

Clinical Characteristics, Dynamic Profile of Radiology and Laboratory Findings in Coronavirus Disease 2019

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Keywords: Coronavirus disease 2019, Covid-19, Emerging infectious disease, Coronavirus pneumonia

Posted Date: May 7th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-25659/v1>

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Abstract

Background Since December 2019, when coronavirus disease 2019 (Covid-19) emerged in Wuhan city and rapidly spread throughout China, more and more data from different area and different stages of disease have been needed.

Methods In this retrospective, single-centre study, we included all 38 confirmed cases of Covid-19 in Weihai from Jan 24 to Feb 24, 2020. Patients were divided into group A by normal Oxygenation Index (OI), group B by abnormal OI (less than 400 mmHg). The dynamic changes in clinical laboratory parameters were tracked from day 1 to day 32 after the onset of the disease at 4-day intervals. Cases were analyzed for clinical, radiological features and laboratory data. Outcomes were followed up until Feb 24, 2020.

Results 38 patients with Covid-19 were included in this study, 68.42% patients were family clustered, and 97.37% patients had a history of exposure. The mean days between exposure and onset were about 5 days. Most patients were men, mean age was 43 years, 52.6% patients had chronic diseases. Most patients had fever or cough, about a third of patients had expectoration or fatigue, and 5 (13.16%) patients had shortness of breath.

Background

In December 2019, a cluster of acute respiratory illness, now known as coronavirus disease 2019 (Covid-19), occurred in Wuhan, Hubei Province, China ^[1-5]. The disease has rapidly spread from Wuhan to other areas. The World Health Organization (WHO) has recently declared Covid-19 a public health emergency of international concern ^[6]. As of April 26, 2020, a total of 2,774,135 confirmed cases, 190,871 deaths had been documented globally ^[7-9]. On the other hand, many patients have recovered after observation and treatment. As of April 25, 77,394 cases had been discharged in China ^[10].

This gives us an opportunity to analyze the dynamic index changes of patients in the whole process, might help identify the defining clinical characteristics, development, changes and severity of the disease.

Here, we describe clinical characteristics, dynamic profile of radiology and laboratory findings in 38 hospitalized patients with laboratory-confirmed Covid-19.

Methods

Cases

For this retrospective, single centre study, we recruited 38 patients of Covid-19 admitted to hospital in Weihai from January 24 to February 12. Covid-19 was diagnosed on the basis of the WHO interim guidance ^[11]. Only laboratory-confirmed cases were included in the analysis. All these patients had chest computed tomography (CT) scans, blood test and arterial blood gas analysis results. Oral consent was

obtained from patients. The study was approved by the institutional ethics board of Weihai Municipal Hospital.

Procedures

We obtained epidemiological, clinical, radiology, laboratory, management, and outcome data from patients' medical records. Clinical outcomes were followed up to February 24, 2020.

Laboratory confirmation of 2019nCoV was done in Weihai Center for Disease Control and Prevention (CDC), a confirmed case of Covid-19 was defined as a positive result real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay of nasal and pharyngeal swab specimens^[12].

The date of disease onset was defined as the day when the symptom was noticed. Oxygenation Index (OI) was calculated by arterial partial pressure of oxygen (PaO₂)/ fraction of inspired oxygen (FiO₂). Normal OI was 400 to 500 mmHg, abnormal OI was defined by lower than 400mmHg according to the Berlin definition^[13], which means impaired respiratory function.

Patients with normal OI were in group A, patients with abnormal OI were in group B.

Statistical Analysis

Categorical variables were described as frequency rates and percentages, and continuous variables were described using mean. Means for continuous variables were compared using independent group *t* tests when the data were normally distributed; otherwise, the Mann-Whitney test was used. We used SPSS (version 19.0) for all analyses. $p < 0.05$ was considered statistically significant.

Results

1. Baseline Clinical Characteristics of Patients (Table 1)

38 patients with Covid-19 were included in this study, 26 (68.42%) patients were family clustered from nine different families.

In total, 37 (97.37%) patients had a history of exposure to the epidemic area (Wuhan) or had close contact with confirmed patients.

The mean days between exposure and onset were about 5 days.

Most patients were men, mean age of the patients was 43 years, 20 (52.6%) patients had chronic diseases, including cardiovascular and cerebra vascular diseases, endocrine system disease, digestive system disease, respiratory system disease, malignant tumor, and nervous system disease.

7 (18.42%) among 38 patients had allergy history, six of them were allergy to β -lactam antibiotics.

Most patients had fever or cough, about a third of patients had expectoration or fatigue, and 5 (13.16%) patients had shortness of breath. Other symptoms included muscle ache, diarrhea or headache.

2. Dynamic Profile of Radiology in Patients of Covid-19

Ground-glass opacity (GGO) and consolidation shadows, unilateral or bilateral distribution, were the most common radiographic features in patients with mild symptoms without obvious chest distress or hypoxia (Figure 1A, 1B).

