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Laboratory data analysis of novel coronavirus (COVID-19) screening in 2510 patients

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ABSTRACT

Background: Novel coronavirus (COVID-19) is highly infectious and requires early detection, isolation, and treatment. We tried to find some useful information by analyzing the covid-19 screening data, so as to provide help for clinical practice.

Method: We collected nucleic acid and hematology data from 2510 patients for COVID-19 infection for retrospective analysis.

Result: COVID-19 and influenza A and B infection rates were 1.3%, 3%, and 3%, respectively. COVID-19 nucleic acid was detected in stool but not in tear samples from 8 positive patients. Among the 32 patients with COVID-19, 15 (47%) and 16 (50%) patients showed decreased lymphocyte count and lymphocyte ratio, 21(66%) and 24(75%) patients showed decreased eosinophil count and eosinophil ratio, and 18 (56%) patients showed increased C-reactive protein. Ten hematological indicators significantly differed in the blood of patients with COVID-19 and those with influenza A and B ($P < 0.05$). Eighteen hematological indicators significantly differed between patients with COVID-19 and negative patients ($P < 0.05$).

Conclusion: The positive rate of influenza A and B infection was higher than that of COVID-19. When pharyngeal swab collection may cause infection, fecal samples can be examined. Evaluation of pharyngeal swab and fecal samples can improve the positive rate of nucleic acid detection. The COVID-19 can cause some hematological indices changes.

1. Introduction

Starting in December 2019, cases of pneumonia with unknown causes began to appear in Wuhan, Hubei province, China. Subsequently, the outbreak of this pneumonia quickly spread throughout the Hubei province, country, and world. This pneumonia was confirmed to result from a novel coronavirus infection according to whole-genome sequencing [1]. On January 13, 2020, the World Health Organization tentatively named the virus as 2019 novel coronavirus (2019-ncov). On February 7, 2020, China officially named this novel coronavirus pneumonia as NCP. Later, on February 11, 2020, the World Health Organization officially renamed the NCP as coronavirus disease 2019 (COVID-19) [2]. COVID-19 is mainly characterized by pulmonary inflammation, which can cause damage to the gastrointestinal tract, liver, and nervous system [3,4]. It can also cause fever, cough, and other symptoms [5,6]. The clinical manifestations are similar to those of other viral infections, and thus differential diagnosis from other viral infections is necessary.

The clinical diagnosis of COVID-19 mainly relies on laboratory virus nucleic acid detection but is affected by virus levels in patients and sample collection methods. False-negative results are frequently observed. Additionally, numerous studies have reported changes in the laboratory detection data of patients with COVID-19 [7,8] and studies typically focus on one or several hematology indices, limiting the applicability of the research results. Therefore, we comprehensively analyzed and compared the laboratory data of screened patients with COVID-19 to provide a basis for the diagnosis and differential diagnosis of this disease compared to influenza.

2. Materials and methods

2.1. Subjects

We collected the laboratory test data from the hospital information

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Table 1
Basic information of 173 novel coronavirus, Influenza A/B virus infections.

Characteristics		Influenza	
	COVID-19 (n = 32)	Influenza A Virus (n = 57)	Influenza B Virus (n = 84)
Median (interquartile) age (years)	50 (37–66)	39 (25–55)	26 (20–33)
Age groups (years) – No.,%			
≤14	0	4 (7)	16 (19)
15–29	2 (6)	13 (23)	37 (44)
30–49	13 (40)	21 (37)	29 (35)
50–69	11 (34)	15 (26)	0
≥70	6 (19)	4 (7)	2 (2)
Sex-No., %			
Male	15 (47)	35 (61)	40 (48)
Female	17 (53)	22 (39)	44 (52)

system for 2510 patients who underwent screening for COVID-19 in the Fever Clinic of Xiangya Second Hospital of Central South University from January 23 to February 25. Thirty-two patients tested positive for COVID-19 nucleic acid, 57 patients tested positive for influenza A virus nucleic acid, 84 patients tested positive for influenza B virus nucleic acid, and the remaining patients were nucleic acid-negative. The basic information of patients is shown in Table 1. The study was approved by the Ethics Committee of the Second Xiangya Hospital of Central South University.

