<u>Journal of Medicinal and Chemical Sciences</u> 6 (2022) 227-238



Journal of Medicinal and Chemical Sciences

Journal homepage: http://www.jmchemsci.com/



Review Article

Medical Evaluation of Test Results Related to Covid 19 in Iranian Hospitals Using QUADAS-2 to Evaluate the Quality of Studies and Meta-Analysis Using Stata / MP v.16 Software

Hoseinali Danesh^{1, 2}, Saeid Rahimi Ghasabeh³, Ramin Rounasi⁴, Ehsan Zarepur⁵, Ali Abdolrazaghnejad^{2, 6*}

ARTICLE INFO

Article history

Received: 2021-10-24

Received in revised: 2021-11-06

Accepted: 2021-11-13

Manuscript ID: JMCS-2110-1304 Checked for Plagiarism: **Yes**

Language Editor: Ermia Aghaie

Editor who approved publication:

Dr. Zeinab Arzehgar

DOI:10.26655/JMCHEMSCI.20222.10

KEYWORDS

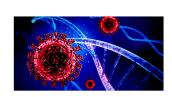
Laboratory Tests Diagnostic Tests COVID-19 PCR

ABSTRACT

The aim of current study was to evaluate the outcome of some laboratory tests and accuracy of diagnostic tests for patients with COVID-19. The QUADAS-2 tool was utilized to quality assessment of diagnostic accuracy studies. For data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. 95% confidence interval for effect size with fixed effect model and Inver-variance method were calculated. Meta-analysis was performed using Stata/MP v.16 software. 469 studies were reviewed, of which the full text of 52 studies was reviewed and finally twenty-two studies were selected for meta-analysis. differences of Alanine transaminase was 3.40 U/L (MD, 95% CI -2.45, 9.25), correlation between Alanine transaminase and severe COVID-19 was not significantly. Stool, feces, rectal swabs 25% (ES, 95% CI 0.32, 0.82), Urine 1% (ES, 95% CI 0.05, 0.58), overall sensitivity of PCR for detection of COVID-19 was 44% (ES, 95% CI 0.19, 0.68), less sensitive observerd when PCR detection of COVID-19. Evidence revealed that at the time of admission of patients with COVID-19, a specific laboratory model can be used to perform relevant tests and make decisions about patients. PCR using sputum samples was highly sensitive for detecting COVID-19 and after that computed tomography of the chest was identified with high sensitivity.

GRAPHICAL ABSTRACT

Computed tomography Study	Sensitivity with 95% CI	Weight (%)
Zhang et al., 2020	0.93 [-0.05, 1.91]	20.00
Xie et al., 2020	0.91 [-0.07, 1.89]	20.00
Li et al., 2020	0.83 [-0.15, 1.81]	20.00
Long, 2020	0.97 [-0.01, 1.95]	20.00
Ai et al., 2020	0.97 [-0.01, 1.95]	20.00
Overall	0.92 [0.48, 1.36]	
Heterogeneity: $I^2 = 0.00\%$, $H^2 = 0.01$		
Test of $\theta_i = \theta_j$: Q(4) = 0.06, p = 1.00		



¹Plastic, Reconstructive & Aesthetic Surgeon, Assistant Professor of Zahedan University of Medical Sciences (ZAUMS)

²Clinical Immunology Research Center at Zahedan University of Medical Sciences, Zahedan, Iran

³Anesthesiologist at Noor Afshar hospital, Iranian Red Crescent Society, Iran

⁴Department of Anesthesiology and Pain Medicine, Iran University of Medical Sciences, Tehran, Iran

⁵Resident of cardiology, Isfahan cardiovascular research center, Isfahan cardiovascular research institute, Isfahan University of Medical Sciences, Isfahan, Iran

⁶Department of Emergency Medicine, Khatam-Al-Anbia Hospital, Zahedan University of Medical Sciences, Zahedan, Iran

^{*} Corresponding author: Ali Abdolrazaghnejad ☑ E-mail: Email: Ali.abdorazzagh@gmail.com
© 2022 by SPC (Sami Publishing Company)

Introduction

Patients have reported early symptoms of fever and cough, and most have complained of chest pain, difficulty breathing, and pneumonia, which are diagnosed clinically by imaging tests such as chest x-rays or computed tomography (CT) scan [1-4]. Common findings of chest CT images in people with COVID-19 (Figure 1) are multifocal bilateral patchy ground-glass opacities consolidation with interlobular septal and vascular in the peripheral areas of the lungs [5-8]. However, CT findings can change as the disease progresses, and the manifestations may be consistent with other viral respiratory illnesses [9-11]. Reverse transcription polymerase chain reaction (RT-PCR) is used to detect COVID-19 based on molecular testing, which aims to detect virus RNA in patient respiratory samples [12-14]. This test is time consuming and laboratory equipment shortages are common around the world, and if the viral genome is not enough, the result will be a false negative [15-17]. Other methods used to diagnose the disease include serological testing of IgM and IgG production in response to viral infection [18-20]. Most of these methods are used when the rate of asymptomatic infections increases or PCR testing is not available [21-23]. In the current study, tried to investigate the characteristics (sensitivity, specificity) of all COVID19 diagnostic tests [24-26]. On the other hand, laboratory data are very important in achieving important results. Therefore, the aim of current study was evaluated the outcome of Laboratory Tests and accuracy of diagnostic tests in Patients with COVID-19 [27-29].