In patients with hypoxia or lower OI (<400mmHg), the lesions spread to both sides, showing diffuse GGO or crazy-paving pattern (Figure 1C, 1D).

In the early stage of the disease, GGO was the main imaging manifestation, unilateral or bilateral, distributed under the lower lobe pleura (Figure 2A).

As the progression of the disease, the infection aggravated rapidly, the lesions spread to both sides, showing multilobed distribution with diffuse GGO, crazy-paving pattern or consolidation (Figure 2B, Figure 3A).

In peak period, the lung involved area slowly increased to the peak. It was manifested by diffuse GGO, crazy-paving pattern, consolidation and substantial strip shadow (Figure 2C, Figure 3B).

When infection was controlled, consolidation shadow was gradually absorbed. Wide range of GGO could be found as the performance after absorption (Figure 2D, Figure 3C).

In dissipating period, the lesion had been basically absorbed and improved, a little fiber strip shadow could be left (Figure 2E).

3. Dynamic Profile of Laboratory Findings in Patients of Covid-19

To determine the major clinical features that appeared during Covid-19 progression, the dynamic changes in clinical laboratory parameters, including hematological, biochemical and coagulation parameters, were tracked from day 1 to day 32 after the onset of the disease at 4-day intervals. At the end of February 24, 2020, data from all patients were analyzed.

Of all 38 confirmed patients, according Oxygenation Index (OI), 34 patients with normal OI (≥ 400 mmHg) were in group A, four patients with lower OI (<400mmHg) in group B.

Time line charts illustrate the laboratory parameters in 38 patients of Covid-19 every 4 days based on the days after the onset of illness.

3.1 Hematological routine parameters (Table 2)

Both White Blood Cell Count and Neutrophil Count in group B were higher than group A (Figure 4A, 4B). Lymphocyte Count, CD4 T lymphocytes and Eosinophil Count in group B were lower than group A, and

below the lower normal limit (Figure 4C, 4D, 4E). There was no significant difference between the two groups in Monocyte Count, Hemoglobin. Significant difference on Platelet Count between two groups could be found in some period of the disease (Figure 4F). Because limited data on Erythrocyte Sedimentation Rate (ESR), no significant difference was tested.

3.2 Biochemical parameters (Table 3)

There was significant difference on Total Bilirubin between group A and group B on days 13-17 after disease onset (Figure 5A), also there were some significant differences between the two groups on glutamic-pyruvic transaminase (ALT) and glutamic oxaloacetic transaminase (AST). The values in group B were higher than group A. Albumin in group B was lower than group A, and usually below the lower normal limit (Figure 5B). Blood Urea Nitrogen (BUN) in group B was higher than group A (Figure 5C), while there were no significant difference on Serum creatinine (Scr).

There were no significant difference between the two groups both in Creatine Kinase (CK) and Creatine Kinase-MB Isoenzyme (CK-MB). Significant difference on Lactate Dehydrogenase (LDH) (Figure 5D) and A-hydroxybutyrate Dehydrogenase were tested. The values in group B were higher than group A.

As for Triglyceride, Cholesterol, High Density Lipoprotein (HDL) and Low Density Lipoprotein (LDL), there were no significant differences between the two groups.

C-reactive protein (CRP) and procalcitonin (PCT) in group B were higher than group A (Figure 5E, 5F).

3.3 Coagulation parameters (Table 4)

Prothrombin Time (PT) in group B were higher than group A (Figure 5G), while there was no significant difference on Activated Partial Thromboplastin Time (APTT). There was no significant difference between the two groups in Fibrinogen and D-Dimer.

Discussion

Covid-19 has been a public health emergency of international concern ^[6]. The population is lack of immune to Covid-19 and generally susceptible. Covid-19 has rapidly spread to the whole country, which has exceeded the total number of patients with severe acute respiratory syndrome (SARS) in 2003, and the number of confirmed and suspected cases is increasing.

At onset, most cases are mild and the survival rate is high. Once the disease aggravate, the death rate will rise ^[14]. Early diagnosis, early recognition and early treatment of Covid-19 are particularly important ^[15].

At present, most descriptive studies divide patients into general group, severe group and critical group according to diagnostic criteria ^[16]. Oxygenation Index < 300 mmHg is the criteria to classify general group and severe group. We chose the lower limit of the normal OI (400 mmHg) as group criteria, hoping to help early recognition and high vigilance on the transition from general type to severe type.

The dynamic data about the whole disease process was not much. We tracked and analyzed 38 patients' all examination results during the whole process of the disease, made dynamic charts, aiming to find the dynamic evolution of different groups through statistical analysis.

Most patients (37/38) in this group had obvious epidemiological characteristics. Before January 24, 2020, all cases were imported, followed by family clustering cases, indicating that Weihai was mainly in the stage of import and family clustering cases, prevention and control work was necessary and important to firmly block the community transmission chain.