2.2. Nucleic acid detection

The COVID-19 nucleic acid test detects the N and 1ab genes, and the quality of nucleic acid extraction is monitored by using an internal standard. A positive quality control, weak positive quality control, and two negative quality controls in each batch were used. When two genes are are amplified and the cycle threshold (CT) value is below the detection limit, the result is considered as positive. A single gene is detected in the influenza A and B nucleic acid test; when the CT value is below the detection limit, the result is considered as positive. The COVID-19 kit was provided by Hunan Shengxiang Biology Co., Ltd. (Changsha, China) and the influenza A and B kit was provided by Jiangsu Master Co., Ltd. (Jiangsu, China). The performance verification results of the COVID-19 kit were as follows: Precision test showed that the kit had good repeatability and the coefficient of variation (CV, %) of CT was less than 5%. Due to the consideration of biosafety, we did not verify the accuracy, but our laboratory participated in the inter laboratory quality assessment organized by Shanghai clinical test center, and all the results passed. The sensitivity of this kit is 200 copies/ml. The interference test showed that the 10% (volume ratio) of whole blood, nasal secretion, 10% concentration of Runhou tablet solution, 10% concentration of hydroxymethozoline solution had no effect on the test results. This kit has no cross reaction with cytomegalovirus, influenza A virus, influenza B virus, Chlamydia pneumoniae, Mycoplasma pneumoniae, Staphylococcus aureus and so on. The performance verification results of influenza A and B virus kit are as follows:Precision test shows that the detection repeatability of the kit is good, and the coefficient of variation (CV, %) of detection CT value is less than or equal to 5%. The accuracy results show that the negative and positive compliance rate is 100% through testing enterprise reference/international standard (or reference). The sensitivity of this kit is 1.00e+04 copies/ml. The interference test showed that the 10% (volume ratio) of whole blood, nasal secretion, 10% concentration of Runhou tablet solution, 10% concentration of hydroxymethozoline solution had no effect on the test results. The kit has no cross reaction with cytomegalovirus, Chlamydia pneumoniae, Mycoplasma pneumoniae, Staphylococcus aureus, etc.

2.3. Hematology indices

We collected blood from patients with COVID-19 using routine methods and evaluated biochemical indicators. The blood routine indicators included lymphocyte count (LYM#), lymphocyte ratio, platelet count (PLT), white blood cell count (WBC), platelet-large cell ratio, monocyte ratio (MONO%), monocytes count (MONO#), red blood cell count, red blood cell volume distribution width-CV, red blood cell volume distribution width-SD, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular-hemoglobin concentration, mean platelet volume (MPV), basophil ratio (BASO%), basophil count (BASO#), eosinophil ratio (EO%), eosinophil count (EO#), hemoglobin, PLT-I, platelet volume distribution width (PDW), thrombocytocrit, immature granulocytes ratio (IG%), absolute value of immature granulocytes, neutrophil ratio, and neutrophil count. Biochemical indicators included myoglobin, albumin (ALB), ratio of albumin to globulin, carbon dioxide combining power (CO_2), serum calcium (Ca), serum alanine aminotransferase (ALT), serum aspartate amino transferase (AST), AST/ALT, serum creatinine, serum creatine kinase (CK), serum CK isoenzyme MB (CK-Mb), serum potassium (K), serum chloride, serum magnesium, serum sodium, serum urea, serum uric acid, serum globulin, serum lactate dehydrogenase, serum inorganic phosphorus (IP), anion gap, serum direct bilirubin, serum total bilirubin, serum total bile acid, serum total protein (TP), D-dimer, C reactive protein, and procalcitonin (PCT).

2.4. Statistical analysis

The median and interquartile range were calculated for continuous variables, and the two-tailed *t*-test and Mann-Whitney test were used as appropriate to compare continuous variables in data from different patient groups. The normality of the distribution was tested by single sample Kolmogorov-Smirnov test. P values less than 0.05 were considered to indicate statistically significant differences. SPSS version 24.0 (SPSS, Inc., Chicago, IL, USA) was used for data analysis. Statistical analysis graphs were generated and drawn using GraphPad Prism 8.00 software (GraphPad, Inc., La Jolla, CA, USA).

3. Results

3.1. Data analysis of nucleic acid detection of COVID-19

A COVID-19 nucleic acid was detected in 32 swabs collected during patient screening. The detection rate was 1.3%. COVID-19 nucleic acid was detected in the stool specimens of 8 positive patients examined. However, COVID-19 nucleic acids were not detected in tear samples from 10 positive patients. During the same period, the detection rates of patients with influenza A and B were 2.3% and 3.3%, respectively

Table 2
Types of nucleic acid test specimens.

