Original Article

Prevalence of social network addiction and its association with depression, anxiety, and stress among Iranian internet users

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Abstract

Introduction: Regarding the invention of smart phones and improved Internet connectivity, the use of social network sites has become an essential part of people's daily life. The present study aimed to determine the prevalence and factors associated with social network addiction among Iranian users at a national level.

Materials and Methods: The statistical population of the present study included all Iranian internet users who use social network sites in 2018 in Iran. Participants were 5,360 individuals recruited from an online survey. Social network addiction was measured using Social Network Addiction Test (SNA-T), and factors associated with social network addiction were measured using Depression, Anxiety and Stress scale (DASS-21). Descriptive and Logistic regression tests were used.

Results: It is indicated that 29.7%, 11.2%, and 0.9% of the participants, had low, moderate and severe addiction to social network sites, respectively. Also, adolescents and youth were significantly more addicted to social network sites than adults. Participants with high levels of depression, anxiety, and stress, were significantly more addicted to social network sites than participants with low levels of depression, anxiety and stress ($P < 0.001$).

Conclusion: The findings highlight the prevalence of social network addiction and co-occurrence with depression, anxiety, and stress among Iranian population. Whether we consider social network addiction as a primary diagnosis or as an outcome of other psychiatric disorders, it should be noted and considered in psychiatric treatment.

Keywords: Depression, Internet, Social network addiction

Introduction

The advent of Social Networking Sites (SNSs) has changed the way individuals connect and communicate with each other (1). SNSs are web-based applications (e.g., Facebook, Twitter, Instagram), where individuals can interact with others in virtual communities, create public profiles, and share written, audio, or video messages (2). Much researches on SNSs use have been published in recent years because of its exponential growth (3,4). For instance, as of December 2017, there were 1.4 billion active users on Facebook on average per day (5). These statistics alone indicate the exponential rise of SNSs and also suggest the potential for addiction.

Social network addiction, also described as pathological SNSs use, refers to a situation where individuals' preoccupation with SNSs, characterized by an inability to regulate their SNSs use, result in a significant negative impact on their daily lifestyle (6). The description of social network addiction has been based on the definition for substance dependence or pathological gambling. It shares characteristics like preoccupation, mood modification, tolerance, withdrawal, and functional impairment (7). While the negative outcomes of such addictions may not always be as devastating as those generated by severe substance addictions, but they affect vulnerable population of adolescents and young adults (8,9). Moreover, they can have a myriad of negative effects on individuals' work, school, social functioning, interpersonal relationships, sleep health (10), and even alterations in the gray matter volumes of the brain (11).

Currently, most existing studies on social network addiction are primarily based on adolescents or young adults (12), and there is a gap of studies in large populations at a national level. Furthermore, although there is empirical evidence that specific populations (e. g., college students) may be more prone to exhibit excessive or addictive tendencies toward social network addiction (13), very few have investigated this phenomenon among adults. Adults are not immune to internet-related addiction, and their use does not differ much in their motivations for SNSs use (14). Therefore, this research seeks to address some of these gaps by assessing social network addiction in a large population at a national level. Thus, this study aims to assess the prevalence of clinically significant levels of social network addiction in Iranian internet users and assess the interplay between the level of social network addiction and the level of depression, stress, anxiety, and demographic features among them.

Materials and Methods

This study was cross-sectional. The statistical population consisted of all Iranian internet users who used SNSs in 2018 in Iran. The sampling was non-probable, using an online survey to obtain the data. The minimum sample size with a 2% margin of error and 99% confidence was 4647, which in the present study, the sample size was 5360 individuals.

Questionnaires were distributed both on channels and forums of SNSs with thematically different topics (ranging from health, psychology, travel, and computers to craft and comic themes) to obtain the most heterogeneous sample. For data analysis and hypothesis testing, SPSS software, version 20 (15), was used. The questionnaire was devised so that every individual could see his/her levels of addiction to SNSs and levels of depression, anxiety, and stress immediately after completing the questionnaires. This kind of questionnaire provoked them to answer the questionnaire correctly so that they could see their results. Finally, 5360 individuals responded to the questionnaires, and their data were analyzed.

Research instrument

A) Sociodemographic Data: Age, sex, relationship status, level of education as well as current job were assessed. Furthermore, information about the name of used SNSs was collected.

B) Social Network Addiction Test (SNA-T): It is a 20-items self-report questionnaire with a 5-point Likert-type (ranging from "not applicable" to "always") which provides an assessment of a participant's problematic usage of social network and severity of usage. Results can be classified participants based on the following intervals: 0 to 30 (none), 31 to 49 (mild addiction), 50 to 79

(moderate addiction), and 80 to 100 (severe addiction). This test designed by the researchers in the present study is adapted from the Internet Addiction Test (IAT, developed by Young). The internal consistency of this test in the present study was high (Cronbach's alpha: 0.91). Also, indices obtained from confirmatory factor analysis showed an acceptable model fit to the Items (χ^2/df: 2.88, GFI: 0.90, CFI: 0.91, and RMSEA: 0.08).

C) Depression, Anxiety, and Stress Scale (DASS-21): The DASS-21 is a 21-item scale score on a 4-point Likert-type scale (3= applied to me very much, or most of the time; 0= did not apply to me at all), consisting of sentences describing negative emotional states. It contains three subscales (depression, anxiety, and stress) and has shown good internal consistency and convergent and discriminant validity (16). In addition, we administered the Persian version of the DASS-21 validated by Asghari, Saed, and Dibajina (17), which showed good psychometric properties in non-clinical Iranian participants.

Those Iranian internet users who used social networking sites over the six previous months entered the study. Incomplete questionnaires were excluded from the study.

At first, information was given about the objectives of the present study to the participants. Then, before entering the study, online consent was obtained from the participants. Finally, participants also completed the questionnaires anonymously.

Results

Of the 5360 participants in the online survey, about one-third (1799) were men, and two-third (3561) were women. Other demographic characteristics are shown in Table 1. The results indicated that 645 participants are classified as being addicted to SNSs. Therefore, we can infer that the prevalence of social network addiction in this study was 12.1%, of which 11.9% of the participants had moderate, and 0.9% had severe social network addiction. Also, 29.7% of the participants had low social network addiction.

Participants were also asked to choose three SNSs which they used most. Table 2 shows the results of the most used SNSs among participants.

Table 1. Demographic characteristics of participants

Variable		Frequency	Percent
Sex	Male	1799	33.6
	Female	3561	66.4
Age (Year)	15 and lower	90	1.68
	16-24	1091	20.35
	25-34	2211	41.25
	35-44	1293	24.12
	45-54	527	9.83
	55 and higher	148	2.76
Marital status	Single	2389	44.6
	Married	2742	51.2
	Divorced	191	3.5
	Widowed	38	0.7
Education	Under diploma	317	5.9
	Diploma	1073	20.0
	Bachelor	2416	45.1
	Master	1239	23.1
	Doctorate	315	5.9
Occupation	Student	1247	23.3
	Employee	1682	31.4
	Worker	56	1.0
	Housewife	887	16.5
	Self-employee	786	14.7
	Other	407	7.6
	Jobless	295	5.5
Depression	Normal	2354	43.9
	Low	719	13.4

	Moderate	1084	20.2
	Severe	518	9.7
	Very severe	685	12.8
Anxiety	Normal	2575	48.0
	Low	439	8.2
	Moderate	1084	19.6
	Severe	476	8.9
	Very Severe	822	15.3
Stress	Normal	2598	48.5
	Low	742	13.8
	Moderate	937	17.5
	Severe	728	13.6
	Very severe	355	6.6
Addiction to social networks	Not addicted	3120	58.2
	Low	1594	29.7
	Moderate	600	11.2
	Severe	45	0.9

Table 2. Most used social network sites

SNS	1. Telegram	2. Instagram	3. WhatsApp	4. Facebook	5. Line	6. Google+	7. Viber	8. Linke in	9. Weblog	10. Tweeter	11. Tango	12. Cloob	13. Wayn
Frequency	5174	3595	1482	990	374	284	171	149	117	86	50	24	2

As evident in Table 2, the most popular SNSs among Iranian internet users were Telegram messenger, and the second and third most popular SNSs are Instagram and WhatsApp, respectively.

An ordered logistic regression analysis was performed with social network addiction status as the outcome variable and demographic variables and depression, anxiety, and stress as predictors. The analysis result is shown in Table 3.

Table 3. Ordered Logistic Regression test results regarding the demographic variables and depression, anxiety, and stress

		Addiction to SNSs				Odds Ratio	0.95 Confidence Interval	P
		Not Addicted	Low	Moderate	Severe			
Sex	Male	1078 (59.9%)	528 (29.3%)	181 (10.1%)	12 (0.7%)	1		
	Female	2042 (57.3%)	1066 (29.9%)	419 (11.8%)	34 (1.0%)	0.9	0.8 , 1.1	0.119
Age	15 and less	42 (46.7%)	28 (31.1%)	17 (18.9%)	3 (3.3%)	1		
	16-24	444 (40.7%)	404 (37.0%)	220 (20.2%)	23 (2.1%)	1.3	0.8 , 2.1	0.319
	25-34	1299 (58.8%)	679 (30.7%)	221 (10.0%)	12 (0.5%)	0.8	0.5 , 1.3	0.286
	35-44	835 (64.6%)	344 (26.6%)	108 (8.4%)	6 (0.5%)	0.6	0.3 , 1.1	0.078
	45-54	391	108	26 (4.9%)	2 (0.4%)	0.4	0.3 , 0.8	0.004

		(74.2%)	(20.5%)					
	55 and more	109 (73.65%)	31 (20.9%)	8 (5.4%)	0	0.4	0.2 , 0.8	0.005
Marital status	Single	1189 (49.8%)	798 (33.4%)	370 (15.5%)	32 (1.3%)	1		
	Married	1785 (65.1%)	737 (26.9%)	208 (7.6%)	12 (0.4%)	0.8	0.7 , 1.1	0.054
	Divorced	126 (66.0%)	47 (24.6%)	16 (8.4%)	2 (1.0%)	0.6	0.4 , 0.8	0.005
	Widowed	20 (52.6%)	12 (31.6%)	6 (15.8%)	0	1.1	0.6 , 2.1	0.787
Have child	Yes					1		
	No					1.1	0.9 , 1.2	0.563
Education	U diploma	140 (44.2%)	103 (32.5%)	66 (20.8%)	8 (2.5%)	1		
	Diploma	595 (55.5%)	316 (29.5%)	147 (13.7%)	15 (1.4%)	0.8	0.6 , 0.9	0.042
	Bachelor	1449 (60.0%)	705 (29.2%)	243 (10.1%)	19 (0.8%)	0.7	0.5 , 0.9	0.003
	Master	737 (59.5%)	388 (31.3%)	111 (9.0%)	3 (0.2%)	0.7	0.5 , 0.8	0.003
	Doctorate	199 (63.2%)	82 (26.0%)	33 (10.5%)	1 (0.3%)	0.7	0.5 , 0.9	0.021
Occupation	Student	547 (43.9%)	441 (35.4%)	234 (18.8%)	25 (2.0%)	1		<0.001
	Employee	1072 (63.7%)	478 (28.4%)	129 (7.7%)	3 (0.2%)	0.5	0.4 , 0.6	0.298
	Worker	27 (48.2%)	25 (44.6%)	4 (7.1%)	0	0.8	0.4 , 1.3	<0.001
	Housewife	555 (62.6%)	243 (27.4%)	81 (9.1%)	8 (0.9%)	0.5	0.4 , 0.6	<0.001
	S. employee	512 (65.1%)	198 (25.2%)	71 (9.0%)	5 (0.6%)	0.5	0.4 , 0.6	<0.001
	Other	261 (64.1%)	113 (27.8%)	32 (7.9%)	1 (0.2%)	0.5	0.4 , 0.6	<0.001
	Jobless	146 (49.5%)	96 (32.5%)	49 (16.6%)	4 (1.4%)	0.6	0.5 , 0.8	<0.001
Depression	Normal	1073 (72.3%)	556 (23.6%)	92 (3.9%)	3 (0.1%)	1		
	Low	419 (58.3%)	227 (31.6%)	73 (10.2%)	0	1.4	1.2 , 1.7	<0.001
	Moderate	564 (52%)	378 (34.9%)	134 (12.4%)	8 (0.7%)	1.4	1.2 , 1.6	<0.001
	Severe	217 (41.9%)	208 (40.2%)	91 (17.6%)	2 (0.4%)	1.4	1.1 , 1.8	0.003
	Very Severe	217 (31.7%)	225 (32.8%)	210 (30.7%)	33 (4.8%)	2.1	1.6 , 2.7	<0.001
Anxiety	Normal	1813 (70.4%)	633 (24.6%)	126 (4.9%)	3 (0.1%)	1		
	Low	256 (58.3%)	140 (31.9%)	41 (9.3%)	2 (0.5%)	1.2	1.1 , 1.6	0.038
	Moderate	539 (51.4%)	367 (35%)	139 (13.3%)	3 (0.3%)	1.3	1.1 , 1.5	0.002
	Severe	223 (46.8%)	171 (35.9%)	75 (15.8%)	7 (1.5%)	1.2	0.9 , 1.5	0.158
	Very Severe	289 (35.2%)	283 (34.4%)	219 (26.6%)	31 (3.8%)	1.4	1.1 , 1.7	0.002
Stress	Normal	1914 (73.7%)	571 (22%)	110 (4.2%)	3 (0.1%)	1		
	Low	423 (57%)	263	55 (7.4%)	1 (0.1%)	1.6	1.4 , 1.9	<0.001

		(35.4%)					
Moderate	425 (45.4%)	365 (39%)	141 (15%)	6 (0.6%)	2.4	1.9 , 2.8	<0.001
Severe	260 (35.7%)	279 (38.3%)	179 (24.6%)	10 (1.4%)	3.2	2.6 , 4.1	<0.001
Very severe	98 (27.6%)	116 (32.7%)	115 (32.4%)	26 (7.3%)	4.9	3.7 , 6.8	<0.001

As presented in Table 3, except for sex and having child, there was a significant statistical relationship between the other variables and social network addiction. Among different age groups, social network addiction was most prevalent in the 16-24 years old participants. Also, 59.3% of the participants in this group had low to severe social network addiction. Addiction to SNSs was seen in 50.2% of the single participants. While most married, divorced, or widowed were in the normal range. The results suggest that participants under

Discussion

Our first aim was to determine the prevalence of social network addiction among Iranian internet users. Results showed that 12.8% of participants (645 persons) were addicted to SNSs, with a range of moderate to severe addiction. Also, 600 (11.9%) people had moderate, and 45 (0.9%) had severe social network addiction. Since most SNSs users were adolescents and youth, most studies of social network addiction are based on teenagers and university samples reporting ranges from 0.8% (18) to 18.3% (19). Our study shows that adolescent and young participants were more addicted to SNSs, as compared to adults. 22.3% of young participants in schools and universities were addicted to SNSs, which is consistent with studies by Pempek, Yermolayeva and Calvert (20), Niemz et al. (19), Ho, Lwin, and Lee (6), and Thompson and Lougheed (21) studies. One of the reasons for such findings is that adolescents are very susceptible to peer influence compared with adults. Becoming part of a peer group is an important developmental goal for adolescents (22), and SNSs offer many opportunities for social connections with peers. