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Post–Intensive Care Syndrome in Covid-19 Patients Discharged From the Intensive Care Unit

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Patients with Covid-19, after discharge from the intensive care unit (ICU), experience some psychological, physical, and cognitive disorders, which is known as the post–intensive care syndrome and has adverse effects on patients and their families. The aim of this study was to evaluate the post–intensive care syndrome and its predictors in Covid-19 patients discharged from the ICU. In this study, 84 Covid-19 patients discharged from the ICU were selected by census method based on inclusion and exclusion criteria. After completing the demographic information, the Healthy Aging Brain Care Monitor Self Report Tool was used to assess post–intensive care syndrome. Sixty-nine percent of participants experienced different degrees of post–intensive care syndrome, and its mean score was 8.86 ± 12.50; the most common disorder was related to the physical dimension. Among individual social variables, age and duration after discharge were able to predict 12.3% and 8.4% of the variance of post–intensive care syndrome, respectively. Covid-19 patients who are admitted to the ICU, after discharge from the hospital, face cognitive, psychological, and functional disorders, and there is a need for planning to prevent, follow up, and care for them by health care providers in the hospice and palliative care centers.

KEY WORDS
Covid-19 survivors, intensive care unit, post–intensive care syndrome

Covid-19 disease is a mild to severe respiratory syndrome that occurs after infection with severe acute respiratory syndrome (SARS) coronavirus 2. It was first identified in Wuhan, China, in December 2019 and has quickly become a pandemic, affecting millions of people and causing significant deaths worldwide. Most people infected with SARS coronavirus 2 develop a mild clinical syndrome such as the flu, approximately 20% require hospitalization, and a significant proportion of them lead to a critical illness (septic shock, respiratory failure, or multiple organ dysfunction) and death.[1] During the first months of 2020, the rapid global increase in mortality has made this epidemic one of the most important emergencies of the World Health Organization.[2] Statistics show that, by May 2021, 160 686 749 cases of Covid-19 disease have been reported worldwide, of which 3 335 948 have died and 139 784 185 have improved.[3]

On February 19, 2020, the first case of Covid-19 was reported in Iran.[4] After a while, Iran became a global epicenter of Covid-19.[5] Iran is still one of the countries dealing with the most cases of Covid-19 infections and subsequent deaths. According to statistics, Iran ranks 14th in the number of Covid-19 cases.[6] In Iran, patients with acute cases of Covid-19 are cared for in hospitals and patients with mild cases are quarantined at home. In addition, the Primary Health Care Network, as the largest health care network in Iran, provides access to primary health care in the most remote regions by providing screening, screening, tracking, and contact tracing activities.[7]

The large number of people with Covid-19 has increased the need for beds in intensive care units (ICUs).[8] It is estimated that approximately 6% to 10% of Covid-19 patients have a severe to critical infectious disease and may need to be admitted to the ICU.[9] Approximately one-third of ICU beds are available to care for Covid-19 patients.[10] Among patients with Covid-19 admitted to the ICU, approximately 60% were discharged from the hospital and returned home.[11] One of the most challenging parts of

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caring for Covid-19 patients are caring for those discharged from ICUs. These patients are likely to face unrecognized care needs leading to irreversible complications. So the long-term survival effects of Covid-19 have become the focus of new research due to concerns about the virus' unknown adverse effects.[12] Previous studies have shown that hospitalization in the ICU can lead to new physical, cognitive, and psychological disorders that persist even after discharge from the hospital and are known as post–intensive care syndrome (PICS). This suggests that survivors of critical illness are likely to experience PICS,[13] which has been described as a "hidden public health disaster."[14] The PICS has an adverse effect on clinical and functional outcomes,[15] so it can reduce the survival rate after discharge from the ICU.[16] It is often associated with an inability to return to work, a negative impact on family income, a decrease in quality of life, and an increased risk of death for the next few years (first 3-6 years).[17,18]

Patients with Covid-19 are often treated with mechanical ventilation, neuromuscular blocking, and sedation therapy[19] in the ICU, and there is a risk of anxiety and depression, posttraumatic stress disorder, and neurological deficits.[20] Reduction of cognitive stimuli due to reduced direct contact of families with patients due to infection control precautions can lead to psychological symptoms.[21] It seems that, because of the mentioned stimulus factors in Covid-19 patients, these patients are likely to face several physical, mental, and cognitive disorders after discharge from the ICU that need to be carefully examined and identified. The aim of this study was to evaluate these disorders in the form of PICS in Covid-19 patients discharged from the ICU and to determine some prognostic factors.