Specimen type	COVID-19		Influenza A Virus		Influenza B Virus	
	Positive cases-No., %	Test cases	Positive cases-No., %	Test cases	Positive cases-No., %	Test cases
Pharyngeal swab	32 (1.3)	2510	57 (2.3)	2510	84 (3.3)	2510
Feces	8 (19)	43	0	6	0	6
Serum	0	31	2 (13)	15	2 (13)	15
Sputum	0	15	0	15	0	15
Bronchial lavage	0	1	0	1	0	1
Nasal swab	0	6	/	/	/	/
Whole blood	0	1	/	/	/	/
Tear	0	10	/	/	/	/

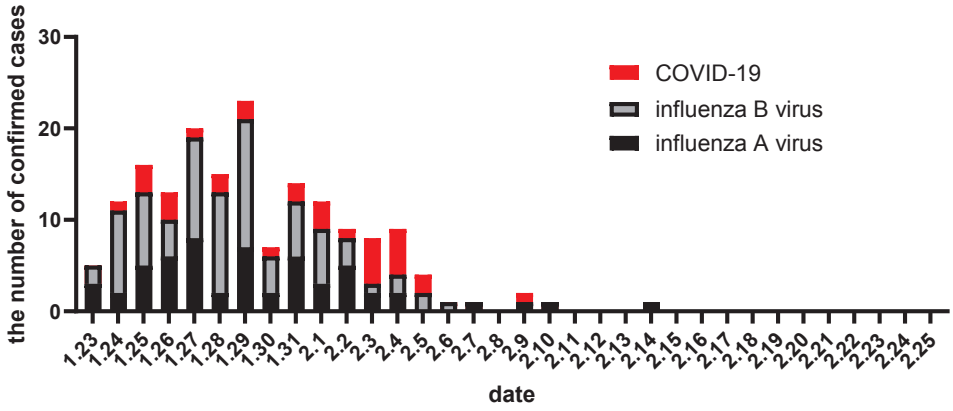

Fig. 1. Changes of nucleic acid positive cases with time.

(Table 2).

Fig. 1 shows that the nucleic acid-positive cases of COVID-19 were mainly detected from January 24 to February 9, with February 3 and 4 showing the largest number of positive cases. During this period, both influenza A and B viruses were also present. No COVID-19-positive cases were detected after February 10.

3.2. Differences in hematology indices between COVID-19-positive and COVID-19-negative patients

In the 32 patients with COVID-19, 15 (47%) and 16 (50%) patients showed decreased lymphocyte counts and proportions, 21 (66%) and 24 (75%) patients showed decreased eosinophil counts and proportions, and 18 (56%) patient showed an increase in C-reactive protein (Fig. 2).

We compared all laboratory hematology indices for the 32 patients with COVID-19 and 2337 negative patients. Patients with COVID-19 showed significantly higher levels of HFLC%, MPV, MONO%, TP, and ALB ($P < 0.05$). In contrast, PLT-I, WBC, lymph, BASO%, BASO, EO, EO, PLT, PCT, absolute value of immature granulocytes, Neot, urea and IP were significantly decreased ($P < 0.05$).

3.3. Differences in hematology indices between patients infected with COVID-19 and influenza A/B viruses

We compared all laboratory hematology indices between 32 patients with COVID-19 and 141 patients with influenza A/B viruses. In patients with COVID-19, six hematology indices, MPV, PDW, TP, ALB, ALT, and CO_2CP, showed increased levels ($P < 0.05$). In contrast, EO %, EO#, IP, and CK-MB were clearly reduced ($P < 0.05$).

4. Discussion

COVID-19 is a highly infectious virus that can be transmitted by droplets, contact, and aerosol and fecal-oral infection [9], making it difficult to prevent and control in China. In addition, because of the increased risk of transmission caused by the movement of people who are planning to return to work and school, improvements in the laboratory detection capacity and speed of diagnosis are needed to facilitate early detection, isolation, and treatment [10].

