

**JCOMS**



Volume 2, Number 4, December 2022

**Journal of  
Current Oncology  
and  
Medical Sciences**

[www.journalofcoms.com](http://www.journalofcoms.com)



## Evaluation of bullying and cyber victimization in adolescents

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### Abstract

**Introduction:** In recent years, with the change in people's lifestyles and the advent of technology, the method of bullying has changed. In the 21st century, bullies use new methods to harass their former peers. This type of bullying is bullying behaviours through electronic and digital media. In addition, its main feature is the lack of dependence on face-to-face communication between the victim and the bully. According to statistics, this problem has affected more than 32% of teens worldwide since 2007.

**Materials and Methods:** The present study was a cross-sectional analytical study examining cyberbullying and victimization rates in adolescents aged 12 to 18. In this study, 254 children of working parents and clients referred to Shafa Educational and Medical Center of Guilan University of Medical Sciences were evaluated by a CBVEQ questionnaire (during 2021).

**Results:** The scores from the factors of victimization and cyberbullying in this study were obtained. They showed that the average score of adolescents was 22.79 in the context of cyber victimization. Moreover, the score was 20.27 in the context of cyberbullying. Besides, Boys were more likely than girls to be victims of cyberbullying. The rate of cyberbullying in adolescents aged 15 to 18 was higher than the younger ages. Furthermore, the lower the parents' educational level, the rate of cyberbullying and victimization increased in adolescents.

**Conclusion:** The findings of this study and a recent study about the extent of cyberbullying and victimization among teenagers suggest that preventive strategies and interventions of parents and schools are needed.

**Keywords:** Bullying, Victimization, Cyber Bullying, Cyber Victimization, Teenager

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Received: 2022.8.26, Accepted: 2022.12.19



## Introduction

In recent years, with people's lifestyle changes and technology introduction into their lives, the way of bullying has also changed. Today, the American Psychological Association considers bullying a form of behavioural aggression in which one person intentionally and systematically harasses and offends another (1, 2).

In the 21<sup>st</sup> century, bullies are using new methods of harassment and bullying than their previous peers. This new bullying refers to bullying behaviour through electronic and digital media. The main feature of this new bullying is the lack of dependence on face-to-face communication between the bully and the victim. This latest type of bullying is called cyberbullying and victimization (3).

Various studies on bullying and cyberbullying found that approximately 43% of children were targeted by bullying and harassment online. Moreover, 70% of students reported experiencing bullying and harassment online. Girls were twice as likely as boys to be victims of cyberbullying (4).

A study investigated the risks of child and adolescent victimization through cyberbullying during the entry/exit restrictions of COVID-19 (5). This study found that with the increasing use of social media among children and adolescents during restrictions, most became cyberbullying victims. Besides, where young people were bullied, most posts and comments contained content about sex and sexual opinions. There were videos about the images of young girls and the trending of videos about school children fighting and insulting each other. A notable finding of this study was the use of fake accounts to commit cyberbullying (5).

As Aguaded (2014) points out, the most thoughtful response to a bullying society requires the development of media competence (6). Consequently, according to studies by Livingstone et al (2017), families and schools should seek to maximize the use of media for learning and entertainment (7, 8). Other researchers pointed to the need to reinforce the idea of educating children to become friends on social media (9).

Furthermore, the parental attachment was critical to preventing adolescent misconduct (10).

According to the social control theory, the individual's association with society is essential in reducing deviant behaviours. Besides, research showed that students with more significant family problems were more involved in cyberbullying. Additionally, school bullying, like cyberbullying, was negatively related to family support for adolescents (10).

Researchers also noted the importance of using evidence-based research on bullying interventions in schools to inform students better and prevent cyberbullying (11).

The issue of victimization and cyberbullying in adolescents has been one of the hot topics in the field of psychiatry and, in the last three years, has been examined by various researchers in different countries (12-17). According to the studies, behaviours that occurred in adolescence were the source of people's problems during childhood.

One of the pathological and destructive behaviours during childhood is bullying. If childhood and adolescence bullying behaviours are not attended to, they become more violent and aggressive in the next years (18). Therefore, paying attention to the issue of cyberbullying and its profound psychological effects is one of the most critical concerns of the country's education at present.

It is necessary to conduct more studies at the national level and in the provinces to solve this cyberbullying crisis. Consequently, the prevalence and distribution of cyberbullying and its psychological effects can be determined, and preventive strategies can be identified to avoid the increasing growth of this harassment. For this aim, this study was conducted on employees' and clients' cyber-sacrificed children of Shafa Educational and Medical Center of Guilan University of Medical Sciences during the year 1400 (2022-2023), and its increasing importance in setting current policies was noted.

## Materials and Methods

The present study consisted of a clinical and cross-sectional trial. The statistical population included adolescents aged 12 to 18 years whose parents were employees of or referrals to Shafa Medical Center of Guilan University of Medical Sciences. The

participants were selected since they were available and eligible for admission. The sample size required for this study was estimated to be 233 people .

The data was collected using an online questionnaire. The questionnaire included patient information and a cyberbullying victim experience questionnaire. First, parents were informed about the research process, goals, and possible consequences of the problem. Then, after obtaining consent to participate in the study, parents were asked to participate in an online questionnaire, which included demographic and bullying and cyberbullying questions .

Subsequently, a safe environment was provided for their children and the parents were reassured that their children won't be harmed. If the child was present, the adolescents were provided additional information about their previous access to cyberspace. However, if the adolescents had previous mental illness in the past that they received the treatment they were excluded from the study.

After completing the re-processing, the individuals were assured that the information obtained would remain completely confidential. Besides, they were told there was no need to mention the person's name, address, or telephone number in the questionnaire. In addition, if the participants thought they had any problems regarding cyberbullying, they were referred to the counsellors and specialists of the Child and Adolescent Psychiatric Clinic of Shafa Hospital.

**Measures**

The Cyberbullying Victim Experience Questionnaire (CBVEQ) was designed and validated by Antoniadou et al. (2016) to assess the cyberbullying experience among adolescents. The scoring method of this questionnaire was in the form of a 5-point Likert scale (1 = never, 2 = once or twice, 3 = sometimes, 4 = most of the time, 5 = every day). This questionnaire had two factors: 1 is the cyber victim factor, 2 is the cyberbullying factor, and each factor had 12 questions (19).

In a study conducted in Iran, Cronbach's alpha coefficient of this scale for cyberbullying, cyber victim, and the whole scale were reported to be 0.75, 0.78, and 0.79, respectively (20).

**Statistical Analysis**

Statistical analyses were presented cross-sectionally. Using the Kolmogorov-Smirnov test, it was found that the scores obtained in the field of victimization and cyberbullying from the CBVEQ questionnaire did not have a normal distribution (P = 0.001). Therefore, Mann Whitney U and Kruskal Wallis tests were used for examining the variables. Besides, a regression model was used to investigate the relationship between independent factors and dependent factors of the study. All data were analyzed in SPSS 26 software, and a significant level below 0.05 is acceptable.

**Results**

Findings showed that about 75% of the parents of the studied adolescents had a diploma to a bachelor's degree (Table 1).

**Table 1.** Personal characteristics of the participants.

Variable	Situation	Number
<b>Gender</b>	Boy	117 (46.1%)
	Girl	137(53.9%)
<b>Age</b>	12-14	115(45.3%)
	15-18	139(54.7%)
<b>(Age) Mean ± SD (min-max )</b>	1/82(12±14/85 18)	
<b>Mothers education</b>	Unlettered	12(4.7%)
	Primary education	1(0.4%)
	High school	38(15%)
	Diploma	101(39.8%)
	Associates degree	17(6.7%)
	Bachelors degree	69(27.2%)
	Masters degree	9(3.5%)
	Doctorate	7(2.8%)
<b>Fathers education</b>	unlettered	3(1.2%)
	Primary education	4(1.6%)
	High school	21(8.3%)
	Diploma	77(30,3)
	Associates degree	22(8.7%)
	Bachelors degree	92(36.2%)
	Masters degree	23(9.1%)
	Doctorate	12(4.7%)

Based on the CBVEQ questionnaire, the scores of the victimization and cyberbullying factors were examined. The results showed that adolescents'

average internet victimization score was 22.79. Moreover, in cyberbullying, the score was 20.27 (Table 2).

**Table 2.** Cyber victim and cyberbullying factors obtained from the CBVEQ questionnaire.

Factor	Number	Range of achievable points	Mean $\pm$ SD	Minimum points earned	Maximum points earned
Cyber victim	254	12-60	8/42 $\pm$ 22/79	12	52
Cyberbullying	254	12-60	8/88 $\pm$ 20/27	12	54

Using the Mann-Whitney U test, it was determined that there is a statistically significant difference between the scores obtained in the Cyber victimization according to gender (P=0.019). According to our study, boys had more cyber victimization than girls.

It was also found that there is no statistically significant difference between the scores obtained in the area of cyber victimization from the CBVEQ questionnaire according to the age groups of children and adolescents under investigation (P=0.093). Adolescents between the ages of 15 and 18 have been cyber victimization little more.

Using the Kruskal Wallis test, it was determined that there is a statistically significant difference between the scores obtained in cyber victimization, according to the education of the mothers (P=0.0001). It was also determined that there is a statistically significant difference among the points obtained in the cyber victimization, according to the education of the fathers, it can be seen (P=0.0001).

Adolescents whose parents had illiterate/primary education have been bullied more than other adolescents. Also, teenagers whose parents had master's/doctorate degrees have been victims less than others. (Table 3).

**Table 3.** Comparison of the points obtained in cyber victimization, according to some individual characteristics.

Variable	Situation	Number	Mean $\pm$ SD	P value
Gender	Boy	117	9.11 $\pm$ 24.3	P=0.019
	Girl	137	7.58 $\pm$ 21.51	
Age (year)	12-14 year	115	7.77 $\pm$ 21.67	P=0.093
	15-18 year	139	8.84 $\pm$ 23.72	
Mother's education	Illiterate/elementary	13	7.2 $\pm$ 27.61	P=0.0001
	Sub Diploma / Diploma	139	8.53 $\pm$ 24.44	
	Associate / Bachelor	86	7.47 $\pm$ 20.3	
	Master's degree/ Ph.D	16	7.92 $\pm$ 18	
Father's education	illiterate/elementary	7	13.08 $\pm$ 31.28	P=0.0001
	Sub Diploma / Diploma	98	8.22 $\pm$ 24.69	
	Associate / Bachelor	114	8.1 $\pm$ 21.72	
	Master's degree/ Ph.D	35	6.64 $\pm$ 19.28	

Using the Kolmogorov-Smirnov test, it was determined that the data on cyberbullying does not have a normal distribution (P=0.001).

Using the Mann-Whitney U test, it was determined that there is no statistically significant difference between the scores of cyberbullying, according to gender

(P=0.732). The amount of cyberbullying in girls and boys was not much different.

It was also found that there is a statistically significant difference between the scores of cyberbullying, according to age (P=0.004). Teenagers in the age group

of 15 to 18 years were more likely to commit cyberbullying.

Using the Kruskal Wallis test, it was found that there is a statistically significant difference between the scores of cyberbullying, according to the education of the mothers of the investigated children (P=0.001). It was also found that there is a statistically significant difference between the points of cyberbullying can be seen according to the education of the fathers (P=0.028).

Adolescents whose mothers had illiterate/primary education have committed cyberbullying more than others. On the other hand, adolescents whose mothers had a master's/doctorate degree did not necessarily bully less than others.

Adolescents whose fathers had a sub diploma/diploma have committed cyberbullying more than others.(Table 4).

**Table 4.** Comparison of the points obtained in cyberbullying, according to some individual characteristics.

Variable	Situation	Number	Mean ± SD	P value
Gender	Boy	117	8.55±20.11	P=0.732
	Girl	137	9.18±20.4	
Age (year)	12-14 year	115	7.48±18.32	P=0.004
	15-18 year	139	9.62±21.89	
Mother's education	Illiterate/elementary	13	9.76±27.61	P=0.001
	Sub Diploma / Diploma	139	9.14±21.35	
	Associate / Bachelor	86	7.43±17.94	
	Master's degree/ Ph.D	16	10.78±20.31	
Father's education	illiterate/elementary	7	8.42±17	P=0.028
	Sub Diploma / Diploma	98	9.64±22.53	
	Associate / Bachelor	114	6.98±18.57	
	Master's degree/ Ph.D	35	10.97±20.17	

In addition, the Spearman Rho correlation coefficient was used. This evaluation showed a positive correlation between the scores of internet victimization and bullying in male children (P = 0.0001). The finding conveyed that in male children, the increase or decrease of scores in cyberbullying was correlated with the increase or decrease of the scores from internet victimization.

Furthermore, a positive correlation was found between internet victimization and cyberbullying scores (P = 0.0001) in female children, using the Spearman Rho correlation coefficient. This finding signified that the increase or decrease in cyberbullying scores was correlated with the increase or decrease in internet victimization scores in female children (Table 5).

**Table 5.** Correlation between the scores of Internet victimization and Internet bullying by gender of adolescents 12 to 18 years.

Gender	Variable	Points earned in cyber victimization	
Boy	Points earned in internet bullying	Spearman Rho	0/337
		P-Value	P=0/0001
		Type of correlation	Positive correlation
Girl	Points earned in internet bullying	Spearman Rho	0/439
		P-Value	P=0/0001
		Type of correlation	Positive correlation

## Discussion

The current study investigated the involvement of adolescents aged 12 to 18 in being bullied and internet victims (through the CBVEQ questionnaire) in Guilan province. This study was one of the first on the frequency and extent of adolescent involvement in cyberbullying in Guilan. Therefore, there was no previous background to compare the findings of this study. However, the results of this study can be compared with future research.

The present study showed that the mean scores of the adolescents were 22.79 in the internet victimization field and 20.27 in the field of internet bullying. The scores reflected a relatively high rate of conflict. The differences between the results of the studies can mostly be related to different methods and tools used to determine the prevalence and involvement of adolescents in cyberbullying.

A comparison of the results with other studies, we showed that the average score of internet victimization was significantly higher in boys than girls. Furthermore, bullying was somewhat higher in boys but not significantly that different from the findings of Chou et al.(2021) study (21).

In li study's the demographic variables, gender and school scores were closely related to cyberbullying. In particular, male students had a higher rate of cyberbullying than female students(22). In addition, according to Goa's research(2016), male students were more likely than female students to commit cybercrime, which is consistent with the current study's results (23).

The present paper's results showed no significant difference between girls and boys regarding cyberbullying. This finding was consistent with the study by Agnes Zsila et al. (2018). However, in Zsila's study, there was no significant gender difference, even in the case of cyberbullying victims. In the current study, boys were more likely than girls to be victims of cyberbullying. The reason for this difference can be the different cultural contexts of countries, differences in friendship groups and intimacy of girls' relationships, and the extent of adolescents' involvement with social spaces (24).

This study showed that cyberbullying in teenagers aged 15 to 18 is higher than among teenagers in lower age groups. The rate of cyber victimization in bullying was also higher in the same age group, but there was no significant difference. This finding is consistent with the study of Ding et al. who reported that older students are less likely to be victims of cyberbullying, there was no correlation. In our study, both cyberbullying and cyber victimization increased with age; The reason for this difference can be attributed to the level of parental support at a younger age in different societies, dependence on friends at a younger age, and the role of empathic relationships in friendships, younger teenagers being more vulnerable, hours of using cyberspace which naturally the higher it is, the more it is and the type of virtual groups that older teenagers participate in. In other words, older teenagers have more courage to do this and parental supervision is less (25).

On the other hand, the findings showed that a higher level of parents' education resulted in a lower rate of internet victimization in adolescents. Moreover, the adolescents whose parents were illiterate or had primary education were more vulnerable to cyberbullying. Internet bullying was also reported more in adolescents whose mothers had primary education. These findings were consistent with a study by Camerini et al. (2020) reported in a systematic review. Camerini et al. (2020) showed that family social support and parental attachment reduced the risk of bullying and cyberbullying. The more accurate and comprehensive the control and supervision of the family, the greater the empathy between family members (4).

Besides, another critical finding in this study was that the rate of scores was relatively high for cyberbullying in adolescents whose parents had a master's/doctoral degree. This finding could indicate that parents who spent more time outside the home and interacted less with their children provided the space for teens to have more access to cyberspace. Especially mothers could have a significant impact on adolescents' skills in their social relationships. This impact is because mothers are usually considered the moral role models of their children in Iran, and there is a deep dependence

between mother and child. In other words, the finding demonstrated that the less interaction between the family members, the more alone time adolescents spend in cyberspace.

As empathy and love at home diminish, children increasingly try to hide their problems from their parents. As a result, they would try to cope with these psychological stresses on their own by turning to high-risk groups. However, the more they work in these groups, the more psychological tensions overwhelm them.

In addition, this study found that an increase or decrease in cyberbullying was associated with an increase or decrease in cyber victimization. In traditional societies, a bully is considered a strong and valuable person. Even the victims, who have tasted the harassment and violence of the social space, try to become a bully themselves after a while to feel more socially accepted by gaining the support and attention of others.

The cyber bullies in traditional societies try to align more people with themselves by gathering fans in cyberspace. On the other hand, adolescents who were victims usually try to hide the violence and refuse to inform parents and teachers in schools. Thus, the necessary legal and social prosecution is not employed for a bully. Consequently, this cycle continues into adulthood and involves more and more people. Bullies continue to operate through physical, verbal, and psychological violence in such a society. Besides, victims suffer extreme stress and anxiety, social isolation, and severe psychological damage by concealing their problems.