MATERIALS AND METHODS

This study is a descriptive-analytical study. Census method was used for sampling. Inclusion criteria include being 18 years and older, hospitalization in the ICU for 48 hours or more solely due to Covid-19, being discharged from the ICU for 4 weeks to 1 year, ability to communicate by telephone, no mental and cognitive illness diagnosis in the past (to prevent the probable effect of past psychological and cognitive damage on the new symptoms of the PICS), and no limitations and physical weakness in the past, such as plagia, paresis, and so forth, according to the patient's history and medical record. In addition, individuals who did not wish to participate in the study and those with cognitive impairment according to the Abbreviated Mental Test (AMT) were excluded from the study. Data were collected from September 2020 to February 2021 from the educational and medical corona centers affiliated with Ardabil University of Medical Sciences. For this purpose, first, the contact information of Covid-19 patients discharged from the ICU was extracted from their file archives, and then they were contacted by phone to complete the questionnaires. From the beginning of corona disease to February 2021, approximately 149 corona patients were discharged from the ICU of Ardabil hospitals, and their information was reviewed for inclusion in the study. Twelve patients died because of complications of the disease; 10 patients were excluded from the study because of a score of less than 8 in the AMT, which indicated a high severity of cognitive impairment; and 43 patients were excluded from the study because of other causes (Figure 1). Finally, 84 eligible patients were

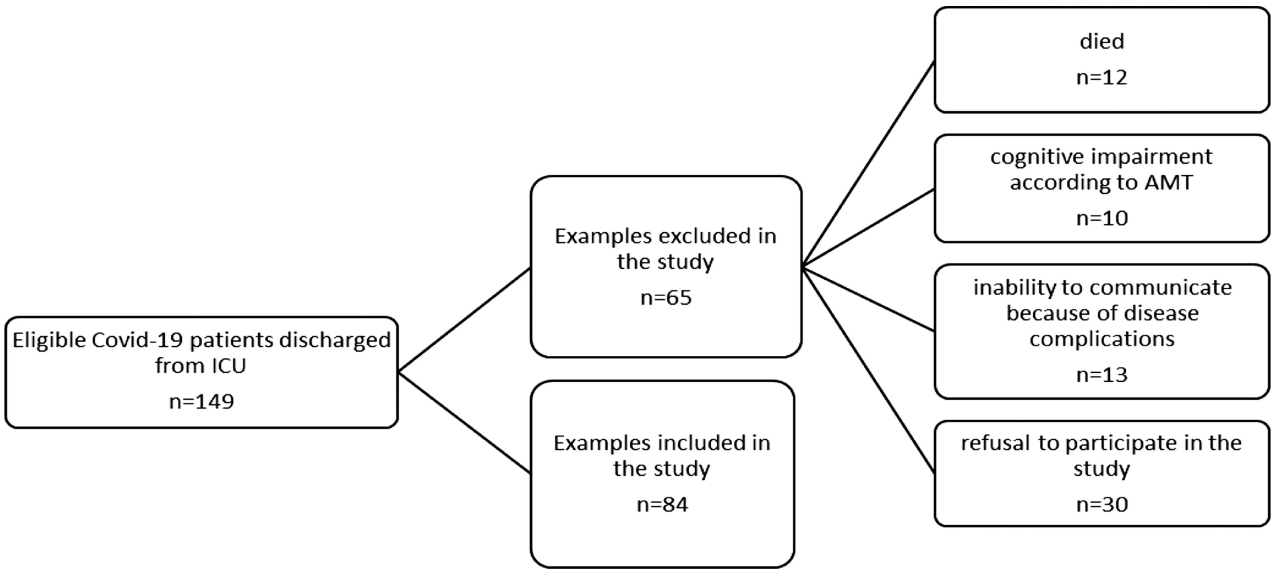

FIGURE 1. Flowchart of patients through the study. AMT, Abbreviated Mental Test; ICU, intensive care unit.

included in the study (56.4% of the total study population in the study period).

