Abstract: In this retrospective COVID-19 study on 105 infected children admitted to Wuhan Children's Hospital, we have revealed two biomarkers (DBIL and ALT) to promptly screen out the severe ones from all the cases with the assistance of a proposed supervised decision-tree classifier. This clinical route achieves a 100% F1-score in the present investigation, which can be expected to facilitate early diagnosis and intervention for pediatric COVID-19 case.

1 Introduction
The outbreak of the Coronavirus Disease 2019 (COVID-19) epidemic has caused worldwide health concerns since November 2019 [1]. A previous study by Wei et al. [2] described the demographical, epidemiological, and clinical features for infected infants. However, compared with adult cases, little attention has been paid to children infected with COVID-19 [2–6]. Detecting the severity of the infection in children is challenging, since most of the paediatric patients have mild symptoms [2] irrespective of illness being moderate or critical therein.

2 Methods
For this retrospective study, we identified 105 infected children admitted to Wuhan Children's Hospital, the solely designated hospital in Wuhan for COVID-19 paediatric patients, from 1 February to 3 March 2020. The epidemiological, clinical laboratory and outcome data were extracted from the medical records of these patients. The study was approved by the Wuhan Children's Hospital Ethics Committee.

Throatswab, analswab, or urine specimens were taken at the time of admission for real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR), which was performed by the Wuhan Huada Gene Biology. Symptoms at the time of admission were collected together with laboratory results, chest radiography and CT findings, treatment received for COVID-19, and clinical outcomes.

Severe patients are generally manually detected according to the guidelines from the National Health Commission, China, using clinical symptoms including shortness of breath, assisted respiration, apnoea, cyanosis, dehydration, and progressive increase of lactate.

In this study, a supervised decision-tree classifier was developed. All clinical measurements from the last available date were used as features and set ‘mild’ and ‘severe’ as labels. ‘−1’ was used to complement incomplete clinical measures to avoid bias. We used standard F1-score [4] to evaluate the performance of the classifier. We started from one feature and increased the number of features in the clinical route until the F1-score converges. We picked the classifier with less incomplete...
measurements for all the patients, when two classifiers with the same number of features performed the same.

3 Results
A total of 105 children, including 64 boys and 41 girls, were infected with COVID-19, of whom 8 were critically ill. The youngest was an infant (1 day old), and the oldest was 15 years old. The boys infection rate (60.95%) was higher than that of the girls (39.05%). This is opposite to a previous report [2]. Children above 6 years have the highest infection rate (60.95%). All the children lived in Wuhan.

Based on the currently available clinical data, we discovered a clinical route that can achieve a 100% F1-score (shown in Fig. 1a). Fig. 1a shows the mild and severely infected paediatric patients over the proposed two-feature-based clinical route. As a result, we have extracted merely two features, i.e. direct bilirubin (DBIL) and alanine transaminase (ALT), by which 8 critically ill paediatric cases can be precisely identified from other 97 mildly infected patients.

4 Discussion
Due to the scantiness of clinical data from confirmed COVID-19 children cases, especially severe ones, it is an urgent yet challenging mission to promptly distinguish the severe ones from the mild cases for early diagnosis and intervention. To this end, with the assistance of machine learning methods, we identified that DBIL and ALT, surfacing from over 300 clinical features, we are able to serve as a combination index to screen out all the critically ill cases. Although the increase of DBIL and ALT has been reported to reflect tissue destruction or injury, for the first time, their combination is revealed as a precise indicator for the severity of COVID-19 paediatric cases, which is quite different from the discovered clinical route for adults [4].

The study was limited to a small number of patients from a single centre in Wuhan. Further studies from multiple centres in a larger cohort would be beneficial to the validation of the proposed route as well as an understanding of the disease.

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