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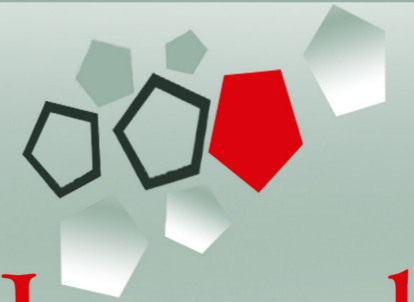
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The effect of cognitive rehabilitation therapy (CRT) on the executive functions of children with autism spectrum disorder (ASD)

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Original Article

Abstract

BACKGROUND: Executive functions (EF) impairments are considered as central deficits in autism spectrum disorder (ASD). The purpose of this study was to determine the effectiveness of cognitive rehabilitation therapy (CRT) on EFs of children with high-functioning ASD (HFA).

METHODS: This was a quasi-experimental study with a pretest-posttest design and control group. The study population included all children with HFA referred to the comprehensive Arman Shayan Rehabilitation Center in Tehran, Iran. Using the high-functioning Autism Spectrum Screening Questionnaire (ASSQ) and clinical diagnostic interviews by two clinical psychologists, 24 children with HFA were selected purposefully and were randomly assigned to experimental or control groups. Subjects in both groups completed the Behavior Rating Inventory of Executive Function (BRIEF) in pretest and posttest. The experimental group received 1-2 sessions (1 hour) per week of CRT for 6 months. Data analysis was performed using analysis of covariance (ANCOVA) in SPSS.

RESULTS: Data analysis showed that the use of CRT resulted in a significant difference between groups in terms of the total EFs score, which was 88.5%, as well as the components of inhibition (57%), orientation (46%), emotional control (42%), initiate (43%), working memory (55%), planning (56%), organizing (36%), and monitoring (36%).

CONCLUSION: CRT, as an evidence-based intervention, seems to be effective in improving neuropsychological functions in children with HFA.

KEYWORDS: Cognitive Rehabilitation Therapy, Executive Function, High-Functioning Autism Spectrum Disorder

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Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by cognitive and neurobiological deficits based on social and non-social information processing defects,¹ and is associated with stereotypical and repetitive behaviors as well as significant conformational constraints¹ and low quality of life (QOL).² There are three major disadvantages associated with ASD, including

socialization disorder, deficit in verbal and nonverbal communication, and restricted and repetitive patterns of behavior.³ In recent years, prevalence estimates of ASD have increased for unknown reasons.⁴ Estimates of the ASD prevalence varied from 1.2500 in the 1970s to 1.150 in 2000.⁵

However, the most recent reports of the US Centers for Disease Control and Prevention (CDC) published in 2014 reported a prevalence of 1 in 110 children in 2011, and 1 in 68 children in 2014;⁵ findings in different countries are not in agreement,⁶ and in a study conducted by Samadi and McConkey in 2015

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in Iran, the prevalence of autism in 2014 was 2.95 per 10,000 children.⁷ According to previous research, children with autism have a lower level of motor skills development, motor coordination, balance, executive functions (EFs), social skills, and attention.⁸

There is evidence to suggest that children with high-functioning autism (HFA) exhibit better social and behavioral outcomes compared to other children with autism.⁹ Individuals with HFA or level 1 autism are considered to be cognitively higher functioning (IQ \geq 70) compared to people with ASD.¹⁰ Individuals with HFA may exhibit deficiencies in the fields of communication, recognition and excitement expression, and social interactions.¹¹ Despite their moderate or high IQ, children with HFA often present a significant dissonance between cognitive abilities that significantly affects their QOL.¹² In recent years, cognitive theories regarding the relationship between brain and behavior in children with autism have been the subject of scholarly studies. One of these well-known theories is the theory of EFs.¹³

The term executive functions refers to mental control processes related to cognitive and emotional self-control needed to maintain targeted behaviors. EFs include processes such as response inhibition, working memory, cognitive flexibility, planning, fluency, and attention control.¹⁴ The theory of executive dysfunction in autism emphasizes an explicit link between frontal lobe failure and executive dysfunction, which suggests that impairment in basic EFs has many social and non-social characteristics of autism.¹⁵

There is growing evidence that children and adolescents with ASD present impairments in the EF items, such as cognitive flexibility, working memory, inhibition, and planning.¹⁶ EF impairments are considered as central deficits in ASD. Studies have found that children with ASD have problems with tasks requiring working memory, inhibition, and

flexibility.¹⁷ Several studies have shown that children with autism have several EF impairments in characteristics such as inhibition and control,¹⁸ cognitive flexibility,¹⁹ and working memory.²⁰

Today, a variety of therapies can be used in children with autism. One of the most novel therapy methods is cognitive rehabilitation therapy (CRT). CRT has recently gained increasing attention as an effective intervention for the improvement of fundamentally cognitive deficits in psychiatric conditions, including schizophrenia, attention-deficit/hyperactivity disorder (ADHD), brain damage, and ASDs.²¹ CRT was developed as a special form of intervention in psychiatric populations with Wagner's research on attention and practice of abstraction in people with schizophrenia in the late 60's.

Since then, CRT has been adapted to various clinical populations, covering many cognitive domains and the different areas of EFs.²² Cognitive rehabilitation is an intervention based on behavioral education that leads to the development of cognitive processes (such as attention, working memory, EFs, social recognition, and metacognition) with the aim of generalization and sustainability.²³ Cognitive rehabilitation is a potentially effective approach toward the remediation of information processing deficits in people with ASD without intellectual disability.²⁴

The goal of CRT is to improve cognitive flexibility, central coherence, and general information processing, reduce perfectionism, and improve response to inappropriate thinking styles.²⁵ Studies on the effect of CRT have been increasing since 1990, and meta-analysis studies have shown that CRT in patients with schizophrenia can lead to improved cognitive functions, and subsequently, improved psychosocial functioning.²⁶ In the same vein, Miyajima et al. investigated the effect of CRT on cognitive processes in children with ASD, and found

that the use of CRT significantly improved the scores of numerical sequences, verbal fluency, and the Tower of London (ToL) task in children with ASD.²³ Eack et al. also found that cognitive rehabilitation can significantly improve cognitive deficits and EFs in people with ASD.²⁴ Moreover, Katsumi et al. argued that the cognitive rehabilitation program had a significant impact on improving cognitive processes, including working memory, verbal memory, attention, and other EFs.²⁷

Despite evidence of EF impairments in people with autism, few studies have investigated the effect of CRT on the EFs of these children.²⁸ EFs are cognitive abilities, sensory growth is considered as the basis for cognitive development in different studies, and EFs and sensory processing play an important role in everyday life, social functioning, and adaptive behaviors of children with autism. Therefore, the development of interventions that affect the cognitive processes of children with ASD in order to improve their EFs is crucial and research on the effectiveness of CRT can be of great importance. Therefore, the present study aimed to determine the effectiveness of CRT on EFs of children with HFA.

Materials and Methods

This was a quasi-experimental study with a pretest-posttest design and control group. The study population included all children with level 1 ASD referred to the comprehensive Arman Shayan Rehabilitation Center in Tehran, Iran, for specialized services during November-March, 2012. From among patients referred to Arman Shayan Rehabilitation Center, using the Autism Spectrum Screening Questionnaire (ASSQ) and clinical diagnostic interviews by two clinical psychologists, 24 children with HFA who were eligible to enter the study were selected purposefully and randomly assigned to experimental or control groups.

The Diagnostic and Statistical Manual of

Mental Disorders, Fifth Edition (DSM5) was used for the diagnosis of ASD. The study inclusion criteria were the necessary diagnostic criteria based on the ASSQ, children of 8-12 years of age with normal IQ (using the Wechsler Intelligence test), normal speech level (as evaluated by a speech therapist), and written parental consent to participate in the study.

The study exclusion criteria consisted of receiving psychological and therapeutic treatments over the last month, children with intellectual or physical disabilities, psychotic symptoms in a child, and history of neurologic diseases such as epilepsy.

To perform this research, first, the purpose of the research was explained to the parents, then, informed parental consent for the child's participation in the evaluations was obtained. The parents were assured that all the contents presented in the training sessions and the results of the questionnaires would be kept strictly confidential and would be analyzed as a group without mentioning the name of the participants. Furthermore, individuals who demonstrated interest in and willingness to participate in the study were entered into the study. The evaluations and interviews were straightforward with no harm to the person, and the participants did not incur any costs. The participants could leave the assessment and interviewing sessions at any time.

Clinical Diagnostic Interview Based on the DSM-5: The diagnostic interview conducted by a clinical psychologist with the parents of children who have been referred for the evaluation of possible autism spectrum disorders to the Arman Shayan Rehabilitation Center, which lasted about 1 hour. This included biographical information, history and examination of current and past diagnostic symptoms. The initial report of the diagnostic interview included how the child developed and how he/she behaved at school, the medical history (including details on the consumed medications, sleep, exercise, and diet), and the

family's status (including parental occupation, number of siblings, and exploring psychiatric symptoms in the whole family). In this research, subjects who received high scores in the ASSQ underwent a clinical diagnostic interview. This interview was conducted to evaluate and diagnose HFA. Subjects who met the DSM-5 criteria for ASD were considered as the final study sample. To measure the validity and reliability of the clinical interviews, the agreement coefficient between interviewers (who were two clinical psychologists) was calculated (agreement coefficient = 0.78).

The high-functioning Autism Spectrum Screening Questionnaire: The high-functioning ASSQ consists of 27 questions completed by the child's parents or teachers. Each question has 3 response choices of "yes", "to some extent", and "no", which, respectively, indicate the scores 2, 1, and 0 in that question. If the parents complete the form, an overall score of 19 or higher indicates high-functioning ASD, and if the teacher completes it, a score of 22 or higher represents high-functioning ASD.²⁹

The validity and reliability of this instrument was determined by Kasechi et al.²⁹ He stated that the Persian version of the high-functioning ASSQ had a satisfactory formal validity and credibility. The retest reliability coefficient of the high-functioning ASSQ was estimated in the parents group ($r = 0.467$) and in the teachers group ($r = 0.614$), which indicated the reliability and validity of the instrument in autistic individuals. The Cronbach's alpha coefficient obtained for the parents and teachers of the healthy children and children with ASD showed that the high-functioning ASSQ items were suitable for the screening of children with high-functioning ASD.²⁹

The Behavior Rating Inventory of Executive Function: The Behavior Rating Inventory of Executive Function (BRIEF) was developed by Joya, Iscott, and Conventi in 2000³⁰ to assess various aspects of the functions of the anterior part of the brain. The BRIEF is an assessment

tool for both parents and teachers to measure EF behaviors at home and at school. The questionnaire is designed for ages 5-18 years and has two parent/teacher report forms, both of which have 86 questions that are scored on a 3-point scale [never (1), sometimes (2), and most often (3)]. BRIEF contains 8 EF components, including inhibition (15 questions), shifting attention or orientation (12 questions), emotional control (9 questions), initiate (7 questions), working memory (11 questions), planning (14 questions), organization (7 questions), and monitoring (11 questions). The overall score of the questionnaire is the sum of the score of these components, and higher scores represent greater EF deficit. The retest reliability coefficient of the questionnaire was 0.81 for the parents' report form and 0.86 for the teacher's report form. This questionnaire has three versions for different ages. In this study, a child and teenage version for ages 5-18 years (parent report form) was used.³¹ In the study by Maleki and Alizadeh Zarei, the reliability and validity of the questionnaire were reported.³⁰ The test-retest reliability of the subscales of inhibition, orientation, emotional control, initiate, working memory, planning, organization, and monitoring was 0.90, 0.81, 0.91, 0.80, 0.71, 0.81, 0.799, and 0.78, respectively, and the overall score of EFs was 0.89. BRIEF had good content validity because all the questions were selected from interviews with parents regarding EFs.³¹ In this study, the parental report form was used to measure inhibition and emotional regulation of children.

Cognitive Rehabilitation Therapy: Forehead lobe Exercise Program (FEP) is one of the interventions of the CRT the effects of which on cognitive and social functions are examined here. The FEP includes the 3 scales of cognitive flexibility, working memory, and planning, which are designed to gradually increase in complexity during the sessions. Each scale consists of a set of tasks that include eye movements and processes, information

organization, fine movements, etc. The therapist encourages problem-solving strategies and provides instructions for using an effective strategy. For this purpose, the FEP system encourages the subject to perform the tasks as accurately as possible. The FEP consists of 44 sessions, each involving paper and pen tasks, house building with blocks, and fine movements.²³

The study participants were 24 children with HFA, who were divided into two equally sized groups of 12 after the evaluations. Before the onset of CRT, in the pretest phase, all subjects in the experimental and control groups completed the BRIEF under the same conditions (the same time and place). Experimental group subjects received 1-2 sessions (1 hour) per week of advanced FEP for 6 months and subjects in the control group received 1-2 sessions (1 hour) per week of other routine therapies, such as occupational therapy or psychotherapy, without FEP for 6 months. After completing the sessions, all subjects in the experimental and control group completed the BRIEF as a post-test under the same conditions. Finally, data analysis was

performed using analysis of covariance (ANCOVA) in SPSS software (version 21, IBM Corporation, Armonk, NY, USA).

Results

The mean age of the participants in the experimental and control group was 9.55 ± 1.485 years and $9.83 \pm 1.258 \pm 1.58$ years, respectively; 62.5% of the subjects were 8-10 years old, and 37.5% were 11-12 years of age. Regarding their school level, 54.1% of the participants were in the third and fourth grades and 45.9% in the fifth and sixth grades. The subjects in the two groups were compared in terms of age ($P = 0.8930$, $t_{-136/0}$) and school level ($P = 0.486$, $X^2 = 443.2$), and the homogeneity of the groups was confirmed.

Table 1 shows the mean and standard deviation of the total score of EFs and their components. As can be seen in table 1, the mean total scores of EFs and their components (such as inhibition, orientation, emotional control, initiate, working memory, planning, organization, and monitoring) were higher in the experimental group than that in the controls in the posttest.

Table 1. Descriptive indexes of executive functions and their components in experimental and control groups

The dependent variable	Group	Pretest		Posttest	
		Mean	SD	Mean	SD
Inhibition	Experimental	26.50	± 4.73	23.00	± 4.306
	Control	25.75	± 3.54	25.08	± 3.260
Orientation	Experimental	23.08	± 2.31	20.58	± 1.920
	Control	22.67	± 3.05	22.17	± 2.580
Emotional control	Experimental	17.50	± 2.43	15.33	± 1.770
	Control	18.00	± 2.25	17.42	± 2.150
Initiate	Experimental	16.00	± 1.53	13.67	± 1.430
	Control	16.25	± 0.87	15.17	± 1.115
Working memory	Experimental	22.17	± 2.08	19.25	± 1.810
	Control	21.75	± 1.96	21.33	± 1.820
Planning	Experimental	28.00	± 1.90	25.50	± 2.060
	Control	28.75	± 2.41	28.17	± 2.120
Organizing	Experimental	15.58	± 1.31	13.25	± 1.760
	Control	15.42	± 1.37	14.50	± 1.440
Monitoring	Experimental	21.33	± 1.77	19.00	± 2.210
	Control	20.83	± 1.85	19.92	± 1.730
Executive functions	Experimental	170.16	± 7.80	149.58	± 7.270
	Control	169.41	± 6.25	163.75	± 6.390

SD: Standard deviation

Table 2. The results of homogeneity of variances and variance-covariance matrices for executive functions and their components*

The dependent variable	Levene's test	P
	F	
Inhibition	1.006	0.3270
Orientation	0.100	0.7540
Emotional control	2.543	0.1250
Initialization	0.028	0.8680
Working memory	0.555	0.6460
Planning	3.158	0.0890
Organizing	2.758	0.1110
Monitoring	0.958	0.3380
Executive functions	1.572	0.2230

*Box's M test: F = 1.820; P = 0.524

Moreover, the results of the statistical distribution of the above variables showed that all variables were distributed in the range ± 1 and the default was the normal distribution of data for the use of parametric tests.

Before applying the parametric test of multivariate analysis of covariance (MANCOVA) for EFs and their components, the homogeneity of variance assumption was examined using Levene's test and the results indicated that this default was set for the total score of the EFs and their components (Table 2). Subsequently, to test the homogeneity of variance-covariance matrices, Box's M test was used. The results of this test were not calculated due to the high multicollinearity in the dependent variables (the total score of the EFs and their components) and the non-observance of this default. Therefore, considering the absence of this assumption for MANCOVA and the existence of multicollinearity risk in dependent variables, one-variable ANCOVA was used to examine the difference between the total score of EFs in

the two groups and MANCOVA was applied to examine the difference between executive function components. In addition, the assumption of homogeneity of the regression line slope and the existence of a linear relationship between the covariate variable and the dependent variable were studied the results of which showed the establishment of these two defaults for the total score of EFs (Table 3).

The results presented in table 3 show that considering pretest scores as auxiliary variables, the use of CRT resulted in a significant difference between the groups in the total score of EFs ($F = 161.526$, $\eta^2 = 0.885$), which was 88.5%. This showed that part of the individual differences in EFs was due to differences in group membership (impact of the intervention). Therefore, the implementation of CRT led to a decrease in the mean total executive function scores of the experimental group participants (Table 1) compared to the control group. Therefore, it can be argued that CRT was effective on the EFs of children with HFA.

Table 3. Results of analysis of covariance of intergroup effects for executive functions in experimental and control groups

Variable	Source of changes	Sum of squares	Average squares	F	P	ETA square	Statistical power
Executive functions	Pretest group	2.961	2.961	0.352	0.5590	0.017	0.087
	Pretest	862.123	862.123	105.848	0.0001	0.834	1.000
	Group	1315.621	1315.621	161.526	0.0001	0.885	1.000
	Error	171.044	8.145				

Table 4. The results of multivariate analysis of covariance for the two groups in the executive functions components

Title of exam	Value	F	P	ETA coefficient	Test power
Wilks' lambda	0.968	26.306	0.0001	0.968	1
Piley effect	0.032	26.306	0.0001	0.968	1
Hotelling's effect	30.064	26.306	0.0001	0.968	1
Biggest root	30.064	36.306	0.0001	0.968	1

In order to use MANCOVA for executive function components, the homogeneity of variance-covariance homogeneity assumptions was examined using Box's M test; the results presented in table 2 indicated that the test was insignificant for the executive function components ($F = 1.028$, $P = 0.4250$). Therefore, considering the existence of this assumption, MANCOVA and the lack of multicollinearity risk in the dependent variables were used to analyze the differences between the executive function components in the two groups. Furthermore, the hypothesis of homogeneity of the regression line slope and the existence of a

linear relationship between the covariate variable and the dependent variable were investigated, which resulted in the establishment of these two defaults for the EFs components (Table 4).

After controlling the effect of pretest, the significance level of Wilks' lambda showed that there was a significant difference between the two groups in at least one of the components of EFs, indicating that 97% of the observed difference in the mean of the executive function components was related to the effect of CRT. The statistical power of 1 also indicates the adequacy of sample size and acceptable statistical accuracy for this conclusion (Table 5).

Table 5. Results of analysis of covariance of inter-group effects of the components of executive functions

Variable	Source of changes	Sum of squares	Average squares	F	P	ETA coefficient	Test power
Inhibition	Pretest group	0.518	0.518	0.299	0.6040	0.0470	0.075
	Pretest	210.741	210.741	115.620	0.0001	0.8920	1.000
	Group	34.311	34.311	18.824	0.0010	0.5730	0.981
	Error	25.518	1.823				
Orientation	Pretest group	0.018	0.018	0.041	0.8470	0.0070	0.053
	Pretest	25.415	25.415	26.134	0.0001	0.6510	0.997
	Group	11.631	11.631	11.960	0.0040	0.4610	0.895
	Error	13.615	0.972				
Emotional control	Pretest group	0.001	0.001	0.001	0.9820	0.0001	0.050
	Pretest	60.742	60.742	44.916	0.0001	0.7620	1.000
	Group	13.837	13.837	10.232	0.0060	0.4220	0.845
	Error	18.933	1.352				
Initiate	Pretest group	0.834	0.834	0.871	0.3870	0.1270	0.124
	Pretest	14.625	14.625	18.228	0.0010	0.5660	18.228
	Group	8.604	8.604	10.724	0.0060	0.4340	0.861
	Error	11.233	0.802				
Working memory	Pretest group	0.732	0.732	0.476	0.5160	0.0740	0.476
	Pretest	22.794	22.794	12.602	0.0030	0.4740	12.602
	Group	31.455	31.455	17.391	0.0010	0.5540	0.972
	Error	25.322	1.809				
Planning	Pretest group	1.054	1.054	0.650	0.4510	0.0980	0.105
	Pretest	42.111	42.111	32.931	0.0001	0.7020	1.000
	Group	22.590	22.590	17.660	0.0010	0.5580	0.974
	Error	17.902	1.279				
Organizing	Pretest group	2.316	2.316	1.413	0.2790	0.1910	0.172
	Pretest	21.228	21.228	15.048	0.0020	0.5180	0.950
	Group	11.170	11.170	7.910	0.0140	0.3610	0.744
	Error	19.749	1.411				
Supervision	Pretest group	2.706	2.706	1.613	0.2510	0.2120	0.189
	Pretest	44.064	44.064	39.389	0.0001	0.7380	1.000
	Group	8.804	8.804	7.869	0.0140	0.3600	0.742
	Error	15.662	1.119				

The results presented in table 5 show that, considering the pretest scores as the auxiliary variables, the use of CRT led to a significant difference between the groups in the components of inhibition ($F = 18.82$, $\eta^2 = 0.57$), orientation ($F = 11.96$, $\eta^2 = 0.46$), emotional control ($F = 10.23$, $\eta^2 = 0.42$), initiate ($F = 10.72$, $\eta^2 = 0.43$), working memory ($F = 17.39$, $\eta^2 = 0.55$), planning ($F = 17.66$, $\eta^2 = 0.56$), organizing ($F = 7.91$, $\eta^2 = 0.36$), and monitoring ($F = 7.87$, $\eta^2 = 0.36$). The effect level of the components of inhibition, orientation, emotional control, initiate, working memory, planning, organizing, and supervision was, respectively, 57%, 46%, 42%, 43%, 55%, 56%, 36%, and 36%. This showed that part of the individual differences in the components of EFs was due to the difference in group membership (the impact of the intervention). Therefore, the implementation of CRT resulted in a decrease in the mean scores of the experimental group participants (according to table 1) in the components of inhibition, orientation, emotional control, initiate, working memory, planning, organizing, and supervision compared to the control group. Therefore, it can be argued that CRT is effective on the EFs of children with HFA.