In this study, in addition to demographic questions, the Healthy Aging Brain Care Monitor Self Report (HABC-M SR), a tool for assessing PICS and AMT signs for assessing cognitive status, was completed by telephone by the assessor. The HABC-M SR is a 27-item tool for assessing cognitive, functional, and psychological symptoms. The cognitive dimension includes 6 questions about memory, alertness, and judgment. The physical dimension includes 11 questions about daily life activities. The psychological dimension includes 10 questions about the symptoms of depression, anxiety, and psychosis. The score range for each item is between 0 and 3. The maximum scores for the cognitive, functional, and psychological dimensions are 18, 33, and 30, respectively. Scores in the 3 subscales and a high overall score are associated with more severe symptoms. Validity and reliability of the HABC-M SR have been confirmed by Wang et al[22] (2019). The tool was used in the study after obtaining permission from the tool designer.[23] Before collecting data, content validity index was calculated for the tool by the 10-specialist panel (including 3 nurses in the ICU, 3 anesthesiologists, and 4 nursing faculty members with enough experience in the field of palliative care). The score range of the content validity index for all items of the tool was 0.90 to 1.00. In addition, internal reliability according to Cronbach α coefficient for the cognitive, functional, and psychological dimensions of the HABC-M SR were determined to be 0.92, 0.96, and 0.65, respectively. The AMT has 10 questions that are given 1 point for each correct answer, and at the end, the total points are calculated. The validity and reliability of this questionnaire are acceptable in Iran, and its best cutoff point for distinguishing people with cognitive impairment from people with normal cognitive status is 8.[24]

To analyze the data, descriptive tests (mean, median, frequency, percentage, and standard deviation) and inferential statistics (linear regression) were performed using SPSS software version 22.

ETHICAL CONSIDERATIONS

After obtaining permission from the ethics committee of Ardabil University of Medical Sciences, people who met the inclusion criteria were selected. The objectives and method of the study were explained to the patients. All the patients' questions were answered, and they were informed that participating in the study was voluntary and could be discontinued at any time during the study. All the participants were informed that the data were collected and managed anonymously and confidentially and the results were not used for purposes other than the study. A verbal informed consent was given by each participant before data collection.

RESULTS

Of 149 eligible patients in the study period, 30 were excluded because of refusal to participate, but 35 (12 deaths, 10 severe cognitive disorders, and 13 ill conditions and inability to communicate) could not answer the researchers' questions because of complications of the disease and were excluded from the study (considering that the purpose of this study was to investigate physical, mental, and cognitive disorders in the form of PICS, in a sense, these 35 people can be considered as people with complications). Finally, data from 84 patients were analyzed. The mean and standard deviation of age, length of stay in the ICU, and duration after discharge (the month or months from the discharge of the patients from the ICU to conducting the research) in participants were 51.67 (15.43) years, 18.42 (17.15) days, and 3.29 (2.09) months, respectively. Other characteristics of the participants and scores of the PICS according to demographic categories are shown in Table 1.

The results of the study showed that the mean (SD) of the PICS score in discharged patients is 8.86 (12.50) and 69% experience mild to moderate degrees of this syndrome. The frequency and mean score of the PICS dimensions are shown in Table 2. In addition, Table 1 shows the average PICS scores and its dimensions in terms of sex, educational status, marital status, presence or absence of comorbidity, and occupation.

A regression test was used to evaluate the relationship between demographic characteristics and PICS. For this purpose, the variables of educational status, sex, marital status, age, length of hospital stay in the ICU, presence or absence of comorbid disease, and duration after discharge were entered into the regression model. Regression results showed that, among the previously mentioned variables, only the variables of age and duration after discharge have a significant relationship with PICS score, because they explain 12.3% and 8.4% of the variance of PICS, respectively (Table 3). Figure 2 shows the scores of PICS and its dimensions according to duration after discharge from the ICU.

DISCUSSION

This study was performed to evaluate the PICS in patients with Covid-19 discharged from the ICU. The results of this study showed that most participants experience some degree of PICS disorders and its various dimensions. According to the mean of items of different dimensions, most of the disorders are related to the dimension of functional disorders. This indicates that most patients have a low physical ability due to the complications of the disease and have more problems in daily activities. Studies on non-Covid patients discharged from ICU wards also mainly indicate more physical and functional problems.[25-27] For example, van der Schaaf et al[27] (2009), in a prospective study of mechanically ventilated patients discharged from the ICU in

TABLE 1 Scores of PICS in the Patients Discharged From the ICU According to Their Demographic Categories

		Frequency (%)	Total Score of PICS	Cognitive Dimension	Functional Dimension	Psychological Dimension
Sex	Female	37 (44)	9.49 (11.89)	0.81 (2.58)	5.81 (8.89)	2.86 (3.13)
	Male	47 (56)	8.36 (13.07)	0.87 (1.93)	4.96 (9.5)	2.53 (3.16)
	Independent *t* test		*t* = –0.12 *P* = .68	*t* = –0.12 *P* = .90	*t* = 0.42 *P* = .67	*t* = 0.48 *P* = .63
Marital status	Single	6 (7.1)	9.83 (16.38)	1.17 (1.83)	5.83 (11.60)	2.83 (4.66)
	Married	72 (85.7)	7.69 (11.63)[a]	0.82 (2.32)	4.35 (8.09)[a]	2.53 (2.99)
	Lone or divorced	6 (7.1)	21.83 (13.60)[a]	0.83 (1.32)	16.67 (13.18)[a]	4.33 (3.26)
	ANOVA test		*F* = 3.80 *P* = .02	*F* = 0.07 *P* = .93	*F* = 5.15 *P* = .006	*F* = 0.92 *P* = .40
Educational level	Illiterate/ primary school	40 (47.62)	10.75 (12.26)	0.83 (2.32)	6.93 (9.46)	3.00 (3.05)
	High school	14 (16.66)	11.71 (16.41)	1.43 (3.05)	7.21 (12.41)	3.07 (2.46)
	Academic	30 (35.72)	5.00 (10.02)	0.60 (1.59)	2.33 (6.20)	2.07 (3.46)
	ANOVA test		*F* = 2.32 *P* = .10	*F* = 0.66 *P* = .52	*F* = 2.58 *P* = .08	*F* = 0.89 *P* = .41
Job	Self-employment	24 (28.57)	8.17 (12.38)	0.54 (1.02)	5.04 (9.16)	2.58 (3.30)
	Employee	18 (21.43)	6.44 (11.92)	0.83 (1.91)	3.39 (7.78)	2.22 (3.26)
	Homemaker	33 (39.29)	9.48 (11.30)	0.70 (2.49)	5.91 (8.98)	2.88 (2.87)
	Retired	9 (10.71)	13.22 (18.21)	2.22 (3.63)	7.89 (12.98)	3.11 (3.79)
	ANOVA test		*F* = 0.63 *P* = .59	*F* = 1.36 *P* = .26	*F* = 0.54 *P* = .65	*F* = 0.23 *P* = .87
Existence of comorbidity diseases	No	32 (38.10)	7.5 (12.38)	0.34 (1.00)	5.00 (9.98)	2.16 (3.12)
	Yes	52 (61.90)	9.70 (12.62)	1.15 (2.68)	5.54 (8.78)	3.00 (3.13)
	Independent *t* test		*t* = –0.78 *P* = .44	*t* = –1.64 *P* = .10	*t* = –0.26 *P* = .80	*t* = –1.20 *P* = .23

