## Prevalence of Gastrointestinal Problems in Patients with COVID-19: A Systematic Review and Meta-analysis

Behzad Badakhsh<sup>1</sup>, Mohammad Karimian<sup>2</sup>, Feizollah Mansouri<sup>3</sup>, Farzad Zarei<sup>4,5</sup>, Somayeh Mahdikhani<sup>6</sup>, Ebrahim Salimi<sup>5</sup>, Ali Gholami<sup>7</sup>, Milad Borji<sup>8,9</sup>, Asma Tarjoman<sup>10,11</sup>, Ali Khorshidi<sup>12,8,\*</sup>

- <sup>1</sup> Assistant Professor of Internal Medicine, Department of Internal Medicine, School of Medicine, Ilam University of Medical sciences, Ilam, Iran
- <sup>2</sup> Assistant Professor of Vascular Surgery, Ilam University of Medical Science, Ilam, Iran
- <sup>3</sup> Professor of Infectious Disease, Infectious Diseases Department, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran
- <sup>4</sup> Department of Nursing, Faculty of Nursing and Midwifery, Kermanshah University of Medical Science, Kermanshah, Iran
- <sup>5</sup> Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran
- <sup>6</sup> Ph.D. Nursing student, Università degli Studi "La Sapienza" di Roma, Public Health and Infectious Diseases, Undergraduate, Italy
- <sup>7</sup> Assistance Professor of Anesthesiology, Clinical Research Development Center of Taleghani Hospital, Kermanshah University of Medical Science, Kermanshah, Iran
- <sup>8</sup> Clinical Research Development, Imam Khomeini Hospital, Ilam University of Medical Sciences, Ilam, Iran
- <sup>9</sup> School of Allied Medical Sciences, Ilam University of Medical sciences, Ilam, Iran
- <sup>10</sup> Student Research Committee, Ilam University of Medical Sciences, Ilam, Iran
- <sup>11</sup> Zoonotic Disease Research Center, Ilam University of Medical Sciences, Ilam, Iran
- <sup>12</sup> Associate Professor of Epidemiology, School of Medicine Psychosocial Injuries Research Center, Ilam University of Medical Sciences Ilam, Iran

# ABSTRACT

#### **Background:**

Considering the prevalence of COVID-19 worldwide, the present study aimed to determine the prevalence of gastrointestinal problems (anorexia, diarrhea, nausea, and vomiting) in patients with COVID-19.

#### Materials and Methods:

The purpose of this study was to determine the prevalence of gastrointestinal problems in patients with COVID-19 using Systematic Review and Meta-analysis methodology. The search was conducted independently by two researchers on international databases, including Web of Science (ISI), Scopus, Embase, Science Direct, PubMed/Medline, and Google Scholar Search Engine. Keywords included "Vomiting", "Anorexia", "Diarrhea", "Nausea", "SARS-CoV-2", and "COVID-19". Data were analyzed using STATA statistic software.

#### **Results:**

The total sample size was 3602 patients. Initially, 1456 studies were included in the study, which reached 33 articles after the final screening. Regarding the prevalence of gastrointestinal problems in patients, the prevalence rate of diarrhea was 6% (95% CI: 0.06 [0.04, 0.08]), anorexia was 13% (95% CI: 0.13 [0.03, 0.24]), nausea and vomiting was 4% (95% CI: 0.04 [0.03, 0.05]), and pharyngalgia was 16% (95% CI: 0.16 [0.02, 0.30]).

#### **Conclusion:**

The results of this study can be used as a guideline for clinical professionals.

Keywords: COVID-19, Gastrointestinal problems, Clinical symptoms, Systematic review, meta-analysis

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## \**Corresponding author:*

Ali Khorshidi, MD

Clinical Research Development, Imam Khomeini Hospital, Ilam University of Medical Sciences Ilam, Iran Telefax: + 98 84 2237143 E-mail: ali\_482002@yahoo.com

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#### **INTRODUCTION**

Gastrointestinal diseases are significantly associated with infectious diseases worldwide (1,2). Common gastrointestinal diseases include diarrhea, nausea and vomiting, and anorexia. Hospital admission of these patients may result in high costs for the health system in all countries (3). Even in some cases, due to gastrointestinal problems, the patient's health may be compromised, and the patient may die (4).

Diarrhea is a common symptom in developing

countries. The causes of diarrhea in patients include functional disorders such as Crohn's disease and Celiac disease, dysfunction of bile acids, or infectious diseases (5,6). Factors such as inadequate hygiene, lack of access to safe drinking water, and other risk factors are contributing to diarrhea (7-9). Another gastrointestinal problem is nausea and vomiting (10).