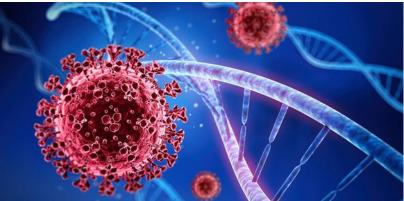


Figure 1: Universities Create New Epidemiological Model to Study COVID-19 Dynamics

Material and Methods

Selection Criteria

Inclusion criteria: patients with COVID-19 infections; Sample size higher than 4 patients; f diagnostic method; Human biological samples (HBS). Case studies, case reports and reviews; other infection were excluded from the study. Studies data were reported by study, years, study design, age, Number of patients, Methods for Evaluation. The QUADAS-2 tool was used to quality assessment of diagnostic accuracy studies [22]. It consists of four main domains comprising patient selection, index test, reference test, and flow/timing. All four domains include two independent judgments: "Risk of bias" and "Applicability". Only the last domain "flow/timing" comprises a single judgment on "Risk of Bias". All seven judgments must be

scored "Yes" or "No" or "Unclear". The purpose of the signalling questions is to help score the QUADAS criterion "Risk of bias" as "Low", "High" or "Unclear". For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. Prior to the screening, kappa statistics was carried out in order to verify the agreement level between the reviewers. The kappa values were higher than 0.80. 95% confidence interval for mean difference with fixed effect model and Inverse-variance method were calculated. deal with potential heterogeneity, random effects were used and I² showed heterogeneity. I² values less than 50% indicate low heterogeneity and above 50% indicate moderate to high heterogeneity. Meta-analysis was performed using Stata/MP v.16 software (The fastest version of Stata).

Results and Discussion

In the review of the existing literature using the studied keywords, 469 studies were found. In the initial review, duplicate studies were eliminated and abstracts of 434 studies were reviewed. At this stage, 361 studies did not meet the inclusion criteria, so they were excluded, and in the second

stage, the full text of 73 studies was reviewed by two authors. At this stage, 52 studies were excluded from the study due to incomplete data, inconsistency of results in a study, poor studies, lack of access to full text, inconsistent data with the purpose of the study. Finally, twenty-two studies were selected (Figure 2).

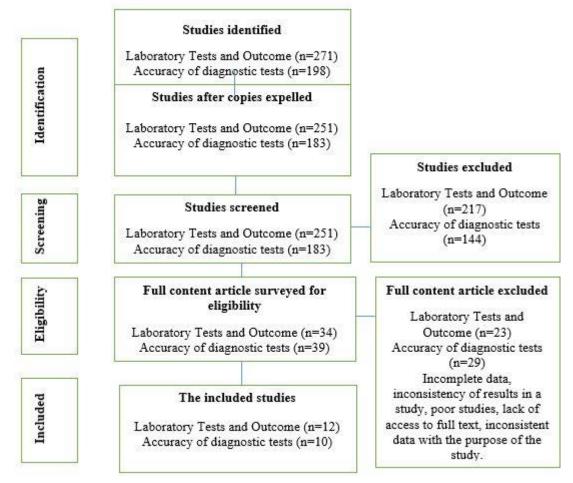


Figure 2: Study Attrition

Characteristics

Twelve and ten studies have been included in present article for laboratory tests and outcome and accuracy of diagnostic tests, respectively.

The number of patients were 2314 with 43.75 mean of years. The range of radiological abnormalities at baseline was between 44-100%. The mean of comorbidity 36.11% (Table 1).

The number of patients were 1662. Reference method in all studies was RT-PCR, one studies nor reported this section. In two studies methods for evaluation, enzyme linked immunosorbent assay (ELISA), in four studies Chest CT and in

three studies RT-PCR were used. The marker gene is presented in Table 1.

Bias Assessment

Qu *et al.*, 2020 [30] and Xie *et al.*, 2020 [31] studies had a total score of 2 and 3/14, this score indicates the low quality of the studies. (0-4, high risk of bias). Eight studies had a total score between 5-9/14 (moderate risk of bias), this score indicates the moderate quality of the studies. Twelve studies had a total score between 10-14/14 (low risk of bias), this score indicates the high quality of the studies [32-35].