Abbreviations: ANOVA, analysis of variance; ICU, intensive care unit; PICS, post–intensive care syndrome.
[a]*Significant differences in the confidence level of 0.95 by Tukey test.*

the Netherlands, found that physical problems were the most common disorder. Review studies also show the prevalence of some functional and physical disorders in SARS and Middle East Respiratory Syndrome survivors.[25] Previous studies have shown that the incidence of physical and functional disorders in non-Covid patients discharged from the ICU is due to factors such as myopathy, long-term use of sedatives and paralytics,[28] joint contracture due to prolonged immobility in the ICU,[29] and decreased pulmonary function.[26] The exact cause of functional disorders in

TABLE 2 Frequency and Mean Score of the PICS and Its Dimensions Among Patients Discharging From the ICU

Category[a]/Variable		Cognitive	Functional	Psychological	Total PICS
Frequency (%)	Lack of disorder	66 (78.57)	38 (45.24)	35 (41.67)	26 (30.95)
	Mild level	15 (17.86)	32 (38.10)	46 (54.76)	47 (55.95)
	Moderate level	2 (2.38)	6 (7.14)	3 (3.57)	11 (13.1)
	Severe level	1 (1.19)	8 (9.52)	0 (0)	0 (0)
Mean ± SD		0.85 ± 2.22	5.33 ± 9.20	2.68 ± 3.14	8.86 ± 12.50
Item's mean[b]		0.14	0.48	0.27	0.33

Abbreviations: ICU, intensive care unit; PICS, post–intensive care syndrome. SD, Standard Deviation.
[a]Categorizing for each variable determined as follows: lack of disorder, acquiring a score of 0; mild level, first one-third of the potential score for every variable; moderate level, second one-third of the potential score for every variable; severe level, first one-third of the potential score for every variable.
[b]Item mean calculated through mean divided by all numbers of items of each variable.

corona patients has not been determined, but pulmonary dysfunction seems to play an important role in the occurrence of these complications.[30]

The results of the study showed that more than 58% of participants experience mild to moderate degrees of psychological disorders after discharge from the hospital. Studies of psychological complications have been performed in Covid-19 patients, and most of them confirm that these patients develop psychological complications even after recovery. For example, Zhang et al[31] (2020) reported a 30% prevalence of depression in Covid-19–recovered patients. Other similar studies have reported psychological effects such as anxiety, posttraumatic stress disorder, depression, and insomnia in patients with Covid-19.[32] It seems that treatment in the ICU with excessive sensory stimulation or sensory deprivation, forced quarantine, and changes in normal living conditions can affect the occurrence of mental disorders in participants.[21]

Although the results of this study showed that cognitive impairments have the lowest mean item among the 3 dimensions of PICS, it cannot be stated with certainty that these patients are less likely to develop cognitive impairments, especially considering that 10 patients (6.7% of the total sample size) were excluded because of high cognitive impairment (score < 8 in the AMT) and the possibility of not answering PICS questions correctly. In the study of Miskowiak et al[33] (2021) on Covid-19 patients discharged from the hospital, 59% to 65% of patients showed objective and clinical cognitive impairments 3 to 4 months after discharge from the hospital. Other studies on non-Covid patients discharged from the ICU show that cognitive impairment is a common complication in these patients. For example, de Azevedo et al[34] (2017) in a prospective study of ICU patients in Brazil showed different degrees of cognitive impairment in mechanically ventilated patients. Kawakami et al[35] (2020) also showed in a prospective study in Japan that patients discharged from the ICU have cognitive impairments. Numerous factors can contribute to cognitive impairment in ICU-discharged patients, including long-term delirium due to deep sedation[36] and the effects of mechanical ventilation as well as postdischarge

TABLE 3 Linear Regression Analyses for Determining Predictor Variables of the PICS After Being Discharged From the ICU

Predictor Variables	R^2	Standardized Coefficient	*F* Score	*P*
Educational level	0.000	0.004	2.77	.97
Sex	0.000	0.02		.87
Married status	0.000	–0.02		.88
Age	0.123	0.35		.02
Hospitalized duration in ICUs, d	0.004	0.06		.58
Comorbidity diseases	0.000	–0.02		.84
Duration after discharge, mo	0.084	0.29		.007

Abbreviations: ICU, intensive care unit; PICS, post–intensive care syndrome. The table showed that "age" and "length of discharge from the hospital" are 2 predictors of PICS and explain 20% of variance of that.