There were more males in this group (22/38), which was consistent with the literature reported ^[12]. The days between exposure and onset were 5 days, indicated that the incubation period of the disease was relatively short, the pathogenicity was strong, and the onset was rapid.

More than half (20/38) patients had chronic medical illness. The combination of chronic diseases usually indicates poor prognosis ^[14], positive treatment to chronic diseases is very important.

Seven patients had allergy history, most of them were allergy to β -lactam antibiotics. So far, there's no relevant evidence about Covid-19 and allergy, but they are both related to our immune system. After infected by Covid-19, cytokine storm induced by virus invasion may affect the immune status. For patients with a history of allergy, it is particularly important to choose proper antibiotics when combined with bacterial infection.

The early clinical manifestations of patients with Covid-19 in this group were mainly fever, often accompanied by cough and other respiratory symptoms. Most of the patients are dry cough, and some patients have fatigue, shortness of breath and other systemic symptoms, which suggests a difference in viral tropism as compared with SARS-CoV, MERS-CoV, and seasonal influenza ^[17, 18].

There is no obvious severe dyspnea at the early stage of the disease. In addition, it is reported that most patients will have dyspnea in the disease progression, while a few patients have hemoptysis, diarrhea and other manifestations ^[12, 19]. Early recognition of signs of disease progression is important.

The most important imaging feature of patients with Covid-19 in the early stage is that HRCT shows multiple patchy ground glass shadows, some with consolidation, involved in one or both lungs, usually located under the pleura, which is very similar to the Middle East respiratory syndrome (MERS) ^[20].

As the disease progresses, the lesions may spread to both sides, showing diffuse GGO or paving stone sign, causing respiratory dysfunction, or even worse, ARDS and death. Dynamic change of image indicates the development of the disease. We listed two cases, showing dynamic imaging changes of Covid-19 CT features.

The changes of imaging were divided into different periods. Early in the disease, we found GGO distributed subpleurally; after progressive of the disease, diffuse GGO, crazy-paving pattern and

consolidation distributed; to the peak stage, the involved area of the lungs slowly increased to the peak and dense consolidation became more prevalent; at absorption period, the consolidation was gradually absorbed, extensive GGO could be observed.; after dissipating, the lesion had been basically absorbed or a little fiber strip shadow could be left.

Pan ^[21] divided the dynamic changes of CT into four different periods according to the days after the initial symptoms, our results basically resembled with the study.

Most patients have normal peripheral blood leukocyte count. Both White Blood Cell Count and Neutrophil Count in group B were higher than group A, mainly associated with bacterial infection. Neutrophilia may be related to cytokine storm induced by virus invasion, but in some severe cases, leukocytopenia may occur.

Lymphocyte Count and CD4 T lymphocytes in group B were lower than group A, and below the lower normal limit. As the disease recovered, the value gradually increased. Lymphocytopenia was common in patients with Covid-19, and in some cases, severe, our finding was consistent with the results of two recent reports ^[12, 22].

Eosinophil Count in group B were lower than group A. Whether eosinophils are reduced or attracted to human tissues by certain factors depends on pathological sections and bone marrow pathology.

Significant difference on Platelet Count could be found in some period of the disease. From the current clinical data, most of the patients with Covid-19 are in the normal range of platelet level, and the incidence of thrombocytopenia is different. 5% of the patients with platelet count $< 100 \times 10^9 / L$, 12% of the patients with platelet count $< 125 \times 10^9 / L$, 36.2% of the patients with platelet count $< 150 \times 10^9 / L$, which may be related to the number of cases and the proportion of light and severe patients^[12, 22, 23].

There was significant difference on Total Bilirubin, ALT and AST between group A and group B. The above indexes fluctuated in different periods, considering the influence of Covid-19 or some drugs with hepatotoxicity. The nutritional status of severe patients is usually poor. Albumin in group B was lower than group A, and usually below the lower normal limit. After the treatment of albumin supplement and nutritional support, the albumin index can increase.

Acute renal impairment may occur during disease processes, related to direct effects of the virus or hypoxia. We found BUN in group B were higher than group A. LDH and A-hydroxybutyrate Dehydrogenase in group B were higher, while there were no significant difference on CK and CK-MB, indicating no obvious myocardial damage.

CRP was normal or slightly elevated and PCT was negative in general patients, consistent with other reports ^[24]. The inflammatory response of most patients in the early stage of the disease is usually relatively light. With the aggravation of infection and disease, CRP and PCT could increase.

In the published descriptive articles on clinical characteristics of patients with Covid-19, prolonged PT, increased D-Dimer and fibrinogen were described, which were more common in severe patients [14, 22, 23]. Coagulation activation could have been related to sustained inflammatory response. We found PT in group B was higher than group A, while there were significant differences on APTT, fibrinogen or D-Dimer, consistent with previous studies [25].

This study has several limitations. First, only confirmed Covid-19 patients were included; suspected but undiagnosed cases were ruled out in the analyses. Second, 38 patients were recruited, sample size is small, especially in severe patients. It would be better to include as many patients as possible in our city, in other cities in China, and even in other countries to get a more comprehensive understanding of Covid-19. Third, grouping standard was more sensitive to identify disease progression, but the severe patients could not be stratified. No distinction was made on data of critical patients and mild severe patients. Forth, not every patient had complete results by every 4 days during the whole course, affecting the observation of the results continuity. However, the data in this study showed dynamic changes of related indexes in different periods.

Conclusion

In conclusion, Covid-19 has spread rapidly since it was first identified in Wuhan and has been shown to have a wide spectrum of severity. Early diagnosis and treatment are important. We described clinical characteristics, dynamic profile of radiology and laboratory findings in 38 hospitalized patients with laboratory-confirmed Covid-19. These findings can help early recognition of general and severe patients.

Abbreviations

Covid-19=coronavirus disease 2019, OI=Oxygenation Index, GGO=Patchy Ground-glass opacity, CT=computed tomography, WHO=World Health Organization, RT-PCR=real-time reverse-transcriptase-polymerase-chain-reaction, PaO₂=arterial partial pressure of oxygen, FiO₂=fraction of inspired oxygen, ESR=Erythrocyte Sedimentation Rate, ALT=glutamic-pyruvic transaminase, AST=glutamic oxaloacetic transaminase, BUN=Blood Urea Nitrogen, Scr=Serum creatinine, CK=Creatine Kinase, CK-MB=Creatine Kinase-MB Isoenzyme, LDH=Lactate Dehydrogenase, HDL=High Density Lipoprotein, LDL=Low Density Lipoprotein, CRP=C-reactive protein, PCT=procalcitonin, PT=Prothrombin Time, APTT=Activated Partial Thromboplastin Time, SARS=severe acute respiratory syndrome, MERS=Middle East respiratory syndrome

Declarations

Ethics approval and consent to participate: Oral consent was obtained from all patients. The study was approved by the institutional ethics board of Weihai Municipal Hospital (No. 202025).

Consent for publication: Not applicable.

Availability of data and material: The data and material during the current study are available from the corresponding author.

Funding: Not applicable.

Competing interests: The authors declare that they have no competing interests.

Authors' contributions: Ailing Liu conceived the study, participated in its design and draft the manuscript. Jing Zhang, Wei Qiao and Wei Zang collected data and helped data analysis. Yingying Zhang did mainly data analysis. Junyang Kang helped to draft the manuscript. Haifeng Teng participated in its design and coordination to draft the manuscript. All authors read and approved the final manuscript.

Acknowledgements: The authors would like to express their appreciation for all of the emergency services, nurses, doctors, and other hospital staff for their efforts to combat the Covid-19 outbreak. We thank all patients involved in the study.