## Conclusions

The findings of this study and the extent of adolescents' involvement with cyberbullying and victimization suggest that the authorities need more effective measures to adopt preventive strategies and interventions for parents and schools. To better formulate preventive cyberbullying and victimization measures, we need to consider all the factors mentioned in this study for designing an interactive model.

## Author contribution

All the authors of this article researched the subject with intellectual participation, wrote the manuscript, and approved the final manuscript.

## Acknowledgments

The authors would like to thank the staff of the Shafa Medical Center of Guilan University of Medical Sciences who helped us in this study, and we would like to thank Guilan University of Medical Sciences.

## Conflict of interest

The authors of this study have no conflicts of interest to declare.

## Statement of Ethics

All methods and procedures were approved by the Animal Care and Use Committee of Guilan University of Medical Sciences, with code IR.GUMS.REC.1400.199

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## Epidemiologic surveillance of cutaneous fungal infection and its causative agents in patients referred to Razi laboratory, Rasht, Iran: A retrospective study from 2016-2021

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### Abstract

**Introduction:** Information on epidemiologic trends of dermatophytosis and its causative agents is essential for the healthcare system to improve its knowledge of associated complications. The main purpose of this study was to determine the distribution of fungal strains and the infection sites of patients with dermatophytosis.

**Materials and Methods:** In this cross-sectional study, the demographical data and clinical characteristics of 641 patients with a positive fungal culture who were referred to Razi pathobiological laboratory, Rasht, Iran, between 2016-2021 were collected. All data were analyzed using SPSS software version 21 by a significant level of < 0.05.

**Results:** Out of 641 patients, 70% were female and the mean age of patients was  $43.98 \pm 16.99$  years. Laboratory analysis demonstrated that *Candida Albicans* (44/9%), *Aspergillus* (31/8%), and *Dermatophytes* (18%) were the most common causes of superficial cutaneous fungal infections. Among the dermatophytes, the most common pathogens were *Trichophyton mentagrophytes* (53%) and *Trichophyton Rubrum* (20.8%), also, the most common site of infection was nail (64.4%).

**Conclusion:** Considering the high prevalence of *Candida Albicans* and *Aspergillus*, especially in females, it is important to determine preventive protocols for fungal infections and better clinical management of the patients involved.

**Keywords:** Dermatophytosis, Fungal Infections, *Trichophyton*, *Candida*, *Aspergillus*, Tinea

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Received: 2022.11.15, Accepted: 2022.12.13



## Introduction

Fungal infections of the skin, hair, and nails are common with an increasing trend all over the world. The most important and common fungal infection is dermatophytosis (1). The globally increased prevalence of superficial and endemic fungal infections over the past 4–5 years with a rise in recurrent episodes, frequent exacerbations, and a severe chronic course has been observed (2). This infection is mainly limited to the surface layers of the epidermis, stratum corneum, and its appendages including hair and nails. Dermatophyte infections are classified according to the affected body site, including tinea capitis (scalp), tinea corporis (body), tinea bar-bae (beard area), tinea pedis (feet), tinea cruris (groin, perineum, and perineal areas), tinea unguium (nails), and tinea manuum (hands) (3–6). Dermatophyte infections are caused by Epidermophyton, Trichophyton, and Microsporum, with 41 species. The frequency of the disease and its type varies in different regions, and this variation depends on the living conditions and geography of that region and other factors such as occupation, age, level of personal hygiene, contact with animals, soil, etc. (7,8).

Another common cause of skin fungal infection is *Candida albicans*, which is a part of the normal flora of the digestive system in humans that can cause infection on the skin. This type of fungal infection usually starts from the perianal area and can spread to the perineum, lower abdomen, groin, and skin. *Candida* species can also lead to chronic fungal infection, onychomycosis, or even fungal infective dermatitis (8,9). Several factors play a role in the pathogenicity of fungal infection (*Candida*, etc.) including aging, obesity, long-term use of antibiotics, and a history of underlying diseases (10,11).

*Aspergillus* is another fungus that is a part of the human normal flora found in the upper respiratory tract and is also found in the surrounding environment (soil, dust, tobacco plants, water, and, food) (12,13). Therefore, a positive *Aspergillus* fungal culture can indicate a secondary infection that has superimposed on a primary skin lesion (caused by excessive washing, a wound, or any other skin injury). Patients with primary infection of cutaneous *Aspergillo*sis also usually have a history of contact of the damaged skin with an

infected object. All types of *Aspergillo*sis are more common in patients with a weak immune system (14–16).

In Guilan, Iran, due to the humidity of this region as well as the prevalence of agriculture and rice farming in this province, the prevalence of skin fungal infections is very high and it brings a lot of diagnostic and treatment costs for the people of the community as well as the healthcare system. The solution to this problem includes obtaining more information about this disease, its widespread prevalence in the province, especially in the hot seasons of the year, and the infectious strains. In this regard, we conduct this study to evaluate the prevalence of various dermatophytosis in Guilan province, Iran.

## Materials and Methods

### Study design and variables

In this retrospective cross-sectional study, demographical data and clinical characteristics of 641 patients with a fungal positive culture who were referred to Razi pathobiological laboratory, Rasht, Iran, from 2016 to 2021, were collected. The data included gender, age, types of infection site (feet, groin, body, nails, hands, scalp, face, perineum, and perineal areas), the strains of the infection (*Trichophyton mentagrophytis*, *Trichophyton rubrum*, *Epidermophyton flucosum*, *Microsporum canis*, *Trichophyton verrucosum*, *Microsporum gypsum*, *Trichophyton tonsurans*, *Trichophyton violaceum*, *Trichophyton schönleini*, *Candida*, *Aspergillus*, *Fusarium*, *Mucor*, *Penicillium*, *Cladosporium*, *Acremonium*, *Pseudoalcheria boidei*, *Mystoma*, *Rhizopus*, and *Alternaria*), and the year of sampling. All patients with positive fungal culture were included and the patients with incomplete data or negative fungal culture were excluded from the study. This study design was approved by the ethical committee of Guilan University of Medical Sciences (IR.GUMS.REC.1400.457).

### Statistical Analysis

Mean and standard deviation are used to describe quantitative variables with normal distribution. Qualitative variables are described using numbers and percentages. The normal distribution of quantitative

study data has been measured using Kurtosis, Skewness, Q-Q Plot, and Shapiro-Wilk test. Also, Chi-Square and Fisher exact tests were used to determine the association between demographical data and comorbidities in LPP patients. Statistical calculations were performed using the IBM SPSS Statistics version 21 with a significant level of less than 0.05.

### Results

In this present study, 88 patients (13.7%) in 2016, 92 patients (14.4%) in 2017, 114 patients (17.8%) in 2018, 121 patients (18.0%) in 2019, 96 patients (15.0%) in 2020, and 130 patients (20.3%) in 2021 were diagnosed to have dermatophytosis with a positive fungal culture. Out of 641 patients, 192 (30%) were male and 449 (70%) were female. The mean age of patients was 43.98±16.99 (3-93) with a mean of 44 years old (Table 1). According to the distribution of fungal infection in patients in scalp 25 (3.9%), body 46 (7.2%), hand 28 (4.4%), feet 66 (10.3%), nail 413 (64.4%), groin 42 (6.6%), face 15 (2.3%), and perineum and perineal

areas 6 (0.9%), nail was the most frequent site of fungal detection.

**Table 1.** Age frequency of studied patients.

Variables	Prevalence	Percentage
0-10	18	%2.8
11-20	32	%4.9
21-30	101	%15.7
31-40	123	%19.2
41-50	126	%19.7
51-60	128	%20.0
61-70	80	%12.5
71-80	26	%4.1
81-90	4	%0.6
91-100	3	%0.5

The frequency of fungal strains in patients represented that Candida and Aspergillus were most frequent in the nail, feet, body, and hand; and Candida and Trichophyton mentagrophytes were most frequent in the groin. While in the scalp, the most frequent fungal strains were Trichophyton mentagrophytes and Candida (Table 2).

**Table 2.** Frequency of fungal strains.

Fungal strains	Infection site								
	Nail n (%)	Feet n (%)	Body n (%)	Groin n (%)	Hand n (%)	Scalp n (%)	Face n (%)	Perineal areas n (%)	
<b>Candida</b>	288 (44.9)	193 (46.7)	24 (36.4)	17 (37.0)	23 (54.8)	12 (42.9)	6 (24.0)	8 (53.3)	5 (83.3)
<b>Aspergillus</b>	204 (31.8)	162 (39.2)	18 (27.3)	9 (19.6)	2 (4.8)	5 (17.9)	3 (12.0)	5 (33.3)	0 (0.0)
<b>Trichophyton mentagrophytis</b>	61 (9.5)	19 (4.6)	10 (15.2)	7 (15.2)	11 (26.2)	5 (17.9)	7 (28.0)	1 (6.7)	1 (16.7)
<b>Trichophyton rubrum</b>	24 (3.7)	10 (2.4)	7 (10.6)	3 (6.5)	2 (4.8)	0 (0.0)	2 (8.0)	0 (0.0)	0 (0.0)
<b>Trichophyton verrucosum</b>	14 (2.2)	5 (1.2)	1 (1.5)	4 (8.7)	1 (2.4)	3 (10.7)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Mucor</b>	11 (1.1)	6 (1.5)	2 (3.0)	1 (2.2)	1 (2.4)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Trichophyton tonsurans</b>	10 (1.6)	2 (0.5)	0 (0.0)	1 (2.2)	8 (0.0)	0 (0.0)	6 (24.0)	1 (6.7)	0 (0.0)
<b>Penicillium</b>	7 (1.1)	3 (0.7)	2 (3.0)	1 (2.2)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Rhizopus</b>	5 (0.8)	2 (0.5)	2 (3.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Fusarium</b>	4 (0.6)	4 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Pseudoalcheria boidei</b>	3 (0.5)	1 (0.2)	0 (0.0)	2 (4.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Epidermophyton floccosum</b>	2 (0.3)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

<b>Microsporium gypsum</b>	2 (0.3)	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Cladosporium</b>	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.6)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Acremonium</b>	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Mystoma</b>	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Trichophyton verrucosum</b>	1 (0.2)	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Trichophyton schönleini</b>	1 (0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (4.0)	0 (0.0)	0 (0.0)
<b>Alternaria</b>	1 (0.2)	0 (0.0)	0 (0.0)	1 (2.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
<b>Total</b>	641 (100)	413 (64.4)	66 (10.3)	46 (7.2)	42 (6.6)	28 (4.4)	25 (3.9)	15 (2.3)	6 (0.9)

A significant association was reported between the gender and age of the patients and the infection site ( $P=0.001$ ), Table 3.

**Table 3.** Comparison the association between age and gender, and infection site.

Infection site	Age (year)			P value	Gender		P value
	<44	44 ≤			Male	Female	
<b>Nail</b>	413 (64.4)	183 (57.4)	230 (71.4)		82 (42.7)	331 (73.7)	
<b>Feet</b>	66 (10.3)	27 (8.5)	39 (12.1)		24 (12.5)	42 (9.4)	
<b>Body</b>	46 (7.2)	27 (8.5)	19 (5.9)		18 (9.4)	28 (6.2)	
<b>Groin</b>	42 (6.6)	30 (9.4)	12 (3.7)		27 (14.1)	15 (3.3)	
<b>Hand</b>	28 (4.4)	17 (5.3)	11 (3.4)		11 (5.7)	17 (3.8)	
<b>Scalp</b>	25 (3.9)	23 (7.2)	2 (0.6)		20 (10.4)	5 (1.1)	
<b>Face</b>	15 (2.3)	8 (2.5)	7 (2.2)	0.001	6 (3.1)	9 (2.0)	0.001
<b>Perineal areas</b>	6 (0.9)	4 (1.3)	2 (0.6)		4 (2.1)	2 (0.4)	
<b>Total</b>	641 (100)	319 (49.8)	322 (50.2)		192 (30)	449 (70)	

While, this association was not observed between the gender and age of the patients and the fungal strains ( $P>0.05$ ), Table 4.

**Table 4.** Comparison the association between age and gender, and fungal stains.

Fungal strains	Age (year)			P value	Gender		P value
	>44	44 ≤			Male	Female	
<b>Candida</b>	288 (44.9)	142 (44.5)	146 (45.3)		83 (43.2)	205 (45.7)	
<b>Aspergillus</b>	204 (31.8)	89 (27.9)	115 (35.7)		50 (26.0)	154 (34.3)	
<b>Trichophyton mentagrophytis</b>	61 (9.5)	41 (12.9)	20 (6.2)		25 (13.0)	36 (8.0)	

<b>Trichophyton rubrum</b>	24 (3.70)	8 (2.5)	16 (5.0)		8 (2.5)	16 (5.0)	
<b>Trichophyton verrucosum</b>	14 (2.2)	9 (2.8)	5 (1.6)		4 (2.1)	10 (2.2)	
<b>Mucor</b>	11 (1.7)	3 (0.9)	8 (2.5)		3 (1.6)	8 (1.8)	
<b>Trichophyton tonsurans</b>	10 (1.6)	10 (3.1)	0 (0.0)		7 (3.6)	3 (0.7)	
<b>Penicillium</b>	7 (1.1)	3 (0.9)	4 (1.2)	0.999	2 (1.0)	5 (1.1)	0.999
<b>Rhizopus</b>	5 (0.8)	3 (0.9)	2 (0.6)		3 (1.6)	2 (0.4)	
<b>Fusarium</b>	4 (0.6)	3 (0.9)	1 (0.3)		0 (0.0)	4 (0.9)	
<b>Pseudoalcheria boidei</b>	3 (0.5)	3 (0.3)	0 (0.0)		1 (0.5)	2 (0.4)	
<b>Epidermophyton flucosum</b>	2 (0.3)	1 (0.3)	1 (0.3)		1 (0.5)	1 (0.2)	
<b>Microsporium gypsum</b>	2 (0.3)	2 (0.6)	0 (0.0)		1 (0.5)	1 (0.2)	
<b>Cladosporium</b>	1 (0.2)	0 (0.0)	1 (0.3)		1 (0.5)	0 (0.0)	
<b>Acremonium</b>	1 (0.2)	0 (0.0)	1 (0.3)		0 (0.0)	1 (0.2)	
<b>Mystoma</b>	1 (0.2)	1 (0.3)	0 (0.0)		0 (0.0)	1 (0.2)	
<b>Trichophyton verrucosum</b>	1 (0.2)	0 (0.0)	1 (0.3)		0 (0.0)	1 (0.2)	
<b>Trichophyton schönleini</b>	1 (0.2)	1 (0.3)	0 (0.0)		1 (0.05)	0 (0.0)	
<b>Alternaria</b>	1 (0.2)	0 (0.0)	1 (0.3)		1 (0.5)	0 (0.0)	
<b>Total</b>	641 (100)	319 (49.8)	322 (50.2)		192 (30)	449 (70)	

## Discussion

The prevalence of surface and skin fungal infections in 20-25% of the world's population indicates the importance of this type of skin disease. The most prevalent fungal infections among the studied patients were candida, aspergillus, and dermatophytes with the majority of Trichophyton mentagrophytes. According to our results, the most common infected sites were nails, feet, and body respectively. It has been identified that in males, the most common infected sites were the nail, groin, and leg; and in females were nails, leg, and groin, which can be related to the type of jobs (farmer), excessive washing of hands and feet, contact with detergents, cosmetic-beauty procedures, obsessive compulsive disorders, and anxiety, which more exposed some parts of the body to fungal strains.

In a study by Salari et al. on Kerman's population, Iran, it was demonstrated that dermatophyte infections were

more common in men, with the majority of tinea unguium and Trichophyton mentagrophytes. Also, the most common non-dermatophyte strain in that study was reported to be Aspergillus species (17), while in our study, Candida species were more common. Another study by Ebrahimi's et al., in Mashhad, Iran, reported that the most common types of infection were tinea corporis (32%), tinea cruris (27%), and tinea capitis (12%) (18), that was in contrast with our results, which can be due to the difference in climate and humidity of the two provinces, as well as the difference in common jobs in these two provinces, while the most common dermatophytes in both studies was reported to be Trichophyton mentagrophytes.

In the current study, the most involved age groups were upper than 44 years, which may be due to skin structural changes, antibiotics and other drug

consumption, higher prevalence of underlying disease, as well as occupational issues and related challenges. Trichophyton mentagrophytes were more prevalent in the age group below 44 years old and Trichophyton rubrum was more common in people over 44 years old. The scalp was the only site of infection where dermatophyte strain was preferred over non-dermatophyte types with 64%. But in face and perineal areas, Candida was the most common cause of infection with a prevalence of 53% and 83%, respectively. Considering that the primary form of Candidiasis and Aspergillosis infections generally occur in cases of immunodeficiency or existence predisposing underlying diseases such as diabetes, the high prevalence of these pathogens on the primary skin lesion (damage caused by excessive washing, moisture, wounds, burns, etc.) have grown secondary.

