelling the Onset of Symptoms of COVID-19. Front. Public Health, 2020:1
7. Wu J, Li W, Shi X, Chen Z, Jiang B, Liu J, et al. Early antiviral treatment contributes to alleviate the severity and improve the prognosis of patients with novel coronavirus disease (COVID-19. Journ. of. Int. Med, 2020;288(1):128- 38.
8. Giammaria D, Pajewski A. Can early treatment of patients with risk factors contribute to managing the COVID-19 pandemic? J glob Health. 2020 ;10(1): 010377.
9. Chaccour C, Casellas A, Di Matteo AB, Pineda I, Montreo Af, Castillo PR, et al. The effect of early treatment with ivermectin on viral load, symptoms and humoral response in patients with non-severe COVID-19: A pilot, double blind, placebo-controlled, randomized clinical trial.; Eclin.Med.The Lancet 2021; 1(32):100720.
10. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Melhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID -19: results of an open-label, non-randomized clinical trial. Int. J. Antimicrob Agents. 2020;56(1):105949.
11. Liu k, Chen Y, Han k. Clinical features of covid -19in elderly patients: A comparison with young and middle-aged patients. J Infect. 2020 Jun;80(6): e14-e18.
12. Cheng ZJ, Shan J. Novel coronavirus: where we are and what we know. Infection 2020; 48: 155-63.
13. Williamson EJ,Walker AJ,Bhaskaran K, et al. Factors associated with COVID-19-related death using Open SAFELY. *Nature*. 2020;584(7821):430-436.
14. Biswas M, Rahaman S, Biswas TK, Haque Z, Ibrahim B. Association of Sex, Age, and Comorbidities with Mortality in COVID-19 Patients; A Systematic Review and Meta- Analysis. Intervirology 2021; 64: 36-47.
15. Chen, J., Lu, H., Melino, G. et al. COVID-19 infection: The China and Italy perspectives. Cell Death Dis .2020;11, 438
16. Onder G, Rezza G, Brusaferrro S. Case-fatality rate and characterstics of patients dying in relation to covid-19 in Italy. JAMA .2020;323: 1775-6.
17. www.mohfw.gov.in
18. Richardson S, Hirsch JS, Narasimhan M, Crawford JM McGinn T. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. JAMA. 2020;23:2052-9
19. Ssentongo P, Ssentongo AE, Heilbrunn ES Ba DM,Chinchilli VM. Association of Cardiovascular disease and 10 other pre-existing comorbidities with COVID-19 mortality. A Systematic Review and Meta- Analysis. PLoS ONE .2020;15(8): e0238215.

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