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Tables

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Figures

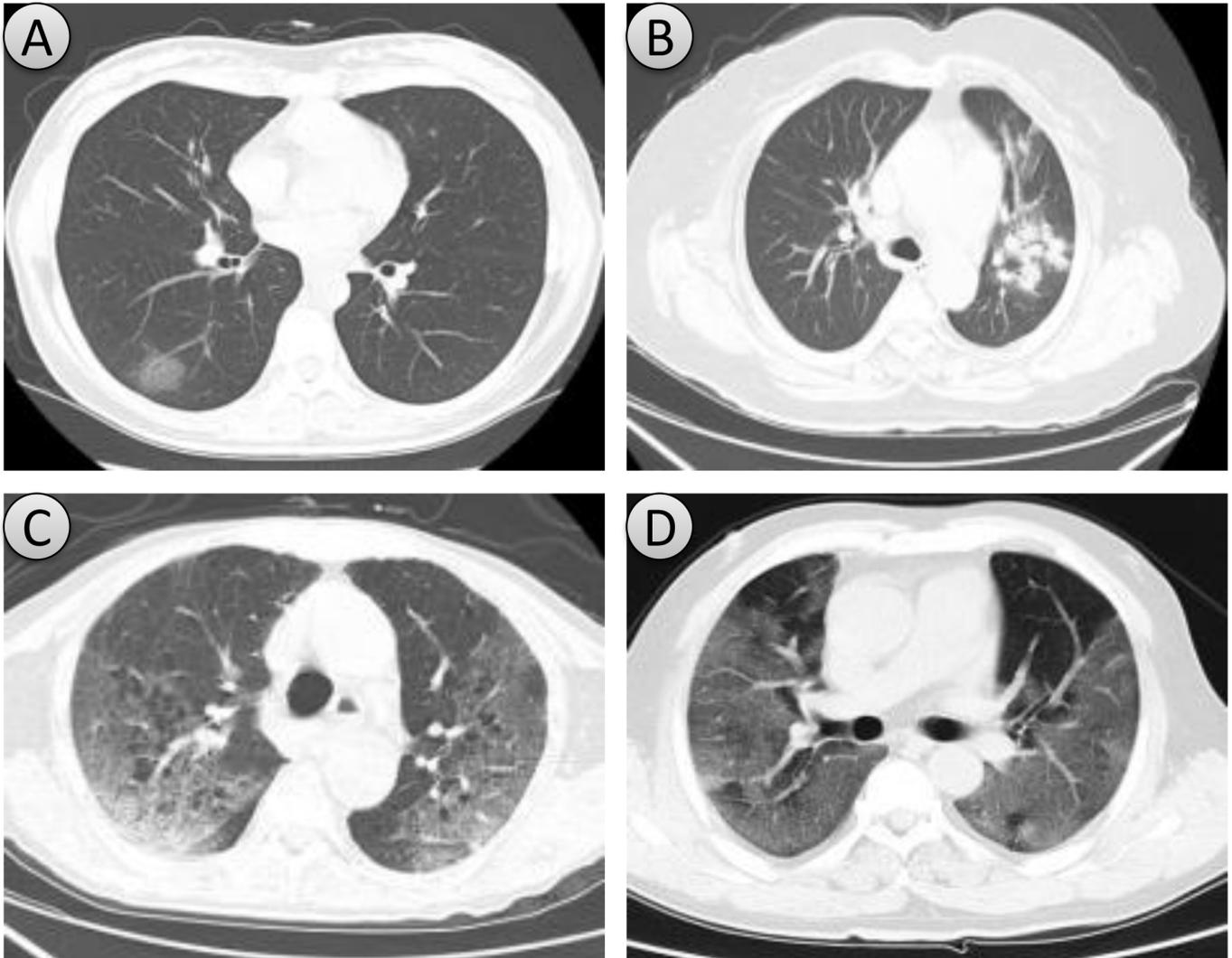


Figure 1

Figure 1

A: Chest Computed Tomography (CT) image of a 34-year-old female with Covid-19, showing small ground-glass opacity (GGO) on right lower lobe. B: Chest CT image of a 60-year-old female with Covid-19, showing limited consolidation shadows on left lung. C: Chest CT image of an 86-year-old male with Covid-19, showing diffuse GGO bilateral distribution. D: Chest CT image of a 55-year-old male with Covid-19, crazy-paving pattern could be found on both lungs.