Abdolrazaghnejad A., et al. / J. Med. Chem. Sci. 2022, 5(2) 227-238

Table 1: Studies selected for systematic review and meta-analysis (Laboratory Tests and Outcome)

Study Years	Number of Mean of age		Radiological abnormalities	Comorbidity
Study fears	patients	(years)	at baseline (%)	(%)
Sun <i>et al.</i> ,2020 [23]	8	32	100	13
Liu <i>et al.</i> ,2020 [24]	13	54	NR	58
Liu <i>et al.</i> ,2020 [25]	78	33	NR	26
Guan <i>et al.</i> , 2020 [26]	1099	47	86	24
Wan et al.,2020 [27]	135	47	100	32
Zhang <i>et al.</i> ,2020 [28]	140	57	99.3	64
Li <i>et al.</i> ,2020 [29]	83	46	100	18
Qu <i>et al.</i> ,2020 [30]	30	51	NR	NR
Gao <i>et al.</i> ,2020 [31]	43	44	NR	NR
Qin et al.,2020 [32]	452	58	44	44
Han <i>et al.</i> ,2020 [33]	95	NR	NR	NR
Wang et al.,2020 [34]	138	56	100	46

Table 2: Studies selected for systematic review and meta-analysis (Accuracy of diagnostic tests)

Study. Years	Number of patients	Reference method	Methods for Evaluation	Marker gene		
Zhao <i>et al.</i> , 2020 [36]	173	RT-PCR	enzyme linked immunosorbent assay	IgM/IgG		
Zhang et al., 2020 [37]	14	RT-PCR	Chest CT	NR		
Yu et al., 2020 [38]	76	NR	RT-PCR	open reading frame 1ab gene and nucleocapsid protein gene		
Xie et al., 2020 [35]	19	RT-PCR	RT-PCR	NR		
Pan et al., 2020 [39]	23	RT-PCR	RT-PCR	NR		
Li <i>et al.</i> , 2020 [40]	78	RT-PCR	Chest CT	NR		
Liu <i>et al.,</i> 2020 [21]	214	RT-PCR	enzyme linked immunosorbent assay	IgM/IgG		
Chan, 2020 [2]	15	RT-PCR	RT-PCR	spike protein gene, nucleocapsid protein gene, helicase protein gene		
Long, 2020 [3]	36	RT-PCR	Chest CT	NR		
Ai et al., 2020 [4]	1014	RT-PCR	Chest CT	NR		

Outcome of Laboratory Tests

Mean differences of White blood cells in patients with COVID-19 was 1.8 ×109/L (MD, 95% CI 0.18, 1.98). Decrease the number of lymphocytes in the blood in patients with COVID-19 was -0.31×109/L (MD, 95% CI -0.41, -0.21). Increased number of neutrophils observed in patients with severe COVID-19, the Mean differences of this parameter was 1.31 ×109/L (MD, 95% CI 0.51, 2.11). A low hemoglobin count observed in patients with severe COVID-19, the Mean differences of this parameter was -4 g/L (MD,

95% CI -6.5, -1.5). The Mean differences of procalcitonin was 0.04 ng/ml (MD, 95% CI 0.00, 0.07), there was no association between procalcitonin and the severity of COVID-19. The range for prothrombin time was 0.31-1.11 seconds and Mean differences was 0.71 seconds, this means was prothrombin time was high in patients with COVID-19. Mean differences of creatinine in patients with COVID-19 was 3.20 μ m (MD, 95% CI -0.70, 7.10), correlation between creatinine and severe COVID-19 was not significantly (Figure 3 and Table 4) [36-38].