Discussion

The aim of this study was to determine the effectiveness of CRT on EFs of children with HFA. The results of the present study showed that CRT significantly reduced the total score of EFs and their components, including inhibition, orientation, emotional control, initiate, working memory, planning, organizing, and supervision, in children with HFA. In other words, CRT was effective on EFs of children with HFA. This finding is consistent with the findings of Miyajima et al.,²³ Eack et al.,²⁴ Eack et al.,³² Marceau et al.,³³ Katsumi et al.,²⁷ and Wykes et al.³⁴ CRT, as an evidence-based intervention, can be effective in improving the psychological

neuropsychiatric processes and the daily functioning of children with autism. In this regard, Glenthøj et al., in a study reviewing researches on the effectiveness of CRT, provided strong evidence of the effect of CRT on improving cognitive processes such as working memory.³⁵ Marceau et al. reported that CRT has a significant effect on EFs and leads to improvements in functions such as inhibition, control, and flexibility.³³ A meta-analysis study and a clinical trial have shown that CRT can significantly improve cognitive and psychological functions.^{34,36} The content of CRT includes repetitive exercises, strategies for modifying cognitive deficits and how to extend the tasks of exercises to daily tasks, and learning. One of the goals of CRT is to improve patients' social compatibility and to improve certain cognitive dimensions. CRT can simultaneously reduce cognitive deficits and behavioral symptoms of patients.³⁷ Studies conducted on the effect of CRT on EFs have suggested that the use of CRT may have altered the brain function of patients in the prefrontal cortex and improved brain structures such as increasing the amount of gray matter in the brain in disorders such as schizophrenia, stroke, and brain damage.³⁸ Similarly, recent research on anorexia nervosa has also reported changes in the activity of the prefrontal cortex during the program's homeopathic program.³⁹ It has also been pointed out that cognitive activation techniques used in CRT are likely to lead to psychological adaptation of the brain through tissue enlargement as a result of neuroplasticity (the ability of the brain to reset itself by creating new neural connections throughout life that leads to more efficient neurophysiological processing). Neuroplasticity allows brain neural cells to adapt to damage and disease in response to new situations or changes in the environment.⁴⁰ Furthermore, Penades et al. reported a significant improvement in brain function of

patients after applying CRT, which may be due to an increase in the transmission of information between the pelvic regions between the prefrontal cortex regions through the pink body.⁴¹ These techniques increasingly relate to computer assignments that are used for common exercises to enhance learning through CRT.⁴¹ The exercises used in most programs include graded changes based on the difficulty level resulting in a program that adapts to the dynamic performance of a person over time.⁴² Penades et al. showed that changes in EFs were accompanied by significant changes in personal autonomy and overall performance after receiving CRT.⁴¹ Despite the empirical evidence that CRT has an impact on the EFs of children with autism, further research is needed to understand the underlying mechanisms for the effectiveness of CRT in EFs of children with autism disorders.⁴³

Conclusion

One of the most important limitations of this study was the use of paper-and-pencil scale administration for measuring the performance of children. It is suggested that in future research, a computer psychological nerve be used to measure cognitive and rehabilitate performance based on the brain function of the subject. The lack of a follow-up phase was another limitation to the study. Therefore, the use of follow-up research projects in future studies can be effective in obtaining reliable results on the therapeutic effects of this approach. Although the results of this study have great implications for the treatment of cognitive and rehabilitate performance in children with HFA, further research is needed to generalize the results of this study.

Conflict of Interests

Authors have no conflict of interests.

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The prevalence of malnutrition in a pediatric hospital of Tabriz City, Iran, in 2016

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Original Article

Abstract

BACKGROUND: Malnutrition is a disorder that results from reduction or imbalance in the absorption of food and energy. It leads to prolongation of hospitalization and increased mortality in patients. Screening reduces the costs, complications, and duration of hospitalization. We have tried to evaluate the prevalence of malnutrition in hospitalized children in Tabriz Pediatric Hospital, Tabriz, Iran, and review the validity of the standard questionnaire of Iran Ministry of Health for pediatric malnutrition.

METHODS: In this descriptive cross-sectional study, 400 patients were examined. All patients were screened for malnutrition status in the first 24 hours, using a primary nutritional assessment form. Patients were divided into two categories: no malnutrition or mild malnutrition and moderate to severe malnutrition. SPSS software was used to analyze the data.

RESULTS: Of the 400 admitted and studied patients, 238 patients were in the age range of 1 to 60 months (group I) and 162 patients were in the age range of 5 to 19 years (group II). In group I, 11 patients were diagnosed with moderate acute malnutrition (MAM). Severe acute malnutrition (SAM) is defined as weight for height of less than -3 Z-score, which means that 7 cases of patients (2.9%) had severe malnutrition or severe weight loss. In group II, there were 20 patients (12.3%) among a total of 162 patients who were overweight, and 10 patients (6.2%) were obese.

CONCLUSION: The results of this study differed from previous studies. Therefore, it is recommended that the Ministry of Health questionnaire be reconsidered, and a restudy is necessary.

KEYWORDS: Body Mass Index, Malnutrition, Overeating

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Introduction

Malnutrition is a nutritional disorder that results from reduction or imbalance in the absorption of energy, protein, vitamins, and minerals,¹ which leads to lower quality of life, increased hospital costs due to increased patient care and prolongation of hospitalization period, delay in recovery, and increased mortality in hospitalized patients.^{2,3}

Malnutrition in patients especially in hospitalized patients has been known for over 20 years.^{4,5} The risk of mortality in children with malnutrition is higher. If children with moderate malnutrition do not receive appropriate treatment support, their disease progresses to severe malnutrition, which is life-threatening. Therefore, malnutrition management is considered a community health priority. In Europe and the United States (US), 40 to 50 percent of hospitalized patients had malnutrition at the onset of admission, and this percentage increased with

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age increasing.^{6,7} On the other hand, malnutrition intensifies during the hospitalization period, which is related to the underlying disease or psychosocial factors. Ultimately, it is possible to see anorexia, increased nutritional requirements, difficult swallowing, and nausea and vomiting.²⁻⁹ Lack of proper nutrition screening despite the high prevalence of malnutrition caused that this disease remains unknown and incurable.^{5,10,17} The Supplemental Nutrition Assistance Program guidelines mention nutrition screening as the first step in nourishing care during admission.¹¹ One of the ways to reduce the burden of severe malnutrition is to prevent it in children younger than two years (who are most vulnerable to injury).¹⁴ Early diagnosis and screening of these patients reduces the complications of the disease, duration of hospitalization, and hospital costs.^{5,10,12} Screening and rapid nutrition interventions also improve the care quality of treatment group.¹⁰ About 12.6% of 6.9 million deaths of children under the age of 5 years, which includes more than 800000 deaths, are due to malnutrition. Rapid diagnosis of patients using screening methods based on weight condition, weight loss and dietary intake, body mass index (BMI), and eating disorders,¹³ and then nutritional interventions such as nutritional counseling, providing educational pamphlets, supplements, and supportive feeding through tubes or intravenously can improve the nutritional status of patients.^{15,16} Complete nutrition assessment is very time-consuming and expensive.¹ The goal of nutritional screening is the rapid identification of patients with malnutrition or at risk of malnutrition.¹² In this study, we have tried to evaluate the prevalence of malnutrition in hospitalized children in Tabriz Pediatric Hospital, Tabriz, Iran, and to review the strengths and weaknesses of the standard questionnaire of Iran Ministry of Health for pediatric malnutrition.

Materials and Methods

In this descriptive cross-sectional study, all children and adolescents who were admitted to Tabriz Pediatric Hospital from the start to end of the study (3-month period in 2016) and their samples reached 400, were evaluated under initial nutritional assessment. The criteria for entering were all children and adolescents who were between 1 month and 18 years old and admitted to different wards. Patient exclusion criteria included admission to the emergency department, neonatal ward, and neonatal intensive care unit (NICU), and admission for less than 24 hours in wards. All studied patients were screened for malnutrition status in the first 24 hours after admission using a primary nutritional assessment form, done by an intern medical student who had enough training to evaluate nutritional indicators. All patients' information such as name, gender, date of birth, weight, and height were recorded.

For patients requiring a nutritional expert assessment, specialist assessment and follow-up sheets were considered in the patient's file. Patients' entry criterion for a nutritional expert assessment was responding yes to each of the information collection form questions, and then they were referred to the nutrition expert for advice, by completing the consultation request form. All completed datasheets included initial evaluation sheets, specialized evaluation, and the patient's nutritional status follow-up reports at the end of the study. All patients were examined in the last 24 hours of hospitalization period, and also if the patients were admitted for more than one week, they were re-evaluated for malnutrition status. In the case of re-admission of children during the study or at least for 3 months, the child was not considered as a new patient.

SPSS software (version 24, IBM Corporation, Armonk, NY, USA) was used for data analysis. Descriptive statistics including frequency distribution tables, percent frequency, mean,

standard deviation (SD), and absolute and relative frequency (percent) were used to describe the research variables. Final results were presented after the analysis in the form of tables and charts. A histogram chart was used for quantitative variables and bar charts and pie charts were used for qualitative variables.

Results

Of the 400 admitted and studied patients, 238 patients were in the age range of 1 to 60 months (group I) and 162 patients were in the age of 5 to 19 years (group II). In both age groups, the number of girls and boys was almost equal. The mean age in the group I was 20.91 months and in group II was 8.12 years. Average of height and weight in groups I was 78.89 cm and 10.42 kg, respectively. In group II, the average height was 16.75 cm and the average weight was 12.36 kg. In this study, group I has been hospitalized for on average 6.82 days, while the other age group was admitted for 5.54 days (Table 1).

Malnutrition in patients of 1 to 60 months old: Z-score table of patients' weight-height shows that the weight distribution chart is a chart which has a normal and bell-shape distribution that has the largest number of patients in the Z-score of between -1 and 1, and the Z-score becomes smaller by getting away of it.

Table 1. Weight-height Z-score distribution in the age group of 1 to 60 months (group I)

Z-score	n (%)	Cumulative percentage
0	2 (0.8)	0.8
-3 >	7 (2.9)	3.8
-3 ≤ -2	11 (4.6)	8.4
-2 ≤ -1	31 (13.0)	21.4
-1 ≤ 0	62 (26.1)	47.5
0 ≤ 1	65 (27.3)	74.8
1	16 (6.7)	81.5
1 <= 2	33 (13.9)	95.4
2 <	6 (2.5)	97.9
3 <	5 (2.1)	100
Total	238 (100)	

Therefore, the variable has a normal distribution. According to the definitions given in the methodology, 11 patients were diagnosed with moderate acute malnutrition (MAM). Severe acute malnutrition (SAM) (severe weight loss) is defined as weight for height Z-score of less than -3, which means that 7 cases of patients (2.9%) had severe malnutrition or severe weight loss.

Malnutrition in the group of 5 to 19 years old: Table 2 shows the patients' Z-score distribution based on BMI. Based on this table, most of the patients were in the range of -1 to 1 Z-score. According to the Iran Ministry of Health definition which has been presented in the methodology, in the age range of 5 to 19 years, overweight is to have a BMI with a Z-score of more than 1 to 2, and obesity is to have a BMI with a Z-score of more than 2. Based on this and according to the table above, in the present study, there were 20 patients (12.3%) among a total of 162 patients aged 5 to 19 years who were overweight and 10 patients (6.2%) were obese.

Table 2. Body mass index (BMI) Z-score distribution in the age group of 5 to 19 years (group II)

Z-score	n (%)	Cumulative percentage
Valid		
-3 >	2 (1.2)	1.2
-3 ≤ -2	7 (4.3)	5.6
-2 ≤ -1	15 (9.3)	14.8
-1 ≤ 0	34 (21.0)	35.8
0 ≤ 1	65 (40.1)	75.9
1	9 (5.6)	81.5
1 <= 2	20 (12.3)	93.8
2 <	5 (3.1)	96.9
3 <	5 (3.1)	100
Total	162 (100)	

Discussion

Of the 400 admitted and studied patients, 238 patients were in the age range of 1 to 60 months (group I) and 162 patients were in the age range of 5 to 19 years (group II). In group I, 11 patients were diagnosed with

MAM. SAM (severe weight loss) is defined as weight for height Z-score of less than -3, which means that 7 cases of patients (2.9%) had severe malnutrition or severe weight loss. In group II, there were 20 patients (12.3%) among a total of 162 patients who were overweight and 10 patients (6.2%) were obese. In the present study, a total of 400 patients were referred and hospitalized in different departments of Tabriz Pediatrics Hospital for one year. According to our searches in the SID, PubMed, MEDLINE, and Google Scholar databases, a similar topic has not been ever studied in Iran. In a study done by Hendrikse *et al.* the study was performed on 226 hospitalized children.¹⁸ Also, in another study which has done by Naber *et al.*, 155 hospitalized children were examined for internal and digestive diseases.³ In the present study, the proportion of males and females has been reported as approximately equal with the relative preference of males. Based on the charts, it seems that with the general increase in age, hospitalization reduced to some extent. Height charts in both groups had a normal distribution. In the term of hospitalization days, patients of group I were hospitalized for 6.82 days on average and those of group II for 5.54 days. Most patients were admitted for 3 days in both groups.

However, the most important indicator in this study was height and weight index based on height, weight, and BMI based on Z-score. Also, 4.62% of patients had Z-scores of more than 2 who were overeating accordingly, which is considered as malnutrition. Accordingly, 13.9% of patients had been malnourished during admission generally. In the study by Naber *et al.*,³ 45% of patients were malnourished while admitting and it was shown that malnutrition often was seen in hospitalized patients. Therefore, the prevalence of malnutrition in hospitalized patients was much lower than that estimated in some previous studies based on the

Ministry of Health standard questionnaire. In the case of group II, evaluation was based on BMI. Accordingly, the distribution of patients' Z-scores in the chart shows that a total of 11.73% of patients in this age group was malnourished while admitting. Accordingly, malnutrition statistics while admitting in the group I had no significant difference with malnutrition in group II. Also, 4 patients had a decrease in the Z-score for more than 2 units, which means that they have suffered acquired hospital malnutrition. In further evaluations, all four patients had suffered from nephrotic syndrome which was not among the exclusion criteria of Iran Ministry of Health questionnaire. Therefore, According to the statistical difference between the present study and the previous studies and also the problems of the Ministry of Health questionnaire, it is suggested to carry out more extensive studies after the current questionnaire reforms.

Conclusion

In group I, 11 patients were diagnosed with MAM, which means that 2.9% had severe malnutrition or severe weight loss. In group II, 12.3% were overweight and 6.2% were obese. The results of this study differed from those of the previous studies. Therefore, it is recommended that the Ministry of Health questionnaire be reconsidered, and a restudy is necessary.

Conflict of Interests

Authors have no conflict of interests.

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The study of factors affecting concentration in classroom among high school students in Divandarreh City, Iran, in 2018

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Original Article

Abstract

BACKGROUND: Concentration is one of the most important requirements of education and learning; so that decentralization and distraction in the classroom is one of the most common educational problems. The purpose of this study was to determine the factors affecting the concentration in the classroom among high school students in Divandarreh City, Iran, in 2018.

METHODS: This cross-sectional study was conducted in 2018 among all high school students in Divandarreh City. The sample size was 370 and the cluster sampling method was used. The research instrument was a questionnaire containing demographic characteristics and concentration in classroom. Exclusion criteria included the lack of consent or incorrect completion of the questionnaire. Finally, the data were analyzed by descriptive statistics [frequency, mean, and standard deviation (SD)] and chi-square test.

RESULTS: In this study, 54% (198 boys) were male and 46% (172 girls) were female. The average score of the factors related to the teacher was 28.98 ± 5.79 , for the factors related to the student was 29.07 ± 5.76 , and for the environmental factors was 8.20 ± 2.48 . The most effective factor in concentration in class was the teacher ethics and his/her appropriate behavior with the students (3.18 ± 1.00) and the least effective factor was relying on booklet (1.94 ± 1.10). There was a significant relationship between gender and the teacher-related factors ($P < 0.001$), student-related factors ($P = 0.004$), and environmental factors ($P < 0.001$).

CONCLUSION: According to the results of this study, by improving the behavior of teachers and professors and empowering them to bring their students together, they can play a major role in increasing the students' learning and concentration.

KEYWORDS: Concentration, Students, Learning, Iran

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Introduction

Education is the most important principle in an educational system and attention and concentration in the classroom is considered as one of its most important foundations. Consequently, lack of attention and concentration will result in a lack of proper learning and ultimately lack of progress.¹

Focus is a behavioral and cognitive process, i.e., it is selective and based on the intended purpose in ignoring other understandable information. In other words, focus means that the mind is clearly drawn from the various simultaneous spaces of thought to the desired goal.² Professors often talk about attention and concentration as a general mental state in which the mind focuses on certain special features of the environment, so they regard the focus as one of the main pillars of education and believe

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that the students who are unable to focus, cannot benefit from appropriate training.³ Regarding the importance of concentration in learning and teaching, especially in the classroom, it can be noted that it is one of the most important needs of education and learning, which aimed at promoting education through decentralization and distraction in the classroom.⁴

It is worth considering the point that it is easy to focus on improving patterns by modifying some patterns.⁵ In a study by Mehralizadeh et al., it was concluded that students had the highest concentration in the front row of the class (58.3%) and the time interval of 10-12 a.m. (43.8%).⁵

There are several factors that influence concentration in the classroom, which can be generally categorized into three categories:

I. The factors associated with the teacher such as his/her skill in motivating and applying the material, having sufficient knowledge and information, the grasp of the subject of teaching in the classroom, the use of educational aids, teacher ethics, and the uniformity of the teacher's voice.⁶⁻⁸

II. Student-related factors such as attendance in class, classroom sleepiness, having individual intellectual involvement, interest in the subject of course, and the desired nutrition before class.⁹⁻¹²

III. Environmental factors such as the presence of sound pollution in the class, the presence of light and ventilation in the classroom, and too many students in class.^{13,14}

The classroom is a special place for learning and transferring experience and knowledge between professors and students; therefore, the need for attention and concentration in class must be taken into consideration more and more.¹⁵ Quality in education is an important issue in the educational system of each country in order to improve their educational status.⁵

One of the important factors in creating

concentration in students is motivation; therefore, it is one of the important factors in learning and progress in students;¹⁶ so that professors can create positive motivation in students and transfer knowledge in different ways, educate their students and encourage them to work more and more to learn, and ultimately improve the educational and academic achievement of students.¹⁷

Materials and Methods

This cross-sectional study was carried out in the academic year of 2018-2019. The statistical population included all high school students of Divandarreh City in Kurdistan Province, Iran. According to the Cochran formula, the P-value of 0.05, and a confidence level of 95%, the sample size was estimated to be 370 people.

Multistage sampling was used, in which boys and girls were considered to be two clusters. The sample size assigned to each cluster was proportional to the size of the floor. The number of classes within school and the number of students in each class would also be selected according to their size. Finally, the volume allocated to each class was selected using simple random sampling.

The criteria for entering the study included students aged 16-19 in the city of Divandarreh in all disciplines and all schools, and the criteria for leaving the study included lack of interest in completing the questionnaire and incorrect completion of the questionnaires.

After approval of the school administrators, informed consent was obtained from all students. It also emphasized the protection of all information about them.

The research tool was a questionnaire about factors influencing concentration in the class which had 25 questions. The aim of this study was to investigate the factors affecting concentration in the classroom from the viewpoint of students (factors related to the teacher, factors related to the student, and environmental factors). The questionnaire

consisted of two sections: demographic characteristics (gender, grade, and academic average) and questions related to concentration from the students' point of view in three sections: faculty affiliation (11 items), student-related factors (11 items), and environmental factors (3 items). The questions were scored in a 5-point Likert scale from 0 to 4 for ineffective, very low, low, high, and very high responses, respectively.

In the study by Mehralizadeh et al.,⁵ the validity of the questionnaire was criticized and verified by reviewing the articles, texts, and counseling with leading experts and professors of the university. To test its reliability by means of a re-test, the questionnaire was given to 15 students in two time intervals of 10 days. By calculating the Spearman correlation coefficient, the reliability was confirmed ($r = 0.77$).

In this study, quantitative variables were estimated based on mean and standard deviation (SD) and qualitative variables based on number and percentage. The abundance of each of their domains and subcategories was calculated based on the Likert scale and the mean and SD of the total in each of the domains and subcategories were also calculated. Data analysis was performed using Stata software (version 12, Stata Corporation, College Station, TX, USA). For all tests, the level of significance was considered as 0.05. For all of the above parameters, the 95% confidence interval (CI) was also calculated.

Results

In this study, 370 high school students from 10 schools in the city of Divandarreh were enrolled. 54% (198 students) were male and 46% (172 students) were female. The mean and SD of students' age was 16.80 ± 0.71 years.

38% (140 students) were at the 10th grade, 48% (177 students) at the 11th grade, and 14% (53 students) at the 12th grade.

In terms of students, the mean score of the

factors related to the teacher was 28.98 ± 5.79 , for the factors related to the student it was 29.07 ± 5.76 , and for the environmental factors was 8.20 ± 2.48 .

Among the factors related to the teacher, the appropriate behavior of the teacher with the students (3.18 ± 1.00) and his/her ability to bring the students together (3.00 ± 1.02) got the highest scores. On the other hand, the difference in teacher's gender with that of student (1.97 ± 1.47) and the use of PowerPoint teaching aids got the lowest scores (2.12 ± 1.18).

Of the factors associated with the students, the most related factors were interest in the subject (3.18 ± 0.99) and active attendance in the classroom (3.08 ± 0.91). In the area of environmental factors, the presence of light and ventilation in the class (2.71 ± 1.10) had the highest correlation with the concentration and the presence of noise pollution in the class had the least correlation (2.74 ± 1.24) with student focus (Table 1).

From the viewpoint of the students in this study, the most effective factor in concentration in the class was the teacher ethics and his/her appropriate behavior with students (3.18 ± 1.00) and the least effective factor in the classroom was relying on the booklet (1.94 ± 1.10).

As shown in table 2, according to Mann-Whitney U statistical analysis, there was a significant relationship between gender and teacher-related factors ($P < 0.001$), student-related factors ($P = 0.004$), and environmental factors ($P < 0.001$).

In the present study, the students' grade point average (GPA) was divided into 4 groups: under 14, 14-16, 16-18, and 18-20, respectively. The frequency of each group was 38 (11%), 96 (25%), 156 (42%), and 80 (22%).

At the end, and for better statistical analysis, the GPA of less than 16 years was considered "weak" and higher than it was considered "strong".