Constipation can lead to increased intracranial pressure as well as impaired rehabilitation treatments for patients with difficulty in controlling intestine movement (11, 12). Symptoms of constipation affect the patients and their care so that it can decrease the quality of life of such patients and disrupt their daily lives (13). Factors that can contribute to constipation include lifestyle, income status, education, physical activity, hormonal changes, and infectious diseases (14, 15).

COVID-19 is a pandemic infectious disease that has spread worldwide. One of the complications of this disease is gastrointestinal problems. However, studies of these complications have reported different prevalence (4,16,17).

### 2. Objectives

The purpose of this study was to determine the prevalence of gastrointestinal problems (anorexia, diarrhea, and nausea and vomiting) in patients with COVID-19 using Systematic Review and Metaanalysis methodology.

## MATERIALS AND METHODS

#### 3.1. Protocol

According to Systematic Reviews and Meta-Analyses (PRISMA) statement (18).

## 3.2. Inclusion and exclusion criteria

PICO elements of the study include, P: patients with Covid-19, I: Clinical symptoms, C: Healthy people. O: anorexia, diarrhea, nausea, and vomiting. Case reports, and Systematic Review and Meta-analysis articles were excluded from the study.

## 3.3. Information sources and search strategy

The search was conducted on the international databases including Web of Science (ISI), Scopus, Embase, Science Direct, PubMed/Medline, and Google Scholar Search Engine. Keywords included "Vomiting" [Mesh], "Anorexia" [Mesh], "Diarrhea" [Mesh], "Nausea" [Mesh], "SARS-CoV-2" [Mesh], and "COVID-19" [Mesh].

### 3.4. Study selection

The research team consisted of senior expert nurses (master) (FZ & ES) who did the primary search in international databases, and in case of any discrepancies between the two researchers, the final research was reviewed by another researcher with another senior nurse (master) (MB). Also, any questions about the procedure and the data contained in the articles were reviewed and approved by a gastroenterologist (BB).

#### 3.5. Data collection process and data items

The form of findings included the prevalence (percent) of the three main variables associated with gastrointestinal complications such as diarrhea, nausea, and vomiting. The age, sample size for male and female patients, and the name of the published journal were also listed in the checklist (table1).

## 3.7. Statistical approach

Data analyses were performed in STATA software, version. 11 (College Station, TX, USA).

### **RESULTS**

The total sample size was 3602 patients. Initially, 1456 studies were included in the study, which yielded 33 articles after the final screening. Regarding the prevalence of gastrointestinal problems in the patients, the prevalence rate of diarrhea was 6% (95% CI: 0.06 [0.04, 0.08]), anorexia was13% (95% CI: 0.13 [0.03, 0.24]), nausea and vomiting 4% (95% CI : 0.04 [0.03, 0.05]), and Pharyngalgia was 16% (95% CI : 0.16 [0.02, 0.30]) (figures 2-5).

#### **DISCUSSION**

In this Systematic review and Meta-analysis study, which examines gastrointestinal problems in patients with COVID-19 for the first time in the world, it has been shown that the incidence of diarrhea in patients with COVID-19 is 6% (95% CI: 0.06 [0.04, 0.08]). In a Systematic review and Meta-analysis study by Rodriguez-Morales and colleagues (43), which aimed to assess the clinical symptoms in patients with COVID-19, the prevalence of diarrhea varied

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-	Author	Age	Country	N (%)	Male N (%)	Female N (%)	Journal	Diarrhea N (%)	Nausea and vomiting N (%)	Anorexia N (%)	Pharyngalgia
1	-Huang et al (2020) (19)	49·0 (41·0– 58·0)	China	41	30(73)	11(27)	Lancet	1(3%)	-	-	-
2	Chen et al (2020) (20)	55·5 (13·1)	China	99	67 (68%)	32 (32%)	Lancet	2(2)	1(1)	-	-
3	Chen et al(2020) (21)	29.88	China	9	-	-	Lancet	1(11)	-	-	-
4	Wang et al(2020) (22)	56	China	138	63 (45.7)	75 (54.3)	JAMA	14 (10.1)	5 (3.6)	55 (39.9)	24 (17.4)
5	Guan et al (2020)(5)	47(31- 73)	China	18	9 (50)	9 (50)	JAMA	3 (17)	-	-	-
6	Zhang et al (2020) (6)	57 (25- 87)	China	140	71 (50.7)	69 (49.3)	Allergy	18(12.9)	7(5)	17(12.2)	-
7	Guan et al (2020)(7)	47.0 (35.0– 58.0)	China	1099	640(58.1)	459(41.9)	The New England Journal of Medicine	42 (3.8)	55 (5.0)	-	-
8	Kui et al (2020) (23)	57 (20–83)	China	137	61(44.5)	76(55.5)	Chinese Medical Journal	11(8)	-	-	-
9	Xu et al (2020) (24)	41 (32- 52)	China	62	35 (56)	27 (44)	BMJ	3 (8)	-	-	-
10	Chang et al (2020) (25)	34 (34- 48)	China	13	-	-		1 (7.7)	-	-	-
11	Henry et al (2020) (26)	0-19	14 Countries	82	43(52.4%)	27(32.9%)	-	1(4)	-	-	-
12	Yang et al (2020) (27)	45.11 ± 13.35	China	85	81	68	Journal of Infection	11(7.38)	2(1.34)	-	-
14	Li et al (2020) (16)	45.1± 12.8		17	9 (52.9)	8(47.1)		2 (11.8)	-	-	-
15	Yu et al (2020) (16)	29-34	China	7	-	-	The Lancet Infectious Diseases	1(14.3)	-	-	-
16	Pan et al (2020) (28)	40 ± 9 (25 - 63)	China	21	6 (29%)	15 (74%)	Radiology	-	-	-	-
17	Ng M et al (2020) (29)	56(37- 65)	Hong Kong	21	13(62)	8(38)		2(10)	-	-	-
19	Song et al (2020) (30)	49 ± 16		51	25(49)	26(51)		5(10)	3(6)	-	-
20	Chung et al (2020) (31)	51 ± 14	China	21	-	-	Radiology	-	1(5)	-	-