Table 3: Detailed QUADAS-2 assessment of all included studies

- 11-11	or Betaire	Risk of		essment		Applica			
2: low 1: unclear 0: high	Patient selection	Laboratory analyses	Outcome	Timing and flow		Patient selection	Laboratory analyses	Outcome	Total score
Sun <i>et al.</i> ,2020 [23]	+	+	+	+	(+	+	+	14
Liu <i>et al.</i> ,2020 [24]	+	?	•	•	(+	?	•	6
Liu <i>et al.</i> ,2020 (25]	+	•	+	•	(+	?	+	9
Guan <i>et al.</i> , 2020 [26]	?	+	•	-	(?	+	-	5
Wan <i>et al.</i> ,2020 [27]	+	•	•	?	(+	•	•	5
Zhang <i>et al.</i> ,2020 [28]	+	+	+	+	(+	+	+	14
Li et al.,2020 [29]	+	+	?	?	(+	+	?	11
Qu et al.,2020 [30]	?	•	•	-	(?	•	•	2
Gao et al.,2020 [31]	?	+	•	•	(?	+	•	6
Qin <i>et al.</i> ,2020 [32]	+	+	+	+	(+	+	+	14
Han et al.,2020 [33]	+	•	+	-	(+	•	+	8
Wang et al.,2020 [34]	+	•	+	•	(+	?	?	6
Zhao <i>et al.</i> , 2020 [36]	+	+	+	+	(+	+	+	14
Zhang <i>et al.</i> , 2020 [37]	•	+	+	?	(+	+	+	11
Yu et al., 2020 [38]	•	+	+	?	(+	+	+	11
Xie et al., 2020 [35]	?	•	•	?	(?	•	•	3
Pan et al., 2020 [39]	•	+	+	?		+	+	+	11
Li et al., 2020 [40]	+	+	+	+		+	+	+	14
Liu <i>et al.</i> , 2020 [1]	+	+	+	+		+	+	+	14
Chan, 2020 [12]	+	•	•	+		•	+	+	8
Long, 2020 [23]	•	+	+	?		+	+	+	11
Ai et al., 2020 [14]	?	+	+	?	(+	+	+	12

Table 4: Data from each studys

Table 4: Data from each studys												
Biomarker	Sun <i>et al.,</i> 2020 [23]	Liu <i>et al.</i> , 2020 [24]	Liu <i>et al.,</i> 2020 [25]	Guan <i>et al.</i> , 2020 [26]	Wan et al., 2020 [27]	Zhang <i>et al.</i> , 2020 [28]	Li et al., 2020 [29]	Qu <i>et al.</i> , 2020 [30]	Gao et al., 2020 [31]	Qin <i>et al.,</i> 2020 [32]	Han et al., 2020 [33]	Wang et al., 2020 [34]
White blood cells (×109/L)	12.5%↓ 12.5%↑	8.3%↑ 6.3%↑	5.31	33.7%↓ 5.9%↑	20.7%↓ 6.7%↑	19.6%↓ 13.3%↑	12%↓ 10.8%↑			3.5-9.5		3.5-9.6
Creatinine (µm)	1			1.6%1	4.4%1					-		64-104
Prothrombin (sec)	1		1		10.9		1	-	1		12.43	9.4-12.5 ↑
Procalcitonin (ng/ml)	62.5%1	83.5%1	0.06	5.5%↑	81.5%↓ 0.7%↑	34.7%1	53%1			>0.05		35.5%1
Hemoglobin (g/L)	12.5%↓ 37.5%↑	,	,	134	133		,			,	,	
Neutrophil (×109/L)	12.5%↓ 25%↑	18.8%↑	3.11			1%9	,			1.8-6.3		1.8-6.3
Lymphocyte (×109/L)	12.5%↓ 25%↑	1%05	0.98	83.2%↓	50%1	75.4%↓	53%↓			1.1-3.2		1.1-3.2
Aspartate Aminotransferase (AST) (U/L)	50%1	8.3%1	20.5	22.2%1	22.2%1					-	•	37%1
Alanine transaminase (ALT) (U/L)	25%↓ 50%↑	8.3%1	18.1	21.3%↑	26	ı	ı	,	ı	ı	ı	32.0
C-reactive protein (CRP) (mg/L)	62.5%1	83.3%1		20.7%1	10.5		0-11				•	
Lactate dehydrogenase (LDH) (U/L)	62.5%1	91.7%1		41%↑	43%↑	1	ı	1	ı		ı	125-242

Abdolrazaghnejad A., et al. / J. Med. Chem. Sci. 2022, 5(2) 227-238

Outcome of Laboratory Tests

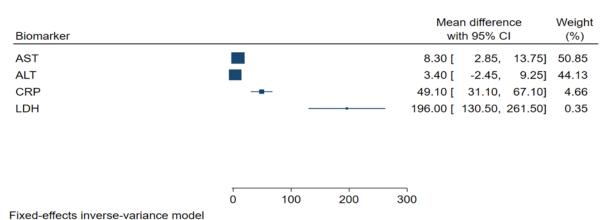
Mean differences of C-reactive protein was 49.10 mg/L (MD, 95% CI 31.10, 67.10), high level of CRP in the blood observed in patients with severe COVID-19. High Lactate dehydrogenase was observed in patients with severe COVID-19, the Mean differences of this parameter was 196 U/L (MD, 95% CI 130.50, 261.5). The Mean differences of Aspartate Aminotransferase was

8.30 U/L (MD, 95% CI 2.85, 13.75), this result showed small difference of Aspartate Aminotransferase in patients with severe COVID-19. Mean differences of Alanine transaminase was 3.40 U/L (MD, 95% CI -2.45, 9.25), correlation between Alanine transaminase and severe COVID-19 was not significantly (Figure 3 and Table 4) [39].