Zamani et al. reported that the prevalence of fungal strains was higher in males rather than females, while the majority of the study's patients were women. The most common type of infection was tinea pedis (30%), thigh dermatophytosis (29%), and body dermatophytosis (15); and the most common fungal strain was Epidermophyton flucosum (31%), Trichophyton rubrum (26%), and Trichophyton mentagrophytes (20%) (19). In a study by Antouri et al., the most common dermatophyte pathogen isolated was reported to be Trichophyton rubrum (76%) and Trichophyton mentagrophytes (11%); also, the most common site was nail (40%). Another investigation demonstrated that Trichophyton rubrum, Trichophyton interdigital, and Microsporum canis were the most frequently detected fungal strains in patients with the majority of tinea pedis and tinea unguium (20). The differences between reported common fungal strains and the site of infection refer to the geographical variation in different regions and also different lifestyles, which makes people susceptible to certain fungal infections. On the other hand, the immunogenic diversity of individuals should be considered in vulnerability to infections, especially opportunistic ones (21,22).

## Conclusions

According to our results, females had a higher frequency of Candida and Aspergillus in nails, feet, body, and hands, and Trichophyton mentagrophyte was

observed more in the scalp, which mostly refers to the type of their everyday activity. Therefore, the public access to some healthcare protocols can be helpful for better clinical management for the prevention and treatment of fungal infections.

## Author contribution

**KGH** and **RGH** participated in the research design and writing the first draft; **HE**, **AD**, and **RR** participated in the performance of the research and analytic tools; **NA**, **ME**, and **PJ** participated in data analysis. All author reviewed and confirmed the final manuscript.

## Acknowledgments

We would like to thank all hospital staff and specialists for their assistance with conforming and recording cases.

## Conflict of interest

No potential conflict of interest was reported by the authors.

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## Evaluation of beta-hemolytic, metallic green sheen, and ONPG test properties *Escherichia coli* isolated from urinary tract infections

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### Abstract

**Introduction:** Uropathogenic *Escherichia coli* strains are the most common cause of urinary tract infections in nosocomial and community-acquired infections. Phenotypic characteristics of *Escherichia coli* isolates in patients with urinary tract infections vary from region to region. Therefore, studying the phenotypic properties of the bacterium is very important.

**Materials and Methods:** In the current study, 100 strains of *Escherichia coli* were detected from urine samples of patients with urinary tract infections in Mazandaran province, Babol. This study aimed to investigate the properties of metallic green sheen, beta hemolysis, and Ortho-nitrophenyl- $\beta$ -D-galactopyranoside (ONPG) test of *Escherichia coli*.

**Results:** The most common bacterium isolated from urinary tract infections was *E. coli* (68.02%). In the present study, the properties of beta hemolysis, metallic green sheen, and ONPG in uropathogenic *E. coli* were 1, 80, and 100%, respectively.

**Conclusion:** The results of this study showed that 20% of *E. coli* strains lacked metallic green sheen, which should be identified through the IMViC test and other biochemical tests.

**Keywords:** Uropathogenic *E. coli*, ONPG test, Metallic green sheen,  $\beta$  hemolysis

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Received: 2022.11.30, Accepted: 2022.12.30



## Introduction

*Escherichia coli* (*E. coli*) is normally found in the intestines of humans and animals (1). *Escherichia coli* is the most common cause of UTI, accounting for 80 to 90 percent of community-acquired infections and 40 to 50 percent of nosocomial infections. More than 50% of women between the ages of 20 and 40 experience a urinary tract infection more than once (2). If left untreated, cystitis can accelerate ascending infections such as pyelonephritis and sepsis with kidney damage (3). *E. coli* that cause urinary tract infections are known as uropathogenic *E. coli* (UPEC) (4). Urinary tract infections are caused by bacteria ascending from around the urethra to the urethra, bladder, and other urinary tract. Colonization of the area around the urethra with pathogenic bacteria is a vital factor in the development of urinary tract infections. Women are more likely than men to get urinary tract infections due to the shorter distance between the urethra and the proximity of the urethra to the anus (5). Phenotypic tests of metallic green sheen in the culture medium of eosin methylene blue agar, hemolysis in blood agar medium, and Ortonitrophenyl beta galactoside are used in the detection of uropathogenic *Escherichia coli*. In EMBs, strong acid producers such as *E. coli* usually form green metallic-colored colonies that show a dark core. Under acidic conditions, the color of eosin Y precipitates, and due to the formation of an amide bond between eosin Y and methylene blue in the medium, dark-colored colonies usually form with a metallic green glow (6). uropathogenic *E. coli* lysis red blood cell by producing hemolysin A by creating a hole in the membrane. HlyA, encoded by the hlyCABD operon, is the most important factor in the UPEC. This toxin gives UPEC the ability to cause tissue damage, cross mucosal barriers, release host nutrients, and damage immune cells (7). The ONPG test detects lactose-negative and delayed lactose-positive bacteria. Prevalence of lactose-negative strains (0-5%) has been reported in studies (8). Given that the beta-hemolytic, metallic green sheen, and ONPG characteristics of uropathogenic *E. coli* have been reported differently, this study aimed to investigate these properties.

## Materials and Methods

### Sample collection and detection

In this cross-sectional descriptive epidemiological study, urine samples were collected from patients referred to Babol Shahid Beheshti Hospital, Mazandaran Province, Babol. A total of 1202 urine samples were collected for 5 months (from November 2020 to March 2020) under the supervision of the Medical Ethics Committee of the Islamic Azad University, Babol branch (Ethics Code 1345). Blood agar, McConkey agar, and Eosin methylene blue (EMB) agar media were used for isolation and identification of UPEC. If the number of colonies of a single microorganism in the urine sample was  $10^5$  colony-forming units per milliliter (CFU / ml) or more, a urinary tract infection would be considered positive. Patients who received antibiotics two weeks before sample collection were excluded from the investigation (9). Strains of *E. coli* were confirmed using the IMViC (Indole, Methyl Red, Voges-Proskauer, Citrate utilization), urease and triple sugar iron agar (TSIA), and other biochemical tests. All confirmed isolates were stored in trypticase soy broth with 15% glycerol at  $-80^{\circ}\text{C}$  until further investigation (10).

### Metallic green sheen

EMB (Eosin Methylene Blue) agar medium is a selective and differential culture medium used to isolate facultative anaerobic bacteria such as *E. coli* (11). To determine the green sheen, *E. coli* colonies are cultivated as streak plate on EMB agar medium, then are kept in an incubator at  $37^{\circ}\text{C}$  for 24 hours. Lactose-fermenting Gram-negative bacteria acidify the environment and under acidic conditions the dyes produce a dark purple complex, which is usually accompanied by a metallic green sheen. metallic green sheen is an indicator of intense fermentation of lactose and/or sucrose. A smaller amount of acid production resulting from slow fermentation develops a brown-pink coloration of growth. Colonies of non-lactose fermenters appear as clear or pink (12).

### Ortho-nitrophenyl- $\beta$ -D-galactopyranoside test

Lactose permease and beta-galactosidase enzymes are needed to break down lactose.  $\beta$ -galactosidase permease exists in the cytoplasmic membrane in which transports lactose into the cell, but cytoplasmic beta-galactosidase hydrolyzes lactose into glucose and galactose. There are strains of *E. coli* that ferment

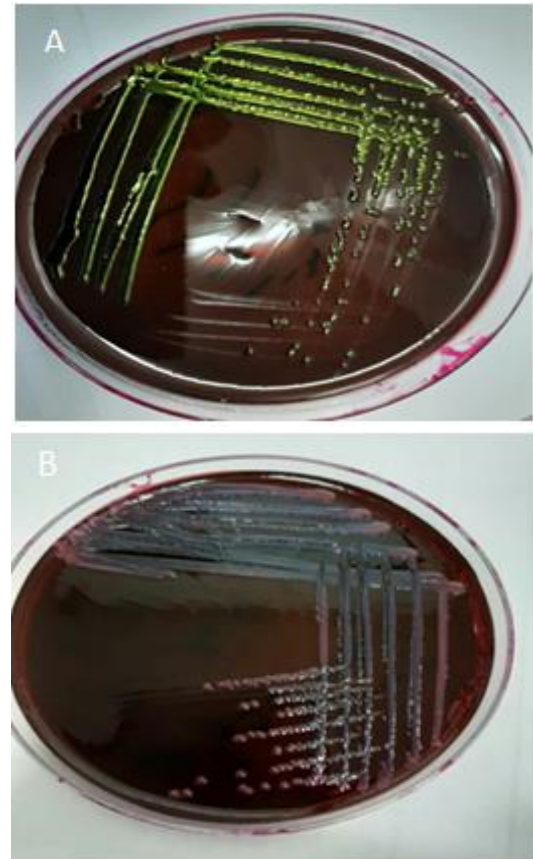
lactose with delay. Some bacteria lack  $\beta$ -galactoside permease enzyme but have  $\beta$ -galactosidase (13). In these strains, there is an insertion sequence between the genes of beta-galactosidase and lactose permease, which may cause a decrease in the expression of lactose permease. To identify delayed lactose fermenting bacteria, the ONPG test is used (14). ONPG is structurally similar to lactose and colorless and enters the cell more than lactose. Inside the cell, ONPG is cleaved by  $\beta$ -galactosidase to o-nitrophenol, which has a yellow color. To perform the test, one ONPG disc is added to a sterile test tube containing 0.1 ml of sterile 0.85% w/v sodium chloride solution (physiological saline). Emulsify the desired colony in the tube containing the disc. Incubate the tube at 37-35 degrees Celsius. Observe the tube at 1- to 6 hour intervals to detect active lactose fermenters. Incubate the tubes for 24 hours to detect late lactose fermenters. If beta-galactosidase is positive, the fluid and disc will turn yellow (15).

### Hemolysis on blood agar

Certain bacteria produce extracellular hemolysin, which hemolyzes red blood cells and releases the hemoglobin contained in them. three types hemolysis create on blood agar medium. Alpha hemolysis creates a green halo around the colony. The hemolysis is produced by oxidation of oxyhemoglobin ( $\text{Fe}^{+2}$ ) to non-oxygen-binding met-hemoglobin ( $\text{Fe}^{+3}$ ) through hydrogen peroxide (16). Beta hemolysis, the complete destruction of red blood cells, shows a clear area around the colony. Gamma hemolysis indicates the absence of hemolysis around the colony. Blood agar culture medium is usually prepared from trypticase soy agar or Columbia agar base with 5% sheep blood. Pure colonies were inoculated using streak plate method on blood agar and then, were kept at 37°C for 24 hours.

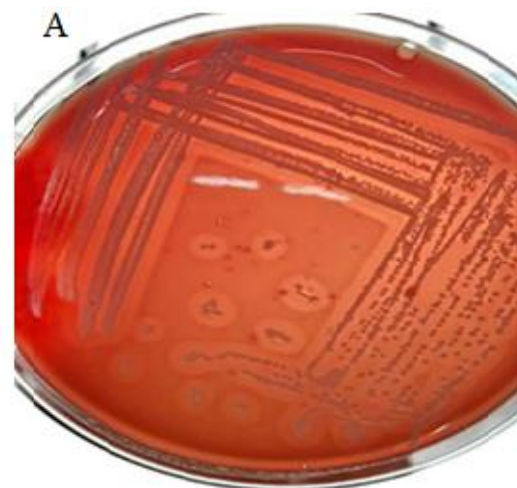
### Results

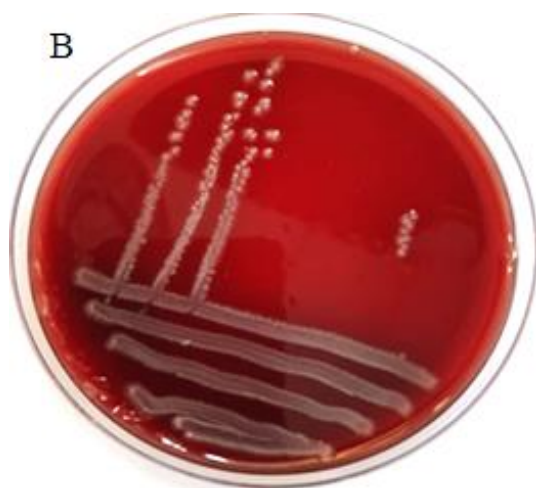
In urine culture, 147 individuals had significant urinary tract infections caused by Gram-negative bacteria. The average age of patients was 58.2 years. The prevalence of urinary tract infections caused by *E. coli* strains was 100 (68.02%). Out of 100 *Escherichia coli* isolates, 80% showed a metallic green sheen but 20% did not have a green gloss (Figure 1).



**Figure 1.** A. Metallic green sheen, B. No green sheen.

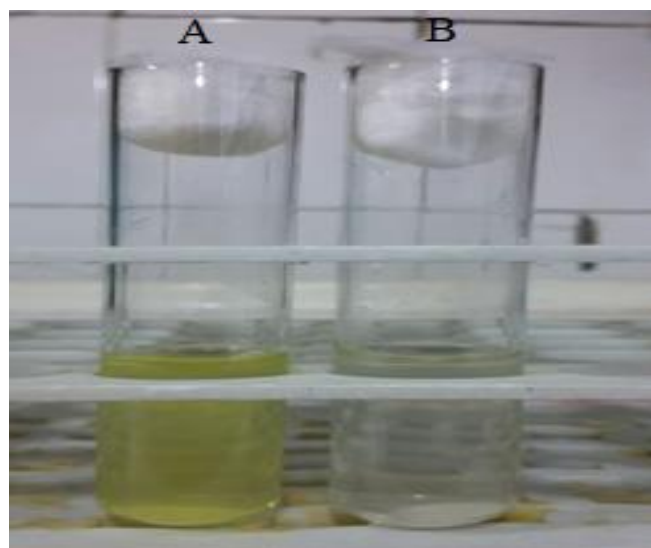
The characteristic of beta hemolysis from 100 tested *Escherichia coli* isolates on Blood agar medium showed that only one (1%) of them had beta hemolysis and the rest (99%) did not have hemolysis (Figure 2).





**Figure 2.** A. Beta hemolysis, B. Gamma hemolysis.

The ONPG test of all *E. coli* strains showed that 100% of the strains had positive reaction (Figure 3).



**Figure 3.** A. Positive ONPG, B. Negative ONPG

## Discussion

*Escherichia coli* is the most prevalent bacterial agent that causes urinary tract infections (UTIs), mainly in women. In our research, the uropathogenic *E. coli* was responsible for 68.02% of urinary tract infections. In a study by Michael W. Dunne and colleagues, it was shown that *E. coli* caused 75.6% of UTIs (17). In another study, was determined that 60.5% of UTI was caused by *E. coli* (18). The results of these studies show that UTIs caused by *E. coli* have almost the same prevalence. In the current research, 80% of uropathogenic *E. coli* showed metallic green sheen in

an EMB agar medium. In the study conducted by Jain et al., all strains of *E. coli* separated from the urine had a metallic green sheen (19). The presence of metallic green sheen has been reported in various studies, but the prevalence of green sheen caused by uropathogenic *Escherichia coli* has not been determined definitively. In our study, only one percent of uropathogenic *E. coli* showed beta hemolysis, but the rest did not cause hemolysis. In the study carried out by Sayan Bhattacharyya, only 10% of uropathogenic *E. coli* were hemolytic (20). In the study conducted by Sonal Jindal, 34% of uropathogenic *E. coli* produced hemolysin and 66% of the remaining isolates did not show hemolysis (21). Noha Mahmoud showed that 15 (30%) uropathogenic *E. coli* isolates were  $\beta$ -hemolytic while 35 isolates (70%) were non-hemolytic (22). The results of these studies show that the production of hemolysin in uropathogenic *E. coli* is different in different regions, which is a common occurrence due to mutations in the gene. Based on our results, 100% of uropathogenic *E. coli* isolates were ONPG positive. In a study by C. LONGHI and et al., 70.9% of uropathogenic *E. coli* presented ONPG positive (23). In another study conducted by Mahshid Deldar Abad Paskeh, all 91 isolates of uropathogenic *E. coli* were ONPG positive (24). The results of these investigations are almost consistent with the present study.

## Conclusions

In conclusion, all uropathogenic *E. coli* don't produce metallic green sheen, so other biochemical features must be considered. A small percentage of uropathogenic *E. coli* cause beta hemolysis, so this test can be used to identify *E. coli* in the laboratory. Almost all uropathogenic *E. coli* are ONPG positive, so this test is not mandatory.

## Author contribution

**MA** designed research, analyzed the data, wrote the manuscript, and performed the interpretation of the results; **RM** wrote the manuscript and collected the specimens; **HKGh** performed the practical experiments and collected the samples.; All authors read and approved the final manuscript.

## Acknowledgments

The authors express their gratitude and appreciation to all people who contributed to this manuscript.

### Conflict of interest

The authors declare that there is no conflict of interest in this manuscript.

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## General health and psychological defense mechanisms of front-line healthcare workers during COVID-19 pandemic in Iran

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### Abstract

**Introduction:** Since December 2019, people throughout the world has been encountering COVID-19 pandemic different populations, especially health care workers have been facing psychological challenges such as high amount of anxiety. In this study, we assessed impacts of COVID-19 pandemic on first-line health care workers psychological well-being in the north of Iran.

**Materials and Methods:** This cross-sectional analytical study was conducted in 4 hot-spot major hospitals of Rasht, during first month of the outbreak in Iran. Physicians and nurses were divided into two categories as low and high risk groups based on their level of exposure to the virus. Standard general health questionnaire (GHQ-28) and defense style questionnaires (DSQ-40) were also used.

**Results:** The mean age of participants was  $30.2 \pm 6.6$ . Of total 199 subjects, 73.4% were females and 26.6% were males. 63.23% of participants were nurses and 36.86% were physicians. Base on the mental health questionnaire, 60.8% and 10.55% of participants experienced mild to moderate psychological stress. There were no significant differences between high risk and low risk groups. Females those who had lost a family member due to COVID-19 and nurses with less developed defense mechanisms were found to be associated with psychological morbidity ( $P < 0.001$ ). Also, in terms of psychological defense mechanisms, nurses working in high risk wards showed more developed mechanisms than their peers.