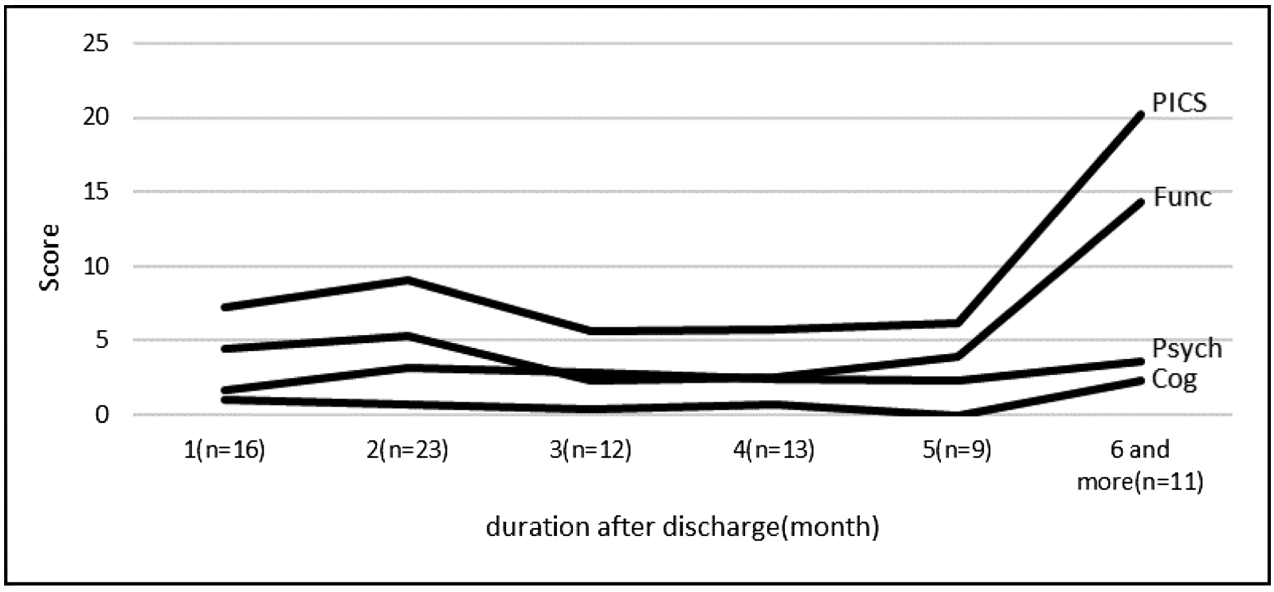

FIGURE 2. Scores of PICS and its dimensions according to duration after discharge from the intensive care unit. Cog, cognitive dimension; Func, functional dimension; PICS, post–intensive care syndrome; Psych, psychological dimension.

stress and anxiety.[37] In patients with Covid-19 disease, the reduction in cognitive stimuli due to reduced family direct contact due to infection control precautions is another factor that can lead to more cognitive impairment in these patients, during and after hospitalization in ICUs.[21]

The results of the regression model showed that age is a predictor of PICS, explaining 12.3% of the variance of PICS in patients discharged from the ICU. This indicates that PICS increases with age. A similar study was not found to show PICS predictor variables in Covid-19 patients, but studies on other patients discharged from ICUs also found that some individual-social variables could predict PICS. Marra et al[38] (2018), in a study in the United States on survivors of critical illness, showed that young age is associated with a lower PICS score. Besides, in various studies, the relationship between old age and mental disorders,[39] functional disabilities, and cognitive disorders[40] has been confirmed. Known or unknown underlying problems that occur with age seem to be an important factor in the development of PICS. In this regard, McNicoll et al[41] wrote that most elderly people (>70%) experience delirium, which can play a role in the development of cognitive disorders and PICS. However, further studies are needed to investigate the causes of the increase in PICS disorders with age in Covid-19 patients after ICU discharge.

Another variable that has the predictive power of PICS in the regression model is the "duration after discharge" from the ICU, explaining 8.4% of the variance of PICS in the participants, so that the amount of PICS score increased with the increase of time duration after patients' discharge. As is shown in Figure 2, PICS score is high in patients who have been discharged from hospital for 2 months. Then, PICS score has decreased in patients who have been discharged for 3 to 5 months. However, PICS score has significantly increased in those patients who have been discharged for 6 months or longer. No study has been found to address this issue in corona patients, but studies on non-Covid patients have shown conflicting results. For example, Herridge et al[42] (2011) showed many functional impairments in acute respiratory distress syndrome patients up to 5 years after discharge, which could be due to lack of necessary rehabilitation after a severe period of illness. On the other hand, some studies have shown a reduction in PICS disorders over time.[38] Different factors can contribute to the conflicting results of PICS over time, some of which may be due to differences in environmental factors,[43] the type and quality of treatment received in hospitals in different countries in the ICU,[44] and, possibly, the provision of palliative care in different geographical areas.[45] Because of the unknown nature of the Covid-19 disease and the numerous complications that may occur in the long term in different systems even after recovery,[46] it is not possible to accurately judge the reason for the increase in PICS score and its cognitive, physical, and psychological dimensions over time.

Although other variables were not statistically significant to PICS, significant conclusions were drawn. For example, Covid-19 patients who lost a spouse were found to have a significantly higher PICS score after discharge from the ICU than patients with a spouse. This issue is probably due to the reduction of social support (family support), because in previous studies, it has been determined that family support in the event of illness is the most important source of support in Iranian society.[47,48] Another

point is that, although underlying diseases affect the severity of Covid-19 disease,[49] this study showed that this variable has no effect on the incidence of PICS in patients discharged from the ICU. Further studies are needed to investigate the effects of underlying diseases on the severity and incidence of PICS after ICU clearance. Hospice and palliative services can contribute an essential role in the response to Covid-19, especially for the patients discharged from the ICU. For Covid-19 patients, training the staff in palliative care, preparing protocols for symptom management, deploying volunteers and specialists to provide psychosocial care and bereavement care, if needed, are some of the services hospice and palliative care centers can provide.[50]

LIMITATIONS

Few studies have examined the adverse effects of being cared for in the ICU for Covid-19 disease, so the results of this study can provide appropriate information for health care and rehabilitation planners of the previously mentioned patients. However, there were some limitations in this study: first, despite contact with all patients treated in the province, 84 patients were included in the study, which is a relatively small sample size, and it may be associated with some variables being not significantly related to PICS. On the other hand, this study is a descriptive-analytic study, and the predictive power of variables is only in their relationship and not their effectiveness. Therefore, it is suggested that interventional or cohort studies be performed to determine the variables affecting PICS. Another point is that, because of the self-reporting nature of the PICS measurement tool in this study, 10 patients were inevitably excluded because of low cognitive scores, so in this study, we could not obtain an accurate estimate of the incidence of cognitive impairment. This means that the actual cognitive impairment in patients with Covid-19 after discharge from the ICU may be greater than that reported in the study.

CONCLUSION

This study followed 149 patients with Covid-19 who had been discharged from the ICU and found that these patients experience cognitive, psychological, and functional disorders in the form of PICS, some degree of illness (because they could not answer the questions), and dying. In addition, the results of the study showed that old age, duration after discharge, and the absence of a spouse are factors that play an important role in the further incidence of the PICS and determine the need to pay attention to these factors. These can provide good evidence-based information for patients treated in the ICU and their caregivers as well as the health care teams in the hospice and palliative care centers for planning to provide physical, cognitive, psychological, and bereavement care for the patients and their families.

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