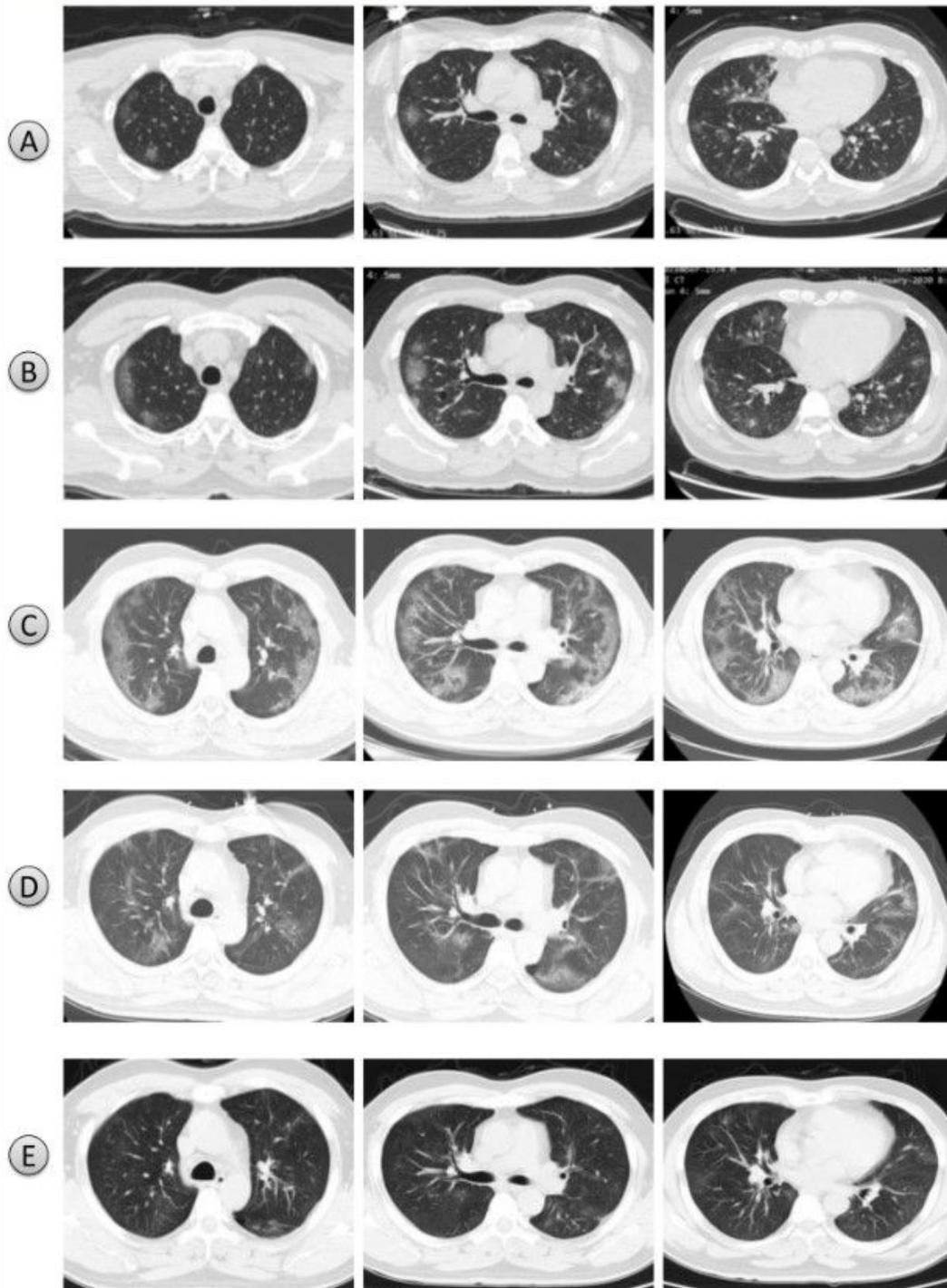


Figure 2

Figure 2

Chest Computed Tomography (CT) images of a 43-year-old male with Covid-19, showing dynamic changes of lesions. A: CT images on day 3 after symptom onset, showing ground-glass opacity (GGO), bilateral, distributed under pleura. B: CT images on day 7 after symptom onset, lesion's area expanded obviously. C: CT images on day 12 after symptom onset, showing diffuse lesions on both lungs. D: CT

images on day 18 after symptom onset, partial lesions had been absorbed. E: CT images on day 25 after symptom onset, most lesions had been absorbed, a little fiber strip shadow left.