**Conclusion:** Majority of physicians and nurses working during COVID-19 pandemic were experiencing levels of psychological distress, mostly in the form of anxiety, sleep dysfunction and depression. Females, individuals who had lost a family member due to the COVID-19 infection and those with less developed psychological defense mechanisms were at higher risk of developing mental morbidity.

**Keywords:** COVID-19, Mental health, Defense mechanisms, Health-care workers, GHQ-28, DSQ-40

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Received: 2022.6.13, Accepted: 2022.12.19



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## Introduction

Since December 2019, world has been experiencing a new infectious disease called COVID-19 (1). This highly contagious virus is mostly transmitted via aerosols of the infected patients through direct contact. COVID-19 symptoms can range from unspecific presentations such as fever, chill, myalgia, headache and cough to severe involvement of the lungs manifesting as acute respiratory distress syndrome (ARDS) and even death (1, 2). According to the published guidelines for the diagnosis and treatment of this virulent and fatal disease, COVID-19 patients are classified into mild, moderate, severe and critical groups based on clinical signs and symptoms, laboratory findings, pulmonary involvement and the need for supportive ventilation and critical care (3, 4). Since the onset of COVID-19 pandemic, there have been nearly 641,915,931 confirmed cases of COVID-19, including 6,622,760 deaths worldwide reported to World Health Organization (WHO) (5). In such epidemics, people undergo a great deal of stress levels. Available information about previous epidemics like SARS (Acute Respiratory Syndrome) in 2003 and H1N1 influenza in 2009 indicate that during epidemics, societies suffered from considerable amount of anxiety and psychological stress which led to serious psychological complications for a lot of individuals (6-8). Medical and paramedical staffs are usually at increased risk of anxiety disorders due to working in a stressful environment, facing unpredictable changes in daily work, unrealistic expectations of patients and excessive exposure to mortality issues (9, 10). First-line health care workers are health those who play a critical role in providing care to the infected patients (10). Similar to SARS and Influenza outbreaks, health care workers who are exposed to COVID-19 disease and unparalleled burden of the disease can greatly suffer from increased stress levels, and experience a higher rate of psychological morbidities (6, 11, 12). A vast body of literature have implied a high prevalence of psychological morbidity among healthcare workers which is mediated by a variety of biopsychosocial factors. Under stressful conditions, individuals use different psychological defense mechanisms which are unconscious psychological processes to prevent anxiety. Based on psychoanalytic theories, defensive mechanisms are unconscious intrapsychic mental

processes that get activated in stressful and threatening situations in order to reduce the unpleasant and annoying signals from consciousness (13, 14). These unconscious mechanisms are psychological strategies that are used to defend against irresistible and unbearable shocks, and are divided into 4 general categories: Pathological category (including psychotic thoughts and projective hallucination), immature category (fantasy, projection, passive aggressive, regression), neurotic (justification, reaction formation, decompensation, displacement, repression) and mature category (humor, sublimation, suppression, altruism, asceticism) (14, 15) which in overall, they are generally summarized in three categories that are the most used defense mechanisms by general population named as mature, immature and neurotic mechanisms (16).

Neurotic and immature styles are kinds of inefficient and non-adaptive exposure mechanisms. On the other hand, mature defensive mechanisms are considered as efficient, normal and adaptive methods (17). Therefore, considering the great negative impact of COVID-19 pandemic on healthcare workers facing this serious challenge, we aimed to assess COVID-19 psychological effects and defense mechanisms of frontline physicians and nurses in 4 hot-spot teaching hospitals in Rasht, Guilan, during first months of outbreak in Iran.

## Materials and Methods

In this comparative cross-sectional study, the study population consisted of physicians and nurses working in 4 COVID-19 hotspot teaching hospitals in Rasht during in April 2020.

The study population were divided into 2 categories as group A and group B. Group A consisted of cases who are directly exposed to COVID-19 patients i.e. physicians and nurses working in high-risk sections such as emergency departments, ICU, respiratory isolation, acute care units and also predetermined wards for admitting COVID-19 patients. Group B included other nurses and doctors who were working in wards that were not in direct contact with COVID-19 patients such as elective patients. Subjects were randomly selected in order to determine their mental health and defense mechanisms. Sampling method was performed based on the total front-line population in 4



mentioned hospital (physicians and nurses) and their ratio with respect to each other.

Present study was approved by Guilan University of medical sciences ethics committee with the code number IR.GUMS.REC.1399.183, and was conducted according to the 2013 guidelines of Helsinki Declaration. A brief explanation about goals of the study and after obtaining informed consent, questionnaires were given to the participants and were filled in person. The questionnaire had 3 parts. The first part included personal, social and occupational data of physicians and nurses such as age, sex, occupation, married status, number of children, education level, work experience, past psychological and psychiatric history and history of death of first-degree relatives due to COVID-19. In the second part, the General Health questionnaire (GHQ-28), which is a valid questionnaire examining mental health status was used. The third part of the questionnaire comprised the Defense Style questionnaire (DSQ-40) containing 40 items, which examined defense mechanisms of individuals.

The 28-item GHQ-28 Questionnaire is a self-report questionnaire which is set to screen four areas consisting of mental symptoms, anxiety, depression and social dysfunction. Each item in this questionnaire scores 0-3 on a Likert scale. The respondents are asked to mark how they have felt during the past 2 weeks. Each of four domains is scored from 0 to 21 and is divided to three groups base on symptoms severity; mild (0-9 score), moderate (10-15 score) and severe (16-21 score). The final score is divided into four groups from 0 to 84. People with score 0-21 experience minimum psychological distress and their health condition are very desirable. Those with scores between 22-42 experience mild psychological distress, however, their general health condition is acceptable. Individuals with 43-63 scores experience psychological distress moderately indicating that their psychological health is at risk. Finally, those who acquired 64-86 scores are described to experience severe psychological distress which means their general mental health is endangered. Farsi version of this questionnaire was previously validated by Molavi et al. which reported 86.5% sensitivity and 82% feature for 28-GHQ in Iran (18).

DSQ-40 comprises 40 questions in a 9 point Likert format and evaluates 20 defensive mechanisms (2 items for each) in three levels of immature, neurotic and mature styles. The Farsi version of questionnaire was validated and standardized by Heidari Nasab et al (19).

The inclusion criteria for high risk group was to be engaged with direct treatment and care of COVID-19 patients. That is why physicians and nurses who were on leave or had no role in the treatment of COVID-19 patients were omitted from the study. In low risk group, participants who had no direct contact with COVID-19 patients were recruited. Those who were unwilling to participate as well as incomplete questionnaires were excluded.

Data were entered to SPSS 21 software. Frequency, percentage and 95% confidence interval were used to determine mental health status and defense mechanisms. Nonparametric Mann-Whitney U test was used to compare mental health levels (the lowest level, mild, moderate and severe) in two groups. Kruskal-Wallis Test, Nonparametric Mann-Whitney test and CHI-Square test were used to compare defense mechanisms and psychological health in 2 groups. Also, ranking and multinomial regression models were used to determine factors associated with mental health status and defense mechanisms of subjects. Spearman's correlation coefficient and Kruskal-Wallis Test were also used to determine the relationship between mental health and psychological defense mechanisms in studied group. P value of less than 0.05 was considered significant.

## Results

In this study, 199 employed doctors and nurses were examined from four hospitals of Rasht ( Poursina, Razi, Alzahra, Dr Heshmat) in terms of psychological effects and defense mechanisms of COVID-19 disease in the north of Iran.

Among these 199 health workers (nurse 126 and doctor 73), 73.37% were women and most of them were in 25-30 age group. The mean age of participants was  $30.24 \pm 6.62$  years. 63.32% of cases were nurses and 36.68% were doctors. In terms of educational degree (regarding the great number of nurses) most of them had bachelor's degree (58.29%). Detailed information of

demographic data is shown in Table 1. Eight people stated that they had lost one of their first degree relatives due to COVID-19 disease. Of total 199 cases, 60 cases (30.15%) were working in low-risk sections

(group B) and 139 cases (69.85%) were working in high-risk wards (group A). According to the results, there was no statistical differences regarding baseline characteristics between 2 studied groups ( $P \geq 0.05$ ).

**Table 1.** Baseline demographic information of study participants and within group comparisons.

		N (%)	Low risk N (%)	High risk N (%)	P- Value
Sex	Female	146(73.37)	46(76.67)	100(71.94)	0.489
	Male	53(26.63)	14(23.33)	39(28.06)	
Age	≤ 25 years old	32(16.08)	14(23.33)	18(12.95)	0.073
	26-31 years old	105(52.76)	29(48.33)	76(54.68)	
	31-36 years old	27(13.57)	4(6.67)	23(16.55)	
	≥36 years old	35(17.59)	13(21.67)	22(15.83)	
	Mean (median) ± SD	30.24 (27.0) ± 6.62			
	Max, Min	(55.0, 22.0)			
Marital status	Single	107(53.77)	35(58.33)	72(51.80)	0.396
	Married	92(46.23)	25(41.67)	67(48.20)	
Number of children	Without child	154(77.39)	48(80.00)	106(76.26)	0.396
	One child and more	45(22.61)	12(20.00)	33(23.74)	
	Mean (median) ± SD	0.36 (0.0) ± 0.72			
	Max, Min	(3.0, 0.0)			
Education	Bachelor degree	116(58.29)	34(56.67)	82(58.99)	0.198
	Master degree	105.03 ( )	1(1.67)	9(6.47)	
	MD. General practitioner	64(32.16)	24(40.00)	40(28.78)	
	MD. Specialist	9(4.52)	1(1.67)	8(5.76)	
History of death in first-degree relatives due to COVID-19	Yes	8(4.02)	3(5.00)	5(3.60)	0.644
	No	191(95.98)	57( )	134(96.40)	
History of previous mental illness	Yes	8(4.02)	3(5.00)	5(3.60)	0.644
	No	191(95.98)	57(95.00)	134(96.40)	
Work experience	< 5 years	129(64.82)	40(66.67)	89(64.03)	0.721
	≥ 5 years	70(35.18)	20(33.33)	50(35.97)	

Regarding the results of GHQ-28 questionnaire (n = 199), Table 2 shows that the majority of physicians and nurses experienced mild (60.8%) and moderate (10.6%) psychological distress. In none of the samples, the level of mental health morbidity was severe.

**Table 2.** Frequency distribution of the studied samples according to different levels of general health based on GHQ-28 questionnaire (n = 199) .

		No.	Percentage	95% confidence interval	
				Up	Low
Mental health level	The lowest limit	57	28.64	22.70	35.20
	Mild	121	60.80	53.91	67.39
	Moderate	21	10.55	6.86	15.39

In examining the normality of the distribution of mental health scores based on Kolmogorov and Shapiro-Wilk test, the distribution of total scores and aspects of mental health did not follow the normal distribution ( $p = 0.05$ ). Hence, non-parametric Mann-Whitney Test and Kruskal Wallis Test were used to compare these

scores in the two groups and also based on individual and social variables. (Table 3) The highest score of general health disorder was in the dimension of anxiety and sleep disorder and the lowest was in the dimension of depressive symptoms.

**Table 3.** Evaluation of general health score normality in each area and total (n = 199).

Mental health	Kolmogorov-Smirnov Test			Shapiro-Wilk Test		
	Probability	df	P-Value	Probability	df	P-Value
Mental symptoms	0.099	199	0.000	0.983	199	0.014
Sleep dysfunction and anxiety	0.116	199	0.000	0.977	199	0.002
Social reaction aspect	0.141	199	0.000	0.946	199	0.000
Depression symptoms	0.171	199	0.000	0.892	199	0.000
Total score	0.092	199	0.00	0.972	199	0.000

In general, there was no statistically significant difference in the total score of mental health in nurses of low-risk and high-risk groups ( $P = 0.239$ ). Likewise, there was no statistically significant difference between the mental dimension score, the anxiety dimension and sleep disorder score, the social action score, the depressive symptom score and the total mental health score of the low risk and high risk doctors.

Table 4 compares the types of defense mechanisms of nurses and doctors in 2 groups. According to the information in this table, ( $p = 0.001$ ). The percentage of neurotic defense style in high risk group nurses was one-fourth of low risk group (10.9% vs. 40%). The percentage of the mature defense mechanism was approximately 20% higher in group A nurses than that of group B (70% vs. 54%) ( $P = 0.001$ ). In doctors' group, although doctors working in high risk wards were having more developed psychological defense mechanisms than low-risk group physicians, the difference was not statistically significant.

According to the results, the defense mechanism in 61.8% of the studied participants was mature. 24% of the subjects showed neurotic mechanism.

**Table 4.** Comparison of defense mechanisms styles in nurses and physicians working in COVID-19 and Non-COVID departments.

Nurses					
Defense Mechanisms	High Risk		Low Risk		P value
	%	No.	%	No.	
Mature	70.33	64	54.29	19	0.001
Immature	18.68	17	5.71	2	
Neurotic	10.99	10	40.00	14	
Physicians					
Defense Mechanisms	High Risk		Low Risk		P value
	%	No.	%	No.	
Mature	60.42	29	44.00	11	0.133
Immature	14.58	7	8.00	2	
Neurotic	25.00	12	48.00	12	

In multiple linear regression analysis, multiple linear regression by Backward method was used to

investigate the relationship between working in high-risk and low-risk work department with mental health.

After adjusting the variables (age, sex, marital status, number of children, education, work experience, defense mechanism and history of death in first-degree relatives due to this disease), there was no relationship between working in high risk or low risk group with mental health status. But, as Table 5 shows, a

significant relationship between mental health score with gender ( $p = 0.026$ ,  $B = 4.06$ ), defense mechanism style ( $p = 0.001$ ,  $B = 3.126$ ) and history of first degree relatives' death due to COVID-19 was found ( $p = 0.068$ ,  $B = -7.57$ ).

**Table 5.** Multiple linear regression model assessing the relationship between demographic variables and mental health.

	Unstandardized coefficients		p-Value	95% Confidence interval	
	Parameter estimation	Standard error		Minimum rate	Maximum rate
(constant)	43.610	8.745	.000	26.363	60.857
Sex	-4.060	1.811	.026	-7.631	-.489
History of death in first-degree relatives due to COVID-19	-7.570	4.119	.068	-15.693	-.489
Defense mechanism	3.126	.956	.001	1.241	5.012

## Discussion

Regarding similar past situations, it is predictable that this pandemic leads to a variety of psychological complications such as post-traumatic stress disorders (PTSD), acute anxiety dysfunction, depression and even suicide in both general population and healthcare workers. Individuals may experience different degrees of psychological reactions (20-23).

In this study, we evaluated the rate of psychological morbidities and types of psychological defense mechanisms of frontline healthcare workers working in COVID-19 pandemic in 4 major hot-spot teaching hospitals in the north of Iran. Studied cases were nurses and physicians divided into two groups of "low risk" and "high risk" considering their exposure rates to the COVID-19 patients. Most of present study cases (69.85%) were working in high-risk departments. In terms of demographic variables, majority of participants were women and were in the age range of 25-30 years, and 69.9% worked in COVID-19 wards. Similar to our study, earlier surveys investigating mental health of health care workers during recent pandemic indicated that most of their participants were

females and worked in COVID-19 wards. However, the mean age of their subjects were higher than ours and healthcare professionals who worked in COVID-19 wards were younger and more likely not in a relationship, in comparison with professionals working in other departments (24, 25). In present inquiry, no significant differences between the two groups of high risk and low risk staff regarding demographic information was found.

This multicenter study revealed that majority of healthcare workers suffered from low to medium levels of psychological distress which were mostly in the form of anxiety and sleep dysfunction. This finding supported the results of previous research evaluating the impact of COVID-19 and other viral outbreaks on healthcare professionals (24-28). In a review by De cock et al. it was confirmed that the psychological impact of COVID-19 pandemic on health care staff was noticeable with considerable levels of anxiety, insomnia and depression(29). In COVID-19 pandemic, health care workers faced with unprecedented challenges including fast decision making, heavy

workload, the pressure to successfully diagnose the suspected patients and act timely, fear of being a silent carrier and passing the disease to their family and friends, hospitalizations of their co-workers, increased pressure and stress when dealing with patients unwilling to cooperate with treatment and isolation, and lack of sources and hospital beds (30).

Regarding personal variables, the level of stress was higher in women and also in those who had lost one of their immediate family due to this disease. This finding is in accordance with previous studies that demonstrated a higher prevalence of psychological morbidities in women in both healthcare workers and general population (24, 31). Women are probably more vulnerable than men in developing depressive symptom, and it is well-known that social supports or supports from their partner can be considered as a protective factor against psychological issues. Furthermore, it is worth mentioning that respondents in most studies were predominantly women and this might have impacted the results (29).