Biomarker				Mean difference Weight with 95% CI (%)
				· / _
WBC				1.08 [0.18, 1.98] 0.13
Lymphocyte		•		-0.31 [-0.41, -0.21] 10.80
Neutrophil		_		1.31 [0.51, 2.11] 0.17
Hemoglobin		_		-4.00 [-6.50, -1.50] 0.02
Procalcitonin				0.04 [0.00, 0.07] 88.19
Prothrombin		-		0.71 [0.31, 1.11] 0.68
creatinine				3.20 [-0.70, 7.10] 0.01
		-	1	
	-5	0	5	10
Fixed offects inverse verience model				

Fixed-effects inverse-variance model

Figure 3: Forest plot showed mean difference of White blood cells ($\times 109/L$), Creatinine (μ m). Prothrombin (sec), Procalcitonin (ng/mL), Hemoglobin (g/L), Neutrophil ($\times 109/L$) and Lymphocyte ($\times 109/L$) in patients with COVID-1



Tixed-effects fifterse-variance model

Figure 4: Forest plot showed mean difference of Aspartate Aminotransferase (U/L), Alanine transaminase (U/L), C-reactive protein (mg/L) and Lactate dehydrogenase (U/L)

Accuracy of Diagnostic Tests

Meta analysis of Computed tomography sensitive was 92% (ES, 95% CI 48%, 100%) among five studies and heterogeneity found ($I^2=0\%$; P=1.00) (Low heterogeneity) (Figure 4). Meta analysis of

Computed tomography specificity was 73% (ES, 95% CI 0.29, 1.16%) among five studies and heterogeneity found ($I^2=0\%$; P =0.87) (Low heterogeneity) (Figure 5 and 6).

Abdolrazaghnejad A., et al. / J. Med. Chem. Sci. 2022, 5(2) 227-238

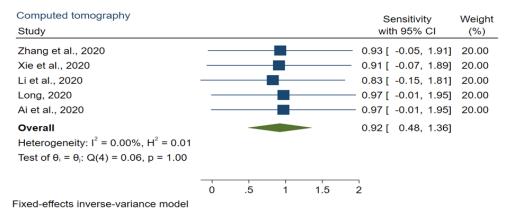
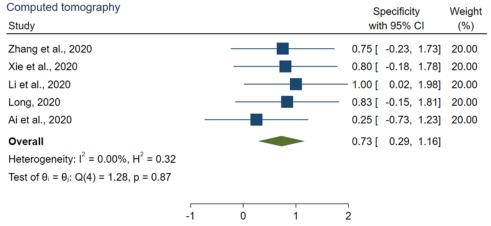


Figure 5: Forest plot showed sensitive of Computed tomography diagnostic for COVID-19



Fixed-effects inverse-variance model

Figure 6: Forest plot showed specificity of Computed tomography diagnostic for COVID-19

Sub group Meta Analysis of Immunological Tests (IgM and IgG):

sensitivity of type of sample:

blood 82% (ES, 95% CI 0.13, 1.51), serum 82% ES, 95% CI 0.16, 1.80), overall sensitivity of Immunological tests was 82% (ES, 95% CI 0.25, 1.39), and heterogeneity found ($I^2=0\%$; P=1.00) (Low heterogeneity). Acording to Test of group

differences there was no significant differences were observed between type of sample for detection of COVID-19 (p=1.00) (Figure 6). specificity of type of sample:

blood 91% (ES, 95% CI 0.21, 1.60), overall specificity of Immunological tests was 91% (ES, 95% CI 0.21, 1.60), and heterogeneity found (I^2 =0%; P=0.99) (Low heterogeneity) (Figure 7).

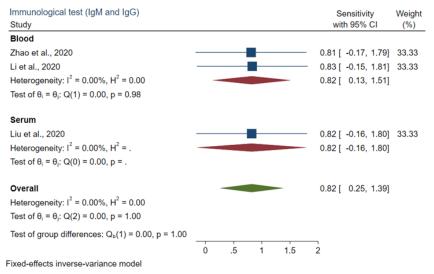


Figure 7: Forest plot showed sensitivity of Immunological tests (IgM and IgG) diagnostic for COVID-19

Abdolrazaghnejad A., et al. / J. Med. Chem. Sci. 2022, 5(2) 227-238

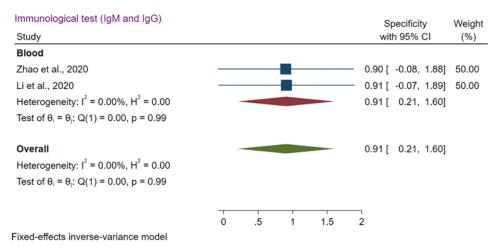


Figure 8: Forest plot showed specificity of Immunological tests (IgM and IgG) diagnostic for COVID-19

