Early Hospitalization Improves the Covid-19 Patients' Prognosis

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The COVID-19 outbreak in Wuhan has subsided but the world is still suffering from it. We present our experience gained during this outbreak from city and hospital perspectives which might inform others to make evidence-based decisions to tackle this devastating pandemic more effectively. We studied the counter-measures adopted by Wuhan Government and analyzed the city's new coronavirus infected disease patient's data obtained from the National Health Commission and one re-purposed hospital to accommodate COVID-19 patients of the counter-measures for the COVID-19 outbreak. There was a significant drop of new-patient after February 18th, 2020. Patients with disease-onset after February 4th had shorter onset to admission days than those with onset before February 4th; and also had less critical-illness and mortality rates. This was due to quicker hospitalization after February 4th. The scores of PCR results at diagnosis, the national early warning score and the time-to-death were not significantly different for critical-illness patients whose onset before vs. after February 4th. The critical and death rates can be decreased by early hospitalization and oxygen therapy for less severe novel coronavirus-infected pneumonia within 7 days after disease onset.

Key words: Counter-measures; COVID-19; SARS-CoV-2; lockdown; outbreak
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The COVID-19 outbreak struck the city of Wuhan unprepared[1] although the memory of SARS is still around. The disease is spreading around the world at a fast pace and has now been declared a pandemic. As healthcare professionals battling with this outbreak over the past one year[2] we feel it is important and timely to share our experiences[3-5]. In this article, we evaluated the consequences of some vital counter-measures to COVID-19 outbreak in Wuhan that will inform other cities currently under the COVID-19 attack.

On January 30th, the World Health Organization (WHO) declared the coronavirus outbreak a Global Public Health Emergency, and March 8th,up-graded it to a pandemic. COVID-19 is now affecting 162 countries and territories around the world including Italy that has now surpassed China in the number of COVID-19 deaths, Iran, Spain, S Korea, Germany, France, the UK and the USA[6-9].

China responded to the outbreak initially with city lockdown on January 23rd and a curfew (residents quarantined to stay at home) on January 26th. More than 10 thousand medical staff with different but relevant skills were recruited rapidly from all over China and arrived in Wuhan to help with this unprecedented medical emergency of such a massive scale. Many existing hospital wards were

re-purposed as infectious diseases wards and new special hospitals (including Fire/Thunder-God and Mobile Cabin hospitals) were constructed within two weeks to accommodate COVID-19 infected patients. Our 1600 bed hospital, the Renmin Hospital of Wuhan University (RHWU), was re-purposed to accommodate new coronavirus infected pneumonia (NCIP) patients only. This article investigates the impact of measures and the speed they were undertaken on the spread, morbidity (need for intensive care) and mortality associated with COVID-19 infection. Many countries have implemented what they perceived were the most appropriate counter-measures based on country specific features of the epidemic but there may be generic measures that may benefit most countries based on our experience in Wuhan. Hence, we present data from the perspectives of the city of Wuhan with around 11 million inhabitants, and data from a large teaching hospital, that may provide important data to inform future decision making.

METHODS

Ethics approval: Thestudywasapprovedby the InstitutionalReviewBoard (IRB)of Renmin Hospital of Wuhan University (RHWU).Written,informedconsentwas waivedinlightoftheurgentneed to collect data in this retrospective study.Datawereanalyzedandinterpretedbythe authors.

Patient and Public Involvement:Patients or the public WERE NOT involved in the design, or conduct, or reporting, or dissemination plans of our research.

DataSources: NCIP patients' data of Wuhan was obtained from the National Health Commission (NHC). We also looked at the medical records of 1446 hospitalized patients admitted to RHWU between January 30th and March 5th (with disease-onset from December 5th to March 3th, 2020).