Although it was expected that individuals working in high-risk departments experience more stress due to the exposure to a new unknown and extremely infectious disease with no certain cure, in present study people in both groups of low risk and high risk experienced the same level of stress and there was no significant difference between nurses and physicians in COVID-19 wards and Non-COVID departments. Similarly, Milenna et al showed that in their research 46 % of healthcare workers working in low risk departments and 48% of high risk section workers were suffering from moderate levels of mental distress during COVID-19 pandemic, and there was not found any differences between the two groups(25). On the contrary, other inquiries implied that healthcare staff who worked in COVID-19 wards were under more psychological pressure and distress than their peers working in non-COVID facilities(24). It is worth mentioning that during the time of research, city of Rasht was considered as one of the high-risk cities in Iran. Therefore, the cases in low-risk group were suffering from psychological stress just like the cases in high-risk group due some reasons such as the new and unknown feature of the disease, diversity in clinical symptoms based on personal variables, relatively long recovering period of this disease and also inability to

distinguish SARS-COV-2 carriers and not-infected elective. Another reason for the lack of significant difference in psychological morbidity between the high risk and low risk groups may be the use of different questionnaires in various studies.

In current study, nurses working in COVID-19 wards had more developed psychological defense mechanisms than nurses in non-COVID wards based on DSQ-40 questionnaire. However, this finding was not statistically significant in physicians group. The reason can be that those working in high-risk departments such as ICU and emergency rooms had more mature mechanisms when confronting different work challenges even before COVID-19 pandemic due to working in critical and stressful situations and facing unpredictable daily challenges and trainings. There is also the possibility that employed people in high-risk sections were hired in such sections due to their developed mechanisms. All of these items can lead to a better stress management and lower psychological morbidity during the pandemic. In multiple regression analyses, possible predisposing factors for the psychological morbidities observed in healthcare staff working during COVID-19 pandemic were found to be being female, loss of a family member due to the COVID-19 disease and having less developed psychological defense mechanisms.

### Limitation

The limitations of the study are the small sample size, not including staff who were infected and were on leave, and also the cross sectional design of the study.

### Conclusions

Present study revealed that majority of physicians and nurses working during COVID-19 pandemic were experiencing levels of psychological distress, mostly in the form of anxiety, sleep dysfunction and depression. Females, those who had lost a family member due to the COVID-19 infection and individuals with less developed psychological defense mechanisms were at higher risk of developing mental morbidity.

### Author contribution

**SMZZ**, introduction author/original researcher (25%); **EM** (10%) and **AV** assistant researcher

(10%), **SSh**, original researcher (10%), **PA** original researcher (10%), **MGr** methodologist/assistant researcher (10%); **NNR** original researcher/ discussion author (25%).

### Acknowledgments

The authors would like to acknowledge physicalthe Poursina Clinical and Research Development Unit Guilan University of Medical Science, Rasht, Iran for their support and contribution to this study.

### Conflict of interest

The authors have no conflicts of interest associated with the material presented in this paper.

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## Surveying medical interns' visual short-term memory and response inhibition function before and after a night shift, sleep quality and smoking habits in Rasht 2020: a cross-sectional study

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### Abstract

**Introduction:** Physicians whether during training years or working years are involved with the shift work system. Night shifts and the sleep deprivation that ensues have many adverse effects both physical and mental. Hence any decrease in doctors' mental capacities will potentially put his and his patients' health at risk, we decided to conduct a study to check medical interns' Visual Short-Term Memory (VSTM) and Response Inhibition Functions changes after a night shift compared to the day before.

**Materials and Methods:** In this study, 32 medical interns from the Guilan University of Medical Sciences were recruited by random sampling. Each participant completed a Pittsburgh Sleep Quality Index questionnaire and was asked about his/her smoking habit and prior night's sleep. Each examinee then was tested in the morning before and after the night shift for VSTM by forward Corsi Block Tapping Test (CBTT) and for Response Inhibition by Stroop Word/Color Test implemented in the PEBL software version 2beta6. The data were coded and analyzed in SPSS v21.

**Results:** There was no significant change in the intern's CBTT and Stroop Test results after a night shift and their VSTM and Response Inhibition Functions remained fairly intact. According to their PSQI results, 29 interns had poor sleep quality and only two had an acceptable PSQI score (5 or less).

**Conclusion:** We argued that the consistent results of the CBTT and the Stroop Color Test could be due to many causes from small sample size to overall lower function under chronic sleep deprivation.

**Keywords:** Night Shift, Intern, Visual Short-Term Memory, Response Inhibition, Smoking, Sleep Quality

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Received: 2022.11.15, Accepted: 2022.12.27





## Introduction

Since the Libby Zion Case and the issuing of “The Law of Libby Zion” based on Bell Commission's work, sleep deprivation (SD) due to night shifts and its toll on doctors' and patients' safety and their overall life satisfaction is of major regard for both doctors and health authorities. High serious and fatal errors are prevalent among sleep-deprived Interns and Residents after the regular night shifts which can easily lead to 36 or 48 hours of SD (1). A higher rate of self-injuries during invasive procedures combined with loose sensory-motor coordination comparable to considerable blood alcohol levels that had resulted in motor vehicle accidents during the commute to the hospital and home makes everyone in contact with a sleepy doctor reasonably anguished (2,3). Many scholars have studied different aspects of SD (acute and chronic) and its effect on different functions of the human brain in acute forms. Working memory and its proposed two subcategories Visual Short Term Memory and Verbal Short Term Memory are regarded as a unit that allows representations to be actively extended over time in the absence of sensory input, making such information available to more complex cognitive operations ranging from mental arithmetic to problem-solving, therefore we assume it as the main storage unit for the data gathered by history taking and physical examination before writing them down or putting an order since short term memory (STM) “must support memory for previously unencountered information, the storage of multiple tokens of the same type, and variable binding” (4-6). As the brain uses the same memory unit to analyze the data and to reference Long Term Memory content, any shortcoming in this capacity is potentially harmful to the efficacy and integrity of the service provided by a doctor or the material learned by an intern or a resident. The other interesting function that seems to keep a human on the perceived (or learned and exercised) right track by mitigating external influence on the decisions he makes is the response inhibition function, which we use to rethink our response to external stimuli right before acting it out a.k.a self-control. Executive function, the cognitive control of behavior, depends on the prefrontal cortex, which is highly developed in higher primates and especially humans. The diverse inputs and back projections to both cortical and subcortical structures

put the prefrontal cortex in a position to exert what is often called “top-down” control or cognitive control of behavior (7). This executive function is crucial to make the right decisions under pressure like when somebody is very sleepy or a doctor is handling a rude or inappropriate patient. Overall sleep quality of a medical student is important for him/her to retain learned material and conduct a healthy lifestyle for years to come (8,9). A chronic poor sleep pattern harms the hippocampus and memory system (10). Speaking of lifestyle; Smoking cigarettes is one of the most harmful risk factors for many health aspects, it is a treatable and preventable cause, but beforehand we need to have a clear assessment of the situation, physicians must be a living example of what they propagate if they believe in it. Due to the lack of study in this area among medical students in Guilan, we decided to conduct a study to evaluate the function of short-term visual memory and inhibit response before and after shift and sleep quality in the internships of educational hospitals in Rasht, Iran.

## Materials and Methods

### Participants

Conducted a cross-sectional analytical study among 32 interns in Poursina Hospital in Rasht during June and July of 2020. Sampling was done by asking available interns if they are interested in participating. The use of self-report questionnaires was limited by clarifying the questions and selecting options that have limited interpretation. Lack of control over variables such as sleep patterns and recreation of the subjects included in the study, which tried to reduce their effect by defining appropriate exclusion criteria. Fatigue and lack of cooperation of the interns after the watch and tightness of the intern program in the hospital were other problems of the project. The exclusion criteria were being on any long-term medication, already having sleeping problems that require using sleeping aids agents and not adherence to the complete study. We used a checklist of two questions regarding being a smoker and starting period of smoking regularly.

### Corsi Block Tapping Test (CBTT)

We conducted a session of testing visuospatial short-term working memory using PEBL (v2.6 portable)

software running on an iLife ZedAir2™ notebook with 14" screen and an ordinary wireless mouse.

Stroop Color and Word Test (SCWT): We used Corsi Block Tapping Test (forward) and Stroop Word Color Test to gather data about the examinee's VSTM and Response Inhibition Function.

### Pittsburgh Sleep Quality Index (PSQI)

We use 19-item self-rated questionnaire pittsburg sleep quality index. It assesses subjective sleep quality in the previous month. The total score ranges from 0 to 21, with higher scores indicating poorer sleep quality. The reliability and validity of the Persian version of the PSQI have been assessed previously in Iran. A total PSQI score > 5 indicates poor sleep quality Thus, those with a PSQI of less than five were considered good sleepers.

All the tests were conducted in a quiet room with an air conditioner and a suitable desk and chair to accommodate the examinee's height and eliminate intruding factors as much as possible. Interns were willing to be tested after the morning report and having their breakfast and we had to comply.

### Sample size

In determining the sample size based on Sarabadani et al.'s study with 95% confidence interval and 90% power, due to the inverse relationship between sleep quality and working memory in students (-0.52), we reached the number 32 as sample size.

### Statistical Analysis

The statistical analysis was performed using SPSS v21 software. Mean and standard deviation (95% confidence interval) were used to describe quantitative variables with normal distribution and median and mean range were used for quantitative variables with the abnormal distribution. Qualitative variables were also described based on number and percentage. The normal distribution of the study quantitative variables was measured using elongation and skewness values, histogram diagram, Q-Q plot diagram and Shapiro-Wilk test. To compare abnormal quantitative variables of visuospatial short-term working memory score and response inhibition score before and after internship shifts using nonparametric Wilcoxon equivalent.

## Results

From the total of 32 interns were entered the study, the results of one intern were excluded due to the exclusion criterion of "regular use of sleep aid agents". The mean age of 31 participants was  $25.42 \pm 0.720$  years with ages 24 to 27 years. Descriptive results which are shown in table 1, exhibited 20 (64.5%) interns were male and 11 (34.5%) interns were female. 14 (45.2%) were smokers with the majority beginning smoking from Physio path/Stager 6 (19.4%). More than half of the participants 16 (51.6%) had slept 4-6 hours during the last night and the duration of the night shift sleeping of 21 (67.7%) of them was 0-2 hours.

**Table 1.** Descriptive result of medical interns.

Age (year)	Mean $\pm$ SD
	25.42 $\pm$ 0.720
Sex	N (%)
Female	11 (35.5)
Male	20 (64.5)
Smoking, n (%)	
Yes	14 (45.2)
No	17 (54.8)
Beginning of smoking, n (%)	
high school	3 (9.7)
Science Basic	3 (9.7)
Stager/Physio path	6 (19.4)
Internship	2 (6.5)
Sleep duration last night (hour)	
2-4	3 (9.7)
4-6	16 (51.6)
> 6	12 (38.7)
Sleep duration night shift (hour)	
no sleep	5 (16.1)
0-2	21 (67.7)
2-4	4 (12.9)
4-6	1 (3.2)

Results of pre-shift and post-shift examinations regarding the visuospatial short-term working memory score and response inhibition score shows in table 2. The Wilcoxon signed rank test on the Corsi block-tapping test and Stroop color-word test exhibited no significant change before and after the night shift. The mean PSQI was  $9.0 \pm 2.49$  with poor sleep quality (PSQI > 5) only in 2 (6.5%) interns.

**Table 2.** The difference of visuospatial short-term working memory score according to CBTT and response inhibition score according to SCWT before and after the night shift in medical interns.

	Before shift Median (IQR)	After shift Median (IQR)	Negative Rank	Positive Rank	Ties	Z <sup>a</sup>	P
<b>Corsi block-tapping test</b>							
Block span	8 (6-8)	11 (9-11)	5	5	21	-0.105	0.917
Total score	88 (54-88)	6.5 (5.5-6.5)	6	14	11	-1.046	0.295
Correct trial	8 (6-8)	11 (10-12)	6	14	11	-1.454	0.145
Memory span	88 (60-96)	6.5 (6-7)	6	14	11	-1.599	0.110
<b>Stroop color-word test</b>							
MRTC	726 (674-812)	747 (654-779)	15	15	1	-0.113	0.910
MRTI	766 (709-824)	794 (725-886)	17	14	0	-0.549	0.583
MRTN	760 (689-812)	752 (677-837)	16	15	0	-0.245	0.806

CBTT: Corsi Block Tapping Test; SCWT: Stroop Color and Word Test; IQR: Inter Quartile Range; a Wilcoxon Signed Rank test. M: mean R: response T: time C: congruent I: incongruent N: neutral.

## Discussion

The consistency of CBTT and Stroop Word/Color Test among examined interns was contrary to our initial expectations. These results could be due to the small sample size. Conducting the test before and after a shift with the same equipment and in the same room suggests that there is little chance for a systematic error; as we assigned random available Interns to the study and sampling was by choosing available random samples.

The second possible explanation is that due to changes in health facilities priorities and more workload and responsibilities put on residents in the COVID-19 era, interns were not as engaged in the shift work and direct contact with the patients as before due to safety regulations and therefore didn't get exhausted.

The other interesting interpretation that we put forward is, by combining the results of these two tests with PSQI results we suggest that the overall and long-term poor sleep quality of the medical interns had put them in a steady low functional capacity that there was no room for reduction of VSTM span or Increase in Response Inhibition Errors and Response Times after one night of acute SD, meaning they could not manifest their best performance cause their night sleep was part of a vicious continuous cycle of poor sleep quality and wouldn't give them enough rest to retrieve their full functional capacity.

45.2% smoker prevalence is quite high for a sample of medical interns and it is highly skewed toward smokers. But regarding the pattern of increase in smokers ratio from 16.6% in 2004 to 23% in 2010<sup>1</sup> and no existing program to actively target this problem, probably the high ratio reported by this study is not far away from reality (11,12).

Combining the results of PSQI scores and the self-declared sleep hours during the night before shift night opens a window into the wrong habit of self-imposed chronic sleep deprivation and derangement in "Sleep Duration" and "Sleep Efficiency" components of sleep hygiene and the necessity of intervention. Limitation of sample size and time limit The availability of interns for review is one of the most important limitations in this study. Also, the impossibility of repeating the test several times and the safe presence in the hospital environment were other limitations of this study.

Focusing the study on surgical interns with the aim of homogenizing the results and better examining them deprived this study of having insight and judgment about the condition of interns in other areas (such as internal, cardiac, ENT, etc.). Insomnia is a part such as the interior having a significant impact on the performance of interns.

Also, reducing the burden of internships and the permanent presence of residents (especially first-year

residents) has been effective in reducing internship fatigue and not changing test results.

The publication of the results of the present study can provide a basis for comparing future studies in each of the areas of smoking or sleep quality with the comparison of the time of this study with the future or statistical samples different from the sample of this study.

Also, educational planners use these results or review the form and content of this study to make more informed decisions about training planning, changing the number of interns on duty and training items provided the day after the intern interns.

## Conclusions

Consistent results of CBTT and Stroop Color Test show that Acute Sleep Deprivation during a night shift among surveyed interns did not affect their VSTM and response inhibition and we suggest it may be the effect of chronic sleep deprivation or the changes due to COVID-19 pandemic caused it. Poor sleep quality and the high prevalence of cigarette smoking among interns need appropriate interference and more research.

## Author contribution

**ZR** and **AD** wrote and compiled this article. **AA** wrote and edited the manuscript comprehensively. All authors confirmed the final version of the paper.

## Acknowledgments

Special thanks to the Clinical Research Development Unit of Poursina Hospital, especially to Mrs. Sedigheh Samimian for her generous guidance and timeless efforts and proceeding.

## Ethical Considerations

The proposal of this study was approved by the Ethics Committee of Guilan University of Medical Sciences IR.GUMS.REC.1399.155.

## Conflict of interest

The authors declare that they have no conflict of interests.

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Original

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## Comparison of the effectiveness of emotion-oriented couple therapy and self-compassion-based therapy on anger rumination in women affected by infidelity

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### Abstract

This study aimed to compare the effectiveness of emotion-oriented couple therapy and self-compassion-based therapy on anger rumination in women affected by infidelity. The method of this quasi-experimental study was with a pretest-posttest design with follow-up. The study population included all couples involved in marital infidelity who referred to Iranmehr Counseling and Psychological Services Center in Rasht in 2020, from which 20 couples (40 people) were selected as the sample by available sampling method. For data collection, Sukhodolsky et al. (2001) anger rumination questionnaire was used and emotion-focused couple therapy and self-compassion therapy sessions were performed for 16 sessions of 4 hours (one treatment every two hours) every week. After three months of treatment sessions to measure the duration of treatment, couples also participated in a follow-up session. Data were analyzed using combined analysis of variance. The results showed that the difference between emotion-focused couple therapy and self-compassion-based therapy on anger rumination was statistically significant ( $F = 13.05$  and  $P = 0.001$ ) and the effectiveness of emotion-focused couple therapy on reducing anger rumination from treatment. It is based on more compassion.

**Keywords:** Emotion-oriented couple therapy, Self-compassion-based therapy, Anger rumination, Marital infidelity

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Received: 2022.11.15, Accepted: 2022.12.13



## Introduction

The family is the core of any society and the center for maintaining mental health. Mental health is the source of human emotions and the center of the most intimate interpersonal relationships and interactions. If there is a rift in the trust and sense of security of the family, it will cause injury to one or both couples. Extramarital affairs undermine the most fundamental component of a relationship, which is trust, and ultimately lead to divorce between couples. Marital infidelity is a crisis for couples and families. Marital infidelity has a significant prevalence in clinical and normal settings, which causes significant disturbances for the perpetrators and their spouses.

Accordingly, some research has addressed the dangers of the consequences of betrayal; For example, 30% of family homicides are committed by women who have been murdered by their husbands due to adultery and suspicion. On the other hand, 22% of family murders are related to the murder of men by their husbands, and in 40% of cases, women kill their husbands with the complicity of their lovers.