Sub group Meta analysis of PCR showed

Sensitivity of type of sample

Stool, feces, rectal swabs 25% (ES, 95% CI 0.32, 0.82), Urine 1% (ES, 95% CI 0.05, 0.58), Blood 7% (ES, 95% CI 0.06, 0.77), Nasopharyngeal aspirate, nasopharyngeal and throat swab 73% (ES, 95% CI 0.24, 1.24), Sputum 97% (ES, 95% CI 0.28, 1.66), Saliva 62% (ES, 95% CI 0.07, 1.31). overall sensitivity of PCR for detection of COVID-19 was 44% (ES, 95% CI 0.19, 0.68), less sensitive observerd when PCR detection of COVID-19 (Figure 9).

The findings of the present study were strong in relation to the first objective of the study (evaluated the outcome of Laboratory Tests) and no high heterogeneity was found between the studies. Present meta-analysis showed higher WBC count, neutrophils, prothrombin time; lower lymphocytes and hemoglobin count observed in patients with COVID-19 [4]. There was no correlation between procalcitonin; creatinine and severe COVID-19. The quality of the studies was moderate to high [5]. The results are consistent with common findings in other viral infections, with a recent systematic review showing that procalcitonin in the management of pneumonia cannot determine whether the infection is bacterial or viral [1]. The exact cause of death from COVID-19 is not yet known, but multiple organ dysfunction and hypoxia can be causes of death [5]. No correlation has been reported between renal function and disease severity at the time of admission [3]. In the present study, high quality studies were used and one of the strengths of their results was that laboratory analysis of patients with COVID-19 was reported at the time of admission. One of the limitations of the study was the lack of definition of the severity of the disease, the period of hospitalization, and follow-up. It is suggested that studies with different populations and comparison of laboratory results be performed in this field [2]. Also, in the present study, a study was conducted in children, which needs to be further studied in different age populations.

The findings of the present study were strong in relation to the second objective of the study (accuracy of diagnostic tests). High sensitivity and low specificity of computed tomography was obseverd; High Sensitivity and high specificity of Immunological tests was obseverd; Sensitivity of PCR detection of COVID-19 was obseverd. The most important findings of the present study were that meta-analysis showed that among all the methods discussed, PCR using sputum samples was highly sensitive to the others methods and is one of the most important methods for detecting COVID-19. These results are supported by the CDC Recommendations, which state that initial testing for SARS-CoV-2 should prioritize the collection of respiratory samples [6]. Computed tomography the second test with high sensitivity was identified, although the specificity for this test was Demonstration in computed tomography of the chest is a very important strategy complementary diagnosis. On the other hand, due to the lower sensitivity of serological tests than other methods, using serological tests to diagnose

in the early / acute stage of the disease can be challenging. One study showed that remodeling of IgM and IgG can occur simultaneously or sequentially in COVID-19, and antibody titers reach 19 after 6 days [5]. It should be noted, however, that the strength of immunological testing is its rapid return time and relatively low

cost, which may be an alternative due to the lack of RT-PCR and its high cost. One of the limitations of this study in examining the second goal is the weakness in the methodology of the studies and the lack of examination of the characteristics of patients and samples.

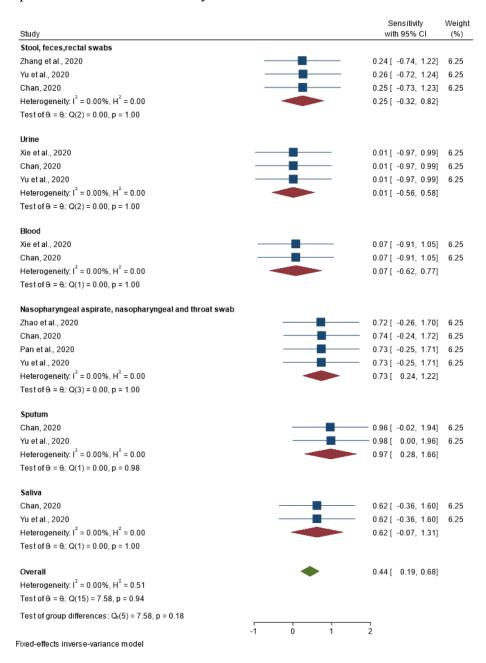


Figure 9: Forest plot showed sensitivity of PCR diagnostic for COVID-19

Conclusion

Evidence showed that at the time of admission of patients with COVID-19, a specific laboratory model can be used to perform relevant tests and make decisions about patients. The laboratory findings in patients with COVID-19 were almost

identical to the results of routine laboratory tests for other viral infections. PCR using sputum samples was highly sensitive for detecting COVID-19 and after that computed tomography of the chest was identified with high sensitivity.

Acknowledgments

The authors express their gratitude to the Vice Chancellor for Research and Information Technology of Zahedan University of Medical Sciences for approving this research and the head of Khatam al-Anbia Hospital as well as all participating families for their cooperation in doing this research.

Future research

It is necessary to conduct further studies with larger sample sizes to investigate administering the right sedative for traumatic children who are admitted to the emergency department. It is also rewarding to use ketamine and midazolam in non-emergency situations where there is enough time to sedate the patient or in emergency departments that are not very crowded.

Funding

The current study was funded by Zahedan University of Medical Sciences.

Authors' contributions

All authors have contributed significantly and met criteria for authorship. All the authors read and approved the final copy of the manuscript.

Conflict of Interest

We have no conflicts of interest to disclose.

ORCID

Hoseinali Danesh:

https://www.orcid.org/0000-0002-0385-2597 Ali Abdolrazaghnejad:

https://www.orcid.org/0000-0002-4121-1643

References

[1]. Mokhtare M., Alimoradzadeh R., Agah S., Mirmiranpour H., Khodabandehloo N., *Middle East J. Dig. Dis.*, 2017, **9**:228 [Google Scholar], [Publisher]

[2]. Etemadi S., Mahmoodiyeh B., Rajabi S., Kamali A., Milanifard M., *Ann. Romanian Soc. Cell Biol.*, 2021, **25**:2417 [Google Scholar], [Publisher]
[3]. Amini A., Shahpoori Arani H., Milani Fard M., *Eurasian J. Sci. Tech.*, 2021, **1**:421 [Crossref], [Google Scholar], [Publisher]

[4]. Givi F., Esmaeili R., Mojab F., Nasiri M., Shadnoush M., *Koomesh*, 2019, **21**:254 [Google Scholar], [Publisher]

[5]. Estebsari F., Dastoorpoor M., Khalifehkandi Z.R., Esmaeili R., Aghababaeian H., *Curr. Aging Sci.*, 2020, **13**:4 [Crossref], [Google Scholar], [Publisher]

[6]. Mohammadi M., Esmaeili R., Fani M., *J. Adv. Pharm. Educ. Res.*, 2019, **9**:111 [Google Scholar], [Publisher]

[7]. Sardari M., Esmaeili R., Ravesh N.N., Nasiri M., *J. Adv. Pharm. Educ. Res.*, 2019, **9**:145 [Google Scholar], [Publisher]

[8]. Hajalimohammadi M., Esmaeili R., Zandi M., Zadeh B.P., *Medico-Legal Update*, 2020, **20**:262 [Crossref], [Google Scholar], [Publisher]

[9]. Azadmehr F., Esmaeili R., Farahani Z.B., Arabborzu Z., *J. Adv. Pharm. Educ. Res.*, 2018, **8**:1 [Google Scholar], [Publisher]

[10].Esmaeili R., Barziabadi Z.F., Khoob M.K., *Nephro-Urol. Mon.*, 2021, **13**:e100728 [Crossref], [Google Scholar], [Publisher]

[11].Soleimani F., Anbohi S.Z., Esmaeili R., Pourhoseingholi M.A., Borhani F., *J. Clin. Diagn. Res.*, **12**:LC01 [Crossref], [Google Scholar], [Publisher]

[12].Maddah Z., Ghalenoee M., Mohtashami J., Esmaieli R., Naseri-Salahsh V., *Med. J. Islam. Repub. Iran*, 2018, **32**:1 [Crossref], [Google Scholar], [Publisher]

[13].Bahoush G., Pahlavani R., Salarinejad S., Zarei E., *PCR*, 2021, **16**: 166 [Crossref], [Google Scholar], [Publisher]

[14].Silva E.H., Lekamwasam S., *J. Prev. Epidemiol.,* 2020, **5**:e03 [Crossref], [Google Scholar], [Publisher]

[15]. Alimoradzadeh R., Mokhtare M., Agah S., *Iran. J. Age.*, 2017, **12**:78 [Google Scholar], [Publisher]

[16]. Alimoradzadeh R., Mirmiranpour H., Hashemi P., Pezeshki S., Salehi S.S., *J. Neurology Neurophys.*, 2019, **10**:1 [Google Scholar], [Publisher]

[17].Abdolrazaghnejad A., Banaie M., Safdari M., Ad. J. Emerg. med, 2018, **2**:1 [Google Scholar], [Publisher]

[18].Akhlaghi N., Payandemehr P., Yaseri M., Akhlaghi A.A., Abdolrazaghnejad A., *Ann. Emerg.*

Med., 2019, **73**:462 [Crossref], [Google Scholar], [Publisher]

[19].Abdolrazaghnejad A., Banaie M., Bang.J.Pharma, 2017, **12**:180 [Crossref], [Google Scholar], [Publisher]

