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Original article

CO-RADS versus Lymphopenia in diagnosing COVID-19

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Abstract

The global spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) generated a pandemic which severely impacted on care delivery worldwide. **Aim of the work**: To assess the correlation between CORADS score and different CBC indices and the sensitivity of CORADs score compared to lymphopenia and neutrophil/ lymphocyte ratio in diagnosing patients with COVID- 19. **Patients and methods** :This study is a retrospective data review study done 106 patients who were visiting the emergency room at Benha University hospital for assessment of symptoms for the possibility of COVID 19.**Results**: Symptoms were variable ; the most common was fever (92.5%), mean total leucocytic count (TLC) 7.5±3.4 (10*3/UL); neutrophil count 5.5±3.3 (10*3/UL), lymphocytic count was 1.42 ± 0.77.CT scan done to all patients where GGO was the most common pattern. CORAD score was ranging from 0 to 5 with mean 3.96±1.59, There was no correlation between CORAD score and different CBC parameters; CORAD scores ≥ 4 had a sensitivity of 71% while CORAD 5 has a sensitivity of 60% in diagnosis. Lymphopenia <2 has a sensitivity of 82%, lymphocytes < 1.5 has sensitivity of 65% and lymphopenia <1.1 has a sensitivity of 40%. Neutrophil lymphocyte ratio > 3 has a sensitivity of 61% but increased to 68% with ratio>2.4.

Conclusion: CORAD score and lymphopenia are rapid and valuable tools in diagnosis of COVID 19. CORAD has a sensitivity 60 to 71% according to the cut off used while lymphopenia has a sensitivity 40 to 82%, neutrophil/ lymphocyte ratio 61 to 68%.

Key Words: lymphopenia, CORADS, COVID 19

Introduction:

The global spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) generated a pandemic outbreak in late 2019-early 2020, which severely impacted on care delivery worldwide [1]

The high pathogenicity of this unusual highly contagious SARS-CoV2 could not be fully understood yet [2]

Coronaviruses may lead to self-limited, mild, and common infections like the common cold, and more severe infections like Severe Acute Respiratory Syndrome (SARS)[3] and Middle East Respiratory Syndrome (MERS)[4].These viruses may lead to clinical conditions with various degrees of respiratory, enteric, hepatic, nephritic, and neurological involvement [5]. The identification of clinical, laboratory and radiologic predictors of early diagnosis and prognosis may assist clinicians in monitoring management strategies.

Real-time Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) demonstrating SARS-CoV-2 RNA in respiratory system samples is the gold standard method for confirming the diagnosis of infection. Although the test is said to be highly specific, its sensitivity varies between 60-89 % [6]. There is conversely, growing evidence that sensitivity of combined nasal and pharyngeal swabs may be insufficient if obtained at a single time point, also depending on the technical characteristics of the test and method of specimen collection. The relatively long turnaround time (TAT) for viral testing together with the low sensitivity of a single real-time reverse-transcriptase polymerase-chain reaction (RT-PCR) assay of nasal and pharyngeal swab specimens also implies that a large number of SARS-CoV-2 patients would not be quickly identified and may not be appropriately managed [7].

Blood tests have an important role in early diagnosis and prognosis of the disease, considering the information they provide to physicians regarding the inflammatory process. This information includes leukocyte count and characteristics such as neutrophil- or lymphocyte-dominance, inflammation (CRP), collateral organ damage (acute renal failure, acute liver failure) and the severity of the disease. Furthermore, biomarkers provide information regarding the nature of pneumonia, so physicians can determine

whether a disease is bacterial or due to other etiologies by analyzing blood test results [8]

The Dutch Radiological Society developed the COVID-19 Reporting and Data System (CO-RADS), which is a categorical assessment scheme on chest CT, from 1 (very low) to 5 (very high) of the likelihood for COVID-19 infection in patients with moderate to severe symptom. CO-RADS looks for typical patterns of COVID-19 infection rather than the extent of these patterns [9].