Various studies have been conducted on the types of injuries caused by adultery. The study found that couples involved in marital infidelity show consequences such as confusion, stress, anger, aggression and mistrust. Negative self-referential processing (including worry and rumination) is a mental quality about self and the future as one of the symptoms of depression that affects a person's ability to deal with life experiences and causes defects in information processing and cognitive biases. It can lead to undiagnosed disorders such as depression in people (1-3). Ruminant in various fields such as anger and self-criticism is a set of passive thoughts that have a repetitive aspect, focus on the causes of the results, prevent problem-solving, increase negative thoughts and increase negative emotions such as anger and stress (4).

Agent analyst approaches have shown that anger rumination consists of two components: first, thinking and visualizing an angry event, and second, a mental review of vengeful actions (5). Therefore, many interventions have been performed to reduce tensions and disorders in marital relationships, the most

important of which is emotion-oriented couple therapy. Emotion-oriented therapy is an experimental therapy that is strongly related to Balbi's (1969) theory through concepts such as focusing on how to deal with basic emotions, interacting with others based on these emotions, and constantly constructing one's emotions from repetitive emotional interactions (6).

Emotion-based couple therapy is a therapy with the origins of Balbi's theory of attachment, which combines the first and third forces of psychotherapy with the systems approach in the family. The use of adult attachment theory in this approach provides a coherent framework for understanding the nature of adult love. The main purpose of this approach is to help couples identify and express each other's needs, main tendencies, and attachment concerns, thus reducing the insecurities of the couple's attachment and fostering a secure attachment between them. This approach emphasizes the role of each couple's emotional experiences and its systematic approach emphasizes the role of interactive cycles in maintaining the problem and integrating the interpersonal and interpersonal world (7).

Studies show that this treatment is effective in reducing the loneliness of women affected by extramarital affairs (8); Improving marital satisfaction and reducing the tendency to extramarital affairs of women affected by domestic violence (9) and reducing sexual violence (10). Wiebe, Johnson, et al. (2017) (11) showed that emotion-focused couple therapy affected increased satisfaction with the emotional relationship and reduced avoidance of attachment and reduced anxiety during the treatment period and 2-year follow-up period. Wiebe, Elliott, Johnson (2019) showed that emotion-focused couple therapy was effective in reducing the avoidance of attachment and sexual satisfaction of couples with a 2-year follow-up period (12).

Another treatment that examines the effect of marital infidelity is self-compassion therapy (13). Self-compassion is about being in touch with your suffering instead of avoiding or cutting it off, creating a desire to alleviate that suffering and being kind to yourself. Self-sufficiency also includes unrealistic judgments about pain, inadequacy, and failure, because personal experience is part of one's larger experiences (13).

Compassion is the ability to transform understanding, acceptance, and love into an inner form. Many people can show compassion to others, but they have trouble spreading the same compassion to themselves. Studies determined that women show less compassion than men, and this may be because women often play a socially caring role (14). Yaarmohammadi et al. showed that self-compassionate education has increased the level of marital intimacy and marital satisfaction (15). Another study showed that self-compassion training can be more effective in reducing marital conflicts in women affected by infidelity who want to improve relationships with their husbands than in forgiveness training (16).

According to what has been said, extramarital affairs are one of the main reasons for divorce and the breakdown of the marriage. Also, society will incur a lot of expenses every year to deal with the mentioned problems. Therefore, conducting the necessary studies to identify the determinants of extramarital affairs and provide solutions for the health of couples' relationships can provide evidence that relying on them and targeting it at the beginning eradicates some problems. Therefore, this study aimed to compare the effectiveness of emotion-oriented couple therapy and self-compassion-based therapy on the rumination of anger in women affected by infidelity.

## Materials and Methods

This study was a quasi-experimental study using a pretest-posttest design with follow-up which was approved by the ethics committee with the code number IR.GUMS.REC.1399.662. The statistical population of this study includes all women affected by infidelity who were referred to Iranmehr Counseling and Psychological Services Center in Rasht during 2020. Sample size with alpha 0.5, Power 0.8, and effect size 0.89. The statistical method of mixed analysis of variance was determined to be 40 pairs ( $n = 80$ ) and 20 pairs were randomly divided into two experimental groups (EFT and CFT groups). The sampling method was purposive.

After completing the Sukhodolsky et al. (2001) anger rumination questionnaire by 20 couples, emotion-focused couple therapy sessions and self-compassion-based therapy for 16 sessions (each treatment one two-

hour session separately for each couple) and weekly on groups The experiment was performed. Finally, after 16 treatment sessions, the post-test group was taken. After three months of treatment sessions, both groups participated in a follow-up session to assess the duration of treatment.

The anger rumination questionnaire was used to collect data. This questionnaire was developed by Sakhodolovsky et al. (2001) and measures the tendency to think about existing anger-provoking situations and recall periods of anger in the past. This scale consists of 19 items and 4 components: 1: the thought of anger (after arguing with someone in my mind I constantly argue with him), 2: memories of anger (I think about the injustices done to me), 3: thoughts Revenge (after a conflict, I have a lot of fantasies about revenge), 4: Understanding the causes (I think about why people mistreat me). Each item is scored on a 5-point Likert scale from never (with a score of 1) to forever (with a score of 5). The creators of this questionnaire obtained its reliability by using Cronbach's alpha coefficient for anger post 0.86, revenge thoughts 0.72, anger memories 0.85 and understanding of causes 0.77. Also, Cronbach's alpha coefficient of the total score of the questionnaire was reported to be 0.93 (Sukhodolsky et al. 2001).

The package of emotion-focused couple therapy sessions in this study was taken from the book *Emotionally Focused Marital Therapy* by Sue Johnson (17). A brief description of emotion-focused couple therapy sessions is presented in Table 1.

The package of self-compassion therapy sessions in this study was taken from Paul Gilbert's book *Compassion-focused therapy* (18). A brief description of self-compassion therapy sessions is presented in Table 2.

In order to describe and analyze the information obtained from the research from descriptive statistics such as frequency, percentage, mean, standard deviation and coefficients of variation and also in the inferential statistics section to control and eliminate the effect of group differences in pre-test from composite or mixed analysis of variance Post hoc tests were used to compare the treatment methods. All these steps using



SPSS statistical software version 26 at a significant level 0.05 occurred.

**Table 1.** A summary of the emotion-focused couple therapy plan.

Sessions (steps and steps)	The content of meetings briefly
Evaluation and coherence	Familiarity, creating therapeutic alliances, examining the motivation for treatment
De-stressing and identifying the negative interaction cycle	Discovering problematic interactions and negative cycles, evaluating attachment injury issues and markers, accessing unrecognized emotions
Assure the injured partner that the injury and blow will not be repeated	Unlocking outstanding attachment experiences, accepting fundamentally unrecognized feelings about injury, Acceptance of the interaction cycle by the couple
Analysis and change of emotions	Access to vulnerabilities, hidden needs, fears and models, promote acceptance by a spouse - expand client dance
Link Reconstruction	The more emotionally involved the hurt partner becomes and the more sensitive the victim's pain becomes
Link Reconstruction	Expressing emotions, increasing identification of attachment needs, accepting emotions, deepening conflict with emotional experience
Deep emotional conflict	Rebuild interactions, discover new solutions to old problems, emotionally responsive partner of the traumatized species
Consolidation and integration	Clients' sincere involvement with their spouse, accepting new situations, creating a secure attachment and turning the relationship into a safe haven, creating a new narrative of the relationship

**Table 2.** Summary of self-compassion therapy training sessions.

Purpose of the meeting	Content	Change the desired behavior	Homework
Introduce and establish a therapeutic relationship, acquaint members with each other, state the rules of the meeting and provide definitions	Pre-test and introduction, explaining the logic of the sessions, defining compassion and the importance of compassion, the difference between a risk-focused mind and a compassionate mind	-	-
Conceptualizing emotion regulation systems and mindfulness techniques	Introducing various emotion regulation systems, teaching techniques (physical examination and moment-to-moment attention), expressing the metaphor of vomiting, and performing the technique of soothing breathing.	Ability to be present at the moment and recognize different emotional states when performing the technique	Practice a soothing role

Explain the concept of self-criticism, its types and functions and introduce the illustration technique	Identify self-criticism, articulate effects, self-criticism with tiger metaphor, empty chair technique and self-critical imagery	The ability to separate the critic himself from the main character	Self-Criticism Benefit Registration Form
Explain the concept of compassionate self-correction and compassionate identity	The difference between compassionate self-correction and self-criticism, the characteristics of the compassionate person, the compassionate self-illustration technique	Trying to gain a compassionate identity	Practice your compassion and your evaluation form
Emphasis on compassionate identity and understanding the concept of anger rumination	Paying attention to compassionate identity by emphasizing the characteristics of the compassionate person, conceptualizing anger rumination and its effects	Evaluate and monitor people's anger	Monitor your anger form
Focus on showing compassion to others and receiving compassion from them	Teach others to practice compassion and receive compassion from them by practicing compassionate chair	Recognize your inner fears of compassion and poison in overcoming them	Practice loving friend
Teaching techniques to cultivate a compassionate mind	Reconstruction of hard emotional memories with emphasis on adopting a compassionate identity, teaching compassionate letter writing techniques, practicing compassionate event recording	Cultivate a system of relief and build a compassionate inner relationship with oneself	Practice self-compassion with illustration, illustration registration form
Provide solutions and summaries	Overview, review of participants' opinions about the educational concepts of homework and the changes made in them, encouraging people to continue doing exercises, conducting post-tests	Motivate to apply the techniques in daily life	Daily form of recording compassion exercises

## Results

The age group of the subjects was 20 to 50 years old, of which the highest percentage, ie 60%, was in the age group of 20 to 30 years. The subjects were self-employed.

The demographic variables of the subjects are shown in Table 3. The results of Chi-square test showed that there is no statistically significant relationship between the frequency distribution of age group, level of

education and employment status of women in the two treatment groups EFT and CFT.

**Table 3.** Frequency of age, level of education and employment status of the subjects in both groups.

	Group	EFT		CFT		P value
Age	<30	1	63	7	36	P=0.282
		2	.2	.8	9	

	31-40	4	40	6	60	1	10	
						0	0	
	>40	4	36	7	63	1	10	
			.4	.7	.6	1	0	
<b>Educa tion</b>	Diplom a	3	30	7	70	1	10	
						0	0	
	Bachelo r	1	59	9	40	2	10	P=0. 312
		3	.1	.9	.9	2	0	
	Masters	4	50	4	50	8	10	
							0	
<b>Job</b>	Housew ife	5	33	1	66	1	10	
			.3	0	.7	5	0	
	self- employ ment	8	61	5	38	1	10	P=0. 26
			.5	.5	.5	3	0	
	Employ ee	7	58	5	41	1	10	
			.3	.7	.7	2	0	

Hypothesis H0 II (1-2): EFT treatment does not affect the rumination of the anger of women affected by infidelity.

Using one-way ANOVA with Repeated Measurements, the anger of women affected by infidelity in three time periods (before the intervention, after intervention and three months after intervention) in the EFT group was examined.

Therefore, the second H0 hypothesis (2-2) that CFT treatment does not affect the rumination of anger in women affected by infidelity is rejected. In other words, self-compassionate couple therapy has been effective in reducing women's anger and its rate has decreased from the pre-test session to the follow-up.

Hypothesis H1 II (3-2): There is a difference between emotion-focused couple therapy and self-compassion therapy based on anger chewing in women affected by infidelity.

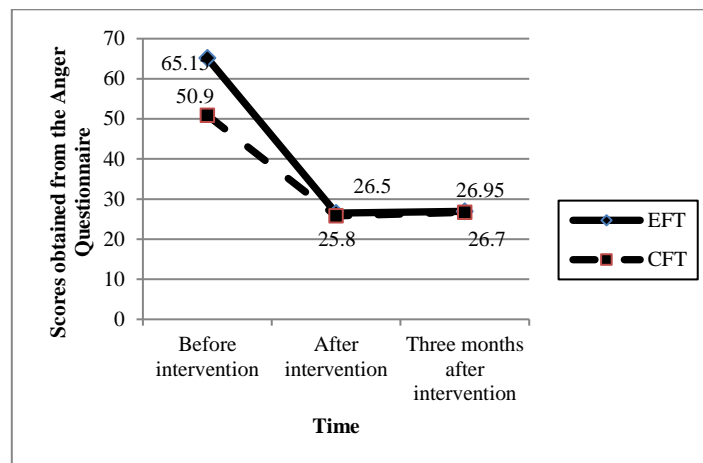
Using the combined analysis of variance test, the results obtained on the rumination of anger of women affected by infidelity in three time periods (before the intervention, after intervention and three months after intervention) in two treatment groups (EFT and CFT) were examined.

Thus, it was found that there is a statistically significant difference between emotion-focused couple therapy and self-compassion-based therapy on the dependent variable of anger rumination (Table 4) (Figure 1).

**Table 4.** Summary of the results of combined analysis of variance to determine the effectiveness of EFT and CFT on rumination of anger in two groups of women affected by infidelity.

Group	Before intervention	After intervention	Three months after the intervention	Intergroup statistical estimation
EFT	65.15± 7.4	26.5± 3.42	26.95± 3.42	F=13.05
CFT	50.9± 10.62	25.8± 4.73	26.7± 26.7	P=0.001

**Figure 1.** Comparison of changes in rumination of anger of women affected by infidelity in the studied periods between the two groups EFT and CFT.



### Discussion

This study aimed to compare the effectiveness of emotion-oriented couple therapy and self-compassion-based therapy on anger rumination in women affected by infidelity. The results of this study showed that both treatments were effective in reducing women's anger rumination but there was a statistically significant difference between the two methods and the effectiveness of emotion-focused couple therapy in reducing women's anger rumination was greater than compassion-based therapy.

On the effect of emotion-oriented couple therapy on reducing anger rumination with the present study by Biasley; Vazhappilly; Girard; Wiebe (8-12).

Explaining this finding, separation chaos is aroused when the security bond is lost - protest, clinging, despair, heartbreak. When attachment returns, the child provides clear clues about his or her needs. Without defense, it demands it. When the expression of attachment responds, the child trusts and accepts the mother's consolation - reassurance - the child is calm. The same process occurs in adult couples.

Emotion-oriented couple therapy identifies the attachment cycle and the basic needs of couples and reconstructs new situations and expresses underlying emotions and offers new ways to deal with emotional issues. During emotion-focused therapy sessions, new experiences occur, challenging the individual's active mental patterns that are reflections of past experiences, and thus causing couples to reconsider their expectations of each other. The result of this process is that spouses find new ways to regulate their emotions. On the other hand, validating emotions, however unpleasant, makes couples feel accepted and therefore relaxed; The therapist's reassurance and calmness have the advantage that couples are not overwhelmed while engaging in emotional experiences. The ability of therapy to properly reflect, accept, and clarify painful experiences enables couples to reorganize and reorganize their experiences. In general, couples' experiences will be easier to tolerate when the couple's experience is understood in a safe environment by the therapist. Research has confirmed that eliminating vicious emotional cycles and rebuilding emotional bonds in this treatment is the most important element in enhancing therapeutic potency. The goal of emotion-focused couple therapy is to increase the effectiveness of communication experiences and reconstruct the couple's interactions, and ultimately create a secure attachment and a sense of security. In this treatment, couples were taught to improve their communication skills and intimacy by identifying their own and their spouse's emotions, awareness, support, and availability, responding promptly to their spouse's emotional needs, and developing safe behaviors (6).

Explaining the effectiveness of compassion-based therapy in reducing anger rumination, it can be said that

this treatment is based on two main processes. The first process refers to all the empirical processes that involve increasing affection and kindness to oneself and others. The behavioral processes of this model also include conditioning, managing to strengthen one's freedom, and helping relationships. In this way, people are taught to observe their thoughts and feelings without judgment and to see them as simply mental events that come and go, instead of seeing them as part of themselves or a reflection of reality. This kind of attitude towards cognitions related to problems prevents the intensification of negative thoughts in the pattern of anger damage.

## Conclusions

The reason that emotion-focused couple therapy has a greater effect on reducing these women's anger chewing than their compassionate therapy may be that EFT expands experience and interaction, and the primary goal of treatment is to gain access to the underlying responses of each couple. It is their reprocessing. These are the answers that often lead to dry and harsh and limited positions of couples. In fact, in this treatment model, the person can have some control over what emotion, when and how to express it. Modify your emotional reactions. Also in emotion therapy, the therapist in all steps while supporting the injured partner and validating and acknowledging secondary emotions, an empathetic reflection of superficial emotions and ensuring that the damage is no longer repeated with timely and effective interventions. Helps the injured partner become more emotionally involved and gain direct experience of their partner's pain and become sensitive. Defined safe. Because he is both the source of the injured person's injury and the solution to his injuries.

Therefore, according to the roadmap that the emotion-oriented therapist has in hand and tries in all steps to meet the needs of the injured couple, such as answering his questions about infidelity and injury, reassuring the injured partner, and providing real evidence of current loyalty. Accepting responsibility for the betrayal by the person hurting and expressing sincere remorse, helping to acknowledge and process any feelings, and finally experiencing the hurt partner as someone available, accountable, and committed. This could be the reason

for the greater effectiveness of this approach in reducing women's rumination.

### Author contribution

**MM**, **SMR** and **HF** participated in the performance of the research and analytic tools. **ZT** and **MRT** participated in the research design and wrote the manuscript and edited and confirmed the final version. All authors reviewed and confirmed the final manuscript.

### Acknowledgments

This article is extracted from the doctoral thesis of clinical psychology with the ethics code IR.GUMS.REC.1399.662. The authors hereby acknowledge and thank all the participants in this research and all those who effectively cooperated in conducting this research.

### Conflict of interest

No potential conflict of interest was reported by the authors.

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## Is there evidence for the use of an herbal "Taryaqe Vabaii" for conditions similar to COVID-19?

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### Abstract

**Introduction:** Vaccination is currently the best option to protect people against COVID-19. On the other hand, some concerns, such as efficacy against new types of viruses, have made it reasonable to consider some additional options available, such as using the capacity of herbal medicines to strengthen the immune system. The present study aimed to investigate the scientific evidence on the possibility of using a herbal compound (anthrax), emphasized in Iranian medical sources, to help control and prevent COVID-19.

**Materials and Methods:** This article is a library retrospective study that is purposeful and with certain criteria by searching the authoritative books of Iranian medicine, including Al-Hawi and Al-Qanun, and some sources of common medications such as reference books of medicinal plants and internal scientific databases and internationally including SID, PubMed, and Google scholar with related keywords, without a time limit.

**Results:** So far, no clinical study has shown the effectiveness of the herbal compound of anthrax (including yellow aloe, saffron, and myrrh) in the paired pains of COVID-19, but there is ample scientific evidence that its components are useful in similar medical conditions. It has been reported to have immune-boosting, antioxidant, anti-inflammatory, and antimicrobial effects.

**Conclusion:** Conducting clinical trials can make the use of cholera opioids more reassuring to help control conditions such as the COVID-19 pandemic, especially in people at higher risk.

**Keywords:** COVID-19, Iranian medicine, Taryaqe Vabaii

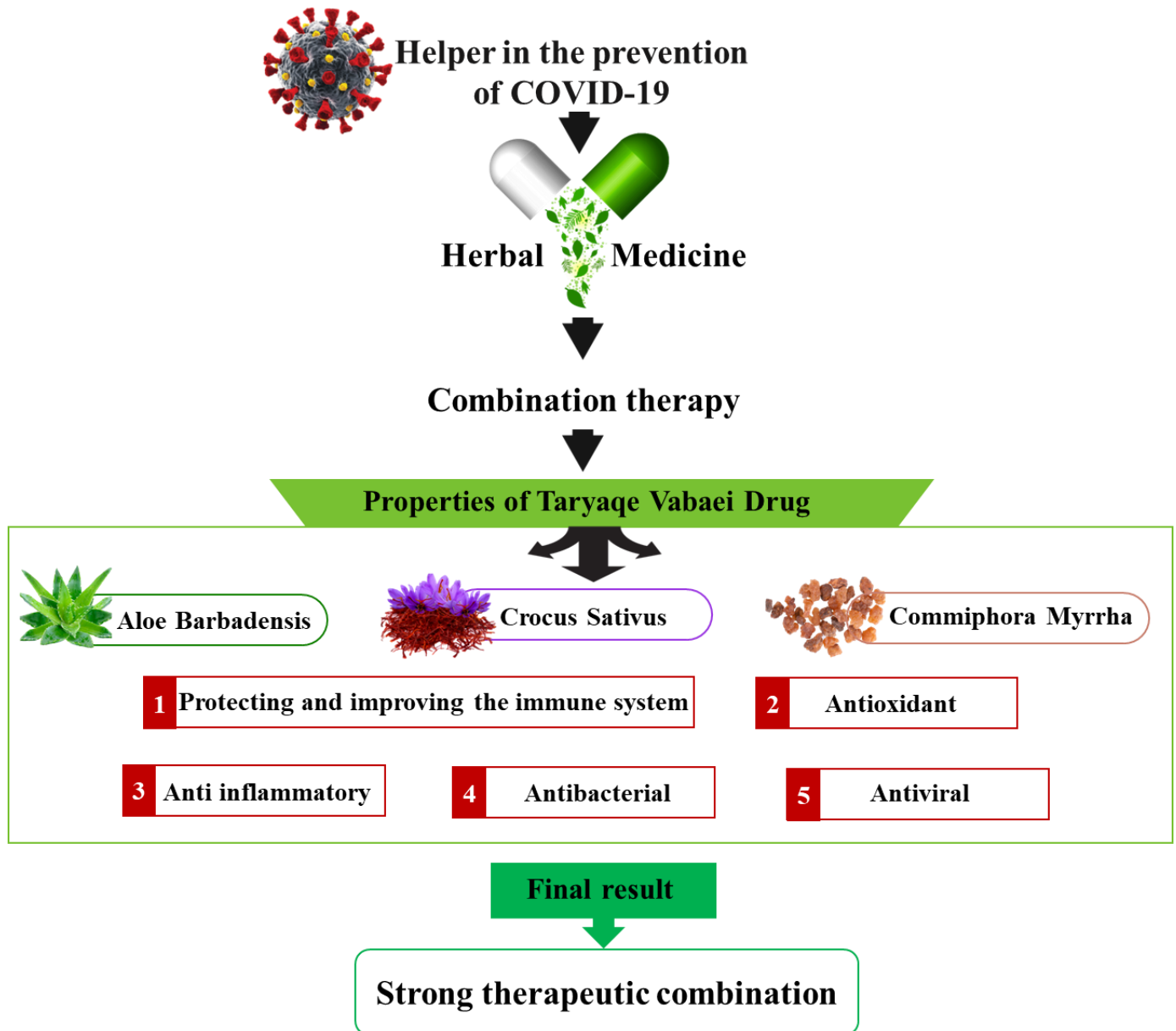
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Received: 2022.6.7, Accepted: 2022.12.13



## Graphical abstract





## Introduction

COVID-19 disease caused by the new coronavirus 2019 The latest coronavirus infectious disease has been discovered, which has led to an epidemic worldwide. The clinical course of COVID-19 varies from mild disease with nonspecific signs and symptoms of acute respiratory illness to severe respiratory pneumonia and septic shock (1).

The early symptoms of the SARS-CoV-2 virus are very similar to other viral infections of the respiratory tract (eg, influenza) and include lung disease, fever, muscle aches, and fatigue (2, 3). According to the World Health Organization, its mortality rate is 3.4% (4). To date, no definitive vaccine or successful antiviral drug has been clinically approved and available. Therefore, prevention and control of infection and observance of hygienic principles by the general public a priority (3, 5).

On the other hand, the development of existing vaccines against SARS-CoV-2 is good news, but there are concerns about safety, allergic reactions, free access, cost-effectiveness and safety on a large scale, unfair distribution, and efficacy against new varieties. And there is a possibility of a lethal mutation of the virus in the body in the future. What is more, according to recent laboratory and epidemiological studies, there is a growing list of mutations in the virus that increase its potential to transmit or help escape the immune response (6). These barriers have made it reasonable and necessary to consider some additional options available, such as using the capacity of traditional herbal medicines, especially natural immune-boosting products. The World Health Organization also supports cooperation with research institutes to select traditional medicine products that can be prescribed for the control and treatment of COVID-19 due to their clinical efficacy and safety (6, 7).

Therefore, because an effective treatment method for this emerging disease has not yet been discovered (2), there is a significant need for preventive policies and the use of traditional medicine experiences (2), especially in people at risk of death. And they are more inclined to it; There are people with diabetes and obesity (8, 9). For this purpose, the present study aimed to investigate the scientific evidence on the possibility

of using a herbal composition based on yellow aloe and emphasized the sources of traditional Iranian medicine which in some scientific articles is referred to as " Taryaqe Vabaii " (10) for Help is written to control this situation.

## Materials and Methods

This article is a review and library review that is purposeful and with certain criteria by searching the authoritative books of Iranian medicine, including; Al-Hawi Fi Al-Tib, Al-Qanun Fi Al-Tib, Elixir Azam, Akbari Medicine, and some sources of common medications such as reference book of medicinal plants and domestic and international scientific databases including SID PubMed, Google scholar, with the keywords of Iranian medicine, plague, diseases Plague, herbal compounds and pandemics of COVID-19, performed without time limit; Information related to the research is often extracted from relevant books and articles, and the content of the study is analyzed based on a specific pattern, and finally, by re-reading the contents.

It should be noted that data analysis has been done in the form of content analysis (Content Analysis). That is, the categories of notes are put together and a theme is extracted from each note, and the collection of these themes or themes that belonged to the notes of a category are put together to form a new note; Then, by summarizing these topics, the outlines were identified. To increase the validity of the study, expert professors were consulted and direct results were obtained from the data obtained from the study samples without opinion analysis. Observance of the principle of fidelity in the expression of the contents by mentioning the source for all the contents, including ethical points, has been considered.

## Results

In the textual studies of Iranian traditional medicine sources, a term called "plague weather" or "fever or plague diseases" has been mentioned, which is largely due to the conditions created in corona-like epidemics (such as influenza and its new strains such as COVID-19) is compatible. Because the term (plague air) means the spread of pollution and infection through the air and is generally used to describe the conditions in which the

air of a geographical area is out of its moderation (temperament) for some reason; In such a way that in its nature and quality, a state of species corruption and infectiousness appears and its consequence manifests itself in the form of a high incidence of diseases with unpleasant and unpleasant complications at the same time among the population of that region. In these texts, the occurrence of such diseases and the pervasive unpleasant complications that result from a single cause such as bad weather is also referred to as "diseases" or "uninvited and migratory diseases" (11).

These sources, while explaining how this condition occurs and how to diagnose it, as well as detail its general symptoms such as fever, respiratory symptoms, lung involvement, and sometimes other organs along with climate and environmental changes (11-13), for prevention and control These conditions, as well as strengthening the body's basic and defensive forces, include recommendations and instructions; 1) Modifying the air of the residential environment, with measures such as daily cleaning of the residential environment, disinfection of home surfaces with cold and dry nature materials such as vinegar and its combination products such as vinegar and halite (Kundel gum or Ferula Foetida), creating proper ventilation with measures Such as frequent smoking (Fumigation) of aromatic plants or their gums in residential environments such as; Pomegranate peel, turmeric, frankincense, halite, camphor and aromatherapy with aromatic agents such as frequent watering at home. 2) Improving nutrition; With measures such as avoiding overeating, reducing the volume and amount of food consumed, using fast-digesting and soft or light foods, tending to consume food to sour taste with cold and dry factors such as vinegar, juice, lemon, orange juice, Tamarhandi, pomegranate and plum juice and the use of beverages such as peppermint and jalab (heated mixture of rose and sugar), use of foods with antioxidant properties (antioxidants) such as onions and garlic. 3) Avoid strenuous work and physical activity Heavy, which leads to weakness of physical strength. 4) Avoid oversleeping. 5) Cleansing impurities and excess body fluids (body fluids) depending on the situation with methods such as diarrhea, urine, feces, and the use of laxatives. And 6) finally, strengthening the heart and brain and avoiding any unnecessary fears and worries;

Today, scientific evidence shows the effects of modulating and strengthening the body's defense system if these recommendations are used correctly (2, 11).

But in addition to these preventive recommendations, including herbal combinations, which are emphasized by the elders of this medical school such as Razi and Ibn Sina, their use has been mentioned as a way to get rid of such conditions; the Use of a herbal composition based on yellow aloe; Aloe is yellow, myrrh and saffron. "Razi" (925-854 AD) was one of the most important medieval medical figures in favor of experimental medicine, in his encyclopedia called "Al-Hawi fi al-Tib" (14) - quoted by Rufus (Greek physician) in this regard He says: I have not seen anyone use this medicine in cholera unless they survived. And that medicine is a combination based on two units of yellow aloe and one unit of mecca and saffron, which should be powdered and a small amount of it should be consumed every day (13). Ibn Sina (1037-980 AD) also mentions this as one of the most important thinkers and scientists of all later periods in his book "Law in Medicine" (14); Among the beneficial compounds that help get rid of and safe from plague or infectious epidemics; Use a combination of aloe vera (two units), myrrh and saffron (one unit each) at a rate of about one dirham (3.5 grams) per day. (12).

Ibn Rushd (1826-1198 AD) also considered the use of this compound in the book "Alcohols in Medicine" useful for the conditions of the plague and its consumption, especially at the beginning of this type of infectious epidemic, makes a person safe. Knows the effects of cholera (15, 16).

According to the scholars of Iranian medicine such as Ibn Sina, a patience has a warm and dry nature and has general properties such as; Absorption power, drying of excess body fluids, is useful in poor quality wounds, and slow healing. He introduces the consumption of about 5 grams of it with hot water twice a day, but with benefits, as an effective laxative and evaluates its effect on cleansing the stomach and digestion (18). Razi, quoting previous physicians such as Disqorides, Galen, Ibn Masouyeh, Hanin Ibn Ishaq, etc., in addition to the mentioned cases, considered yellow patience useful in various inflammations and ailments and considered it as the protector and protector of the body and one of

the best Medications for stomach upsets (19). Hakim Gilani also considers the consumption of food, sprinkling on the stand, and eating (smoke) of yellow aloe in great conditions to have great properties (20).

Ibn Sina Murr has a warm and dry nature and has general properties such as; Openness in evaluating the win-win analysis of all types of winds and at the same time the property of receiving, linting, preventing the infectivity of materials, and eliminating the infection of wounds and also preparing the materials (surplus and waste) for expulsion from the body. Smoke introduces it as an air modifier and highly drying agent and introduces myrrh as one of the prominent combination drugs due to its many benefits. He found it useful for respiratory ailments such as chronic whooping cough and shortness of breath, as well as a loose stomach and bloating (18). Razi mentions the same properties in his encyclopedia, quoting former physicians (19).

Finally, Ibn Sina saffron has a warm and dry nature and has general properties such as; Astringent, which knows the winning analysis and preparation of materials (excess and waste) for excretion from the

body. It is also described as invigorating, administering, and strengthening the heart, respiratory system, stomach, liver, and spleen (21). In addition to the above, Razi is also considered a food digester, appetite suppressant, sexual stimulant, respiratory facilitator, and an excellent booster for the respiratory system (22).

It is noteworthy that according to the sources of Iranian medicine, the use of the above-mentioned combination is not allowed in any situation and its use is recommended, especially in cold weather conditions or in people with a predominance of cold temperament. Therefore, in hot weather or hot weather, its consumption should be done with caution. And in such cases, it is better to use a minimum amount, ie half a derm or half a pound (about two grams) or its occasional consumption, and of course with rose or a potion with honey or sugar to reduce its possible side effects (20, 23).

The compositions and main effects of the Taryaqe Vabaii in Iranian traditional medicine and modern medicine studies are briefly mentioned in table 1 and 2.

**Table 1.** The nature and therapeutic effects of the components of "Taryaqe Vabaii" in Iranian traditional medicine.

Elements	Nature	Properties
<b>Aloe barbadensis</b>	Warm and dry	Astringent, desiccant of excess body fluids, useful in poor-quality and slow-healing wounds, all kinds of abscesses and swellings, and conditions of infectious epidemics transmitted through the air, laxative.
<b>Crocus sativus</b>	Warm and dry	Astringent, digestive and preparing substances for elimination from the body, invigorating, regulating, strengthening the heart, respiratory system, stomach, liver and spleen, digesting food, reducing appetite, sexual stimulant, facilitating breathing and an excellent tonic for the system breathing
<b>Commiphora myrrha</b>	Warm and dry	Opener and opener of ducts and vessels, dispels all kinds of wind, astringent, lint remover, prevents infection of materials and removes infection of wounds, prepares materials for elimination from the body, improves air and is extremely drying, useful in respiratory ailments such as Chronic wet cough and shortness of breath, as well as loose and weak stomach and flatulence

**Table 2.** Components and major medical effects of " Taryaqe Vabaii " in modern medicine studies.

Elements	Compounds	Properties
<b>Aloe barbadensis</b>	Anthracene derivatives, glycosyls such as aloin, hydroxyanthraquinones such as alo-amudin, alkyl chromones including allorsin, flavonoids, saponins, cinnamic acid, essential oil	Anti-influenza, antibacterial, immune-enhancing and wound-healing functions, anti-inflammatory and pain-relieving, antioxidant and increasing T lymphocytes, anti-cancer effects, laxative or laxative effect
<b>Crocus sativus</b>	Apocarotenoid glycosides, especially crocin, picrocrocin, volatile oil, containing safranal and	Anti-virus, antioxidant, bronchodilator, anti-inflammatory, anti-depressant, modulating and

	picrocrocin decomposition products, carotenoids and fixed oil and starch	strengthening the function of the immune system, heart and blood vessel tonic, anti-cough, pain-reliever, reducing fat and blood sugar, anti-coagulant, inhibition of cell proliferation and sedative
<b>Commiphora myrrha</b>	Volatile oil, which mainly includes sesquiterpenes, triterpenes and mucilages	Antimicrobial, astringent, anti-flatulent, expectorant, anti-secretion, antiseptic and wound healing, anti-hyperglycemia, antioxidant, liver protector, pain reliever and anti-inflammatory, anti-tumor and anti-coagulant.

## Discussion

COVID-19 is the latest coronavirus infectious disease to be discovered, leading to epidemics worldwide. The clinical course of COVID-19 varies from mild disease with nonspecific signs and symptoms of acute respiratory illness to severe respiratory pneumonia and septic shock. It can be transmitted by air (mainly) and so on. The pathogenesis and clinical features of COVID-19 are similar to the clinical manifestations of epidemic fever (1). In the sources of traditional Iranian medicine, it is referred to as the "disease of cholera" (11).