Table 1. Mean, standard deviation (SD), and total score of questions about the factors related to concentration in the classroom from the point of view of high school students (n = 370) in Divandarreh City, Iran, in 2018

Questions	Sum	Mean ± SD
Teacher's skills in motivating (applied submission)	1103.00	2.98 ± 1.04
Proper time management of the teachers	1022.00	2.76 ± 0.93
Use of PowerPoint tutorial tool	785.00	2.12 ± 1.18
Large volume of teaching materials in one session	874.00	2.36 ± 1.33
Positive mental history from teacher	992.00	2.68 ± 1.10
Good speed of teaching	997.00	2.69 ± 1.00
Uniformity of the teacher's voice (being monotone)	820.00	2.21 ± 1.19
Appropriate teacher's correspondence with students (teacher ethics)	1180.00	3.18 ± 1.00
Teacher's ability to bring students together with him/her	1112.00	3.00 ± 1.02
Teacher's knowledge and information about discussion	1110.00	3.00 ± 1.02
Teacher's different gender with students	731.00	1.97 ± 1.47
Desired nutrition before class	1036.00	2.80 ± 1.09
Sleepiness in the class	930.00	2.51 ± 1.36
Having a student base on the topics presented	946.00	2.55 ± 0.95
Focusing on other students	954.00	2.57 ± 1.12
Being interested in subject curriculum	1178.00	3.18 ± 0.99
Individual intellectual conflict	1089.00	2.94 ± 1.16
Active presence in class	1139.00	3.08 ± 0.91
Belief in learning the content during teaching	1072.00	2.90 ± 1.02
Relying on the booklet	719.00	1.94 ± 1.10
Students with different gender in class	790.00	2.13 ± 1.46
Read prepared pamphlets or reference books before class	902.00	2.43 ± 1.21
Presence of noise pollution in the class	1014.00	2.74 ± 1.24
Presence of light and ventilation in the class	1006.00	2.71 ± 1.10
Large number of students in the class	1017.00	2.74 ± 1.27

SD: Standard deviation

According to the chi-square test, there was a significant relationship between the GPA and the concentration of students ($P = 0.009$); as 90% of the students with a strong GPA had high concentration level in the classroom (Table 3).

Discussion

Results of this study showed that teachers' ethics had the greatest impact in the field of teachers related factors and being interested in subject curriculum and active presence in class

had the greatest impact in the student related factors; and in the field of environmental factors, the presence of light and good ventilation had the most impact. A relationship between GPA and concentration among the students was observed, and also a significant relationship between gender and all 3 groups of factors (factors related to the teacher, factors associated with students, and environmental factors) affecting the concentration in the class was revealed.

Table 2. Mean and standard deviation (SD) and total scores of the factors related to concentration in the classroom (factors related to the teacher, factors related to the student, and environmental factors) from the point of view of high school students in Divandarreh City, Iran, in 2018

Concentration factors	Sex	N	Mean rank	95% CI for mean	Sum of ranks	Mean ± SD.	P
Factors related to teacher	Male	198	180.00	27.00-29.00	35745.00	28 ± 6	< 0.001
	Female	172	191.00	28.00-30.09	32890.00	29 ± 5	
Factors related to student	Male	198	170.00	27.00-29.01	33780.00	28 ± 6	0.004
	Female	172	202.00	29.00-30.00	34855.00	30 ± 5	
Environmental factors	Male	198	177.00	7.00-8.00	35177.00	7 ± 2	< 0.001
	Female	172	194.00	8.00-8.00	33458.00	8 ± 2	

SD: Standard deviation; CI: Confidence interval

Table 3. Investigating the relationship of grade point average (GPA) with concentration in the classroom from the point of view of high school students in Divandarreh City, Iran, in 2018

Variable		Concentration			Total [n (%)]	P
		Mild (Poor) [n (%)]	Moderate [n (%)]	Severe [n (%)]		
GPA	Weak	0 (0)	19 (14)	115 (86)	134 (100)	0.009
	Strong	3 (1)	7 (3)	226 (96)		

GPA: Grade point average

In the present study, it was evident that the interaction between the teacher and the students had the greatest impact. Such results are consistent with the results of the study of Ghadami et al.¹⁸ that they, too, characterized the teacher's moral behavior such as rhetoric teaching skills level, the scholarship and experience of the teacher as well as ethics and maintaining respect of the students as the most important factors in establishing communication from the viewpoint of the students. Contrary to the results of the present study, the study of Haresabadi et al.¹⁹ showed that proper time management in presentations by professors was the most important factor related to the teachers. Also in the study of Mehralizadeh et al.,⁵ Nazari Vanani et al.,²⁰ and Firouznia et al.,⁶ the teacher's ability to motivate and apply the curriculum has been identified as the most important factor in this field.

In the study of Yasayi et al.,²¹ the greatest factor in the absence of students in classrooms was the lack of interest in the subject as well as the inappropriate ethics of the professor.

In the study of Nazari Vanani et al.,²⁰ the motivating factor by the teacher played the most important role in the presence of students in the classroom. These results are similar to those of Haresabadi et al.¹⁹ and Fasihi Harandi et al.²² However, the studies of Mehralizadeh et al.,⁵ Nojomi et al.,¹⁰ and Ghorbani et al.¹⁴ have described sleepiness as the most important factor in this field.

Hughes in his study showed that lack of interest in the subject was one of the main causes of student absenteeism in the classroom.²³ Also, Gump showed that the attractiveness of syllabus was one of the most

important motivational factors in the classroom.⁷ The third area that was considered in this study was the environmental domain, in which the most important factor was the presence of light and ventilation in the classroom. These results are in accordance with the results of the studies by Haresabadi et al.¹⁹ and Mehralizadeh et al.⁵ In the study of Habibipour and Seif,²⁴ the inappropriate physical space of classes was mentioned as a major factor in absenteeism in the classroom. Decentralization in the classroom can cause lack of motivation and finally absenteeism in the classroom.

From the viewpoint of the students in the present study, the use of audiovisual teaching aids, such as PowerPoint, played a very small role in the student's concentration, which was consistent with the results of the Nazari Vanani et al.²⁰

The other results of the present study showed that there was a significant relationship between sex and the factors related to the teacher ($P < 0.001$), student-related factors ($P = 0.004$), and environmental factors ($P < 0.001$). So that female students showed more importance to these factors; these results are in line with the results of the study by Klohnen and Luo. In their study, the viewpoint of male and female students about the effect of environmental factors on concentration was significant, meaning that female students, due to their psychological characteristics, showed more importance to these factors.²⁵

On the other hand, in the present study, there was a significant relationship between the students' GPA and their concentration in

the classroom, so that students with a better grade had a better concentration; therefore, it could be concluded that the concentration has a direct relationship with academic achievement.

Conclusion

According to the overall results of the study, the most effective factor in the classroom was the teacher ethics and appropriate behavior with the students, so that teachers can improve their behavior to promote education and increase the efficiency and concentration of students. On the other hand, the use of educational tools like PowerPoint has had the least impact. Unfortunately, in the current modern society, some of the professors, regardless of the needs of their students, simply take the boring PowerPoint slides to the classroom with students actually do not need, and according to the results of this research, it is not the correct way. In area of environmental factors, by improving the light and ventilation of the classroom, as well as decreasing the number of student population in the class, one can expect a significant improvement in the quality of education.

Conflict of Interests

Authors have no conflict of interests.

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The overhang rate in posterior teeth restorations among a sample of patients from Sari City, Iran, in year 2017

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Original Article

Abstract

BACKGROUND: Overhang is the extension of restoration material from the prepared cavity. Restoration overhangs have an important role in plaque accumulation, caries, severe gingival inflammation, and periodontal diseases. Therefore, the aim of this study was to determine the frequency of restoration overhanging, and the managements in order to reduce its prevalence and subsequent complications.

METHODS: This descriptive cross-sectional study was conducted on 277 patients, who had at least one restoration in the proximal surface of posterior teeth. At first, all the patients were examined using a mirror, and dental floss under the light of the dental chair. In cases in which the existence of the overhang was suspected, Bitewing radiography was operated on respective regions. Data were analyzed using SPSS software.

RESULTS: 120 teeth had overhangs (19.60%) and 492 (80.39%) exhibited no overhangs. From 120 restorations with overhang, 76 (63.33%) were amalgam restorations, and 44 (36.66%) were composite restorations. In total, 55.83% of them (67 restorations) were in maxilla and 44.16% (53 restorations) were in mandible. The prevalence of overhang in mandible was as 37.73% in mesial regions, 54.71% in distal regions, and 7.54% in mesial-occlusal-distal (MOD) regions; in addition, the prevalence rate in maxilla was as 38.80% in mesial regions, 58.20% in distal regions, and 2.98% in MOD.

CONCLUSION: The overall frequency of restoration overhang was 19.60%, most of which was in amalgam restorations in comparison to composite restorations; and it is mostly seen in distal surfaces of maxillary teeth.

KEYWORDS: Prevalence, Overhang, Posterior Teeth, Composite Resin Restoration

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Introduction

Loss of teeth due to decay and periodontal diseases cause several issues in function (chewing, speaking, etc.) beauty, health, and patient comfort. Thus, restoration and prosthesis treatments are used to return proper function to dental system of patient.^{1,2} Amalgam has still been the most common restorative material which is used to restore decays.³ High fracture

resistance of this material in posterior teeth and cores, demonstrating low technique sensitivity, having favorable results concerning microleakage, and being affordable are the reasons why we use amalgam in our treatments.⁴

The main cause of gingival inflammation is due to bacterial plaques, calculus, overhang, orthodontic treatment, radiation therapy, smokeless tobacco, iatrogenic factors, the restoration materials, and the design of removable partial dentures.³ Overhang is the extra-amount of restoration which is out of prepared cavity.⁵ Overhang in amalgam

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restorations is a considerable issue in oral hygiene.⁴ The most common local factor causing periodontal disease in adults is overhanging dental restorations, and despite all efforts and techniques, Class II composite restoration will result in marginal overhang.⁵ In the past, it was difficult to create a good proximal contact with composite resin, as this material cannot be condensed like dental amalgam. However, now we can establish tight proximal contact using special separation rings.⁶

A review study on the prevalence of overhanging dental restorations reported the interproximal overhang from 25% to 76%.⁷ Restoration methods,³ and variable morphologies in cervical aspect of the tooth such as furcation, fluting, and concavities are the most common causes of poor restorations with overhang, which makes it difficult to place a wedge and matrix band, and to make marginal adaptation.⁴ Overhanging margins of dental restorations are the risk factors for periodontal diseases by changing the ecologic balance of the gingival sulcus to a desired area for growing disease-associated organisms (mainly Gram-negative anaerobic species), inhibiting patient's access to remove plaque, and it also causes caries.^{3,7-11} The position of gingival margin, compared to restoration margin, has direct effect on adjacent periodontal tissues; so the incorrect restoration margin or subgingival margins can be associated with reduction in bone height, high plaque accumulation, severe gingival inflammation, deep pockets, and periodontal disease.¹²⁻¹⁹ In summary, restorations must be based on tooth anatomy considering quality and proximal surface condition, contour, embrasures, and the ending level of margins.²⁰

The aim of this study was to assess the overhang frequency in patients, and the managements in order to reduce its prevalence and subsequent complications.

Materials and Methods

This descriptive cross-sectional study was

performed to investigate the prevalence of overhang (OH) in posterior teeth restorations. This study was completed over a period of 6 months, from May to October 2017. All individuals who visited a private dental office, Sari, Iran, and had at least one restoration in proximal surface of posterior teeth (molar and premolar), were included. People, with trismus or mental disorders such as mental retardation, which hindered effective communication, were excluded. Moreover, patients with restorations, that the existence of overhang in them was suspected but not confirmed, were excluded. Eventually, 277 patients were examined by two expert dentists. Written informed consent was obtained from all the participants.

At first, all the patients were examined by a mirror, and dental floss (Oral B, P & G GrossGerau, Germany) under the light of dental chair. In case of sticking or tearing of the flossing tape, the existence of overhang was suspected, and to confirm clinical findings, Bitewing radiography was operated on respective regions. Radiographies were conducted with Kodak photographic film (Estman Kodak, New York, NY, USA) and radiographic equipment (Planmeca ProXTM; Planmeca Oy, Helsinki, Finland).

The data were analyzed using chi-square test via SPSS software (version 23, IBM Corporation, Armonk, NY, USA).

Results

According to the mentioned inclusion and exclusion criteria, 277 patients were included in this study. In total, 612 teeth had restorations in proximal surfaces and according to examination, 120 teeth had overhangs (19.61%) and 492 teeth (80.39%) exhibited no overhangs, the difference was statistically meaningful [$\chi^2 = 228.118$, degree of freedom (df) = 1, $P < 0.001$].

Among all the successful restorations, 359 restorations (72.96%) were carried out

Table 1. The frequency of restorations without overhang according to the surfaces

Site	Surface	Mesial	Distal	MOD	Total
Maxilla		146 (67.59)	65 (30.09)	5 (2.31)	216 (43.90)
Mandible		145 (52.53)	123 (44.56)	8 (2.91)	276 (56.10)
Total		291 (59.14)	188 (38.21)	13 (2.64)	612 (100.00)

The amounts are presented as number (percent).

MOD: Mesial-occlusal-distal

using amalgam, and 133 restorations (27.03%) were performed using composite. There was a statistically significant relationship between the types of restoration and the overhang frequency ($\chi^2 = 5.125$, $df = 1$, $P = 0.024$).

Furthermore, out of all restorations with no overhangs, 216 were in upper jaw; and with respect to dental surfaces, 146 were in mesial, 65 in distal regions, and 5 in mesial-occlusal-distal (MOD) regions. On the other hand, 276 of restorations without overhangs were in lower jaw. With respect to dental surfaces, 145 were in mesial and 123 in distal (Table 1).

From 120 restorations with overhang, 76 (63.33%) were amalgam restorations, and 44 (36.67%) were composite restorations. In total, 55.83% (67 restorations) of them were in maxilla and 44.16% (53 restorations) were in mandible.

The prevalence of overhang in maxilla was as 38.80% in mesial, 58.20% in distal, and 2.98% in MOD regions. In addition, the prevalence rate in mandible was as 37.73% in mesial, 54.71% in distal, and 7.54% in MOD regions (Table 2).

There was no statistically significant relationship between teeth location and restoration success ($\chi^2 = 0.003$, $df = 1$, $P = 0.096$).

Discussion

Overhang is one of the most common factors

that cause periodontal disease in adults.²¹ Restoration overhangs cause plaque accumulation, caries, and periodontal diseases.²² We assessed overhang using clinical examination methods (dental floss), and bitewing radiographies. In this study, overhang and successful restoration frequencies were 19.6% and 80.4%, respectively, with a statistically meaningful difference. In other studies by Sikri and sikri,²⁰ Quadir et al.,²² Svensson,²³ and Pack et al.,²⁴ the restoration overhangs frequency was high, too.

The relationship between the prevalence of overhangs and restorative material (amalgam and composite) was significant in the present study. This finding could be attributed to dentist ability in accessing and isolating teeth during restoration, cause composite more sensitive technique than amalgam. However, there was no statistically significant relationship between teeth location and restoration success. Similar to our study, Quadir et al.²² reported no significant relationship between the prevalence of overhangs and teeth location ($P = 0.063$). These results are not consistent with those obtained by some other studies,¹⁰⁻²⁵ as their results revealed that overhang frequency was higher in the maxilla than the mandible, which was attributed to the easy accessibility of the mandibular teeth.

Table 2. The frequency of restorations with overhang according to the surfaces

Site	Surface	Mesial	Distal	MOD	Total
Maxilla		26 (38.80)	39 (58.20)	2 (2.98)	67 (63.33)
Mandible		20 (37.73)	29 (54.71)	4 (7.54)	53 (36.67)
Total		46 (38.33)	68 (56.66)	6 (5.00)	120 (100.00)

MOD: Mesial-occlusal-distal

Tavangar et al.²⁶ assessed overhang frequency with respect to jaw side, and found no significant relationship. Moreover, they found a higher frequency of overhang in distal surfaces and in posterior teeth ($P = 0.498$),²⁶ which was consistent to the other study performed in Pakistan.²²

These inconsistencies may be attributed to a relatively smaller sample size obtained from a private dental office in this study, compared to those treated by different dentists.

Amalgam is still the most common restorative material used in restorations, and according to studies, the highest frequency of overhang is related to amalgam restorations.¹ We found higher frequency of overhangs in amalgam restorations, which could be due to inaccuracy of the dentists to place wedge or not to use it, and incorrect using of matrix bands. Tough, in addition to the mentioned factors, variation in dental malformations is also considerable.

Conclusion

The prevalence of overhanging restorations was 19.60% in this study. In total, 55.83% and 44.16% of restorations with overhang were in maxilla and mandible, respectively. Amalgam restorations had more overhanging margins than composite restorations, whereby most of them were observed in distal surfaces of maxillary teeth, which may be a result of difficult accessibility of this area, during restoration, for dentists.

Conflict of Interests

Authors have no conflict of interests.

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The relationship between internet addiction, family relations, and psychological well-being in adolescents

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Original Article

Abstract

BACKGROUND: Internet is one of available modern communicational media that has created a new world for users; so that this virtual world may have irrecoverable implications. Hence, this study was conducted to examine the relationship between internet addiction, family relations, and psychological well-being among the adolescents.

METHODS: In this descriptive and correlational study, statistical population consisted of all adolescents in Urmia City, Iran. The sample size obtained to 65 adolescents, who were addicted to internet; they were enrolled using convenient sampling method in some schools in Urmia. To collect the data, Internet Addiction Test (IAT), Family Assessment Device (FAD), and Warwick-Edinburgh Mental Well-being Scale (WEMWBS) were employed. The data were analyzed using Pearson correlation and multiple linear regression tests through SPSS software.

RESULTS: There was a reverse significant relationship between internet addiction and family relations (-0.878) and subjective well-being among the adolescents ($P < 0.050$ for both).

CONCLUSION: According to obtained findings, it can be stated that internet addiction may lead to reduction in family relations and subjective well-being among the adolescents.

KEYWORDS: Addiction, Internet, Family Relations, Adolescent Well Being, Adolescent

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Introduction

Subjective well-being means cognitive and emotional understanding of life and health by the person, based on two components of cognition and emotion.¹ Cognitive aspect of subjective well-being indicates general evaluation of life satisfaction, and emotional aspect expresses high experience of positive

affect and low experience of negative affect.² Bordwine and Huebner believe that people with high subjective well-being have a higher control sense experiencing more life satisfaction and success.³

Family is based on the deepest mental and social relations, so that a healthy family is the base for healthy persons and society;⁴ family plays a vital role in life of people as the most important social-emotional unit of society. In fact, it can be stated that personality of person is formed in family.^{5,6}

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Family is the base for socialization process in person; so that the role of family is underlined in learning optimal and non-optimal social behaviors, and majority of researchers do agree on this matter that aggressive and offensive behaviors are rooted in family environment.⁷

Internet addiction consists of excessive, unreasonable, and problematic use of internet.⁸ This problem was introduced by Ivan Goldberg in 1995.⁹ According to the American Psychological Association, internet addiction is an unhealthy pattern of internet use that leads to functioning disorder along with undesired inner states during a two-month period.¹⁰ Internet addiction is along with some symptoms such as anxiety, depression, irritability, restlessness, obsessive ideologies, withdrawal, emotional disturbance and disruption of social relationships, reduced social relationships in the real world, and reduced educational performance.¹¹ Considering the relationship between excessive use of internet and personal-family relations among adolescents, this study was undertaken to examine the relationship between internet addiction, family relations, and psychological well-being among the adolescents.

Materials and Methods

This was a descriptive and correlational study. Statistical population consisted of all adolescents in Urmia City, Iran, and the sample size obtained to 60 adolescents, who were addicted to internet. They were selected using convenient sampling method in some schools in Urmia; internet addiction of these members was confirmed by Internet Addiction Test (IAT). To collect the data, IAT, Family Assessment Device (FAD), and Warwick-Edinburgh psychological Well-being Scale (WEMWBS) were employed.

IAT: This test is used to assess internet addiction and consists of 20 items preparing by Kimberly Young to evaluate dependency of

persons to internet and computer.¹² Widyanto and McMurrin reported the reliability of IAT equal to 89%;¹² Asgari and Marashain reported the reliability of Persian version of this test as 97% and 97% using two methods of Cronbach's alpha and Ballad methods, respectively.¹³

FAD: This scale consists of 60 items that is designed based on the McMaster model of family functioning to evaluate 7 factors including problem solving, relationship, roles, emotional response, emotional participation, behavior control, and general function.¹⁴ The internal consistency of this test was 72%-92%, and the correlation of obtained scores of questionnaire retest 66%-76%.¹⁵ Zadehmohammadi and Malek Khosravi obtained the correlation coefficient of Persian version of this scale as 56%-80% retesting subscales, and Cronbach's alpha varied between 88% and 90% for subscales and 90% for total scale.¹⁶

WEMWBS: This scale was designed by Tennant et al.,¹⁷ and consisted of 14 items based on a 5-point Likert scale (from never = 1 to always = 5). Minimum and maximum scores of this scale can be 14 and 70, respectively, and higher score shows better mental well-being. Cronbach's alpha coefficient of this scale was 89% and 91% for student sample and population members, respectively; reliability coefficient of retest (after one week) was 83% ($P < 0.001$).¹⁷ The correlation between total score and items of this instrument varied between 80% and 85%; simultaneous calculation of validity coefficient of WEMWBS with general health scale obtained as 43%, 74% for cognitive well-being, 73% for short form of happiness-depression questionnaire, 77% for 5-item world health questionnaire, 48% for emotional intelligence, and 53% for subscale of life satisfaction.¹⁷ Rajabi reported Cronbach's alpha of this scale as 78%, 75% for optimism, 52% for positive relationship with others, and 55% for being energetic;¹⁸ simultaneous validity

Table 1. Pearson correlation between internet addiction and family relations

Variables		Family relations	Internet addiction
Pearson correlation	Internet addiction	-0.878	1
P (2-tailed)		< 0.001	
Number		65	60
Pearson correlation	Family relations	1	-0.878
P (2-tailed)			< 0.001
Number		65	65

coefficient of this scale with 10-item general self-efficacy scale and 12-item social support scale obtained to 55% and 34%, respectively.¹⁸

The obtained data were analyzed using Pearson correlation and multiple linear regression tests through SPSS software (version 22, IBM Corporation, Armonk, NY, USA).

Results

Statistical sample consisted of 65 boys at age range of 15-18 year who had the same economic-social level, and 80% of them were educating in first and second grades of high school.

According to table 1, Pearson correlation coefficient was -0.878; and this correlation coefficient was significant ($P < 0.001$); hence, it can be stated that there was a reverse and significant relationship between internet addiction and family relations.

According to table 2, Pearson correlation coefficient obtained as -0.908; and this correlation coefficient was significant ($P < 0.001$); hence, it can be stated that there was a reverse and significant relationship between internet addiction and subjective well-being.

As table 3 shows, both the variables (family relations and mental well-being) had prediction ability and of these variables, subjective well-being (-1.747) had the highest prediction ability.

Discussion

The results indicated a negative significant relationship between family relations and mental well-being; in other words, more internet addiction indicates lower score of family relations and mental well-being. This finding is in line with results of Park et al. study that found parental attitudes; family relationships, family cohesion, and coping with violence are in relation with internet addiction.¹⁹

Moreover, Ling-Yan et al. concluded that people addicted to internet were at a low level in terms of the score of adaptability and cohesion in family.²⁰ Senormanci et al. found that people addicted to internet had higher scores of depression, intensive anxious attachment, and significant disorder in family functioning.²¹

Studies conducted by Weinstein and Lejoyeux²² and Bozkurt et al.²³ showed that internet addiction was related to mood disorders such as depression, anxiety disorders, and attention deficit hyperactivity disorder (ADHD).

Finally, the results of studies undertaken by Ozturk et al.²⁴ and Sharma and Sharma²⁵ indicated a significant negative relationship between internet addiction and psychological well-being.

Table 2. The Pearson correlation between internet addiction and subjective well-being

Variables		Subjective well-being	Internet addiction
Pearson correlation	Internet addiction	-0.908	1
P (2-tailed)		< 0.001	
Number		65	65
Pearson correlation	Subjective well-being	1	-0.908
P (2-tailed)			< 0.001
Number		65	65

Table 3. Results of multiple linear regressions to predict internet addiction

Variable	B	Standard error	Beta	T	P
Constant	96.329	2.268		42.482	< 0.001
Family relations	0.350	0.137	0.849	2.560	0.013
Subjective well-being	-2.076	0.394	-1.747	-5.270	< 0.001

These results show that internet addiction is an impulse control disorder and maladaptive pattern of internet usage that leads to a clinical disorder or disease creating psychological, educational, and occupational problems in life of people.²⁶

Conclusion

According to the findings, it is confirmed that there is a negative and significant relationship between internet addiction, family relations, and subjective well-being; in other words, excessive usage of internet would lead to mental disorders and tension in personal and family relationship.

Conflict of Interests

Authors have no conflict of interests.

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Prevalence and determinants of behavioral risk factors of non-communicable diseases among a selected slum population in Bangladesh

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Original Article

Abstract

BACKGROUND: Low and middle income countries and also the underprivileged population both are susceptible for the increased burden of non-communicable diseases (NCDs), and the practice of their behavioral risk factors (BRFs) is the main cause. However, these BRFs and their determinants among the slum population of Bangladesh weren't adequately evaluated. The present study was carried out with the aim to find out the prevalence and determinants of BRFs of NCDs among a selected slum population in Bangladesh.

METHODS: This cross-sectional study was conducted in purposively selected Rayerbazar slum of Dhaka city, Bangladesh, in 2017. A total of 192 adult (aged 18 to 65 years) residents were enrolled in this study using the convenient sampling method. A semi-structured questionnaire, adopted version of World Health Organization (WHO) STEPS instrument was used for data collection. Ascertainments of the risk factors were conducted as per the WHO STEPS guideline. Both descriptive and multivariate statistics were performed using the SPSS software.

RESULTS: The majority of the respondents (72.4%) were men, and the mean \pm standard deviation (SD) of the ages was 37.0 ± 13.6 years. Half (50%) of the respondents were tobacco users. Almost all (98.4%) reported insufficient fruit and vegetables (FAVs) intake. Almost 7 out of 10 (67.7%) of the respondents reported to perform inadequate level of physical activity (PA). However, very negligible (2.6%) proportion of the respondents reported alcohol consumption. The group of the respondents with the age above the mean age (≥ 35 years) reported higher use of tobacco whereas, the group of the respondents with the age below the mean age (< 35 years) reported a higher level of inadequacy of PA.

CONCLUSION: BRFs of NCDs were substantial among the selected slum population of Bangladesh, where age was the major determinant. Health promotion and health education measures are recommended for slum population of Bangladesh to aware them of the BRFs of NCDs.

KEYWORDS: Non-Communicable Diseases, Behavioral Risk Factors, Slum Population

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Introduction

Non-communicable diseases (NCDs), mainly cardiovascular diseases (CVDs), cancers, chronic respiratory diseases, and diabetes mellitus (DM) are the leading causes of deaths

globally. Statistics shows that 41 million (equivalent to 71%) of global deaths are caused by the NCDs.^{1,2} This massive burden of disease is potentially contributed by few identified behavioral risk factors (BRFs), such as tobacco use, harmful use of alcohol, inadequate level of physical activity (PA), unhealthy diet [insufficient fruit and vegetables (FAVs) intake] and excessive dietary salt intake.¹

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Tobacco alone causes death of over 7.2 million people annually worldwide, and 4.1 million deaths have been attributed to excess salt/sodium intake followed by 1.6 million to inadequate level of PA.³ Moreover, approximately 3.3 million annual deaths (5.9% of global deaths) are attributable to alcohol consumption⁴.

Low and middle income countries of the world are victimized more due to NCD burden. Over 85% of all NCD induced global premature deaths (aged between 30 to 69 years) are taking place in low and middle income countries.¹ In Bangladesh, NCDs are attributed to the 67% of all deaths, and there is 22% risk of premature death from target NCDs.² CVDs alone cause 30% of all deaths in this country followed by 12% and 10% due to cancer and chronic respiratory diseases, respectively.⁵ Moreover, in terms of prevalence of BRFs, 44% people use any form of tobacco, 93% consume insufficient FAVs, 38% are involved in inadequate level of PA, 25% are overweight and obese, 21% are hypertensive, and 5% suffer from DM based on a national survey. When these risk factors were clustered, it was found that three-quarter (76%), nearly 4 out of 10 (37%), and 1 out of (12%) had two or more, three or more, and four or more risk factors, respectively.⁶ Furthermore, 60% of Bangladeshi people are used to add extra salt to their meal.⁷

The burden of NCDs as well as their potential risk factors are supposed to be more alarming among the slum population as they are the underprivileged group in society and have poor level of health education and practice.⁸ However, there was no clear statistics reporting the prevalence of NCDs among the slum population in Bangladesh. Furthermore, the extents of prevalence of BRFs along with their determinants among slum population in Bangladesh were not adequately studied. The current study was designed to explore specifically the prevalence of BRFs

of NCDs as well as their determining factors among the selected slum population in Bangladesh.

Materials and Methods

Study design, setting, and population: This was a cross-sectional study conducted in Rayerbazar slum in Dhaka city of Bangladesh in 2017. The slum was situated in Mohammadpur area of Dhaka North City Corporation. The slum was selected purposively considering as one of the largest slums in Dhaka city. A total of 192 adult (aged 18 to 65 years) residents were enrolled in this study using the convenient sampling method according to their availability during the data collection period. Those who had a history of any major NCD were excluded from the study.

Data collection instrument and process: A semi-structured questionnaire suggested by the World Health Organization (WHO), namely the STEPS instrument was used and it was modified to be appropriate.⁹ The questionnaire comprised of socio-demographic information (sex, age, education, occupation, and monthly income) as well as the history of BRFs of NCDs (current tobacco use, insufficient FAVs intake, inadequate level of PA, and alcohol consumption). Data were collected by face-to-face interviews. The respondents were inquired about their socio-demographic background and BRFs status. The respondent's FAVs intake was assessed in serving size using WHO STEPS show-card (1 standard serving size = 80 g of fruit and vegetables). FAVs intake was defined as insufficient when it was < 5 servings/day. PA was assessed in metabolic equivalent of task (MET) technique which was calculated for the two domains of moderate PA (walking and moderate working and/or exercise) and vigorous PA (running and vigorous working and/or exercise) as per the WHO STEPS guideline. The level of PA was defined as inadequate when it was < 600 MET/week.⁹

Statistical approach: Data were analyzed by SPSS software (version 21, IBM Corporation, Armonk, NY, USA). Descriptive statistics was performed to illustrate the respondent's socio-demographic factors as well as BRFs. Binary logistic regression analysis was carried out considering the BRFs as dependent variables and socio-demographic factors (adjusted) as independent variables in order to identify the determinants.

Both verbal and written informed consents were taken from each respondent prior to data collection.

Results

Men respondents were in majority (72.4%). The mean age of all respondents was 37.0 ± 13.6 years and majority (53.6%) were 35 years old and above. Half (50.5%) of them were illiterate. The majority of the subjects were employed (72.4%) and had monthly family income of 15000 and above in Bangladeshi currency (61.5%) (Not presented in table).

Half (50%) of the respondents were tobacco users (Table 1). Among them, three-quarters (75.0%) and one-fifth (18.8%) were smoking tobacco users and smokeless tobacco users, respectively, and the rest used to take both forms. The mean duration of tobacco use was 10.4 ± 4.7 years (not shown in table). Almost all (98.4%) were habituated to take insufficient FAVs (Table 1). The total mean of the FAVs intake among the subjects was 2.4 ± 0.8 servings per day (not shown in table). Nearly 7 out of 10 (67.7%) were habituated to perform inadequate level of PA (Table 1). The total mean of MET of the PA of the participants was 792 ± 1511 per week (not shown in table). However, the prevalence of alcohol consumers was negligible (Table 1). When the prevalence of these risk factors were clustered, the investigations revealed that all (100%) of the respondents had at least one risk factor, and 9 out of 10 (91.1%) and one-

quarter (26.0%) had at least two risk factors and three risk factors, respectively.

Table 1. Prevalence of behavioral risk factors (BRFs) of non-communicable diseases (NCDs) among a selected slum population in Bangladesh (n = 192)

Non-communicable diseases risk factors	n (%)
Tobacco use (current)	96 (50.0)
Insufficient FAVs intake (< 5 servings/day)	189 (98.4)
Inadequate level of PA (< 600MET/week)	130 (67.7)
Alcohol consumption (current)	5 (2.6)

FAVs: Fruit and vegetables; PA: Physical activity; MET: Metabolic equivalent technique

Yes responses were counted for all risk factors. One serving = 80 g

Moreover, binary logistic regression model revealed a middle-to-higher age (≥ 35 years) and the lower age (below 35 years) as the significant determinants of tobacco use and inadequate level of PA, respectively. Other socio-demographic factors had not been found to be as the significant determinants of any BRFs among the population, but the educational status, occupational status, and monthly family income also had little influence on inadequate level of PA; whereas monthly income had a minor effect on the tobacco use (Table 2).

Discussion

In Bangladesh, NCDs related burden as well as their contributing risk factors among the underprivileged slum population were not explored sufficiently, although they are the most vulnerable group for these diseases. Available data also did not reflect the determining factors of BRFs of NCDs adequately. In the current study, the BRFs were evaluated specifically with and without clustering along with their determinants among the underprivileged population of one of the larger slums in Dhaka city. The study revealed that these risk factors were posed remarkably among the population with potential socio-demographic determinants.

Table 2. Binary logistic regression model considering behavioral risk factors (BRFs) of non-communicable diseases (NCDs) as dependent variables and socio-demographic factors (adjusted) as independent variables among a selected slum population in Bangladesh (n = 192)

Socio-demographic factors	Non-communicable diseases risk factors (p; OR; 95% CI)			
	Tobacco use	Insufficient FAVs intake	Inadequate level of PA	Alcohol consumption
Sex				
Women	0.320; 0.6; 0.2-1.7	0.939; 0.9; 0.1-39.7	0.264; 0.5; 0.2-1.6	0.997; 0.0; 0.0
Age (years)				
35 and above	< 0.001; 3.8; 2.0-7.1	0.742; 0.6; 0.1-8.0	0.002; 0.3; 0.2-0.7	0.153; 5.3; 0.5-53.5
Educational status				
Illiterate	0.890; 0.9; 0.5-1.8	0.619; 0.5; 0.1-6.5	0.361; 1.4; 0.7-2.7	0.107; 0.1; 0.1-1.5
Occupational status				
Unemployed	0.863; 0.9; 0.3-2.7	0.911; 0.8; 0.1-35.5	0.169; 2.3; 0.7-7.2	0.997; 0.0; 0.0
Monthly income (BDT)				
15,000 and above	0.474; 1.3; 0.7-2.4	0.809; 0.7; 0.1-8.9	0.188; 1.5; 0.8-3.0	0.629; 0.6; 0.1-4.3

OR: Odds ratio; CI: Confidence interval; FAVs: Fruit and vegetables; PA: Physical activity; BDT: Bangladeshi Taka (currency); MET: Metabolic equivalent technique; The outcomes for the men sex, age below 35 years, literate and employed respondents, and monthly income below 15,000 BDT were the references for respective socio-demographic factors. Insufficient FAVs intake = < 5 servings/day; Inadequate level of PA = < 600 MET/week

The prevalence of almost all of the BRFs was found to be noticeably higher among the current study population in comparison to the data from Bangladeshi national level survey.⁶ Tobacco users were found to be remarkably higher among the population in this study compared to the medical and nonmedical undergraduate level students of the country revealed by another study, whereas FAVs intake behavior and level of PA were almost symmetrical.¹⁰ The lower socio-economic status along with low level of education of this slum population might be the main reason for this disproportionately higher prevalence of BRFs than these two studies.^{6,10}

Moreover, tobacco users and inadequate level of PA performers were found higher in this study than the other relevant studies conducted among the slum population in Dhaka city, although the scenario of FAVs intake behavior was similar.^{11,12} The higher proportions of men sex, illiteracy, and unemployment status of the population of this study than the slum population of other studies of the country might be the responsible factors for these dissimilar findings.^{11,12} The prevalence of alcohol consumption was negligible similar to the other studies, and this scenario was actually the reflection of proper

restricting strategies of culture, society, religion as well as the positive controlling role of the Bangladeshi government. Furthermore, available studies reported that nearly 60% of the slum population in Bangladesh are used to practice added salt during their meal that indicates an alarming situation.^{11,13} However, the disproportionate men and women respondents as well as purposively selection of a single slum and conveniently selection of the study subjects can be considered as the notable limitations of this study. Yet, in this study, the specific remarkable clustered prevalence of the BRFs of NCDs has been explored among the slum population, indicating the higher possibility of future NCD burden among them.

Conclusion

In a conclusion, BRFs of NCDs were found to be substantial among the selected slum population in Bangladesh. The respondent's age was the significant determinant of tobacco use and inadequate level of PA. Proper health promotion and health education measures are recommended in order to control the BRFs of NCDs among the slum population.

Conflict of Interests

Authors have no conflict of interests.

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The predictive value of C-reactive protein (CRP) and procalcitonin chemical biomarkers in the premature diagnosis of infection in brain ischemic stroke

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Original Article

Abstract

BACKGROUND: The infections are common complications after the ischemic stroke. The aim of this study was to evaluate the anticipatory value of C-reactive protein (CRP) and procalcitonin (PCT) biomarkers in diagnosis of stroke-induced infection.

METHODS: In the current prospective study, 184 patients with cerebral ischemia were enrolled. Serum samples were obtained from patients. The CRP and PCT, white blood cells (WBCs) and monocytes, and final infections were evaluated.

RESULTS: In the first 72 hours, the analysis for CRP revealed that the sensitivity was 41.60%, the specificity was 100%, positive predictive value (PPV) was 100%, and negative predictive value (NPV) was 82.90%. PCT showed that the sensitivity was 85.41%, the specificity was 98.54%, PPV was 95.34%, and NPV was 95%.

CONCLUSION: According to our findings, the evaluation of CRP and PCT with simultaneous clinical observation could be considered as a good step in start of antibiotic therapy.

KEYWORDS: C-Reactive Protein, Procalcitonin, Infection, Ischemia

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Introduction

In 25-65 percent of the patients, the infection occurs in the first few days after ischemic stroke.^{1,2} Pneumonia (the infection of pulmonary parenchyma) and the urinary tract infection (UTI) are the most common infectious complications after the ischemic stroke.³ It has been stated that increasing the probability of infection during the acute phase of stroke is

due to immune suppression.⁴ The central nervous system (CNS) adjusts the function of immune system through a complicated path including hypothalamus-pituitary-adrenal axis (HPA axis) and the vague nerve as well as sympathetic nervous system (SNS).^{5,6} The results of many studies reveal that there is an independent association between the infection caused by stroke and the poor functional outcome after that.⁷⁻⁹ Therefore, in case the infection emerges in the incipient stage of the illness, antibiotic treatment is recommended.¹⁰ However, the clinical gold standard method is

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time-consuming for diagnosis and delays the antibiotic treatment. Thus, the simple precise diagnostic markers are required to determine the amount of risk. In the other studies, the C-reactive protein (CRP), white globules, and monocytes were examined as the accepted inflammatory markers regarding their easy and common measurement. Procalcitonin (PCT) is selected to differentiate infection from general inflammation.¹¹⁻¹⁷ All of these biomarkers are available due to easy and quick interpretation.

The values of blood markers such as white blood cell (WBC), CRP, and monocyte as a predictor of infection resulting from the stroke have not adequately been explored; however, they are assessed routinely after the admission of patients. In a study, the biomarkers like CRP, WBC, monocyte, and PCT were sensitive enough to diagnose the infection caused by stroke, but in another one, they did not have enough sensitivity. Thus, due to lack of evidence we cannot be certain about their role in predicting the infection caused by stroke.^{13,14} Approximately, one-third of deaths and serious complications are caused by the subsequent complications especially infection.

The changes of the immune markers and stress, the reduction of human leukocyte antigen-DR isotype (HLA-DR) for instance, or increasing the serum level of catecholamine occur during the incipient stage of stroke and justify the high inclination of these patients to bacterial infection after stroke. It is imagined that these blood markers can predict the occurrence of post-stroke infection to a high extent. Thus, considering the importance of early treatment in patients with stroke, its high incidence, the dramatic infection resulting from that, and taking this point into account that early treatment of these patients has a great influence on their life style and function, in this study we attempt to investigate the predictive value of CRP and PCT chemical biomarkers in the premature diagnosis of the ischemic stroke. First, we are to evaluate the

diagnostic value of each biomarker in predicting the incipient phase of infection and then proceed with specifying that which one has a better diagnostic value.

Materials and Methods

This prospective longitudinal study was conducted on the patients explored in the course of January, 2014 to March, 2015. It was approved by the Ethics Committee of Mazandaran University of Medical Sciences, Sari, Iran (code number: 458, date: December 24, 2013).

First, the experimental studies were carried out; then the patients were followed-up clinically before manifestation of infection and the relationship between this occurrence and the experimental level of each parameter was measured. The sampling method was non-probable and purposeful. The study was carried out in Razi Hospital in Qaemshahr, Iran, and Bou Ali Sina Hospital in Sari. The inclusion criterion was that all the patients should be afflicted by the acute ischemic stroke (AIS) in the first 72 hours before admission. All of the patients signed a consent form for entrance and 10 cc blood was taken from the patients voluntarily, considering the ethics. Stroke was verified by computed tomography (CT) scan or magnetic resonance imaging (MRI). The neurologic disorder was scored using the rating system of the National Health Center for Stroke. The infection caused by stroke includes every infection in the first 5 days of hospitalization.^{13,14} Infection is diagnosed by the standards of the center for disease control (CDC).¹⁵ With regard to the outbreak of the type of infection, they fall into three categories including pneumonia (the infection of pulmonary parenchyma), urinary tract infection (UTI), and other infections. The pneumonia is confirmed when there is at least one of the following criteria (the first or subsequent part): 1. examination of abnormal respiration or pulmonary infiltrates in the chest radiography [chest X-ray (CXR)], 2. productive cough along with purulent sputum, the positive microbial culture from the lower respiratory

tract secretions or the positive blood culture. The diagnosis of UTI is based on the two following cases: the fever ≥ 38 °C, the positive nitrite in the urine sample, leukocyte $> 40\%$ in each microliter of urine, and bacteria $> 10^4$ in a type of pathogen microbe. Other infections are verified if the fever is above 38 °C, WBC is above 11000 in each milliliter or CRP is ≥ 10 m/l, and if the clinical manifestation of infection exists. Determining infection is based on the country's standard protocol. The time of diagnosis depends upon the beginning of clinical manifestations and symptoms that lead to the beginning of diagnostic measurements, as a result, the infection is diagnosed. In order to prevent the entrance of people who had infection before stroke, the patients with the fever of more than 38 degree before admission, those who had infection 3 days before stroke, and people who need mechanical intubation were not allowed in the study. The other excluding criteria included being immunosuppressive and being afflicted by human immunodeficiency virus (HIV) and the other immune system deficiencies. The blood samples were taken at the first 72 hours of hospitalization and after three days to examine WBC, monocyte (Sysmex KX-21N, Kobe, Japan), and the level of CRP and PCT. The amount of CRP was measured by immune turbid metric assay (Pars Azmoon Co., Tehran, Iran). The serum level of PCT was measured using enzyme-linked immunosorbent assay (ELISA) (Kryptor PCT®, BRAHMS, Hennigsdorf, Germany).¹⁶ The statistical analysis was carried out using SPSS software (version 18, SPSS Inc., Chicago, IL, USA). The

descriptive statistical indexes such as mean, standard deviation (SD), median, and absolute and relative frequencies depending on distribution were calculated. The difference between the groups was evaluated by Kruskal-Wallis or chi-square tests. In addition, the simple logistic regression test, the measured biomarkers, and the existence of infection were investigated and P-value ≤ 0.0500 was considered as the significant level.

Results

The study consisted of 184 members, among which 108 people (58.7%) were men and 76 people (41.3%) were women. The mean of the age of study members was 68.52 ± 9.48 years. The lowest age was 48 years and the highest was 91 years. All of the patients were examined in terms of being afflicted by infection in the hospitalization process. To sum up, 48 patients (26.1%) afflicted by a kind of infection were specified. 10 patients (4.5%) were afflicted by urine infection among which 7 were women and 3 were men. In investigating the infection of respiratory system, it was revealed that 33 patients were afflicted by the infection. Totally, 5 male patients were afflicted by the other infections. All of the patients were investigated in terms of the number of white globules, monocytes, CRP, and PCT, and after three days the experimental markers were evaluated. Comparing the two durations of the experiment revealed that all of the experimental characteristics had significant statistical distinction ($P = 0.0001$) (Tables 1-3).

Table 1. Result of laboratory tests in the first 72 hours

Laboratory test	First 72 hours		
	Men Mean \pm SD	Women Mean \pm SD	Total Mean \pm SD
WBC (/ μ l)	7776.36 \pm 1723.33	7143.77 \pm 1440.21	7515.07 \pm 1638.33
Monocyte	2.45 \pm 0.98	2.23 \pm 0.88	2.36 \pm 0.88
CRP	7.40 \pm 4.25	6.32 \pm 2.16	6.95 \pm 3.58
PCT	465.81 \pm 259.12	347.46 \pm 176.06	416.93 \pm 235.32

WBC: White blood cell; CRP: C-reactive protein; PCT: Procalcitonin; SD: Standard deviation

Table 2. Result of laboratory tests in the second 72 hours

Laboratory test	Next 72 hours		
	Men	Women	Total
	Mean \pm SD	Mean \pm SD	Mean \pm SD
WBC	13116.42 \pm 6060.83	11577.35 \pm 10874.29	12480.72 \pm 8397.54
Monocyte	3.25 \pm 1.86	2.69 \pm 1.29	3.02 \pm 1.67
CRP	13.51 \pm 10.27	10.71 \pm 7.32	12.35 \pm 9.25
PCT	1205.74 \pm 1202.84	713.77 \pm 615.24	1002.53 \pm 1000.00

WBC: White blood cell; CRP: C-reactive protein; PCT: Procalcitonin; SD: Standard deviation

Table 3. Results of biomarkers in these cases

Biomarkers		First 72 hours		Next 72 hours	
		Infection		Infection	
		Yes	No	Yes	No
CRP	Positive	20	0	44	126
	Negative	28	136	4	10
PCT	Positive	41	2	47	29
	Negative	7	134	1	107

CRP: C-reactive protein; PCT: Procalcitonin

This study was an attempt to evaluate the predictive value of CRP and PCT. In exploring the patients' CRP in the first 72 hours of admission of irritation, ability of the screening test in the diagnosis of patients was 41.60%, the sensitivity showing the ability of screening in diagnosis of the elderly was 100%, the positive predictive value (PPV) of patients was 100% in the first 72 hours with regard to CRP which represents that all of the infected patients had high CRP and the negative predictive value (NPV), which is the probability of not being infected, was 82.90%. Having been investigated, CRP was 91.60% after three days of admission, sensitivity was 93.15%, the PPV was 81.48%, and the NPV was 96.92%. The investigation of PCT in the first 72 hours of hospitalization revealed that irritation was 85.41%, sensitivity was 98.54%, the PPV was 95.34%, and the NPV was 95.02%. In addition, according to the experiment three days after, the PCT of irritation was 97.91%, sensitivity was 78.67%, the PPV was 61.84%, and the NPV was 99.07%.

Discussion

The results of this study revealed that totally 48 patients (26.1%) were afflicted by one of the infections. It was specified that 10 patients

(4.5%) were afflicted by the urine infection and in exploring the respiratory system, it was represented that 33 patients were infected. Totally, 5 male patients were afflicted by the other infections. In this study, it was attempted to evaluate the predictive value of CRP and PCT. Investigating the CRP of the patients in the first 72 hours represented that the admission of irritation was 41.60%, sensitivity was 100%, the PPV was 100%, and the NPV was 82.90%. Investigating PCT in the first 72 hours revealed that sensitivity was 85.41%, specificity was 98.54%, the PPV was 95.34%, and the NPV was 95.02%. In a study carried out by Tian *et al.* in china, the role of PCT in the cerebral ischemia was investigated. The results revealed that the amount of PCT was significantly higher in the patients with cerebral ischemia than in the control group.¹⁸ As the results of the current study, in the study carried out by Fluri *et al.*, the predictive role of CRP, PCT, and WBC in the creation of infection in stroke was investigated. They examined 383 patients with stroke, 66 of which were afflicted by the post-stroke infection. The results suggested that in the patients with high rate of such factors, the incidence of pneumonia and urine infection was higher in the first 5 days after admission.¹⁹ In the research conducted by Worthmann *et al.*, the role of inflammatory factors in the cerebral ischemia infection was investigated. In their study, they measured the role of inflammatory factors in 56 patients. The results revealed that the incidence of infection after stroke was more in the patients with high inflammatory factors like CRP.²⁰ The results of Welsh *et al.*'s study

represented that CRP had a high connection with the occurrence of the serious subsequent complications. They revealed that the CRP biomarker accompanied the complications of stroke independently.²¹ In another study carried out by Deng *et al.*, the role of PCT was evaluated in the outcome of cerebral ischemia. In a prospective longitudinal study in which they examined 378 patients, they revealed that PCT in the cerebral ischemia was applicable as a predictive marker in the short-term complications of cerebral ischemia.²² The study of Wang *et al.* manifested that in the patients with weaker clinical results and higher mortality, the amount of PCT and the CRP biomarkers was significantly higher. In addition, comparing the PCT and the CRP markers in these patients represented that the amount of PCT in the time of admission had a significant relationship with the clinical results after the release of the patients; however, this finding was not verified in case of CRP.²³ Our research also verified the above-mentioned results, but in our study, the results after releasing from hospital were not evaluated. To confirm the results of this study, in another study carried out by Xie *et al.*, the role of PCT and the CRP biomarkers in the pneumonic survival after stroke was investigated. First, they examined 207 patients with cerebral ischemia, 91 cases of which were afflicted by pneumonia and 39 cases passed away.²⁴ The irritation and feature of PCT in the diagnosis of pneumonia were 84.6% and 71.2%, respectively. In addition, the amount of PCT and the CRP biomarkers was higher in the infected group. They declared that measuring the inflammatory markers and PCT was useful in the prediction of the cerebral ischemia complications.²⁴

Conclusion

This study reveals that the inflammatory factors that appear with the positive or negative biomarkers in the experiments, have a determining role in the prognosis of patients

afflicted by the cerebral ischemic stroke, and maybe in the future, with regard to this effect, we can help the patients recover through applying new therapeutic strategies. However, considering the convenience and the speed of the experiment, it can be used as a part of tools of checking sepsis. Measuring the level of CRP and PCT along with a proper clinical evaluation can be a guide for antibiotic treatment and can enhance the patients' pre-consciousness. In case of using this test, both the strengths and weaknesses of these biomarkers should be taken into account for making decision. Measuring the serum level of PCT with acceptable irritation and feature can help antibiotic treatment, but it cannot be used as the only diagnostic marker and replaced by the clinical judgment of the physician. The researchers of this study support the measuring value of the level of CRP and PCT as a part of investigating diagnosis; and to reach more certain results, they consider conducting more research in this area necessary.

Conflict of Interests

Authors have no conflict of interests.

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A study on nurses' viewpoint about methods of free visit in intensive care units in Besat hospital affiliated to Kurdistan University of Medical Sciences, Iran, 2015-2016

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Original Article

Abstract

BACKGROUND: In spite of the evidence of advantages of visitation, the ban on visit in Iran's intensive care units (ICUs) is still underway, and this issue is always a challenging topic that encounters different behaviors in dealing with the phenomenon of visiting. The purpose of this study was to investigate the barriers and strategies for establishing a free visit system in ICUs from the viewpoints of health care providers.

METHODS: In this descriptive study, 100 nurses working in ICU were evaluated. The data were collected using a demographic information registration form and a questionnaire on attitudes and views about visit in special units which were analyzed by SPSS software using t-test and chi-square test.

RESULTS: 33.3% of cases were men and 66.7% of them were women. Most of the cases (67.9%) were married. The shortest work experience in the ICU was 5 months and the longest was 132 months. The average work experience of the cases in the ICU was 60 months.

CONCLUSION: The majority of nurses believe that free visit can interfere with nursing cares. This interference involves direct intervention, more time spent explaining to the patient's family, and creating a busy environment that is the cause of the errors. The time of the visit is largely regulated by healthcare providers, their attitudes towards the topic, as well as their concerns about this issue.

KEYWORDS: Viewpoint, Intensive Care Units, Nurses

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Introduction

Many families experience having one of their loved ones admitted to the intensive care unit (ICU) each year. Hospitalization in these units has potentially damaging implications for the patient and the family, and they suffer from many problems that their negative effects are unavoidable.^{1,2}

Fear of losing a family member, fear of the

future, fear of financial burden of illness on the family, changes in family roles, anxiety and confusion, depression, loneliness, and disappointment are among the threats that affect the integrated family system at this time.^{3,4}

According to this fact that over 75% of patients admitted to the ICU are not able to participate in making decision for therapeutic purposes and in half of them the decision is made by family members, these threats and stress with a lack of awareness can significantly reduce the ability to decide for

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medical purposes as well as the interaction between the family and the treatment team, and in a long period can cause many physiological and psychological illnesses and post-traumatic stress disorder (PTSD) symptoms can be found in more than one third of cases.⁵⁻⁸

The needs of patients admitted to the ICU and their families have been studied many times and the presence of the patient along with the family and vice versa has been identified as one of the five basic needs. Providing information, support, reliability, comfort, and convenience for the patient and the family are among other needs for both groups.^{9,10}

In the other studies, being away from family members or limitation of visit is one of the stressful conditions. On the other hand, the benefits of free visits to the patient should not be ignored. These benefits include: increasing patient satisfaction, paying attention to patient needs, emotional effects, increasing sensory stimulation, accelerating the recovery process, and reducing stress due to recovery of physiological conditions such as blood pressure, heart rate, intracranial pressure, and hormonal markers of stress.¹¹⁻¹⁵

The benefits of free visit for the family such as increased satisfaction, paying attention to family needs, and reduction of stress, anxiety, depression, and PTSD symptoms have been proved. Nurses also are not deprived of advantage as persons who have the most interaction with these two groups.¹⁶

On the other hand, there is no evidence of increased risk of infection, increased psychological and psychological stress for the patient and the family, or intervention in treatment that the treatment team members are worried about.¹⁷

With all above, special units have always had a limitation of visits and the personnel of these departments consider the patient's isolation as one of the unavoidable principles

of treatment.¹⁸ The idea of this project is presented by the researcher by touching the problems and the needs of the patients and the families in the field of visit in the ICU and their problems.^{19,20}

This study is designed to investigate the obstacles and strategies of free visit administration with the approach of determining the factors related to the views and attitudes of nurses, doctors, and senior managers of hospitals toward free visit, determining the level of awareness about the needs of the patient admitted to the ICU and his/her family and the benefits of free visit, and determination of the most important cultural and physical obstacles.

Materials and Methods

This descriptive study was conducted in the ICU of Besat Hospital affiliated to Kurdistan University of Medical Sciences, Sanandaj, Iran, in 2015-2016. Sampling was done according to the studied population in three parts of the nurses and head nurses working in the ICU with a minimum education of bachelor degree, physicians practicing in ICU, and management systems with members of educational and clinical supervisors of hospital, matron, interior manager, and hospital chief. 100 samples were selected using available sampling method.

Data collection tools consisted of individual information form and a questionnaire of "views and attitudes about visiting in ICUs". Personal information included variables such as age, gender, level of education, marital status, kind of work shift, nursing history, and work experience in the ICU. "The view and attitude about visit in ICUs" questionnaire is based on the five-choice Likert scale (absolutely agree, agree, no idea, disagree, and absolutely disagree), which is graded from 0 to 4.

The researcher referred to research environments, and provided information about the importance and aims of the research

to the authorities of the centers. Then, the researcher referred to the chosen hospital in different shifts and selected the persons who had proper criteria for entering the study and informed them about the confidentiality of the information and made them confident. So the written testimonial was achieved before taking the questionnaires to the cases.

Sampling was continued until the sample size reached the predetermined value. Data were then analyzed using SPSS software (version 19, SPSS Inc., Chicago, IL, USA) and descriptive statistical tests (average, medium).

Results

The average age of the participants in the project was approximately 36 years with a standard deviation (SD) of 7.7 years, the lowest age was 25 years and the highest was 48 years.

The results showed that the lowest work experience in the ICU was 8 months and the highest was 112 months. The average work experience of the patients in the ICU was 50 months. 87% of the studied cases disagreed with free visit. 47% of the cases had one of their first-degree relatives admitted to the ICU during the recent year.

Table 1 shows that the studied cases considered nurses (40%) and their agreement as the key factor in the implementation of the free visit system.

Table 1. Distribution of groups about free visit in the viewpoint of the studied cases

Involved groups	Percent
Patients	20
Patient's family and relatives	24
Nurses	40
Doctors	10
Senior managers	6
Total	100

Table 2 shows that the studied cases considered patient's family and relatives (65%) as the most beneficiaries and doctors (3%) as

the least beneficiaries in the implementation of the free visit system.

Table 2. Distribution of beneficiary groups by establishing a free visit system

Involved groups	Percent
Patients	20
Patient's family and relatives	65
Nurses	7
Doctors	3
Senior managers	5
Total	100

The results showed that with implementation of the free visit in the ICUs, nurses (45.4%) and patients (42.5%) were the most damaged ones. The average score of nurses' knowledge about the benefits of free visit was 8.25, which is a medium level of knowledge. The highest score was 20 and the lowest was 0. The total points were calculated in three groups of 0 to 7 (weak), 8 to 14 (moderate), and 15 to 20 (excellent).

The average score of doctors' knowledge about the benefits of free visit was 7.32, which is within the range of average knowledge.

The average score of senior managers' knowledge about the benefits of free visit was 9.78, which is within the range of average knowledge.

The average score of nurses' attitude toward free visit was 42.66, which is within the range of average attitude. The highest score was 100 and the lowest was 20. The total scores were calculated in three groups of 20 to 45 (weak), 46 to 75 (moderate), and 76 to 100 (excellent).

The average score for doctors' attitude toward free visit was 61, which is within the range of average attitude.

The average score of senior managers' attitude toward free visit was 46.84, which is within the range of average attitude.

Discussion

The recent study showed that nurses, doctors, and other treatment staff did not have a positive attitude toward visit without

limitation, which is because they believe that the free visit will interfere with nursing care and this interference will directly cause taking more time to explain to the patient's family and creating a busy environment that is the cause of the error.

The recent study showed that the studied cases, according to their patient's critical condition in the ICU, did not consider free visit beneficial and even considered it harmful to the patient. This was the most common reason for the negative attitude of the studied cases.¹⁴

The present study showed that 80% of the studied cases were unaware of the changes in patient's vital signs due to free visit, while the results of the research showed that free visiting could stabilize the patient's vital signs and physiological status.¹³ A study showed that patients who had free visit had a more stable physiological status than patients who had no free visit.¹² Moreover, it showed that the high number of patients in the ICU according to the number of nurses and the necessary physical space was one of the obstacles for free visit, which defined strategies should be considered for it such as increasing nurses in ICUs.¹¹

One of the major obstacles for free visit in ICUs was the increased probability of getting infected of the patients by the visitors, which necessary protective equipment such as gloves and masks and other protective equipment should be provided for visitors to prevent the transmission of infection to patients.

In a study, the levels of bacterial and fungal contamination in the air and surfaces in two units with free and limited visit were checked and no significant difference was found between them. Cumulative prevalence of pneumonia, urinary tract infection (UTI), and sepsis in the comparison group was not significantly different with the control group after assimilating age, sex, and duration of hospitalization.¹⁰

The recent study shows that the most important element in discussing cultural barriers of implementing free visit system is

family. Therefore, the family faces a crisis when having one of its members hospitalized in the ICU. Hospitalization in the ICU is potentially unwelcome to the patient and family and has many problems that their negative effects are unavoidable. Fear of losing one of the family members, fear of the future, fear of financial burden of the disease on the family, changes in family members' roles, anxiety, distress, depression, loneliness, and hopelessness are among the threats that affect integrated family system. Having a patient hospitalized in ICU is accompanied by special stresses and challenges for family members which include loss of control, change in role, fear of the future and patient's health, and disappointment.

Conclusion

With the arrival of family members into the ICU and observation of their patient surrounded by the light, various sounds, and different types of tubes and monitors, they feel a lot of insensibility and ask about their patient from anyone they see, because they have entered an unknown and vague world. The experience of hope in the families with a patient admitted to the ICU is significantly different from a family having a patient hospitalized in other parts. Because these families' patients are in critical conditions and between death and life, even if the duration of hospitalization for the patient in the ICU would be short, life of family members are affected for weeks or months in different ways. Therefore, to eliminate these obstacles, educating families about visit and helping them with crisis management is very helpful.

Conflict of Interests

Authors have no conflict of interests.

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The effectiveness of stress management training on mental health status of addicts referred to addiction treatment clinic

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Original Article

Abstract

BACKGROUND: Stress management is the ability of individuals to reduce stress and adapt to stressful situations. The objective in the present study was to investigate the effectiveness of stress management training on mental health of addicts quitting substance abuse referred to Raha addiction treatment clinic in Babol, Iran.

METHODS: In this quasi-experimental study, available sampling method with pre-test and post-test design was used along with the control and intervention groups. A sample of 36 members of the community (drug quitting clinic) were selected and randomly assigned into the two test and control groups, then a pre-test was performed on them through the General Health Questionnaire (GHQ) with a reliability of 78%. For the test group, the stress management skill group intervention was trained in 10 sessions per week with each session lasting 90 minutes. At the end of the session, the post-test was executed on both the test and control groups. The t-test and chi-square tests were employed to compare the quantitative variables between the two groups and the qualitative variables using the SPSS software, respectively.

RESULTS: The results of the study showed that group intervention has been effective on the mental health of addicts quitting substance abuse; as a result, participation in the therapy group and cognitive interventions leads to increasing the mental health of patients quitting substance abuse.

CONCLUSION: According to the results of this study, it can be declared that stress management training has been effective on all mental health scales such as symptoms of somatization, anxiety, disorder in social actions, and depression and leads to a decrease in mental symptoms and mental health improvement in addicts quitting substance.

KEYWORDS: Stress Management, Training, Mental Health, Addicts

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Introduction

Stress is general human reactions relative to the incompatible and unpredictable internal and external factors; so stress arises when the balance and compatibility of the individual disappears due to the external and internal factors.¹

Stress is referred to any internal or external

factor imposed on an individual and affects his psyche, causing disorders, disturbances, and loss of balance. Hans Selye, the founder of scientific research on the phenomenon of stress, describes stress as the degree of wear and tear of the body due to the pressures of life.^{2,3} Psychologists have defined stress as the expectation of compliance, coping, and adaptation by the organism.⁴

According to Alborzkouh et al., when facing

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stress, the individuals should be equipped with the necessary confronting skills in order to reduce the effect of stress. If stress is managed and effective confronting skills are provided, the individuals will be able to deal with the needs and challenges of life in a better way.⁵

Addiction is a physical, mental, and psychological illness which due to its progressive nature, threatens the health of the individual, family, and society in all aspects of life.⁶ In fact, this is a major personal and social problem that, in addition to its physical and psychological impacts on the addicted individuals, threatens the health of the society socially, economically, politically, and culturally, and like any other chronic disorder, needs treatment managing over time.⁷ The results of some studies have shown that psychiatric disorders are more common among individuals with substance abuse compared to the healthy ones; these disorders mainly include anxiety and depression.⁸ In a study, Wells *et al.* found that in patients with substance abuse, the prevalence of psychiatric disorders (anxiety and emotional disorders) is longer in life.⁹ A study by Lowe *et al.* also revealed that 35% of patients with substance abuse suffer from mental disorders, among which depression and panic disorder with values of respectively 15.9% and 10.4% had the highest rates and these disorders cause functional impairment and a decline in the quality of life (QOL) in 17 to 61% of them. These mental disorders exacerbate the drug abuse and reduce the QOL in these individuals.¹⁰

A wide range of psychological treatments including cognitive-behavioral therapies, stress management, biofeedback, supportive psychotherapy, anger control, cognitive restructuring, muscle relaxation, lifestyle changes, and meditation have been effective in improving the QOL and promoting mental health as well as control of the substance abuse of these patients.^{11,12}

The population quitting substance abuse is

one of the groups that are facing high stress and need to be paid particular attention for eliminating their symptoms. Investigations have shown that the prevalence of stress among the addicts in the first 3 months of quitting is much deeper than that of the longer periods¹³ and these factors themselves can be a strong motivation to return to addiction and create a defective round. Based on the studies, the improper thoughts and attribution of a person as well as the way information is processed, and the positions and interpretation of situations have a great influence on the creation and continuity of stress.¹⁴

There are varied and ambiguous studies in relation to the subject matter studied. Therefore, the current study was accomplished aiming to examine whether stress management training affects the mental health of addicts who are quitting substance abuse.

Materials and Methods

The present study was a quasi-experimental and applied study based on the objective and was performed with a pre-test and post-test design and a control group. The test group were subject to the group counseling through stress management group training method during 10 sessions. The training sessions were performed regularly once a week with each session lasting two hours. The control group did not participate in the training sessions.

The statistical population of the study included 114 drug addicts with the age range between 20 and 35 years old who had referred to the Raha addiction quitting clinic in Babol, Iran, in 2015. In this study, the available sampling method was used. To perform the study, the researchers first referred to the clinic and began to conduct the investigations after receiving the required license and permission. The subjects in the statistical population were selected according to the age conditions mentioned and the mental health questionnaire was performed for them. In

addition, the subjects were selected from all the participants whose mental health questionnaire score was more than 35. Then, 36 individuals were randomly selected and assigned to the test and control groups each consisting of 18. The number of 36 people was selected so that in case of drop of the subjects, at least 15 people remain in each group.

The study inclusion criteria were addicts quitting drug abuse, gaining the required score of the mental health and self-esteem questionnaire, lack of suffering from severe physical illnesses or severe mental disorders, lack of consuming psychotherapy drugs in the past two months, and willingness to attend the treatment sessions.

To measure the effect of group stress management training on mental health, the pretest and posttest were used for both groups. The time interval between the pre-test and post-test was about 3 months.

Similarly, the study exclusion criteria included the subject unwillingness or indisposition, lack of conditions for the continuation of the study for any reason, absence of more than 2 sessions.

A written consent form was received from the participants to attend the sessions. To

reduce drops or absence, part of the sessions was focused on the importance of psychological interventions in improving mental health.

This questionnaire was proposed by Yaghubi¹⁵ to distinguish between the individuals with mental disorders and the ones referring to general medical centers. This questionnaire includes 28 items. The subject's answer to each item is determined in a four-point Likert range of much less than the usual, less than the usual, as usual, and more than the usual, with the low and high levels in all options indicating health and lack of health in the individual, respectively.

The scoring method of the questionnaire options was based on the simple Likert model with the options given a score of 3, 2, 1, and 0, respectively.

Yaghubi reported a 76% correlation coefficient between the general health questionnaire (GHQ) and the psychological checklist in Australia.¹⁵ In a study in Chile, Arya and Dierolf reported a sensitivity of 76% for the 12-item general health questionnaire.¹⁶

The stress management training package was taught to the test group through 10 weeks (10 sessions of 90 minutes) (Table 1).

Table 1. Stress management training sessions held on the mental health of the addicts

Session	Session
First	Familiarization of the group members with each other, making contracts, analyzing the concept of stressors and stress responses, and muscle relaxation for 16 muscle groups
Second	Evaluation of the previous session, informing and training of muscle relaxation for 8 muscle groups
Third	Evaluation of the previous session, relationship among the thoughts, emotions, mental imagination, and muscle relaxation intervention for 4 muscle groups
Fourth	Evaluation of the previous session, negative thoughts, cognitive deviations, breathing, visualization, and gradual passive muscle relaxation intervention
Fifth	Evaluation of the previous session, and replacing the rational thoughts with self-training for heat and heaviness
Sixth	Evaluation of the previous session, effective coping strategy, and self-training for heart rate, breathing, stomach, and forehead
Seventh	Evaluation of the previous session, training effective confronting responses and self-training with imagination and self-induction
Eighth	Evaluation of the previous session and managing anger and meditation
Ninth	Evaluation of the previous session, training of expression and breath counting meditation
Tenth	Social support and personal stress management and post-test

Table 2. Frequency and percentage of participants by age

Group	Age (year)	Number		%	
		Test	Control	Test	Control
	20-25	7	2	38.9	11.1
	26-30	6	9	33.3	50.0
	31-35	5	7	27.8	38.9
	Total	18	18	0.100	0.100

Results

The data obtained were analyzed using descriptive statistics including mean and standard deviation (SD) and inferential statistics methods. The test hypotheses were examined with the help of the SPSS software (version 22, IBM Corporation, Armonk, NY, USA).

The data presented in table 2 show the age range of the subjects ranging from 20 years to 35 years. Most of the subjects in this study were 20-25 years old in the test group and 26-30 years old in the control group as 38.9% and 50% of the subjects, respectively. The degree of education of the subjects ranged from the diploma to the bachelor's degree.

Table 3 indicated the distribution of the pre-test scores of the participants in the mental health variable and its components including somatization, anxiety, interpersonal relationships, and depression. Descriptive indicators such as mean, SD, inclination, and stretch were indicative of a desirable normal distribution of the group scores. The distribution of the scores in figures 1, 2, and 3 is demonstrated as a bar graph. Therefore, parametric statistical methods could be used for data analysis.

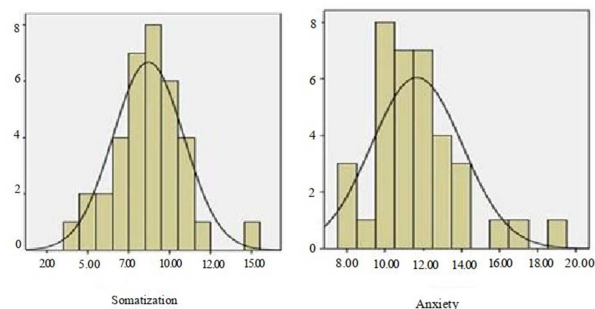


Figure 1. Bar graph of scores of anxiety and pre-test somatization

Table 4 represents the distribution of the posttest scores in the mental health variable and its components including somatization, anxiety, interpersonal relationships, and depression.

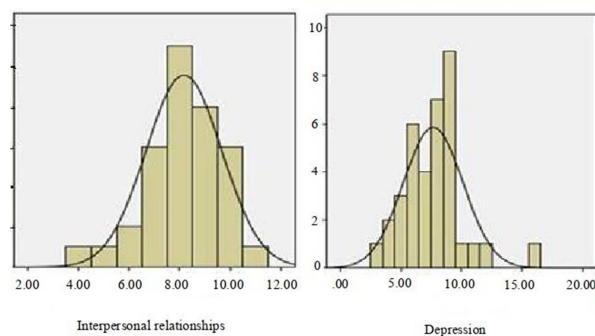


Figure 2. Bar graph of scores of interpersonal relationships and pre-test depression

Table 3. Summary of statistical indicators related to pre-test scores of subjects

Components	Number	Minimum score	Maximum score	Mean \pm SD	Variance
Make-up	36	4	15	8.69 \pm 2.14	4.62
Anxiety	36	8	19	11.66 \pm 2.37	5.65
Interpersonal relationships	36	4	11	8.16 \pm 1.50	2.25
Depression	36	3	16	7.66 \pm 2.44	6.00
Total score	36	23	60	36.19 \pm 6.34	40.20

SD: Standard deviation

Table 4. Summary of statistical indicators related to posttest scores of subjects

Components	Number	Minimum score	Maximum score	Mean	SD	Variance
Make-up	36	1	13	6.16	3.46	12.03
Anxiety	36	3	18	8.44	4.23	17.91
Interpersonal relationships	36	3	11	6.38	2.16	4.70
Depression	36	0	17	4.72	3.79	14.43
Total score	36	9	59	25.70	12.45	155.00

SD: Standard deviation

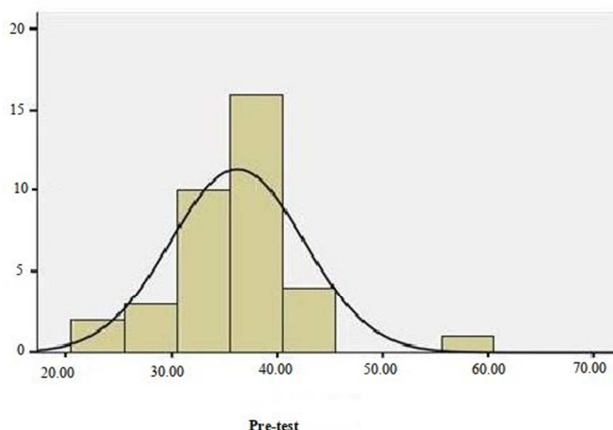


Figure 3. Total pre-test mental health scores

The scores of the descriptive statistics such as mean, SD, inclination, and elongation showed a desirable normal distribution. The distribution of the scores in figures 4, 5, and 6 is demonstrated as a bar graph.

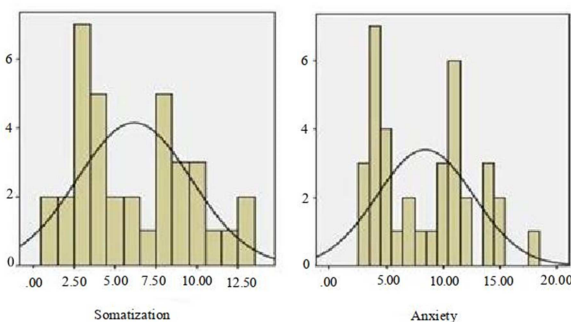


Figure 4. Scores of anxiety and post-test somatization

Therefore, parametric statistical methods could be used for data analysis. For the variance homogeneity between the test and control groups, the Levin test results showed that in the mental health questionnaire, the

significance level of the homogeneity score of the variances in the degree of freedom of 1 between the two groups and 34 within the group was more than 0.05 and hence, all variables had variance homogeneity in the two test and control groups.

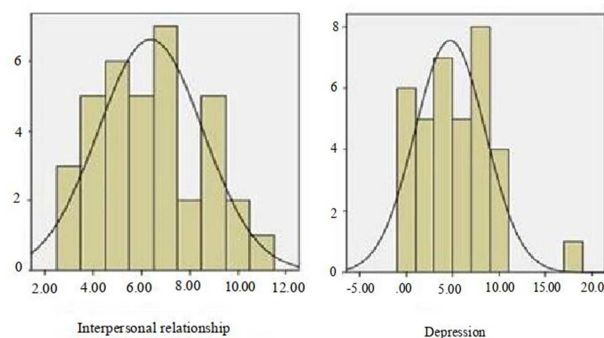


Figure 5. Scores of interpersonal relationships and post-test depression

Main hypothesis

The stress management skills group training sessions improve mental health among the drug abusers.

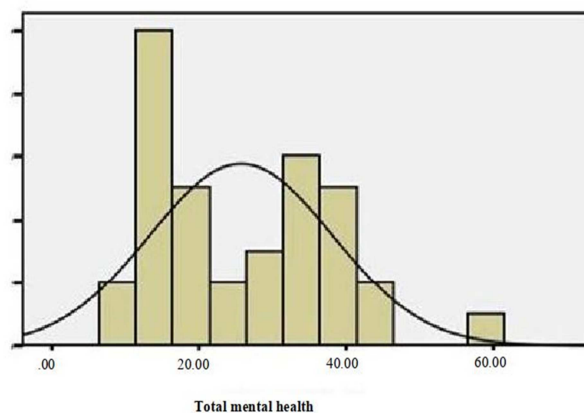


Figure 6. Total post-test mental health scores

Table 5. Covariance analysis of life expectancy in the test and control groups

Scale	SS	DF	MS	F	P
Impact of pre-test variable	424	1	424.0	20.2	0.001
Impact of independent variable	3663	1	3663.0	174.9	0.001
Error	691	33	20.9		
Total	29246	36			

SS: Some of squares; DF: Degree of freedom; MS: Mean squares

In table 5, the effect of the pre-test scores on post-test scores was adjusted using covariance analysis. Therefore, after implementation of the stress management skills group training sessions for the two groups, there was a significant difference in the mental health factor between the two groups and the main hypothesis was confirmed.

Secondary hypotheses

Hypothesis 1: Training of stress management is effective in reducing the somatization symptoms among the drug abusers.

According to table 6, after implementation of the stress management skills group training sessions for the two groups, there was a significant difference in the somatization factor between the two groups and the hypothesis was confirmed.

Hypothesis 2: Training of stress management is effective in reducing the anxiety symptoms among the drug abusers.

Table 7 indicates the covariance statistical index analysis with the significant difference between the symptoms of anxiety in the test and control groups. In this table, the effect of pre-test scores on post-test has been adjusted using the covariance analysis. After performing the group training, the stress management skills were significantly different between the two groups in the test and control groups in the anxiety symptoms factor, so the

hypothesis was confirmed.

Hypothesis 3: Training of stress management is effective in reducing the symptoms of impaired social functioning among the substance abusers.

In table 8, the effect of pre-test scores on post-test was adjusted using the covariance analysis. After implementation of the group training, there was a significant difference regarding the stress management skills between the two groups in terms of the impaired social functioning. Therefore, the hypothesis was confirmed.

Hypothesis 4: Stress management training is effective in reducing symptoms of depression among the quitting drug abusers.

In table 9, the effect of the pre-test scores on the post-test was adjusted using the covariance analysis. Given this table, there was a significant difference between the two groups after the implementation of the stress management skills group training between the two groups in depression symptoms. So the hypothesis was confirmed.

Discussion

The findings of this study showed that the stress management training program increased mental health among the test group compared to the control group.

Table 6. Analysis of covariance scores of the somatization scale of the test and control groups

Scale	SS	DF	MS	F	P
Impact of pre-test variable	6.02	1	6.02	1.93	0.174
Impact of independent variable	265.9	1	265.90	85.30	0.001
Error	102.8	33	3.11		
Total	1790.0	36			

SS: Some of squares; DF: Degree of freedom; MS: Mean squares

Table 7. Covariance analysis of life expectancy scores in the test and control groups

Scale	SS	DF	MS	F	P
Impact of pre-test variable	23.1	1	23.1	5.12	0.050
Impact of independent variable	463.8	1	463.8	102.90	0.001
Error	148.6	33	4.5		
Total	3194.0	36			

SS: Some of squares; DF: Degree of freedom; MS: Mean squares

Table 8. Covariance analysis of scores of the impaired social functioning scale in the test and control groups

Scale	SS	DF	MS	F	P
Impact of pre-test variable	9.56	1	9.56	5.7	0.050
Impact of independent variable	85.4	1	85.42	51.2	0.001
Error	54.9	33	1.66		
Total	1634	36			

SS: Some of squares; DF: Degree of freedom; MS: Mean squares

This finding is in line with the results of the studies conducted by Robbins,¹⁷ Moeller,¹⁸ Lutgendorf et al.,¹⁹ Williams and Schneiderman,¹² Davison et al.,²⁰ Lowe et al.,¹⁰ Lash et al.,²¹ and Ghasemi Zad et al.²² Based on the investigations, stressful events affect humans emotionally, cognitively, and physiologically.

Therefore, in order to adapt to the environment, humans need to be knowledgeable and equipped with skills to cope with stress, as the stress levels beyond the tolerance level endangers the health of individuals.²³ Stress management techniques help reduce the stress in individuals by reducing the level of stress, and it makes them accept an attitude towards life that includes greater ability to adapt to events they cannot change. In addition, stress management aims

to enhance the sense of control, self-efficacy, self-esteem, effective coping, and social support. This will reduce the changes in negative mood and social isolation and improve mental health.²⁴

The results of this study revealed that by challenging negative thoughts and attitudes associated with the drug abuse and modifying them, training time management, and encouraging patients to increase their enjoyment of activities and planning activities enhancing success in the everyday life, symptoms of stress along with the drug intake greatly improve. Moreover, training proper communication skills (daring and self-expression styles) and useful skills (art of listening to, asking, saying no, etc.) to these patients, along with behavioral exercises (playing role during the session) lead to an increase in the level of the desirable social relationships, resulting in receiving the increased social support and this is one of the factors improving the depressed mood and QOL in these patients.

Conclusion

By and large, it can be declared that studies indicate a low level of mental health among the drug abusers, since in most cases, addiction affects mental health of individuals.

Table 9. Covariance analysis of life expectancy in the test and control groups

Scale	SS	DF	MS	F	P
Impact of pre-test variable	78.52	1	78.52	17.40	0.001
Impact of independent variable	217.60	1	217.60	48.22	0.001
Error	148.90	33	4.51		
Total	1308.00	36			

SS: Some of squares; DF: Degree of freedom; MS: Mean squares

Mental health of the families of the drug abusers is affected as well and it exacerbates the underlying problems of the family and, in addition to harmful impacts on the life of the individual, also affects the family and relatives of the drug users.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

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LncRNAs: A new trend in molecular biology of diseases; A review

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Review Article

Abstract

BACKGROUND: Non-coding ribonucleotide sequences, including short and long-term ribonucleic acid (RNA) molecules, are a major part of the gene expression products, which have recently been identified on a large genomic scale. The long non-coding RNAs (lncRNAs) have a length of greater than 200 nucleotides. Only a small fraction of the function of lncRNA molecules is known to date.

METHODS: PubMed, Scopus, Embase, and Google Scholar were searched from January 2000 to May 2018. Based on the study inclusion and exclusion criteria and specific keywords, 92 original, relevant, experimental studies with moderate bias were selected. lncRNAs were evaluated as a new trend in molecular biology of diseases.

RESULTS: Our analysis showed that the presently available evidence confirmed that lncRNAs can be a tool for the diagnosis and prognosis of many diseases and alternative therapies.

CONCLUSION: lncRNAs are an emerging field of investigation as they are suggested to regulate key biological processes, including cellular proliferation and differentiation, and their aberrant expression is associated with many diseases. An improved understanding of the role of lncRNAs in disease would provide valuable information about key biological-promoting pathways and might be highly useful for diagnostic, prognostic, and alternative therapies assessments. This knowledge might also lead to advancement in the management of disease through the development of novel, personalized lncRNAs-based therapies.

KEYWORDS: Long Non-Coding RNA, Autoimmune Disease, Neurodegenerative Diseases, Cardiovascular Diseases, Immune System Diseases

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Introduction

The 20000 gene encodes a protein in the human genome, accounting for less than 2% of the entire human genome sequence.¹ It is very important that 90% of the genomes be actively transcribed, but they do not have the potential to encode protein.² Each of these sequences organizes cell structures, regulates gene

expression patterns, and ultimately determines cell identity and function.³ This non-coding transcript can be divided into the two categories of short non-coding ribonucleic acids (snRNAs) such as microRNA, and long non-coding RNAs (lncRNAs). More than 80% of transcripts are in the lncRNA cells.⁴ These RNAs are very similar to mRNAs regarding processing and presence of polyadenylation signals.⁵

lncRNAs have a length of more than 100 to 200 nucleotides, and their transcription is accomplished by RNA polymerase II.⁶⁻⁸

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Research on the lncRNA promoter showed that the transcription of this class is regulated by the protein-coding RNA transcription factors. It is also hypothesized that the transcription of lncRNAs complies with the same rules in coding-RNA transcription, and the processing involves the capping, polyadenylation, and alternative splicing.⁹

lncRNAs have recently been identified on a massive genomic scale, and only a small part of their function is known. By analyzing the human genome, it is estimated that there are about 23,000 lncRNAs that is greater than the number of mRNAs, and this is comparable to protein-encoding RNAs.¹⁰ lncRNAs sequences have encompassed about 90% of the human genome and spread throughout the genome.¹¹ Studies have shown that lncRNAs act as a mediator between DNA and proteins, and play an important role in cellular function.²

Currently, lncRNAs have emerged as fundamental approaches to biology. Several common features among lncRNAs, which support their independence and biological significance, include the following¹²: 1) Genes encoding lncRNAs a) have epigenetic symptoms compatible with a transcriptional gene (H3K4me3 in the promoter gene, H3K36me3 all over the gene length), b) are transcribed through the RNA polymerase II enzyme, c) are under the regulation of well-defined transcription factors, and d) are expressed in abundance and a special texture. 2) Transcripts for lncRNAs a) often undergo polyadenylation, and b) are undergoing processing through their conventional processing location motifs. Moreover, studies have shown that the inappropriate expression of lncRNAs can cause various disorders and diseases, and lncRNAs are directly linked to several human diseases such as various cancers,¹³ neurodegenerative disease, autoimmune disease, and inflammatory disease.¹⁴ In this review article, we aimed to investigate the biology of lncRNAs and their role in human diseases.

Materials and Methods

PubMed, Scopus, Embase, and Google Scholar

were searched from January 2000 to May 2018. Based on the inclusion and exclusion criteria and specific keywords, such as long non-coding RNA, autoimmune disease, neurodegenerative disease, cardiovascular disease, and immunological disease, 92 original, relevant experimental studies, which were written in English with moderate bias, were selected. lncRNAs were evaluated as a new trend in molecular biology of diseases.

Types of lncRNAs: The types of lncRNAs in terms of transcription and genetic location are classified into the 5 categories of sense, antisense, intronic, intergenic, and bidirectional. In the sense category, the transcription of lncRNAs takes place in a single-gene expression of exons. In the antisense category, the transcription of lncRNAs is performed from the opposite field exons in a gene. In the intronic category, the intron of a transcriptional gene is carried out. The intergenic lncRNAs are independent and are located between two other genes. The bidirectional lncRNA has a common promoter with another gene, but is transcribed in the opposite direction.¹⁵ Based on this specific classification, the study of lncRNA subunits can help identify potential functional relationships between lncRNAs and the related protein-associated genes.

The biological evolution of lncRNAs: The lncRNA sequences, in contrast to their rapid biological evolution, display obvious and weak indications of natural selection.¹⁶ Contrary to protein-coding genes, which are the result of all or part of the doubling of a sequence and diversity, many lncRNAs exhibit a low degree of evolutionary pressure and have different evolution with the coding genes.¹⁷ There are different sources for the appearance of lncRNAs.^{17,18} Chromosome rearrangements can produce lncRNAs from sequences that were not previously transcribed. The collapse of the protein-coding gene framework can create lncRNAs that include some early coding

sequences.¹⁶ The non-coding RNAs retrotransposition during the duplicate process can produce a reverse transcriptional gene or a false pseudogene. Local sequential repeat sequences may also create a new lncRNAs. This phenomenon is seen in the '5' X-inactive specific transcript (Xist). The insertion of a moving element can also produce lncRNAs such as a cytoplasmic RNA of 200 nucleotides (brain cytoplasmic 200-nucleotide or BC200). Unlike mRNA and many non-coding RNA classes, mammalian lncRNAs lack the known orthogonal species in non-mammalian species. The only exception, in this case, is that the RNA contains telomeric repeats (Terra) maintained between human and yeast.¹⁹ Only about 12% of lncRNAs of mice and humans are preserved in other species.²⁰

Biology of lncRNAs: Like other non-coding RNA genes, lncRNA genes lack specific structural indices. The lncRNA genes are usually shorter than protein-coding genes and have fewer exons than they have.²¹⁻²³

Transcription regulation and chromatin alteration patterns of lncRNA genes are similar to those of encoding proteins. The processing signal of the lncRNA molecules, although sometimes performed at a lower processing efficiency, is similar to that of the transcription codons of protein-coding genes.^{23,24} Repetitive elements have also been reported in lncRNAs, which assist in the interaction with their family members in other RNAs and play an essential role in the lncRNA performance mechanism.²⁵ The main part of the lncRNA molecules are polyadenylate, but sometimes their 3' end is seen in another form. In humans, there are about 80 lncRNAs with circular isoforms.²⁶ A little of lncRNAs, due to the formation of a three-spiral structure at the end of the 3', and some of others by snoRNA molecules at both 5' and 3' ends are stable.^{27,28}

lncRNAs have an openreading frame (ORF) without coding the protein, but when lncRNAs come along with the ribosome in the

cytoplasm, other ORFs of these molecules may play the role of mRNA metabolism.²⁹ Frame reading open upstream of lncRNA genes plays an important role in regulating the expression and stability of lncRNA molecules.^{30,31} The lncRNAs can be translated in a way that the transcribed lncRNAs from the downstream are protected from the ribosomal scan and can freely perform their function in the cytoplasm without interfering with the ribosomes. lncRNAs may also direct agents to the ribosomal or modulate the stability of lncRNAs by affecting the pathways of RNA degradation.³² lncRNAs are preferably in the nucleus, can also be seen in the cytoplasm, and are expressed in specific cells and at low levels. lncRNAs can express the gene through alternative splicing, transcription, and post-transcription.³³ The transcription of lncRNAs takes place between the encoding genes and often from the opposite DNA strand.³⁴

The shape and second form of lncRNAs: The formation of a secondary structure is of particular importance for lncRNAs.³⁵ The rate of formation of the secondary structure coincides with the expression level of lncRNAs, in such a way that more organized, more stable lncRNAs, and therefore, lower expressions are observed. Higher C/G content is also associated with greater organization, higher stability, and lower expression of lncRNAs.³⁶ The prediction of secondary stemring structures is useful in identifying lncRNA function. Mfold software, which is widely used, is designed to predict the secondary structure of RNA.³⁷ For this purpose, newer programs, such as CompaRNA, have been developed.^{38,39} Studies have uncovered the many functions of lncRNAs and their strategic roles in the advancement and development of intracellular pathways. The pattern suggested by these studies indicates that the performance characteristics of lncRNAs may be due to their unique structure in bringing together specific regulatory components, including specific

proteins and tissue-specific RNAs, and the subsequent interactions with these DNAs.⁴⁰

The mechanisms of lncRNAs function:

Various research methods have been developed to uncover the functional and molecular mechanisms of lncRNAs. The most efficient approaches to discovering the function of lncRNAs include high-performance lncRNA expression analysis, obtained data validation, and lncRNA-protein interactions evaluation. All of these approaches are possible with special laboratory processes.⁴¹

Studies on the role of lncRNAs in the regulation of the gene expression pattern indicate the complexity of their control mechanism; these molecules are involved in different levels of gene expression regulation, including regulation at the transcriptional level and after transcription. Regulation at the transcription level involves the role of lncRNAs in the epigenetic inactivation of some genes. However, regulatory levels after transcription, which are affected by the action of lncRNAs, include⁴² mRNA degradation protection, pre-mRNAs processing, translation suppression, acceleration of mRNA degradation, mRNA translation activation, and collaboration with microRNAs. The protection of mRNA from degradation by miRNAs in antisense lncRNAs is achieved through these lncRNAs forming a hybrid with the mRNA molecule. Pre-mRNAs processing involves the competing of some lncRNAs with mRNA in binding to the process regulator proteins, and thus, affecting the mRNA values of the mature cell in the cell. Translation suppression is achieved through the imperfect interference of lncRNAs with the mRNA and invoking of the translation inhibitors. 4) The degradation of specific mRNAs is accelerated through the cooperation of some lncRNAs with other mRNA degrading proteins. The mRNA translation activation has been observed in some antisense lncRNAs; these lncRNAs are part of their structure that perfectly

complements the end of the '5 mRNA molecule. They attach to the mRNA, stabilize it, and help call the ribosomes to the mRNA. The result of such an approach is increase in translation. Moreover, some of the lincRNAs act in the same direction (in collaboration with) or reverse to the activity of the microRNA molecules, and thus, play a prominent role in activating or inhibiting the expression of the gene.⁴³

A theory was proposed by Wang and Chang, which showed different modes of gene expression regulation by lncRNAs. According to this theory, lncRNAs are influenced by gene expression through four mechanisms, which are described in the following section. This division was also proposed by Perin et al.⁴⁴ Typically, many of the lncRNAs can be performed by a set of these processes. These mechanisms include splicing, decoy, guide, and scaffold. In splicing, some of the lncRNAs are used to stimulate a cell through a method, such as cellular stress and temperature change, along with growth factors, in order to activate a gene. In decoy, a number of lncRNAs bind to transcription factors preventing the binding of these factors to the gene, and thus, prevent the transcription and inhibit the gene. In the guide mechanism, lncRNAs have the ability to bind to ribonucleoprotein and cause changes in chromatin, and thus, lead to epigenetic changes. In the scaffold mechanism, lncRNAs aggregate the protein complex and bind to the target gene, causing changes in the chromatin structure and transcription to the inhibitor or activation.