Aim of the work

The objective of this work was to assess the CORAD score in patients with positive RT PCR for COVID 19 and its relation to different CBC indices and the sensitivity of CORADs score compared to lymphopenia and neutrophil/ lymphocyte ratio in diagnosing patients with COVID- 19 disease.

Patients and methods

This study is a retrospective data review study done in the period from Feb to July 2021 on patients 106 patients of both sexes who were visiting the emergency room at Benha University hospital in the period from May 2020 to December 2020 for assessment of symptoms for the possibility of COVID 19, approval from local authority for patient reveal of data and the study was approved by Benha Faculty of Medicine ethical committee MOHP NO:0018122017 certificate NO : 1017

Inclusion Criteria: all patients 'above 18 years' visiting the emergency Room for assessment of their symptoms, after diagnosis of COVID being established by RT PCR naso and oropharyngeal swab.

Exclusion criteria: Children < 18 years; Negative PCR patients for COVD 19;Patients with incomplete data.

1-CT chest: (Toshiba Aquilion Prime 160; Toshiba medical system Japan) was used for examining all patients. Images were reconstructed with a 1-mm slice thickness in all cases. CT scans delivered from the medical records were interpreted by 2 separate radiologists who were blinded by the PCR results and the final report after agreement was documented.

CO-RAD scoring was calculated based on the Dutch Radiological Society standardized criteria. The COVID-19 Reporting and Data System (CO-RADS) included data of clinical finding and laboratory test results in addition to CT records. The degree of suspicion ranged from very low to very high (CO-RADS categories 1–5), while category

0 reflects negative infection and category 6 establishes RT-PCR-positive SARS-Cov-2 infection at time of examination [9]

2- Complete blood count (CBC) with differential white blood cells count was done by automated hematology system) Sysmex XE 5000, Sysmex America, Inc., Sysmex® XE-5000 Analyzer).

All possible infection control measures will be arranged in all cases, consisting of prompt sanitation of CT facility and patient's isolation, also during sample withdrawal and transport to the laboratory.

The Collected data was be tabulated and analyzed by suitable statistical methods using the statistical package SPSS (Statistical Package for the Social Sciences) version 26 (IBM Corp., Armonk, NY, USA).numerical data were expressed as mean and standard deviation, frequency table was expressed as number and percentage, correlation between CORAD score and CBC indices were done using Pearson correlation, with r is the correlation coefficient, P value was considered significant if >0.05

Results

This study was carried out on 106 patients who were visiting the emergency room in Benha University hospital for assessment of their symptoms, PCR was positive in the enrolled cases and CT scan CBC was done to all.

46(43.4%) were females while 60 (56.6) were males. The average age was 45± 16.11 years .

Symptoms were variable ; the most common was fever (92.5%), dyspnea in 35%, sore throat in 27.4%, cough in 51.9%, other symptoms as anosmia, diarrhea vomiting , headache, abdominal pain, joint pain were present, (table 1)

Complete blood count was done to patients showing mean toal leucocytic count (TLC) 7.5±3.4 ($10*^3$/UL); absolute neutrophil count 5.5±3.3 ($10*^3$/UL) and percentage 7±15, absolute lymphocytic count was 1.42 ± 0.77 ($10*^3$/UL) and percentage 21.77±11.5($10*^3$/UL). Table 2 shows the different CBC indices for patients.

CT scan done to all patients were reviewed where GGO was the most common finding, while nodular was the least common, opacities coinciding with old healing infection , cavitation was found on top of consolidation in one case, other findings was traction bronchiectasis, septal thickening, bronchial wall thickening, pleural effusion.

The different CT features are shown in table 1.

CORAD score was ranging from 0 to 5 with mean 3.96±1.59, fifty 1 patients were CORAD 5, 11 patients CORAD 4, 4 were CORAD 3 , 3 patients with CORAD 2 and the rest were CORAD 1(59% vs. 22%, respectively).

There was no correlation between CORAD score and different CBC parameters; neither lymphopenia, high N/L ratio predicts the CORAD score. Table 3, Figure 1.