[20].Pakniyat A., Qaribi M., Hezaveh DR., Abdolrazaghnejad A., *J. Acute Dis*, 2018, **7**:241 [Crossref], [Google Scholar], [Publisher]

[21].Rahmati J., Fathi H., Sultanova N., Davudov M.M., Danesh HA., *Int. J. Otorhinolaryngol. Head Neck. Surg.*, 2020, **9**:86 [Crossref], [Google Scholar], [Publisher]

[22].Rakei S., Rad H.I., Arbabisarjou A., Danesh H.A., *Drug Invent. Today*, 2019, **11**: 3123 [Google Scholar], [Publisher]

[23].Rakei S., Rad H.I., Irandegani F., Danesh H.A., *Drug Invent. Today*, 2019, **12**: 2809 [Google Scholar], [Publisher]

[24].Danesh H.A., Focus Med. Sci. J., 2018, 4 [Crossref], [Google Scholar], [Publisher]

[25].Danesh H.A., Saboury M., Sabzi A., Saboury M., Jafary M., Saboury S., *Med. J. Islam. Repub. Iran*, 2015, **29**:172 [Crossref], [Google Scholar], [Publisher]

[26].Abdolrazaghnejad A., Banaie M., Safdari M., *Adv. J. Emerg. Med.*, 2018, **2**:1 [Google Scholar], [Publisher]

[27].Akhlaghi N., Payandemehr P., Yaseri M., Akhlaghi AA., Abdolrazaghnejad A., *Ann. Emerg. Medicine*, 2019, **73**:462 [Crossref], [Google Scholar], [Publisher]

[28].Abdolrazaghnejad A., Banaie M., *Bang. J. Pharma*, 2017, **12**:180 [Crossref], [Google Scholar], [Publisher]

[29].Pakniyat A., Qaribi M., Hezaveh DR., Abdolrazaghnejad A., *J. Acute Dis.*, 2018, **7**:241 [Crossref], [Google Scholar], [Publisher]

[30].Mehr S.S., Ramezani A., Kashi M.A., Krimpalis S., *J. Mat. Sci.*, 2018, **53**:14629 [Crossref], [Google Scholar], [Publisher]

[31]. Mehr SS., Ramezani A., Kashi M.A., *J. Mat. Sci, Mat. Elect.*, 2018, **29**:18771 [Crossref], [Google Scholar], [Publisher]

[32].Nickavar A., Abolhasan Choobdar F., Mazouri A., Talebi A., *Iran. J. Neonatol.* 2018, **9**:1 [Crossref], [Google Scholar], [Publisher]

[33].Nejad N.H., Saboute M., Hosseini R., Tahoori M., Otukesh H., *J. Comp. Pediat.*, 2019, **10**:e74359 [Crossref], [Google Scholar], [Publisher]

[34].Hoseiny-Nejad N., Cheraghi T., Nikpour S., Sheikhvatan M. *I. Pedia.*, 2018, **28**:e63588 [Crossref], [Google Scholar], [Publisher]

[35].Saboute M., Mazouri A., Khalesi N., Hoseiny Nejad N., Razaghian A., *Iran. J. Neonatol.* 2017, **8**:83 [Crossref], [Google Scholar], [Publisher]

[36]. Hoseiny Nejad N., Sadat Sharif A., Otukesh H., Hekmat S., Sakhaei M., *Pediatric Nephrol.*, 2021, **36**:1 [Crossref], [Google Scholar], [Publisher]

[37].Bahoush G., Zarei E., *Open Aces. Maced. J. Med. Sci.*, 2020, **8**:233 [Crossref], [Google Scholar], [Publisher]

[38].Bidari A., Hassanzadeh M., Naderkhani M., Mesgarha M.G., Mohammad A.P., Azadeh A., Hossein H., Zarei E., Khodadost M., *Med. J. Islam. Repub. Iran.*, 2021, 35:1 [Crossref], [Google Scholar], [Publisher]

[39]. Nazari Sabet M, Ahmadipour E, Zamansaraei S., *J. Prev. Epidemiol.*, 2021, **6**:e07 [Crossref], [Google Scholar], [Publisher]

[40].Farnood F., *J. Ren. Endocrinol.*, 2020, **7**:e05 [Google Scholar], [Publisher]

HOW TO CITE THIS ARTICLE

Maryam Ziaei, Mahjoubeh Keykha, Faeze Kazemi, Ali Abdolrazaghnejad. Comparing the Sedative Effect of Oral Midazolam Versus Oral Ketamine on Children Aged 1-7 Years in Need of Radiologic Procedures, *J. Med. Chem. Sci.*, 2022, 5(2) 227-238

DOI: 10.26655/JMCHEMSCI.2022.2.10

URL: http://www.jmchemsci.com/article 140521.html