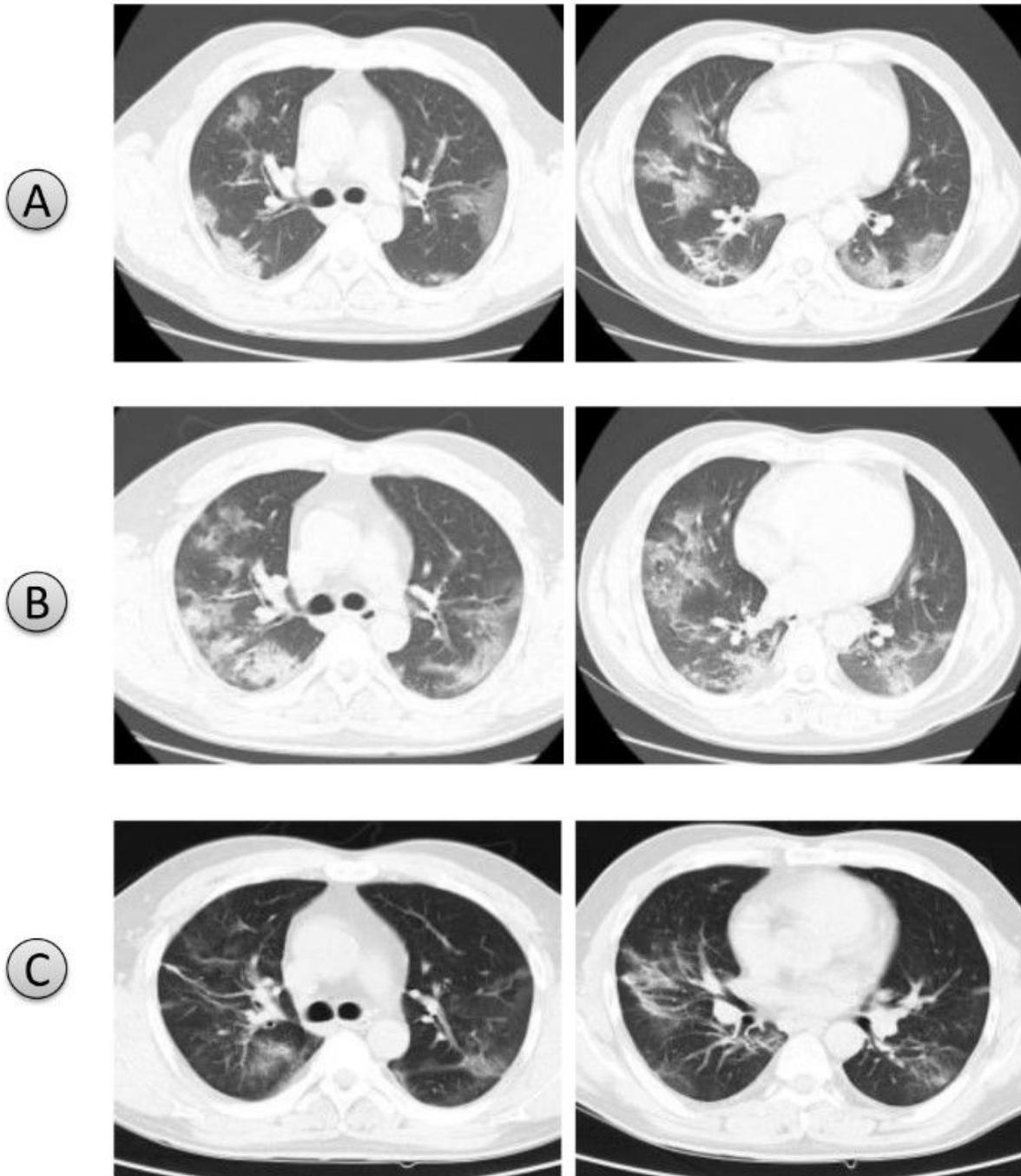


Figure 3

Figure 3

Dynamic changes of a 39-year-old male's chest CT images. A: CT images on day 8 after symptom onset, showing multiple GGO on both lungs, mainly distributed under pleura. B: CT images on day 12 after

symptom onset, lesion's area expanded, with partial consolidation. C: CT images on day 16 after symptom onset, lesions had been absorbed obviously.

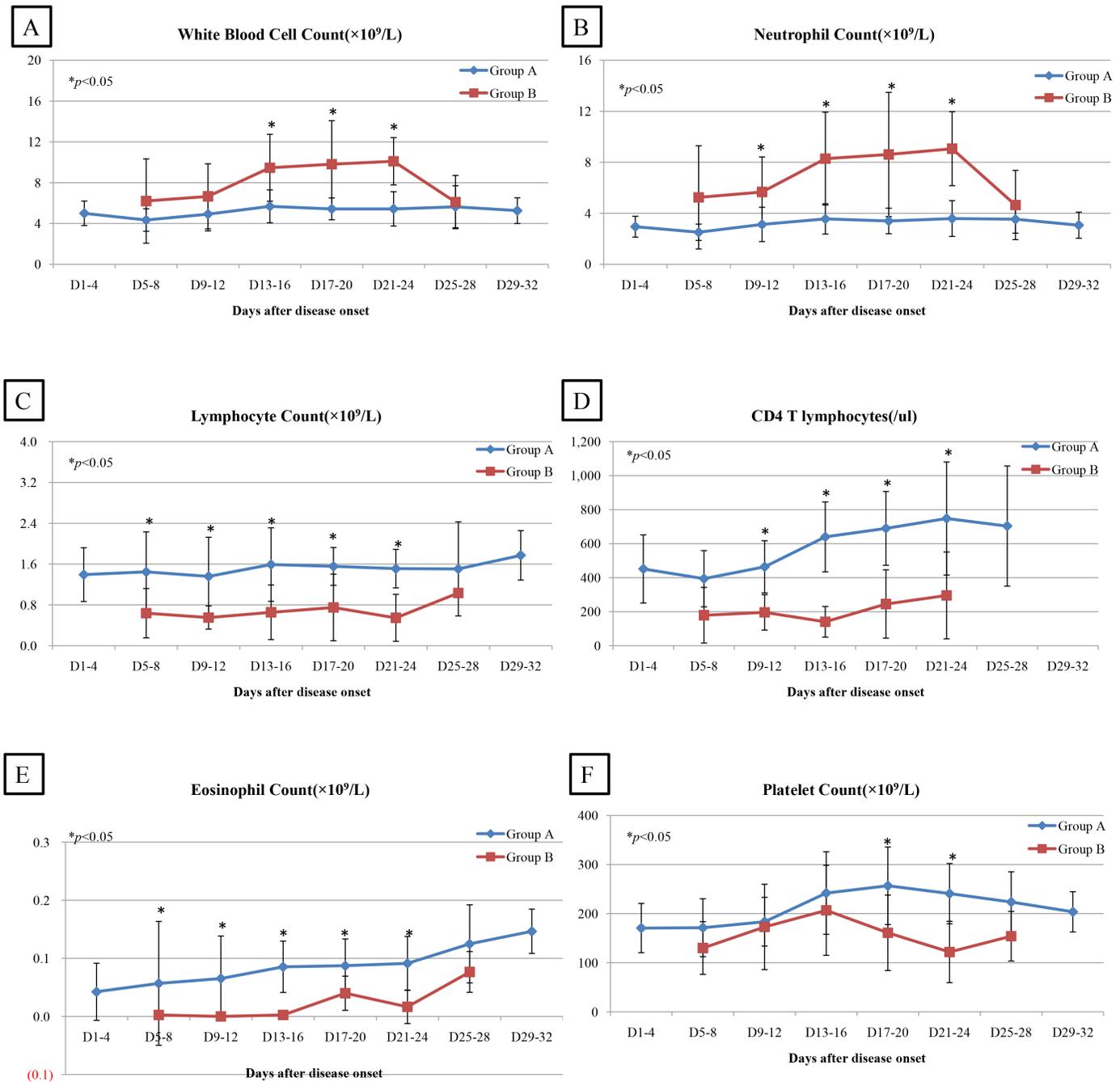


Figure 4

Figure 4

Dynamic Profile of Laboratory Parameters in 38 Patients of Covid-19. Group A: patients with normal Oxygenation Index (OI) ($\geq 400\text{mmHg}$) Group B: patients with lower OI ($< 400\text{mmHg}$) * $p < 0.05$ for group A vs group B.