In these sources, various herbal medicines have been described for these conditions by the great scholars of Iranian medicine, especially "Razi and Ibn Sina" under the title of epidemics. As these two prominent scientists of traditional Iranian medicine in the period of Islamic civilization (3-4th century AH) (14), while describing the conditions of airborne epidemics under the title of "plague air" (11) - in the book *Al-Hawi Fi Al-Tib* (13) and *Al-Qanun Fi Al-Tib* (12) and the "plague diseases" created by it, have also pointed out how and how to protect people in these conditions (24) and while providing health advice, some of the effective herbal compounds in prevention And people suffering from this type of infectious epidemics (25, 26), including, daily use of a plant combination based on yellow aloe, consisting of yellow aloe (*Aloe barbedensis*) (2 units), Mecca Myrrha (1 unit) ) And saffron (*Crocus sativus*) (1 unit) at a rate of about 3.5 grams - also emphasize as an "opium or antidote" (1). New scientific evidence also suggests the usefulness and possibility of using this combination in such circumstances. for example; A 2013 clinical trial by Nigar Z and Itrat M at the National Institute of Unani Medicine Hospital, Bangalore, on a plant compound called *Tiryqa wabai* to

investigate its immune-stimulating effects in the elderly. This plant composition consisted of three ingredients: saffron, saffron, and myrrh. The results of this study showed that this herbal compound at a dose of 500 mg three times a week for 45 days has immunosuppressive effects. Significant increase in total lymphocyte count (TLC) (P-Value <0.001), lymphocyte percentage (P-Value <0.001), absolute lymphocyte count (ALC) (P-Value <0.001) and count (P-Value <0.001) It resulted in CD4 without any side effects (10).

In the study of other sources of modern medicine, it has been shown that each of these plants contains effective compounds and substances and has scientific documents that confirm the properties mentioned in the sources of traditional Iranian medicine. For example; *Aloe barbedensis* shrub with the scientific name (*Aloe barbedensis* Mill. Or *Aloe Vera* L.) of the Liliaceous family, whose medicinal part consists of dried leaf sap (27). This plant (*aloe vera*), also known as the "miracle plant" or "miracle plant", is a medicinal plant that has been used in various cultures for more than 3,000 years (28). And is one of the most studied and used medicinal plants in the world, whose medicinal and phytochemical properties are well documented (29, 30). In general, this plant has compounds such as anthracene derivatives, glycosyls such as alloys, hydroxy anthraquinones such as allo-amodine, alkyl chromones including allorzines, flavonoids, saponins, cinnamic acid, ether oil, etc. It has antimicrobial and antiviral properties (*plum-amodine* inhibits the growth of *H. pylori* and is effective against 4 methicillin-resistant strains of *Staphylococcus aureus*. It also inactivates coated viruses on types 1 and 2). Herpes simplex virus as well as varicella zoster virus, pseudo rabies, and influenza virus have a direct antiviral effect, anti-inflammatory and analgesic effect (by its

salicylates and by inactivating bradykinin, inhibiting the production of histamine and reducing synthesis) Prostaglandin), wound healing (by increasing the amount of granular tissue collagen), anti-cancer effects (by amoudine present in the plant) and laxative or laxative effect (mainly through anthraquinones by stimulating the colon mucosa and increasing its movements) have been mentioned (27).

Since the advent of COVID-19, there has been informed about the use of this plant alone or in combination with other herbal remedies against COVID-19. In one of these studies, to accurately determine the best drugs from a set of 10 aloe vera metabolites, molecular docking, and adsorption, distribution, metabolism, excretion, and toxicity (ADMET) properties were performed. The reactivity of the major protease COVID-19 (Mpro) (responsible for the replication of coronaviruses) with 10 isolated aloe vera compounds showed that; The most stable complex is ferralolide or ligand 6 ( $-7.9$  kcal / mol) followed by aloe vera or ligand 1 ( $7.7.7$  kcal / mol) and alveresin or ligand 8 ( $7.7.7$  kcal / mol). Lipinski confirms ligand 6 as the best drug candidate based on ADME analysis. In other words; Virtual screening results of 10 aloe vera-derived metabolites based on binding scores, hydrogen bonding interactions, and Lipinski's five-dimensional law show that the three molecular substances are ferrolide (ligand 6), aloe vera (ligand 1), and aloe vera (ligand protease 3); An enzyme that plays a key role in regulating post-translational proteins, particularly the cleavage of viral polyproteins into functional protein units. In the meantime, ligand 6 or ferralide is known as the best drug candidate. Because in addition to full obedience to Lipinski's law five, it shows the highest connection energy. (5)

It should be noted that among the several proteins that play a key role in COVID-19 viral infection and are currently considered for potential therapeutic purposes; "Corona core protein" or (3CLpro / Mpro) is known as one of the most important drug targets studied in the research and development of anticoagulants-19, especially in terms of the number of patents and the number of potential drug candidates (31). The protein is a proteolytic enzyme that is essential for the cleavage of viral polyproteins into several active protein units. Its choice as a drug target is justified by the fact that its active site is fully preserved and is not affected by mutations (32).

In addition, each of the top three aloe vera compounds has biological activity. Korizaki et al. Reported the antioxidant, anti-cancer, and antifungal activity of ferralide (Ligand 6) (33), while Ligand 1 exhibits anti-cancer and anti-inflammatory activity (34), and Ligand 8 has an anti-inflammatory effect (35).

Aloe vera also contains antiviral secondary metabolites (anthraquinones) that, like lupinavir (an antiretroviral), can act alone or in combination with SARS-CoV-2 protease 3CLpro (36). To this end, aloe vera can be considered an herbal medicine with a high potential to fight Quid-19 to manage this disease in the world. Several experimental studies have shown that aloe vera has extraordinary virulence properties with a wide range of action (5).

In addition to its inherent antiviral properties, aloe vera also has anti-inflammatory and immunomodulatory properties. Thus, an herbal medicine based on aloe vera extract can reduce the risk of acute respiratory distress - the leading cause of death associated with COVID-19 - by reducing pro-inflammatory factors and boosting the immune system. And since combination therapies based on viral protease inhibitors are the best treatment option; Aloe vera and its major secondary metabolites can play an important role in the management of COVID-19 (5).

In addition to its secondary metabolites, which have antiviral properties, aloe vera also contains "zinc" (40.8ppm). Therefore, its use as an herbal medicine brings this trace element to the patient. Although this chemical is essential as an enzymatic cofactor, a slight increase in its intracellular concentration inhibits the proliferation of retroviruses, including SARS-CoV-1, which is important in the management of COVID-19 (36, 37). Thus, all of this scientific evidence raises growing interest in the immediate formulation of aloe vera as an essential drug for the management of COVID-19 (5).

In other studies, the properties of aloe vera such as; It is anti-influenza, antibacterial, immune-boosting and wound-healing, anti-inflammatory, antioxidant, and thymophyte T lymphocyte proliferation (38). Its dry extract, due to its anthraquinones and pre-anthraquinones, is mainly used as a cleansing agent (39). The leaf pulp and its leachate act against various microorganisms (40) and the ethanolic extract in it causes a significant and dose-dependent increase in the total number of white blood cells and macrophages

(41). In acute gastric mucosal lesions, this extract has been used to inhibit gastric acid secretion and to protect the stomach (42). Aloe vera gel has the same therapeutic effects on the mucous membranes of the gastrointestinal tract as it does on external wounds. The dry extract of aloe also stimulates the vagus nerve by creating a bitter taste and then increases the secretion of gastric juices, thus improving digestion. This bitter substance also acts as a cardiovascular tonic (43). In addition, its anti-diabetic and lipid-lowering effects have been proven in human studies (44). Therefore, it can be useful in people with underlying diseases such as diabetes and obesity who are at higher risk for these types of complications and diseases.

However, from the point of view of toxicity, the harmlessness of the extracts of this plant has been experimentally proven both in laboratory conditions and in vivo (5). However, its use is prohibited in pregnant women, lactating women, and children under two years of age, and if used for more than 2 weeks, there is a possibility of hypokalemia. Therefore, its long-term use should be avoided. Its use with anti-diabetic drugs is also associated with an increased risk of hypoglycemia, and concomitant use with digoxin can lead to hypokalemia and digoxin toxicity. To prevent these side effects, concomitant use of this plant with these drugs should be avoided (27). In one study, a decrease in serum thyroid hormone levels was also reported by patience (45), which seems to be better used with caution in hypothyroid patients.

But in the case of saffron, the scientific evidence of modern medicine shows that; Saffron or Saffron with the scientific name of *Crocus sativus* from the family Iridaceae, whose medicinal part consists of stigma and cream, has compounds such as apocarotenoid glycosides, especially crocin, picrocrocin (4%), volatile oil (1.3-0.4%) containing safranal and products. It is obtained from the decomposition of picrocrocin, carotenoids, and fixed oils and starches. Safranal, picrocrocin, crocetin, and crocin are among the active ingredients of saffron and for them, properties such as stimulation of gastric juice secretion (in small amounts) and stimulation of uterine smooth muscle (in large amounts) have been stated, so its use is not recommended in pregnancy. Is (27, 46). It should be noted that the most common effective doses of saffron, which are used in clinical studies and are safe and significantly lower than toxic doses (> 5 g per day),

are 30 to 50 mg per day. Be (47). Its lethal dose is between 12 and 20 grams (27).

Regarding the use of saffron during the COVID-19 epidemic, there is a lot of scientific evidence that justifies its use during this epidemic. A review of the potential role of saffron during and after COVID-19 infection, focusing on immune, respiratory, renal, and cardiovascular functions; The findings indicated that saffron due to its anti-inflammatory, antioxidant, and other medicinal properties attributed to the bioactive compounds of saffron, can help in pre-and post-infection management strategies. Also, due to its antidepressant properties, it can not only be useful in the management of these post-hospital disorders (subacute and chronic). It can also help boost the safety of ordinary people and manage depression, stress, and anxiety caused by long-term quarantine, isolation, or quarantine (6). Regarding its antidepressant properties (48), it has been reported that saffron is more effective than a placebo or approximately equivalent to therapeutic doses of fluoxetine and imipramine (49).

In addition, many in vitro and in vivo studies have confirmed saffron as an antiviral, antioxidant, bronchodilator, anti-inflammatory, and potent immune enhancer that affects humoral as well as cellular immunity (6). Even saffron petal extract (SPE) is beneficial due to the presence of flavonoids, anthocyanins, and tannins. In one study, intraperitoneal injection into mice for 14 days was associated with an increase in white blood cell count and antibody response, without any change in blood parameters (50). There is also strong scientific evidence for the antiviral effects of saffron, including anti-HSV-1 and anti-HIV-1 (6). Recently, in silicon analysis for pharmacokinetic, toxicological, and ADMET parameters (absorption, distribution, metabolism, excretion, and toxicity) of bioactive saffron molecules, it has been observed that crocetin has a high drug rating against SARS-CoV-2. Crocin and crocetin have a high affinity for the main protease SARS-CoV-2 and crocetin, as a drug molecule, shows transmission through the lipid bilayer (51).

It is interesting to note; Twenty-one percent (21%) of COVID-19 management trials focused on non-vaccine approaches such as immunomodulators (18%) and dietary supplements (3%) (52). Studies related to saffron can be included. In this regard, a review study has claimed that no other spice is as attractive and

excellent as saffron (6). Because saffron is rich in B vitamins, vitamin C, carotenoids, and phytochemicals, it can boost immunity. Saffron compounds have been recorded in several herbal medicinal formulas that are used to treat cardiovascular and central nervous system diseases, as well as to strengthen the immune system and treat depression (53). Clinical trials show that saffron extract is effective in patients with diseases of the central nervous system (CNS) such as Alzheimer's and mental disorders such as depression if administered 20-200 mg per day for ten days to several weeks (6). In addition, crocetin and crocin are useful in the treatment of neurodegenerative disorders associated with memory impairment (48, 54).

A double-blind randomized placebo-controlled clinical trial was performed to determine the immunomodulatory effects of saffron and it was observed that saffron increased IgG levels and decreased IgM levels compared to baseline and placebo. In addition, it increased the percentage of monocytes compared to the placebo. Therefore, short-term daily use of 100 mg of saffron was suggested temporarily without any side effects due to its immunomodifying activities (55).

The results of a study also showed that the use of saffron petal extract at a dose of 75 mg/kg increases the antibody response without changing the hematological and histological parameters of the rat spleen (50). Another experimental study after consuming milk and milk with saffron for 6 weeks, and evaluating innate immunity by measuring the percentage and number of monocytes, neutrophils, eosinophils, basophils, platelets, and total white blood cell count, CRP concentration, and Complement concentration of C3 and C4 and humoral immunity by measuring the percentage of lymphocytes and concentrations of IgG, IgM, and IgA; Showed that 3 weeks after saffron consumption, the number of monocytes and serum IgG concentration increased significantly (P-Value <0.05) and P-Value = 0.01 (total white blood cell and platelet count also showed a significant decrease). P-Value <0.05) After 6 weeks, the number of monocytes and IgG concentration decreased significantly compared to the third week (P-Value <0.05) and P-Value <0.001) and the number of platelets increased significantly (P-Value <0.05). ) Found. These results showed that saffron consumption strengthens the innate and humoral system and has anti-inflammatory properties.

Of course, these effects depend on the duration of saffron consumption (56).

Modulating the safety of bioactive compounds of saffron can help as a management strategy against SARS-CoV-2. Its immunomodulatory activity may include direct targeting of Toll-like receptors (TLRs) and may also be attributed to nuclear factor (NF- $\kappa$ B), activating protein 1 (AP-1), and downstream signaling pathways (57).

Saffron has been shown to increase the ratio of IFN- $\gamma$  to IL-4 in human lymphocytes and thus affect the balance of Th1 and Th2 in them (58). These properties may help modulate the immune response during SARS-CoV-2 infection. A study on sensitized guinea pigs showed that the total and differential white blood cell (WBC) counts were positively affected by saffron and safranal extracts (59).

Regarding the anti-inflammatory effects of saffron, studies have shown that saffron reduces inflammation by inhibiting the activity of cyclooxygenase enzyme and the release of inflammatory cytokines and the production of nitric oxide and nitrite, endothelin-1 and the secretion of total protein, and the absorption of inflammatory cells. Prevents lungs in sensitized guinea pigs. This property helps to control excessive pneumonia in SARS-CoV-2 patients due to the release of cytokines and proinflammatory chemokines and thus can be useful in the management of SARS-CoV-2 (6). Other scientific evidence regarding saffron also indicates that; The stigmas of this plant are used as an antitussive, expectorant, and antioxidant in Greek medicine (38). The antitussive effect of safranal and crocin in saffron stigmas and petals has been documented in an experimental study in Guinea (60). Radical inhibitory, analgesic and hypolipidemic effects (61), antihypertensive activity, anticoagulant activity, inhibition of cell proliferation, and sedation of saffron extract compounds have also been reported in animal and human studies (38, 62). Saffron and its compounds are also an effective treatment for coronary artery diseases, neurodegenerative disorders, bronchitis, asthma, diabetes, fever, and colds and a promising natural remedy in the treatment of metabolic syndrome (63, 64).

Finally, new findings show that; Myrrh or Myrrh with the scientific name *Commiphora molol*. Engl. ex Tschirch from the family Burseraceae, genus *Commiphora*, is a fragrant resin gum from the shrub

"Moran". This small tropical tree is widely distributed in East Africa, Saudi Arabia, and India and contains compounds such as volatile oil (10-2%), which mainly include terracotta sesqui, triterpenes (30-30%), and mucilages (60 to 30%) and properties such as antimicrobial, astringent, anti-flatulence, expectorant, anti-secretion, antiseptic and wound healing have been mentioned (27, 65-67).

Also, scientific studies related to "Mor Maki" have shown that; It is used to treat a variety of diseases such as obesity and fat disorders. In addition, it has anti-hyperglycemic, antioxidant, liver protective, analgesic, and anti-inflammatory activities (68). In addition, myrrh is used as an antimicrobial, antiseptic, static, antiviral, and leukocytopenia agent (46). It also has anti-tumor (38) and anticoagulant (69) activities. Traditionally, cold sores have been used to relieve nasal congestion and coughs due to modulated immune response and antimicrobial activity. Antioxidant effects are a possible mediator in protection against myocardial necrosis, inhibition of platelet aggregation, and also increase fibrinolysis by myrrh resin extract (38).

Studies on COVID-19 also show that Commiphora myrrha is one of those medicinal plants that can be used for such conditions. For example, Fatima S et al. In a review study of the herbal approach to COVID-19 management; This herbal medicine has been considered one of the medicines that are considered useful in Greek medicine for epidemic fever, which is similar to the epidemic conditions of COVID-19, along with other herbal medicines such as yellow aloe and saffron (1). Nikhat S and Fazil M also evaluated the use of smoke of this drug as useful due to the similarity of epidemic fever conditions and COVID-19 (15).

## Conclusions

By reflecting on the scientific findings of these plants and a closer look at the sources of traditional Iranian medicine, it is recommended to conduct more clinical trials on the plant composition of opium poppy, to confirm its effectiveness and safety, to use it to strengthen Make the body's defense system more reassuring in situations such as the Quwid-19 pandemic, especially in people at higher risk.

## Author contribution

SS and MZ wrote the manuscript and edited and confirmed the final version.

## Conflict of interest

No potential conflict of interest was reported by the authors.

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