Table 4 shows the sensitivity of CORAD scoring in diagnosis of COVID disease; taking CORAD scores 4 and 5 as cut off, the sensitivity will be 71% while CORAD 5 has a sensitivity of 60% in diagnosis. On the other hand, lymphopenia<2 has a sensitivity of 82% , but if lymphocytes < 1.5 will be taken as cut off, sensitivity will drop to 65% and to 40% with lympopenia <1.1. neutrophil lymphocyte ratio > 3 has a sensitivity of 61% but increased to 68% with ratio>2.4.

Table (1): symptoms and radiological features of study group

		No (106)	**%**
Sex	Female	46	43.4
	Male	60	56.6
Fever	Yes	98	92.5
Fatigue	Yes	20	18.9
Dyspnea	Yes	38	35.8
Sore throat	Yes	29	27.4
Cough	Yes	55	51.9
Other symptoms	Yes	83	73.3
Comorbidities	Yes	30	28.3
Radiological features	GGO	68	64.2
	Crazy paving	39	36.8
	Consolidation	24	22.6
	HEAL	21	19.8
	Nodular	12	11.3
	Others	6	5.6
	NAD	20	18.9
	Cannot be interpreted	5	4.7%

Table (2): CBC and CORAD score of the study group

N (106)	Range	Mean±S.D
Age (years)	7-85	45.1±16.11
TLC(10*^{3}/UL)	1.80-16. 6	7.5±3.4
Lymphocytes absolute (10*3/UL)	0.4-3.8	1.42±.77
Neutrophil absolute(10*^{3}/UL)	.5-14.3	5.5±3.3
Monocyte absolute(10*^{3}/UL)	0-1.3	.6±.7
PLT (10*3/UL)	52-365	203.4±62.6
Lymphocyte %	5-52	21.77±11.5
Neutrophil %	11-92	69±15
Monocyte %	0-87	1±1
HG(gm/dl)	7-18	13±1
CORAD score	0-5	3.77±1.77

Table (3): correlation between CORAD score and CBC variables

	R	P value
Neutrophil (absolute)	.110	.271
Lymphocyte absolute	-.133	.183
Neutrophil lymphocyte ratio	.107	.285
HGB%	-.125	.198
PLTX	-.133	.175
TLCX	.038	.199

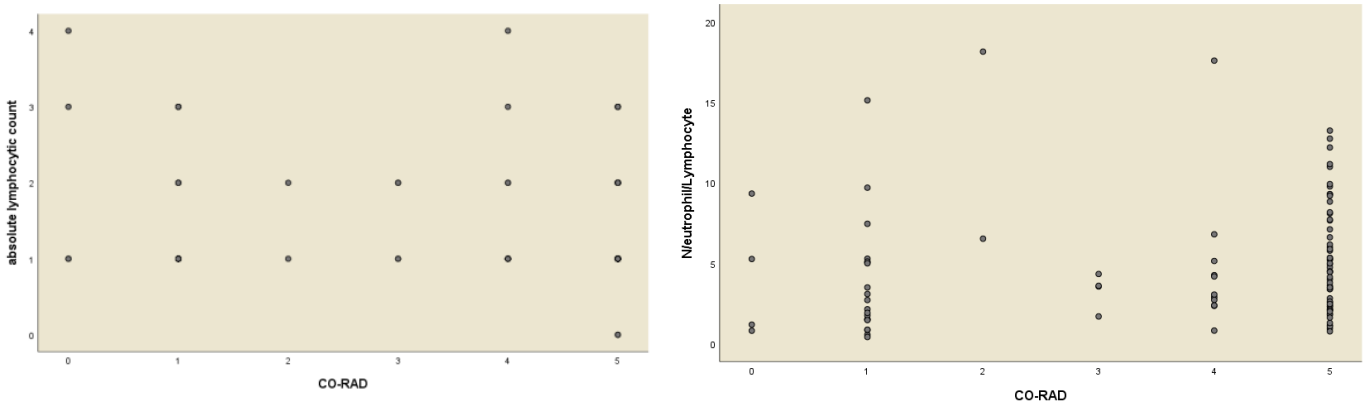

Figure 1: correlation between CORAD score with absolute lymphocyte count and N/L ratio

Table (4) Sensitivity of CORAD score and absolute lymphocytic count to diagnose COVID 19

	Number of cases	Sensitivity %	Total
CORAD			**106**
4≥	**75**	**71**	
5	**64**	**60**	
Lymphocytes			**102**
<2	**84**	**82**	
<1.5	**66**	**65**	
<1.1	**41**	**40**	
N/L ratio			**102**
>3	**62**	**61**	
>2.4	**69**	**68**	

Discussion

Due to the high infectivity and mortality rates of COVID-19, early diagnosis is very important .The definitive diagnosis is done by using real-time PCR analyses. Many factors such as the increased number of samples, and insufficient lab capacities, the time it takes to receive results can be prolonged. Therefore, every parameter allowing for early diagnosis is vital. In this study, the possibility of diagnosing COVID-19 early in ER visits by a simple methods such as a CBC and CT chest, has been assessed [10].

This study found that 46(43.4%) were females while 60 (56.6) were males. The average age was 45± 16.11 years. In a former study the median age was found to be 47 and 52.1% of the patients were males [11]. Another study revealed that 56% of all patients were male and the median age was 59 [12]. Furthermore, another study conducted showed a median age of 41 and 56% of the patients were males [13]. Thus, it can be said that COVID-19 is seen more frequently in males and in middle-aged patients.

The presenting symptoms were variable ; the most common was fever (92.5%), dyspnea in 35%, sore throat in 27.4%, cough in 51.9%, other symptoms as anosmia, diarrhea, vomiting , headache, abdominal pain, joint pain were present. This agrees with a study done earlier [10]. Upon evaluation of common complaints

during ER visits, fever, cough and sore throat were the most common, followed less often by myalgia, malaise and fatigue. The results of this study were found to be noticeably compatible with that of previous researches; also revealed fever and cough to be the most common complaints [11 & 14] . In a study done by a group of researchers, fever and cough and less frequently nausea, vomiting and diarrhea, were observed [11] . A study showed that fever (40/41 patients [98%]), cough (31/41 patients [76%]) and myalgia or fatigue (18/41 patients [44%]) were the most commonly seen symptoms at onset [15].

In our study CT scan done to all patients where GGO was the most common finding(64.2%), while nodular was the least common(11.3%), opacities coinciding with old healing infection, cavitation was found on top of consolidation in one case, other findings was traction bronchiectasis, septal thickening, bronchial wall thickening, pleural effusion. The different CT features are shown in (table 2) this agrees with that study which found that the most common patterns of disease included GGO, observed in 125 patients (96.2%), followed by crazy-paving pattern (n = 68; 52.3%) and parenchymal consolidations (n = 75; 57.7%) .Related CT features were found as follows: fibrosis (n = 53; 40.8%), subpleural lines (n = 28; 21.5%), reversed "halo sign" (n = 5; 3.8), pleural effusion (n = 6; 13%), and lymphadenopathy (n = 20; 6.2%). Lobar involvement, lesion distribution, and disease localization in the pulmonary parenchyma were also observed [16] .

Also the study done on chest CT findings have been reported in 10%–70% of RT-PCR test–proven COVID-19 cases, including consolidation (51.5%), linear opacity (40.7%) , septal thickening and/or reticulation (49.6%), crazy-paving pattern (34.9%) , air bronchogram (40.2%), pleural thickening (34.7%), halo sign (34.5%) , bronchiectasis (24.2%), nodules (19.8%), bronchial wall thickening (14.3%), and reversed halo sign (11.1%). The following lesion distributions have been reported: unilateral (15.0%), multifocal (63.2%), diffuse (26.4%), single and/or focal (10.5%), middle or upper lobe involvement (49.3%–55.4%), peripheral location (59.0%), and central and peripheral location (36.2%) [17].

In our study CBC was done in 102 from 106 patients and we found that TLC was (1.80-16. 6+10*^{3}/UL)with mean ± S.D (7.5±3.4) so TLC count was variable in patients with Covid 19 it may be normal ,decreased or even increased in some patients, this agrees

with a study which showed normal or decreased white blood cells upon admission, but leukocytosis was seen in some ICU patients, including 54% of 41 COVID-19 patients in one study., absolute lymphocytes (0.4-3.810*^{3}/UL) with mean ± S.D (1.42±.77)[15].

In one of the larger studies, it was shown that 83.2% of 1099 patients included had lymphopenia upon admission, and lymphopenia was even more prominent and lower in severe cases absolute neutrophil (5-14.3*3/UL) with mean ± S.D (5.5±3.3)[11]. In a study by Ai et al., There have also been reports of normal and even decreased neutrophils in COVID-19 patients compared to healthy controls [18]. In this study, haemoglobin range was (7-18 gm/dl) mean ± S.D (13±1). In some studies, lower concentrations of hemoglobin were reported in 41–50% of cases upon admission [19] and they were also seen in the elderly, although results were still within the normal range.

In this study absolute lymphocytic count was 1.42 ± 0.77 (10*^{3}/UL) and percentage 21.77±11.5 (10*^{3}/UL), lymphopenia at different cut off values was calculated at <2, <1.5, <1.1 with sensitivity (82%, 65, 41%) respectively this agree with Huang et al.,2020 who found that laboratory abnormalities reported in COVID-19 patients include lymphopenia (>40% patients) [15]. Lymphopenia is the predominant hematologic finding associated with SARS-CoV-2 in the literature and is reported to predict disease severity [20].

In this study N\L ratio was increased and different cut off values>3, >2.4 was calculated with sensitivity (61.68%) respectively. The neutrophil-lymphocyte-ratio (NLR) seems to be consistently increased in patients with severe COVID-19 [21]. Further studies have shown the prognostic value of the NLR[14]. It was noted that higher NLR upon admission was an independent predictor for severe pneumonia in COVID-19 patients [22].

In our study CORAD 4, 5 sensitivity (61, 70%) respectively in comparison to RT PCR. In another study, the ‘imaging group’ CO-RADS 4/5 performed best with AUC of 0.865 when compared to RT-PCR and 0.902 when compared to the final clinical diagnosis [23].

In this study, there was no correlation between CORAD score and different CBC parameters; neither lymphopenia nor high N/L ratio predicts the CORAD score.

Conclusion: CORAD score and lymphopenia are rapid and valuable tools in diagnosis of COVID 19. CORAD has a sensitivity 60 to 71% according to the cut off used while lymphopenia has a sensitivity 40 to 82%, neutrophil/ lymphocyte ratio 61 to 68%.

References:

1-N. Chen, M. Zhou, X. Dong et al., (2020):"Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study," The Lancet, vol. 395, no. 10223, pp. 507–513.

2-Zhu N, Zhang D, Wang W, li X, yang B, Song J, et al;(2020) China Novel Coronavirus Investigating and research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med. ;382(8):727-33.

3- Chan JF, li KS, To KK, Cheng vC, Chen h, yuen Ky.(2012): Is the discovery of the novel human betacoronavirus 2c EMC/2012 (hCov-EMC) the beginningof another SArS-like pandemic? J Infect.;65:477-89.

4- Zaki AM, van Boheemen S, Bestebroer TM, osterhaus AD, Fouchier rA.(2012) :Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia.N Engl J Med.;367(19):1814-20.

5- Ahmet N,Tezcan K,Ceyhun V,CelCuk Y,Ali T,Hakan C (2020): Can the neutrophil/lymphocyte ratio (NLR) have a role in the diagnosis of coronavirus 2019 disease (COVID-19)?REV ASSOC MED BRAS 2020; 66(6):746-751

6-Fang Y., Zhang H., Xie J., Lin M., Ying L., Pang P., Ji W.(2020): Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology. 200432 .https://doi.org/10.1148/radiol.2020200432].

7-Han H, Luo Q, Mo F, Long L, Zheng W (2020) : SARS-CoV-2 RNA more readily detected in induced sputum than in throat swabs of convalescent COVID-19 patients. Lancet Infect Dis 0. https:// doi.org/10.1016/S1473-3099(20)30174-2 .

8-Bekdas M, Goksugur SB, Sarac EG, Erkoc¸oglu M, Demircio ˘ glu F. (2014): Neutrophil ˘ /lymphocyte and C-reactive protein/mean platelet volume ratios in differentiating between viral and bacterial pneumonias and diagnosing early complications in children. *Saudi Med .J.* 35(5), 442–447

9- Mathias Prokop , Wouter van Everdingen , Tjalco van Rees Vellinga , Henriëtte Quarles van Ufford , Lauran Stöger , Ludo Beenen , Bram Geurts , Hester Gietema , Jasenko Krdzalic, Cornelia Schaefer-Prokop, Bram van Ginneken , Monique Brink, :CO-RADS:A categorical CT assessment scheme for patients suspected of having COVID-19—Definition and evaluation. Radiology. 2020 Aug;296(2):E97-E104. doi: 10.1148/radiol.2020201473

10- Eren Usul ˙ Ishak S, Burak Bekgoz & Ali S¸ahin :(2020) The role of hematological parameters in COVID-19 patients in the emergency room 10.2217/bmm-2020-0317 C 2020 Future Medicine Ltd .

11-Guan WJ, Ni ZY, Hu Y *et al(2020):* Clinical characteristics of coronavirus disease 2019 in China. *N. Engl. J. Med*. 382(18), 1708–1720 .

12- Li Q, Guan X, Wu P *et al* (2020): Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *N. Engl. J. Med.* 382, 1199–1207 . 13- Xu XW, Wu XX, Jiang XG *et aL*(2020): Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 368, m606 .

14 - Yang AP, Liu J, Tao W, Li HM (2020) : The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int. Immunopharmacol.*84,106504

15- Huang C, Wang Y, Li X *et al* (2020) : Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 395(10223), 497–506.

16- Marco F1 , Franco I , Giorgio M1 , Simona C1 et al.,(2020) : Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis

17- Adams HJA, Kwee TC, Yakar D, Hope MD, Kwee RM : Chest CT Imaging Signature of Coronavirus Disease 2019 Infection: In Pursuit of the Scientific Evidence. Chest. 2020 Nov;158(5):1885-1895. doi: 10.1016/j.chest.2020.06.025. Epub 2020 Jun 25. PMID: 32592709; PMCID: PMC7314684.

18- Ai J, Zhang HH-YH-C, Xu T (2020): Optimizing diagnostic strategy for novel coronavirus pneumonia, a multicenter study in Eastern China. medRxiv. DOI:10.1101/2020.02.13.20022673].

19-Lippi G, and Plebani M : Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med. 2020. DOI:10.1515/cclm-2020-0198]

20-Tan L, Wang Q, Zhang D, et al (2020.): Lymphopenia predicts disease severity of COVID-19:65, a descriptive and predictive study. *Signal Transduct Target Ther*. ;5:33. [PMC free article] [PubMed] [Google Scholar].

21-A. Khartabil, H. Russcher, Ajam van der Ven & Y. B. de Rijke (2020) A summary of the diagnostic and prognostic value of hemocytometry markers in COVID-19 patients, Critical Reviews in Clinical Laboratory Sciences, 57:6, 415-431, DOI: 10.1080/10408363.2020.1774736

22-Feng Z, Yu Q, Yao S, et al (2020):Early prediction of disease progression in 2019 novel coronavirus pneumonia patients outside Wuhan with CT and clinical characteristics. medRxiv. 2020. DOI:10.1101.02.19.20025296

23-Van Berkel B, Vandevenne J, Coursier K, Alberts V, Van Offenwert J, VerduycktJ, Grieten M, et al., (2021): Chest CT Diagnosis of COVID-19: Accuracy using CO-RADS and CT-Involvement Scoring.*Journal of the Belgian Society of Radiology.* 105(1):17, 1–7. DOI: *https://doi. org/10.5334/jbsr.2342*.

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