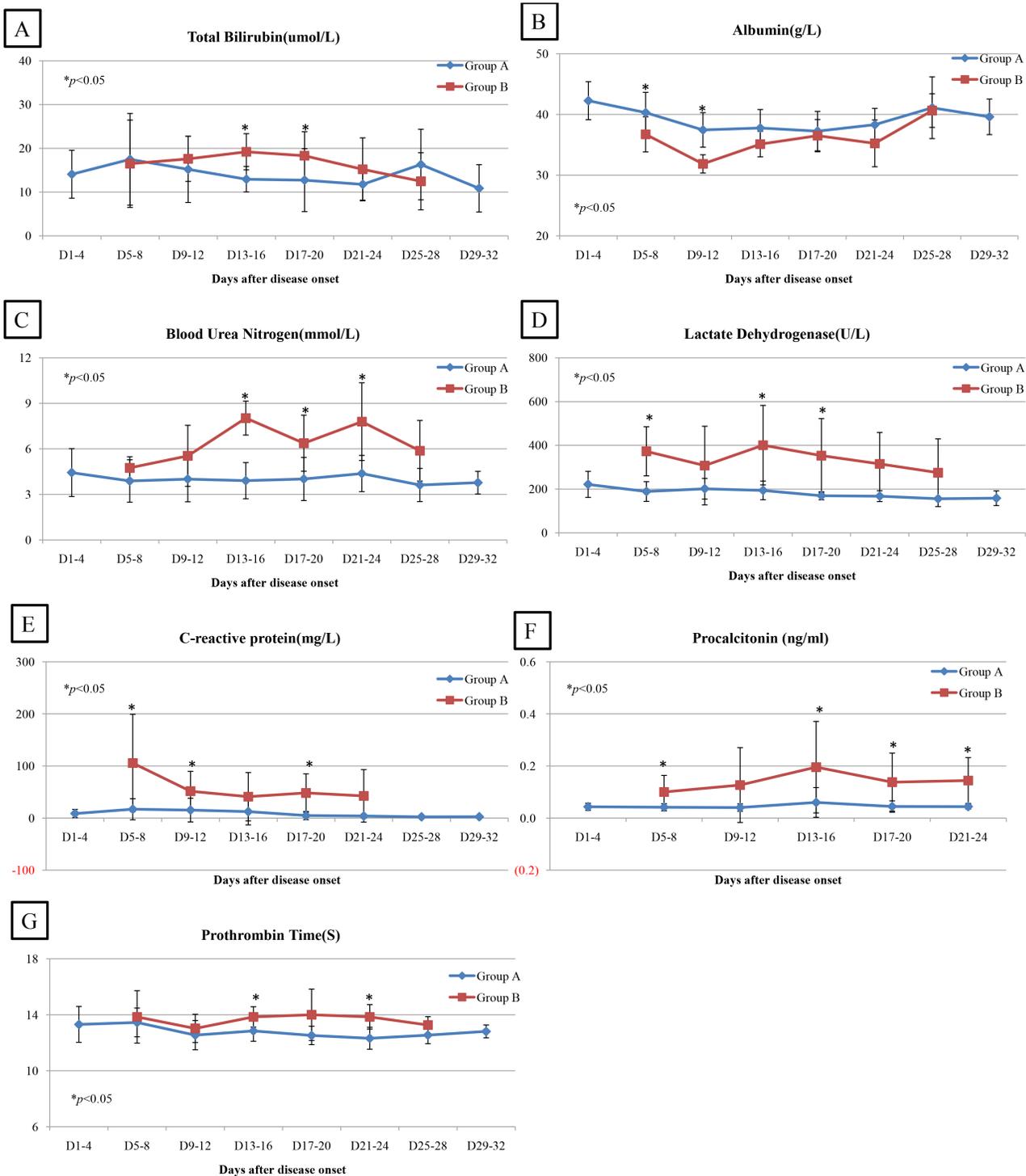


Figure 5

Figure 5

Dynamic Profile of Laboratory Parameters in 38 Patients of Covid-19. Group A: patients with normal Oxygenation Index (OI) ($\geq 400\text{mmHg}$) Group B: patients with lower OI ($< 400\text{mmHg}$) * $p < 0.05$ for group A vs group B.

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