LncRNA-DNA interactions: Approximately, all the lncRNAs mentioned so far act by regulating the transcription of target genomic locus in cis- (nearby genes) or trans- (distant genes) acting manner through binding to the target DNA by identification of specific chromatin structures or as an RNA-DNA heteroduplex or RNA-DNA DNA triplex. Therefore, RNA molecules can interact with

single-stranded DNA by Watson-Crick base pairs (duplex) or can interact with double-stranded DNA by inserting into the major groove of the double helix DNA structure with sequence specificity (triplex).⁴⁵ Previously, it has been reported that lncRNAs can form a stable duplex with promoter sequences⁴⁶ or can form a triplex structure at ribosomal RNA promoters in fibroblasts.⁴⁷ Local chromatin changes can result from the transcription of lncRNAs that are not induced by the non-coding transcript.⁴⁸⁻⁵⁰ In a study, the mechanisms of local gene regulation by twelve lncRNAs were evaluated five of which regulate the expression of their neighboring genes in a cis-acting manner. Surprisingly, none of the five cis-regulators required the lncRNAs transcripts themselves, but this procedure depended on lncRNAs transcription processes such as lncRNA promoters enhancer activity, transcription, or splicing of the lncRNA.⁵⁰

LncRNA-RNA interactions: Numerous classes of lncRNAs act by RNA-RNA interactions. For example, the Epstein-Barr virus (EBV) non-coding RNAs (EBER2) form base pairs with nascent transcripts of the locus from the latent EBV genome and recruit the PAX5 transcription factor to the terminal repeats. Recruitment of PAX5 transcription factor regulates the expression of nearby genes to the TRs, and thereby, regulates the lytic replication cycle of EBV.⁵¹ A major mechanism of gene expression modulation in circRNAs is RNA binding. Until now, studies have indicated two functional consequences of RNA-RNA binding via circRNAs. The first is a reduction in the availability of partner RNA transcripts through direct base pairing, in particularly, with microRNAs. The second consequence is a reduction in alternative RNA transcription by competition for transcriptional machinery components. As 'sponges' for microRNA, circular RNAs can efficiently 'titrate' microRNA from its functional target genes. For example, the ciRS-7 includes 70 sites

for miR-7 binding which controls mid-brain development through 'titrating' of miR-7 transcripts.^{26,52} CiRS-7 is fully resistant to target destabilization mediated by miR-7, so it intensely suppresses the miR-7 function, which leads to an increased number of miR-7's targets. Similarly, the Sry circRNAs, a circRNA in testis, act as a sponge for miR-138.⁵² Generally, the lack of 5' phosphate and 3' OH ends in circRNAs results in more stability than that of linear RNAs and this proposes that long non-coding RNAs can temporally modulate the gene expression via base-pairing interactions and modification of their secondary structures.

Controlling the destruction of mRNA molecules: The frequency of mRNA has a direct correlation with protein output, and factors affecting this frequency play their role through the effect of the transcriptional mRNA and its degradation rate. The mRNA can be decomposed through various processes during transcription or after the completion of transcription. One of these processes is the STAU1-mediated decay of the STAU1 agent by mRNA, which results in the decomposition of active mRNAs. The formation of the open pair between the Alu elements in lncRNAs and the Alu elements in the UTR'3 of the STAU1 target mRNA molecule causes the formation of STAU1 binding sites. This event is associated with the activation of the STAU1 agent and its attachment to the mRNA. This finding uncovers a new approach to invoking proteins to mRNA, and to decompressing mRNA through them.⁵³

Controlling of gene expression: LncRNAs are commonly expressed at low levels, retain little consensus among species, and often display specific tissue/specific expression patterns of the cell.^{21,32}

LncRNAs have different effects on gene expression. One of the first functions identified in lncRNAs is the variation in gene expression by alteration of the chromatin structure. In humans, a large number of lncRNAs have been

identified with different roles in gene expression. Human lncRNAs participate in a range of biological processes, including epigenetics, alternative splicing, and RNA destruction and translation.¹⁷ Furthermore, the role of lncRNAs has been shown to disable chromosome X and genetic imprinting as well as growth and differentiation.⁵⁴

Studies have shown that lncRNAs are also involved in protein translation. For example, an antisense lncRNAs for quinone-carboxy-terminal hydrolyzate (UCHL1-AS) mRNA can enhance mRNA stability and increase UCHL1 protein synthesis. This activity is dependent on the presence of a SINEB2 containing replication.⁵⁵ Beta-secretase-1 antisense (BACE1-AS) is a natural antisense transcript for BACE1 mRNA (Beta positioning enzyme in amyloid precursor protein), which is associated with mRNA stability and increased BACE1 protein levels.⁵⁶

Epigenetic functions: The epigenetic concept was first introduced by Waddington Conrad in 1942 as a theme for expanding evolutionary and developmental programs and processes related to an undifferentiated egg, including complete cleansing and re-projection at a point in the cellular cycle. Although this perception remains valid, the term “epigenetic”, in its current application, includes inherited gene expression changes that do not result from genetic code key differences. Epigenetics is defined as stable and inherited changes in the chromatin structure and is different from the phenomenon of mutation that occurs at the DNA sequence level. Epigenetic events, by changing and modifying the pattern of euchromatin to heterochromatin, and vice versa, regulate the expression of multiple genes. The most important of these events may include the methylation of some of the cytosine openings in the CpG dinucleotides (particularly near the promoter of some genes), as well as the reactions of methylation,

acetylation, and other changes on histones.⁵⁷ Many lncRNAs have diverse epigenetic activities. Some lncRNAs can interact with chromatin-altering enzymes and cause changes in the transcriptional activity of some of the genes, or some other extinction.⁵⁸

Xist, including the best-known lncRNAs, is responsible for initiating and extending the inactivation of chromosome X in somatic cells in women.⁵⁹ It is thought to be necessary to silence hundreds of genes based on chromosome X. Xist, which has a small repeat region called RepA, and is transcribed from both chromosomes X.⁶⁰ Tsix is another antisense of the RepA sequence, and it attaches to this sequence in the Xist transcript of one of the chromosomes X. This prevents the Xist from binding to its chromosome X, which is associated with active chromosome X activation. In the next step, another Xist transcript containing RepA is free, with polycomb repressive complex 2 set to a chromatin-modifying complex in the X-inactivation center of the other chromosome X, causing it to be deactivated.⁶⁰ Moreover, Tsix apply their regulatory function to a portion of the chromatin adjacent to their coding gene. This type of regulation is called the cis type. Another epigenetic event, in which the expression of the gene is responsible for lncRNAs, is a genomic role.⁶¹ The expression of the implanted genes depends on their parent origin, and the differential expression level between the two involved alleles can vary from gene to gene. Because of the role played by genes in the development of mammals, their expression should be carefully regulated.⁶² In a study by Rinn et al., another lncRNA called HOTAIR was discovered that regulates the expression of human HOX genes trans.⁶³ Subsequent studies showed that HOTAIR regulates the expression of the gene in the form of trans in conjunction with chromatin-modifying sets, including PRC2, LSD1, and COREST/REST.⁶³⁻⁶⁵ HOTAIR serves as a guide as well as a framework for guiding

these collections to their intrinsic target genes. COREST/LSD1 sets up lysine 4 from histone H3, and PRC2 performs methylation of lysine 27 from histone H3. These events are associated with the inactivation of the HOTAIR target genes.⁶⁵ HOTAIR was one of the first lncRNAs to be known to play a critical role in the epigenetic regulation of cancer.⁶⁶ 34a-miR is a kind of microRNA that can decrease the HOTAIR stability; this process plays a role in the development of prostate cancer.⁶⁷ It can be emphasized that many of the role-bearing sites have an expression, and code the lncRNAs that play a major role in regulating the adjacent protein-encoding genes in the form of cis.⁶⁸ ANRIL is also a lncRNA identified in 2013, and its coding site is located on the 9p21 chromosomal bar. This site is considered as a hotspot for multidisciplinary diseases and is associated with cardiovascular disease (CVD), cancers, diabetes, glaucoma, and endometriosis. It has been determined that ANRIL regulates the expression of its adjacent gene, B/CDKN2A, using epigenetic mechanisms and via polycambotic proteins as cis, and therefore, plays a significant role in controlling the proliferation and aging of the cell.⁶⁹ Other roles of lncRNAs in post-transcription expression control include regulating the intermittent processing, maintaining the state of pluripotency, and controlling the flow of molecules between the nucleus and the cytoplasm discussed below.

Role in the alternating processing mechanism: Since a single mRNA may be constructed of several proteins with non-tangled functions, intermittent processing of pre-mRNA increases the complexity of the proteome in the cells. For the first time in connection with metastasis, a lncRNAs plays a critical role in the pre-mRNA intermittent processing. MALAT1 is in the nucleus speckle, which involves several proteins involved in the intermittent processing of mRNAs. It seems that MALAT1 provides a molecular

scaffold for the function of these proteins. MALAT1 also regulates the phosphorylation of SR proteins. SR proteins are serine/threonine-rich proteins involved in the regulation and selection of processing sites in pre-mRNAs. MALAT1 can regulate the level of the SR proteins by regulating the phosphorylation of SR proteins, thereby influencing the processing of many pre-mRNAs.⁷⁰ This lncRNA target is a microRNA-Ago2-RISC complex, and the extinction of Ago2 expression results in the formation of constant levels of MALAT1 in the cell. An increase in the expression of 9-miR is also associated with a decrease in the level of this lncRNA in the cell.⁷¹

The role of lncRNAs in diseases

Cancer: A lncRNA was identified in lncRNA-ATB in 2014, which was activated via the TGF- β messenger pathway and adjusted several stages of the hepatocellular carcinoma metastasis process through two independent mechanisms. In the first mechanism, this transcript acts as a ceRNA, and by arresting members of the miR200 family, it reduces their access to their transcripts. This event induces the expression of another lncRNA called 2Zeb1, which increases its values by decreasing E-cadherin, followed by a change from epithelial to mesenchymal state and increased metastasis. In the second mechanism, lncRNA-ATB binds to IL-11 mRNA and increases its stability. Increase in the levels of IL-11 by lncRNA-ATB activates the STAT3 molecule. This is associated with an increase in the intrinsic tendency of cells to survive and their success in the formation of a colony in new tissue. The expression of lncRNA-ATB is a valid predictor of the incidence or non-recurrence of disease and estimates of the overall survival rate in patients with hepatocellular carcinoma.⁷²

lncRNA-EPS is one of the types of lncRNAs that are effectively expressed at the time of the

final differentiation of the types of blood cells. Silencing this lncRNA prevents the differentiation of blood cells and induces apoptosis in them. At the same time, its aberrant expression is associated with inhibition of apoptosis in blood cells. LincRNA-EPS is capable of suppressing the expression of a pro-apoptotic gene called Pycard, and thus, the inhibition of apoptosis.^{73,74} High levels of Pycard inhibit the proliferation of blood cells and induce apoptosis or differentiation in these cells.⁷⁵

DiGeorge syndrome: DiGeorge syndrome is a heterogeneous disorder characterized by evolutionary deformity, cognitive and behavioral disorders, and an increased risk of psychiatric disorders. This syndrome is caused by the removal of the chromosomal region 22q11.2. This region encodes a REST regulated lncRNA called DGCR4, which indicates the potential role of this lncRNA in regulating neural evolution and the phenotype of the disorder.⁷⁶

Cardiovascular Disease: Antisense non-coding RNA in the INK4 locus is indicated as a risk factor for CVD.^{77,78} Myocardial infarction associated transcript (MIAT) is related to MI.⁷⁹ As yet, the studies of circulating lncRNAs serving as cardiac biomarkers make less progress due to the instabilities of lncRNAs in body fluids as usually expected. Long intergenic non-coding RNA predicts cardiac remodeling (LIPCAR), is well known as a mitochondrial lncRNAs, is related with cardiac remodeling and chronic heart failure, and is suggested to be a potential cardiac biomarker.⁸⁰

Multiple sclerosis: Multiple sclerosis (MS) is a complex autoimmune disease, and recent immunological studies have demonstrated abnormal activity of cluster of differentiation 8 (CD8⁺) T cells in the pathology of MS.⁸¹ Because lncRNAs are involved in the differentiation and activity of CD8-T cells, they may be important in MS development and progression. lncRNAs

derived from the promoter of the T cell chain of α are responsible for regulating the use of downstream genes, and thus, the production of various T cell receptors.⁸² In recent studies, researchers have found that the locus associated with the α interleukin-2 receptor is code-labeled with some lncRNAs, one of which, called M21981, greatly increases with T cell activity. It is important to note that this locus is associated with MS talent.⁸³ Tmevpg1 is another lncRNA that may interfere with MS. This lncRNA is transcribed in human and mouse immune cells from a cluster of cytokine genes that includes interferon γ ⁸⁴. Tmevpg1 is believed to be involved in controlling TME infection sustainability.⁸⁴ TME infection is used as a laboratory model for MS because it is characterized by chronic inflammatory demyelination associated with apoptotic oligodendrocytes and axonal degeneration.⁸⁵ These observations suggest that lncRNAs can be responsible for regulating CNS immune responses.

The role of lncRNAs as diagnostic and prognostic factors: The discovery that lncRNAs are key regulators of diseases, including cancer and its progression, have been associated with prospects for the use of these molecules as diagnostic and therapeutic targets. The expression of many lncRNAs such as ANRIL, HOTAIR, and MALAT-1 is limited to specific tissue and a specific disease, and can be used as prognostic markers. The number of lncRNAs used as biochemical markers for diagnosis and prognosis is increasing, and some have been approved for clinical use.⁸⁶ One of the main advantages of lncRNAs is their high stability and their presence in body fluids, especially when exposed to nanoparticles such as exosomes and apoptotic body.⁸⁷ Therefore, they can be measured by blood, urine, or saliva sampling, and then, using the Real-Time polymerase chain reaction (PCR) method.⁸⁶⁻⁸⁸ Some lncRNAs can act as a diagnostic agent or as a prognostic factor. For example, a lncRNA called the prostate cancer

antigen 3 (PCA3) is associated with prostate cancer to a large extent, and is commonly used to determine the risk of prostate cancer from urine specimens and avoid unnecessary prostate biopsy.⁸⁹ All lncRNAs, with a determining role in diagnosis and prognosis, affect the cell cycle processes that create a specific phenotype, such as proliferation, invasion, and survival.⁹⁰⁻⁹²

Conclusion

lncRNAs are non-coding transcripts of protein that interact with other molecules through their molecular structure and have vital roles in controlling different types of cellular processes, such as growth, division, and cell differentiation. Furthermore, lncRNAs have a role in different human diseases and their dysregulation cause viral disease. Therefore, lncRNAs have a potential application as a biomarker for screening, diagnosis, prognosis, treatment response prediction, and treatment evaluation. By increasing the trend in studying lncRNAs, gradually a deeper understanding of these molecules is achieved.

Conflict of Interests

Authors have no conflict of interests.

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The incidence of permanent congenital hypothyroidism: A systematic review and meta-analysis

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Review Article

Abstract

BACKGROUND: One of the most prevalent endocrine disorders is congenital hypothyroidism (CH). The most important complication of this disorder is mental retardation. This study was carried out to evaluate CH prevalence based on newborn screening of CH in different countries through a meta-analysis study.

METHODS: The researchers in this study searched the literature among PubMed/Medline, Scopus, Google Scholar, ISI Web of Sciences and Web of Knowledge, and Science Direct databases. The evaluations were carried out using a researcher-made checklist including goals and research questions. Meta-regression with the Mantel-Haenszel method was performed using a random effects model and Egger's test (ET) and Begg's test (BT) by the STATA software.

RESULTS: A total of 10875 studies were found in the initial literature search related to CH. Ultimately, based on the eligibility criteria considered in the present study, 25 studies were categorized as qualified for systematic review and meta-analysis. The estimate of the CH prevalence among the screened neonates in the studies based on the random effects model was 4.85 per 10000 [95% confidence interval (CI): 4.04- 5.66].

CONCLUSION: Due to the importance of CH related diseases especially for detection of type of hypothyroidism, it is necessary more surveillance be carried out in all countries. Based on Different studies, recognition of the most CH patients is before age 1 year so it helps to reduction the risks of developmental delay, and delayed physiological development and mental retardation.

KEYWORDS: Congenital Hypothyroidism, Hypothyroidism, Prevalence, Meta-Analysis

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Introduction

One of the most prevalent disorders in children is congenital hypothyroidism (CH). Newborn screening for CH has been addressed in developed countries for more than 40 years. However, this plan has been started in developing countries in recent years.¹ The first CH screening was conducted in North America. Screening helps early diagnosis of infants with CH and prevents side effects resulting from this complication. Since most of

the infants with CH have normal appearance with no sign of disease, they can be identified through blood test for CH.² It is estimated that 25% of 127 million of birth population worldwide undergo CH screening.³ Given the preventable and treatable nature of this disorder, it is clear that delay in treatment of CH may cause neurological and intelligence quotient (IQ) problems.⁴ The most usual type of CH is primary hypothyroidism which is diagnosed by T4 and thyroid-stimulating hormone (TSH) levels, so infants must be diagnosed properly and treated quickly to prevent permanent CH and physical delays.⁵ It

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is notable that some parents of the children with CH discontinue thyroid hormone replacement based on the inappropriate medical advice and sometimes without a follow-up.⁶ Incidence rates of CH vary in different parts of the world and in various times. It was reported in the range of 1:1000 to 1:4000.⁷ Based on a study in French during the 20-year period, the permanent CH incidence was 1:10000, while this rate was found to be about 1:1800 in Greece over an 11-year period. There is some evidence that CH incidence has been increased from 1:4094 to 1:2372 in the United States in 1987 and 2002, respectively. One justifying reason is changes in the diagnostic strategies.⁸ There have been numerous studies carried out worldwide with different prevalence rates of CH, therefore the aim in this study was to evaluate the overall prevalence of CH through a systematic review and meta-analysis.

Materials and Methods

The study researchers searched and identified studies on CH with reports regarding the children with CH diagnosed during neonate screening program all around the world from January 1, 2010 to June 8, 2016. All the eligible studies were listed by searching the international databases such as Google Scholar, Scopus, PubMed/Medline, Web of Science, and Science Direct. Various combinational terms were searched for to find a large range of literature, including: "Congenital hypothyroidism", "Congenital hypothyroidism and prevalence", "Congenital hypothyroidism and incidence", and "Congenital hypothyroidism and epidemiology"; the search was limited to no patent and in the 2010-2016 period in the Google Scholar. Moreover, to search in PubMed, all studies in English on human with medical subject headings (MeSH), in the abstract, title, and text were investigated.

All essential data from the listed references

were investigated by two of the researchers (Asrin Karimi¹ and Maryam Parvareh). Appraisal was performed using a checklist containing the study objectives and other research questions. Some studies with no inclusion criteria were deleted.

The following information was extracted from the enrolled studies: year of study, number of detected newborns with permanent CH, sample size, country, author, and title based on the standardized form. The prepared data was reviewed twice by two reviewers independently. All gathered articles were assessed according to the critical checklists STROBE and MOOSE.

Data analysis was performed using the STATA software version 12. Heterogeneity of the studies was appraised by the I^2 statistics. This value was $I^2 = 98.4\%$ ($P < 0.100$). The I^2 statistic was employed to evaluate the percentage of the observed variability due to heterogeneity rather than chance and varied from 0 to 100%, with values of 0% and 100% expressing no observed heterogeneity and significant heterogeneity, respectively. The random model was used while $I^2 > 50\%$, otherwise the fixed effect model was performed. Thus, the random model was used due to $I^2 > 50\%$.⁹ The presence of study bias was determined by the funnel plot and conducting the Begg's test. $P < 0.050$ was considered to indicate a statistically significant difference. Furthermore, the univariate approach was employed to evaluate the causes of heterogeneity among the studies and the Egger test was conducted to assess potential study bias.

Results

A total of 10875 studies were found in the initial literature search related to CH. After precise screening of the abstract, title, and text of some of the studies, 10782 ones did not meet the inclusion criteria and some were duplicated, hence they were excluded and

about 93 articles were selected for reading carefully. Ultimately, based on the eligibility criteria considered in the present study, 25 studies were categorized as qualified for systematic review and meta-analysis (Figure 1) (Table 1).

The estimate of the CH prevalence among the screened neonates in the studies based on the random effects model was 4.85 per 10000 [95% confidence interval (CI): 4.04- 5.66] (Figure 2). According to the meta-regression graphs (Figure 3), there was no relationship between the prevalence of CH and year of publication of the studies ($P = 0.440$) and the prevalence of CH and sample size ($P = 0.300$) (Figure 4). Thus, the prevalence of CH among the screened neonates did not change based on the year of publication of the studies and the sample size significantly.

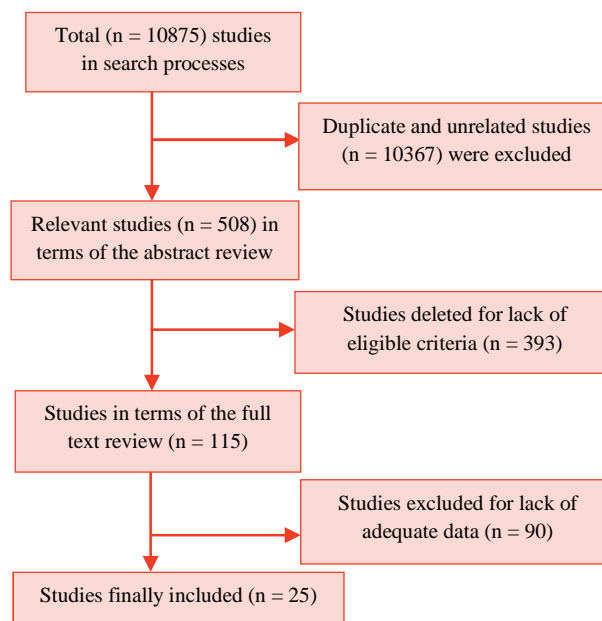


Figure 1. Flow of data in different phases of the systematic review

Table 1. Characteristics of the studies selected

Authors	Study area	Number of neonates screened	Number of neonates with permanent CH
Bekhit and Yousef ¹⁰	Egypt	731743	204
Zhao et al. ¹¹	China	5142148	1922
Deladoey et al. ¹²	Canada	1660857	620
Hettiarachchi and Amarasena ¹³	Sri Lanka	78,167	47
Palhares et al. ¹⁴	Brazil	32278	16
Anastasovska et al. ¹⁵	Macedonia	9757	8
Al Hosani et al. ¹⁶	UAE	698 629	373
Chen et al. ⁴	Taiwan	3000000	1482
Ascurra et al. ¹⁷	Paraguay	53360	35
Al-Jurayyan and Al Jurayyan ¹⁸	Saudi Arabia	1,007,350	306
Samardzic et al. ¹⁹	Montenegro	40758	17
Kaur et al. ²⁰	India	6813	5
Kocova et al. ²¹	Macedonia	215077	83
Cornejo et al. ²²	Chile	2,478,123	273
Wintergerst et al. ⁵	America	751,144	409
Aminzadeh et al. ²³	Iran	47,075	142
Golbahar et al. ²⁴	Bahrain	17806	6
Atas et al. ²⁵	Konya-Turkey	93,897	43
Juan-Fita et al. ²⁶	Spain	71,595	38
Kusdal et al. ²⁷	Kocaeli-Turkey	28,188	39
Hussain et al. ²⁸	Malaysia	12928	2
Sun et al. ²⁹	China	442,454	183
Gopalakrishnan et al. ³⁰	India	13426	11
Woo et al. ³¹	America	92,800	11
Cameo et al. ³²	Colombia	34,363	19

CH: Congenital hypothyroidism; UAE: United Arab Emirates

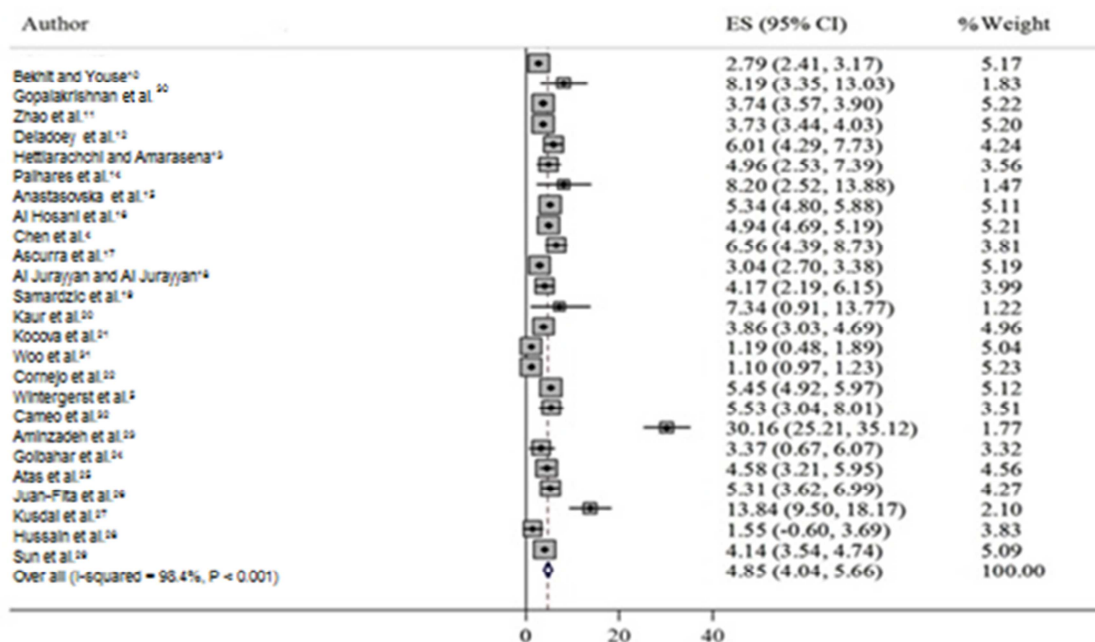


Figure 2. Forest plot of the prevalence of the studies on congenital hypothyroidism (CH) conducted worldwide in the 2010-2018 period
CI: Confidence interval

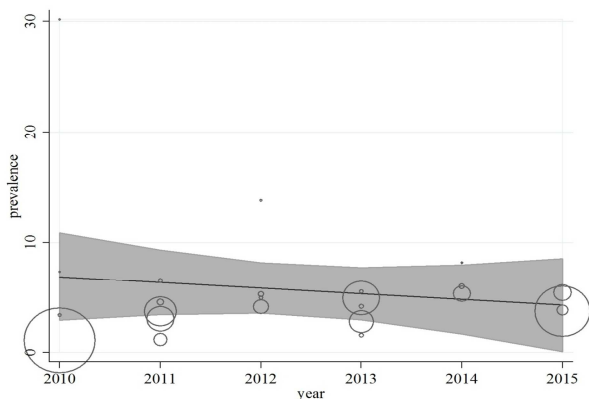


Figure 3. Meta-regression plot of congenital hypothyroidism (CH) prevalence based on the year of publication

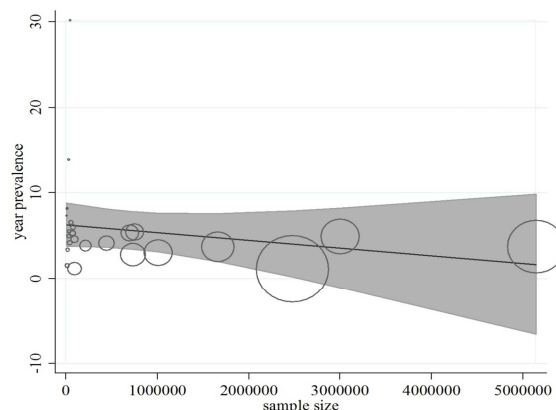


Figure 4. Meta-regression plot of congenital hypothyroidism (CH) prevalence based on the sample size

The Egger’s test was performed to assess the small study effect ($P < 0.001$).

Discussion

The current study reported a systematic review and meta-analysis on the CH screening program in newborn children based on 25 sample studies among a total of 14793617 neonates.

As it seems, it is the first time that the prevalence of CH is reported considering all studies published in this field worldwide. The pilot CH screening was implemented in 1972 in North America for the first time.³³ In this study, the overall prevalence of the permanent CH was 4.85:10000 neonates. Meanwhile, the studies conducted in other parts of the world

have reported an incidence rate of 1-50% for the transient CH among the children with CH.³⁴ It is accepted that about 10-15% of the children diagnosed of the primary CH have transient type of CH at last.³⁵ Different fractions of the incidence of the two types of CH has been reported from different countries with different cultures, nations, and races.^{6,36} In addition, the incidence of total CH varies in different parts of the world. For instance, a CH incidence rate of 1:10,000 vs. 1:2000 has been reported among the blacks in comparison with the Hispanic and native American people, respectively.¹⁴ Transient CH may be the result of some maternal factors such as the excessive iodine intake, iodine deficiency, anti-thyroid medication, or existence of antibodies against thyroid tissue during pregnancy. One of the limitations of the study was that the different incidence rates of the permanent CH reported in different studies may be unreliable, because confirmation of the permanent CH needs to follow up patients for 3 years after the first diagnosis. The prevalence of CH is significantly depending on the study area, thus it is important that countries report correct and accurate information in order to make decisions about the deployment of the best solutions and conduct more studies to gain knowledge on the cause of CH in those areas. In some studies, the incidence of permanent CH was higher than that of the transient CH. The prevalence of permanent and transient CH was 1:3587 and 1:16667 live births, respectively.¹⁴ Other limitations were observed in the studies found based on the search, as most of them did not distinguish children based on gender after determining the type of CH (transient or permanent). Some studies indicated that the CH incidence was higher in girls compared to boys.^{4,37} It was found in recent studies that practically all screening programs report a predominance for the female gender, about 2:1 female-to-male ratio.³⁸ The female/male ratio varies in

different studies, for instance, it was 19.6% higher among women than men⁴ and 3:1 in Saudi Arabia.³⁸ A male preponderance of 1:1.41 was also reported in a study in East Azerbaijan Province, Iran, probably due to the high prevalence of consanguineous marriages.³⁸ Different studies have reported a variety of CH incidence trend over time, for instance in a study¹⁰ conducted in Taiwan, the CH incidence increased by 10% from 1997 to 2004 and decreased after 2005. The peak incidence rate in the 1997-2008 period in this population was 7.68:10000 infants in 2001. The female/male ratio differed during the 12 years of study. In comparison with the present study, this study did not show significant incidence of CH over the study period. That may be due to the diagnosis criteria or registry systems.

Conclusion

More surveillance of CH-related diseases, especially for detection of the type of hypothyroidism needs to be carried out in the future. Data obtained from the studies on patients with CH show that most of the patients with CH are diagnosed before the age of 1 year and that early diagnosis can decrease the risks of developmental delay, mental retardation, and delayed physiological development.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

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Is there any difference in executive function and social adequacy between the children with dyslexia or dyscalculia disorder?

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Short Communication

Abstract

BACKGROUND: Review of literature indicates that there is difference between various types of learning disorder based on functional skills. This study aims to compare the executive function and social adequacy of children with dyslexia and dyscalculia.

METHODS: This descriptive fundamental research was a comparative causative type study. The statistical population included all children with dyslexia and dyscalculia in Tehran Province, Iran, in 2018. Using available sampling method, 43 children (24 with dyslexia and 19 with dyscalculia) were selected from learning disorder centers. Fellner questionnaire was used to assess the social adequacy of the children, and to evaluate the executive functions, Parental Reflective Functioning Questionnaire (PRFQ) was used. The data were analyzed using multivariate analysis of variance (MANOVA).

RESULTS: There was no significant difference between the various components of executive functions and social adequacy of children with dyslexia and dyscalculia ($P > 0.050$).

CONCLUSION: Based on the research findings, function of children with dyslexia and dyscalculia is equivalent in executive function and social adequacy.

KEYWORDS: Executive Function, Dyslexia, Dyscalculia

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Introduction

The dyslexia disorder (reading disorder) term was presented in 1962 by Samuel Kirk. He used this term for children who had little progress in reading, writing, and mathematical computing, and introduced learning disruptions into the educational curriculum.¹ Dyslexia disorder refers to a unitary structure or disorder that is associated with defect and deficiency in the development of academic skills.² According to different studies that were performed, dyslexia and dyscalculia disorder (math dyslexia) have separate cognitive

profiles. In a division, the disturbances are divided into two parts: auditory-verbal and visual-motor, the problem of reading is in the auditory-verbal class and mathematical problem is in the visual-motor category.³ Weakness in visual-motor skills leads to problems in mathematics and handwriting, which is often independent of dyslexia disorder. The problems of this group of children include problems in social awareness and judgment. These problems are not linguistic and in neuroscience texts are associated with a set of nonverbal learning disorder.⁴ Neuroscientists believe that children with non-verbal learning disabilities experience internalized problems like

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depression and anxiety more than those with dyslexia disorder. A review of various studies suggests that about 75% of children with learning disabilities have problems in social skills.⁵ Studies indicate that executive functions play an important role in this disorder. Children with learning disabilities have difficulty executing tasks.^{6,7} Therefore, the main objective of this study is to compare social adequacy and executive functions among children with dyslexia disorder and dyscalculia disorder.

Materials and Methods

The method of this research was fundamental and in terms of the purpose and the type of data collection, it was a causal-comparative type. The statistical population consisted of all children with dyslexia disorder in Tehran Province, Iran, in 2018. Due to the research constraints, the subjects were selected through the available sampling method from the learning disorders centers (2 centers) in Tehran Province. Since for experimental research, at least 15 samples per group are sufficient, the sample size was considered as 43 children (24 children with dyslexia disorder and 19 children with dyscalculia disorder). Sample inclusion criteria were: definitive diagnosis of dyslexia disorder, definitive diagnosis of dyscalculia disorder, age range of 7 to 12 years, and being at the elementary school level. In addition, the existence of any common disorder other than dyslexia disorder and dyscalculia disorder, the presence of writing disorder, physical disability, and intelligence quotient (IQ) less than 85 were considered as the exclusion criteria for sample. For collecting data, Parental Reflective Functioning Questionnaire (PRFQ) and Fellner social adequacy questionnaire were used.

Parental reflective functioning questionnaire (PRFQ): This questionnaire has 86 items that are used to determine the level of executive performance of children aged 6 to 11 years, but

the parental version of the behavior questionnaire includes 63 items. Responses to questions were never (1), sometimes (2), and most often (3). This questionnaire assesses working or active memory, change (cognitive flexibility), emotional control, inhibition, start-up, and planning/organizing and organizing/monitoring materials as executive functions. For this questionnaire, the internal consistency coefficients have been reported using Cronbach's alpha coefficient from 0.70 to 0.80, and for its retest reliability, after four and a half weeks, correlation coefficients have been reported between 0.78 to 0.90.⁸

Fellner social adequacy questionnaire: It is a questionnaire with 47 questions that is based on Fellner's theory and four dimensions of cognitive skills and abilities, behavioral skills, emotional adequacy, and motivational and anticipatory factors. In this questionnaire, each statement contains 7 options: quite agree, agree, somewhat agree, I have no idea, somewhat disagree, disagree, and quite disagree. The parents should choose an option that more reflects the feelings and views of their child. The alpha coefficient obtained from a researcher-made social adequacy questionnaire after removing the questions that had a solidarity correlation with the total score was 0.88, which shows acceptable internal consistency coefficient. In addition, for the purpose of using the reliability method, the rearrangement was 0.90 after 4 weeks.⁹ After identifying the centers that would cooperate, the questionnaire was distributed to the children by parents' consent, so that in the two centers, after determining the subjects by the psychology center, the questionnaires were delivered to parents by the researcher. In the second center, the questionnaires were delivered by the relevant psychologist. By providing the explanation, the parents responded to the questionnaire. Before entering the samples, they were given the necessary information about the goals,

duration of the research, and how they would collaborate during the study. After obtaining informed consent from them, they were selected as members of the sample group. It should be noted that the provisions contained in the Helsinki Statement were observed in this study. Descriptive statistics such as frequency, percentage, mean, and standard deviation (SD) and inferential statistics such as multivariate analysis of variance (MANOVA) were used to analyze the data. All data were analyzed by SPSS statistical software (version 20, IBM Corporation, Armonk, NY, USA). P -value < 0.050 was considered as statistically significant.

Results

Among the subjects, 74.4% (32 persons) of all children were boys. The mean age of children with dyslexia disorder was 9.22 years and mean age of children with dyscalculia disorder was 8.68 years. The t -test result confirmed that the two groups were similar in age ($t = 224.1$, $P = 0.228$). The mean and SD of the variables in the research are presented in table 1 by the two groups. In order to compare executive function and social adequacy (dependent variables), two groups of children with reading disorder and children with math learning disorder (independent variables) were used for MANOVA. Regarding the parametricity of this

test, its preconditions were evaluated before implementation. For this purpose, the Kolmogorov-Smirnov test (K-S test), Levene's test, and Box's M test were used. The results of these tests showed the use of MANOVA according to the pre-test of parametric test.

As shown in table 2, the P -value for meaningful tests of MANOVA in comparison with the two groups in terms of social adequacy (and its components) and executive functions (and its components) were higher than the P -value defined ($P = 0.050$). Therefore, there is no possibility of using MANOVA. This indicates that there is no significant difference between the two groups in terms of executive functions and its subscales ($P > 0.050$).

Discussion

Based on the results, the two groups did not have a significant difference in performance and social adequacy. The review of scientific evidence in this field reveals contradictory findings in the comparison of the two groups in terms of executive functions. For example, according to Nabizadeh research, children with non-verbal learning disabilities have difficulty performing executive functions (according to the function of the brain hemispheres), which separates children from dyslexia disorder in mathematics.¹⁰

Table 1. Mean and standard deviation (SD) of two groups in the research variables

Variables	Group	Dyslexia disorder	Dyscalculia disorder	Total
		Mean \pm SD	Mean \pm SD	Mean \pm SD
Active memory		22.12 \pm 3.32	21.94 \pm 2.48	22.04 \pm 2.95
Flexibility		15.12 \pm 3.43	15.63 \pm 2.75	15.34 \pm 3.12
Emotional control		20.16 \pm 3.19	21.68 \pm 3.18	20.83 \pm 3.24
Inhibition		19.20 \pm 5.62	19.75 \pm 4.79	19.37 \pm 5.21
Start		14.20 \pm 3.12	13.94 \pm 2.93	14.09 \pm 3.00
Planning/organizing		25.50 \pm 3.70	26.63 \pm 3.25	26.01 \pm 3.51
Organizing/monitoring material		11.91 \pm 3.11	12.63 \pm 2.43	12.23 \pm 2.82
Supervision		16.91 \pm 2.76	18.10 \pm 2.84	17.44 \pm 2.83
Overall executive score		145.16 \pm 23.60	150.15 \pm 17.46	147.37 \pm 21.04
Behavioral skills		115.75 \pm 20.01	121.14 \pm 14.28	118.44 \pm 17.17
Motivational and anticipatory affiliates		26.83 \pm 6.25	28.01 \pm 4.08	27.35 \pm 5.37
Cognitive skills		9.33 \pm 3.33	8.74 \pm 4.48	9.07 \pm 3.84
Excellence		10.46 \pm 2.97	11.05 \pm 2.39	10.72 \pm 2.72
Overall score of social adequacy		162.38 \pm 26.53	169.63 \pm 20.13	165.85 \pm 23.92

SD: Standard deviation

Table 2. Significance analysis of multivariate analysis of variance (MANOVA) in comparison of two groups in research variable

Variables	Test	P	F	P
Social adequacy	Pillai's trace	0.107	1.143	0.351
	Wilks lambda	0.893	1.143	0.351
	Hotelling's trace	0.120	1.143	0.351
	Roy's largest root	0.120	1.143	0.351
Executive functions	Pillai's trace	0.385	1.566	0.155
	Wilks lambda	0.615	1.566	0.155
	Hotelling's trace	0.627	1.566	0.155
	Roy's largest root	0.627	1.566	0.155

F: Fisher-Snedecor (F)

In the study of Saghafi et al., programming and attention indexes in students with non-verbal learning disorders were similar to those of students with dyslexia. Also, the results of this study showed that the flexibility of students with non-verbal learning disorders was more than students with dyslexia, and dyslexic students, on the other hand, had a better memory than students with non-verbal learning disorders.¹¹ In analyzing the data obtained, there is no significant difference between them. We should point out that the degree of similarity between dyslexia disorder and dyscalculia disorder is partially demonstrated in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), the problem of learning and using scientific skills. DSM-V is based on the high correlation between problems in the accounting and reading. This can be an explanation for the results. Another factor that can explain heterogeneity in research is the great tendency of brain activity of children with dyslexia disorder and dyscalculia disorder. Peters et al. performed a study in which the children's brain activity in 4 groups (control group, dyscalculia disorder, dyslexia disorder, and dyscalculia disorder/dyslexia disorder) was compared during a math design that allowed them to separate the various processes that might be associated with specific or common neural roots of these disorders.¹² The limitations of the present study were to find children who had only a dyslexia disorder or dyscalculia disorder. Hence, the low sample

size of the research makes the distribution of results difficult. Since today, effective interventions for the treatment of dyslexia disorder have been designed, it is suggested that parents pay attention to the symptoms of these abnormalities before that the children enter school.

Conclusion

The results of the present study showed that there was no significant difference between the type of dyslexia disorder and dyscalculia disorder in terms of social adequacy and executive function. These results explain that homogeneity of these types is considered in terms of the structures that were studied.

Conflict of Interests

Authors have no conflict of interests.

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