Table 1: Clinical characteristics of the study subjects

-	Author	Age	Country	N (%)	Male N (%)	Female N (%)	Journal	Diarrhea N (%)	Nausea and vomiting N (%)	Anorexia N (%)	Pharyngalgia
21	Zhou et al (2020) (23)	56·0 (46·0–67·0)	China	191	191	119 (62)	Lancet	9 (5)	7(4)	-	-
22	Shi et al (2020) (32)	49.5(11)	China	81	81	39(48)	The Lancet Infectious Diseases	3(4)	4(5)	1(1)	-
23	Hsih et al (2020) (33)	45.0 (39-51)	China	2	2	1(50)	Journal of Microbiology, Immunology and Infection	1(50)	-	-	-
24	Yang et al (2020) (34)	59.7 (13.3)	China	52	52	17 (33)	Lancet Respir Med	-	2(4)	-	-
25	Ma et al (2020) (35)	-	China	50	50	22(44)	The Lancet	3(6)	-	2(4)	-
26	Qui et al (2019) (36)	8.3	China	36	36	13(36)	The Lancet Infectious Diseases	-	2(6)	-	1 (3%)
27	Du et al (2020) (37)	34.10	China	67	67	35(52.2)	The Lancet Infectious Diseases	2(3)	-	8(11.9)	20(29.9%)
28	Xu et al (2020) (38)	43.9 ± 16.8	China	50	50	21(42)	Journal of Infection	-	-	-	-
29	Zhang et al (2020) (39)		China	28	28			3 (10.7)	-	-	-
30	Chen et al (2020) (46)	51(36-64)	China	249	249	123(49.4)	Journal of Infection	8(3.2)	-	-	-
31	Zhang et al (2020) (40)	46.65±13.82		573	295(51.5)	278(48.5)		45(7.9)	22(3.8)	-	-
32	Sun et al (2020) (41)	-	China	8	6(75)	2(25)	World Journal of Pediatrics	4(50)	4(50)	-	-
33	Zhang et al (2020) (42)	65.0 (56.0- 70.0)	China	28	17(60.7)	11(39.3)	Annals of Oncology	3 (10.7)	-	-	-

between 2% and 13.8%. The differences between the results of this study and those of Rodriguez-Morales and colleagues (43) indicate that in this study, the prevalence of diarrhea in patients with COVID-19 were studied in 28 studies, while Rodriguez-Morales and colleagues (43) studied diarrhea in only six articles. Another Systematic Review and Metaanalysis study that investigated the prevalence of diarrhea was done by Nasiri and co-workers (44), with a total prevalence of 5.7 (3.8-8.6) in 13 studies. Anorexia was also reported in five articles with a prevalence of 10.1 (1.0-57.2), which is consistent with Systematic review and Meta-analysis of Nasiri and co-workers (44)

### **CONCLUSION**

The results of this study can be used as a guide for clinical professionals.

## Author contributions:

All authors contributed to the initial discussion.

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Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran (3009984) / clinical research development center of Imam Khomeini Hospital affiliated to Ilam University of Medical Sciences, Ilam. Iran.

#### **CONFLICT OF INTEREST**

The authors declare no conflict of interests related to this work.

Systematic review and Meta-analysis

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Fig.4: Prevalence of nausea and vomiting in studies entered into the Systematic review and Meta-analysis

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Fig.5: Prevalence of pharyngalgia in studies entered into the Systematic review and Meta-analysis

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