Our results show that during the same period, the positive rate of influenza A/B infection, which lead to influenza outbreaks, was higher than that of COVID-19 infection. Therefore, COVID-19 must be differentiated from influenza A/B to ensure appropriate patient management. No patients diagnosed with COVID-19 and influenza A/B infection had coexisting conditions. Whether the viruses compete between each other requires further clinical studies. Our results showed that the detection of COVID-19 infections was concentrated between January 24 and February 9 and peaked on February 3 and 4, with no positive cases after February 9. This is because cases that in other parts of China were imported from Wuhan, and the state enacted timely prevention and

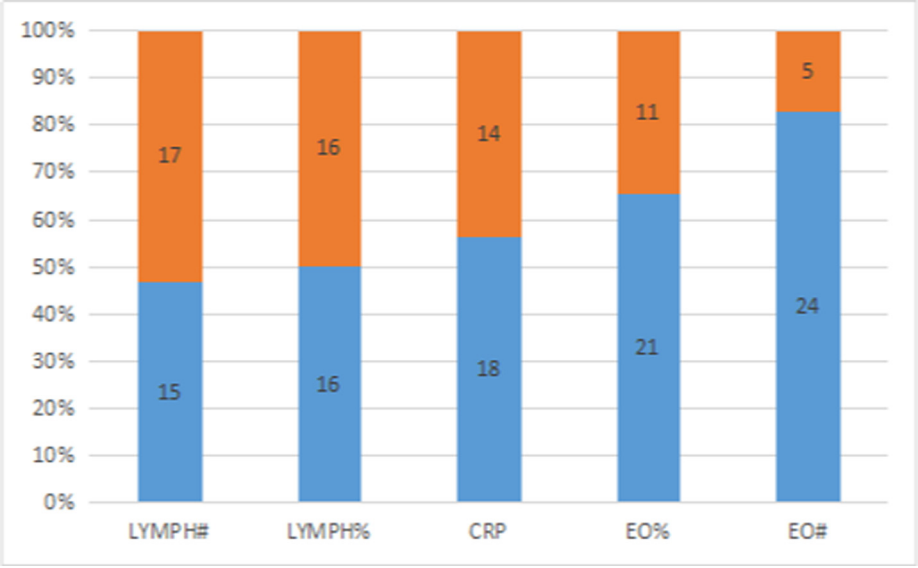

Fig. 2. Changes of hematology indices novel coronavirus infected patients.

control measured. Therefore, after the incubation period of the virus, the positive rate of both patients infected with COVID-19 and those infected with influenza A/B was significantly decreased. The number of diagnosed cases in the country has decreased to the hundreds, and 28 provinces have reported no new cases for several days.

We also detected COVID-19 in stool samples from eight positive patients, demonstrating that stool samples can be used for nucleic acid testing, or a combination of pharyngeal swab and stool samples can be used to improve the positive detection rate when there is a high risk of infection during pharyngeal swab collection. However, viral nucleic acid was not detected in the tears of positive patients, suggesting that the first infection was not related to the eye.

At present, there is no mention of changes on eosinophils in the latest diagnosis and treatment plan released by the Chinese government. With the increase of the COVID-19 research, we have seen some reports of eosinopenia [10]. However, compared with the published literature, our study found that the proportion of eosinophil changes was higher, among which 21 (66%) and 24 (75%) patients showed a decrease in eosinophil count and proportion. This may be related to our research object is the COVID-19 screening patients, these patients are in the early stage of the disease, the body's emergency response is more intense, so the decline of eosinophils is faster. But, the relationship between eosinophils and disease severity needs further study.

We also comprehensively compared all laboratory hematology indices in patients with COVID-19 to those in patients who were negative and those infected with influenza A/B. Compared to negative patients, HFLC%, MPV, MONO%, TP, and ALB were increased, whereas PLT-I, WBC, LYMPH#, BASO%, BASO#, EO%, EO#, PLT, PCT, IG%, NEOT#, urea, and IP were decreased. Compared to patients infected with influenza A/B, MPV, PDW, TP, ALB, ALT, CO_2CP were increased, whereas EO%, EO#, IP, and CK-MB were reduced. Changes in MONO%, WBC, PLT, PLT-I, LYMPH#, EO%, EO#, NEOT#, serum urea, ALT, TP, and ALB were consistent with the results of previous studies [11–14]. Hematology indices, such as HFLC%, MPV, PCT, PDW, IG%, CO_2CP, IP, and CK-MB were not mentioned. Therefore, these hematology indices can provide useful information for the COVID-19.

CRediT authorship contribution statement

Hu Yun: Funding acquisition, Investigation, Data curation, Formal analysis, Writing - original draft. **Zhuoran Sun:** Writing - review & editing. **Jun Wu:** Writing - review & editing. **Aiguo Tang:** Data curation, Formal analysis, Writing - original draft. **Min Hu:** Writing - review & editing, Methodology. **Zhongyuan Xiang:** Conceptualization, Project administration, Funding acquisition, Investigation, Methodology.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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