Case definition: Aconfirmedcaseof NCIP for hospitalization wasdefinedasapositiveresultonreal-timereverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of nasal and pharyngeal swab specimens (Chinese guideline for COVID-19, Edition 7). Only laboratory-confirmed cases wereincluded intheanalysis. Anonymized data regarding the onset-date of clinicalsymptomsandsigns, date of hospital admission, occupation and laboratory tests etc. was extracted from electronic medical records. We defined the degree of severity of NCIP (critical-illness vs. non-critical-illness) at the time of analysis using the NCIP guideline of China CDC (Edition 7). Critical-illness was defined as having any of the following conditions after NCIP diagnosis: 1. Respiratory failure requiring mechanical ventilation; 2. Shock; 3. Non respiratory complications causing organ failure and requiring intensive care.

Study Definitions: The onset to admission days wasdefinedastheperiod betweenthepotentialearliestdateof symptoms (i.e., dry cough,fever,fatigue,myalgia, altered taste, sore throat etc.) anddate of hospital admission.

Scales of scores for RT-PCR testing were defined as 1-6 for the sum of positivity of shelf protein (+-+++) and open reading frame (+-+++). This was evaluated on the report at diagnosis.

Patients with disease-onset between Dec.23th-February 3rd were assigned to group of before Feb.4 and patients' onset between February 4th to March 3rd was assigned to group of after Feb.4.

LaboratoryTesting RT-PCRassayswereperformedinaccordance withtheWHO protocol.

National Early Warning Score (NEWS): NEWS is an aggregated weighted score of 0–20, based on measurements of heart rate, systolic blood pressure, arterial oxygen saturation, respiratory rate, level of consciousness, temperature and supplemental oxygen[11].

StatisticalAnalysis: Non-parametric analyses were used to compare non-normally distributed numerical variables, and the results were expressed as the median and interquartile range. Categorical variables were summarized as counts and percentages. In this retrospective observational study,all statistics weredeemed to be descriptive only.We usedPrism,Version8,toplotthenumbersofpatients, percentage of morbidity and mortalityongraphs. Alltheanalyseswere performed with SPSS, Version 22.0, and $p<0.05$ was considered statistically significant.

RESULTS

Fig. 1A shows the timeline of the counter-measures and events undergone by Wuhan city and our hospital. In Fig.1B, the black line represents daily new cases. The green triangle represents the first peak of the new cases and after the first peak; the number of new cases remained high and only began to decline on February 18th (Blue triangle). There is a massive surge (sharp rise and fall) of new cases on February12th as all the suspected cases before February 12 were counted as new-onset cases without RT-PCR confirmation for fast hospitalization and treatment start. The green line represents daily recovered cases and there is almost an intercept of the green line (curve) and black curve on February 19th right after the sharp drop of the daily new-cases curve (black) on February 18th.

Our repurposed hospital was opened for NCIP from January 30th. The number of daily hospital admissions showed a similar pattern to city epidemiology of the outbreak (Fig.1C). The 1st peak of newly admitted patients appeared at the time when the facility was first opened for NCIP admissions and the second peak appeared between February 5-7th, coinciding with the rise of the city new cases. The red curve represents the death numbers of each day which showed February 9th had the highest number.

There was a significant difference (Fig.2A left) in the disease-onset to admission days whose onset before vs. after February 4th (11days (IQR 8-16) vs.7days (IQR 3-10), n=1096/197, p=0.000), including dead patients (Fig. 2A, middle: 10.5, interquartile range, 7 to 14 vs.3, interquartile range, 2.5 to 6.5 n=98/5, p=0.002). and critical-ill patients (Fig. 2A, right: 11 days (IQR 8-15) vs. 7 days (IQR 4-12.25), n=236/28, p=0.001).

Fig.1 Counter-measures for COVID-19 outbreak and effects on COVID-19 epidemiology.

(1)Timeline for countermeasures;
(2)Timeline of daily new cases and recovered COVID-19 cases in Wuhan;
(3)Timeline of daily new admission and deaths in our hospital.

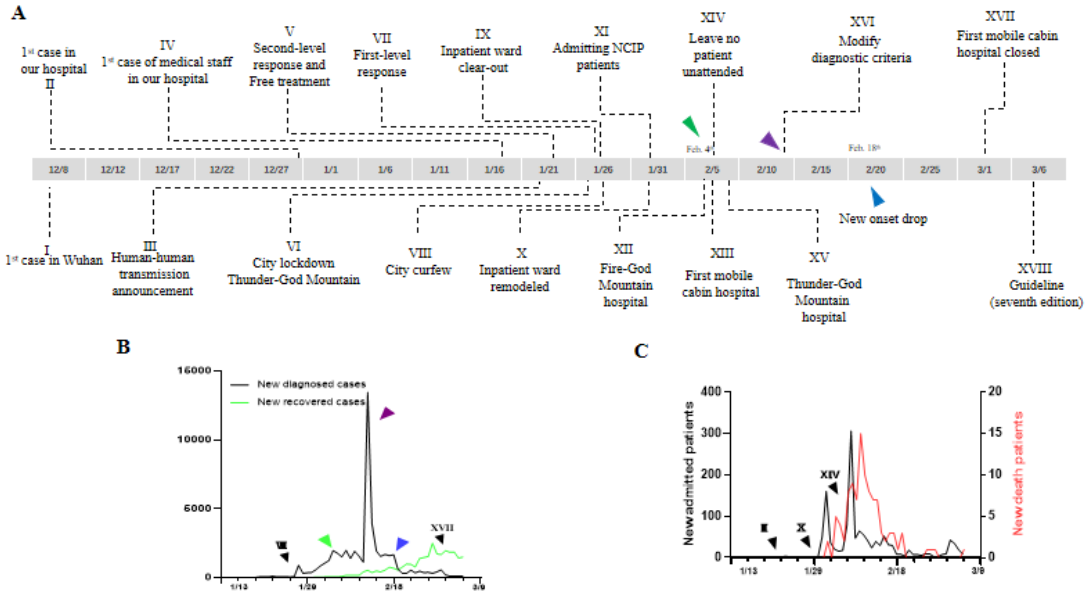
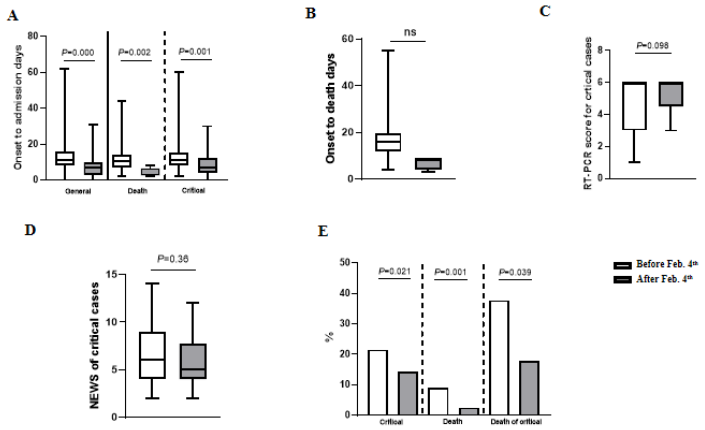


Fig. 2 Effects of days to admission on COVID-19 prognosis

A)Onset to admission days for all cases, death cases and critical cases before vs. after February 4;
B)Onset to death days for dead cases before vs. after February 4;
C)The scoring of RT-PCR results for virulence evaluation before vs. after February 4th for critical-illness cases;
D)Comparison of NEWS for critical-illness patients before and after February 4;
E) Comparison of critical-illness rates, mortality rates and mortality rate of critical-illness cases before and after February 4.



The severity of cases onset before vs. after Feb. 4 are not significantly different represented by 1) time-to-death for dead patients (Fig. 2B: 16 days (IQR 12-19.75 vs. 8 days (IQR 4-9), n=98/5, p=0.50), Scores of RT-PCR testing for viral replication of critical cases: (Fig. 2C,*p*=0.098), NEWS of critical-ill patients (Fig. 2D: 6 (IQR 4 -9) vs. 5 (IQR 4-7.75)). Meanwhile, the sex and age compositions are not significant different as well (data not shown).

However, there was a significant difference in the critical rate, death rate and death over critical rate for patients' onset before vs. after February 4th (Fig.2E left: 21.5% vs. 14.2%, n=236/28,*p*=0.021; Fig. 2E middle: 8.9% vs. 2.5%, n=98/5,*p*=0.001; Fig.2E right: 37.7% vs. 17.9%, n=98/5,*p*=0.039).

DISCUSSION

There have been several recent reports on the COVID-19 outbreak[12-14] but most of these are based on data from January 2020. This study represents the most up-to-date data on the Wuhan COVID-19 outbreak. The peak growth of newly diagnosed NCIP cases in Wuhan was from February 4th to February 18th. We analyzed daily reports of NCIP data from NHC, and related this with affected patients' data from our hospital, in order to evaluate the impact of the counter-measures. This study is the first report to examine how long it took for Wuhan to see the turning point of the transmission following the city lockdown and curfew, and important information for cities currently experiencing a surge in NCIP new cases. Our data demonstrates that critical-illness and mortality rates can be reduced with early hospitalization and treatment, possibly oxygen therapy within 7 days of onset.

After Fire/Thunder-God Mountain and Mobile Cabin hospitals were quickly opened the patient admission facilities were significantly enhanced. All the suspected cases before February 12th were counted as new onset cases admitted to these available wards after February 12th. Moreover, all diagnosed patients were required to be admitted to hospital which facilitated earlier supportive treatment with oxygen (almost inaccessible when quarantined at home). Meanwhile medical specialists with different but relevant skills arrived in Wuhan quickly and other important medical resources were quickly mobilized.

February 4th-18th represents the peak platform after city curfew (January 26th), indicating that a period of 9-24 days elapsed before the beneficial impact of a tight curfew was seen. However, this does not necessarily indicate a longer incubation time than has been reported since there are too many confounding factors.February 18th is likely the turning point for the Wuhan COVID-19 epidemic although a considerable number of asymptomatic patients were still undiagnosed[15]. There is a cross of the new case curve and recovery case curve further supporting that period time was the turning point for the Wuhan battle against this outbreak.

Critical-ill patients whose onset after February 4th usually took an average of 7 days to get admitted, benefitted from the strategy of fast diagnosis in the absence of RT-PCR (Guideline Edition 5, February 12th). The reception capacity for COVID-19 patients has been greatly enhanced since February 5th and all the patients were required to be hospitalized once diagnosed. This strategy allowed patients whose onset after February 4th to have much lower critical-illness rate and mortality rate (drop dramatically).

The high mortality rate of COVID-19 cases in Italy shows that virulence doesn't appear to diminish with transmissions[16]. Meanwhile, the age, sex and the critical status (evaluated by NEWS, death time for dead and viral load measured by RT-PCR at diagnosis) are not significantly different between those two groups (disease onset before vs. after Feb. 4th) suggesting all of these do not account for the improved prognosis of NCIP but only early hospitalization. No antiviral drug has proven

effective so far. However, oxygen therapy facilitated by early admission has been proved effective[17] for critical-ill patients. We rationale that NCIP at early/milder stage can also be prevented from progressing to more severe status with early oxygen therapy because our data showed that early oxygen therapy (accessible mostly at hospital) has less critical rate and death rate.

We have gained important insights regarding the clinical features of COVID-19infection[18-20]. We need not only to focus on preventing the transmission but also target on lowering the critical-illness and mortality rate of this disease. The massive mobilization of resources to increase the capacity to support the COVID-19 patients even at milder stage (with oxygen therapy) is likely the most cost-effective way for achieving the above two goals. This is a key learning point for many countries currently in the middle of this pandemic.

We think that the turning point of the epidemic may have happened around February 18th which is 24 days after the strict enforcement of the city curfew took effect[21]. The critical-illness and death rates decreased due to quicker hospital admission and prompt oxygen therapy for early onset patients (within 7 days), especially for those NEWS higher than 6. Wuhan appears as if it is going to win this battle and the experiences and lessons, we learned from Wuhan will hopefully enlighten others who are currently in the fight against COVID-19.

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DECLARATION OF INTERESTS

I declare there is no conflict of interest.

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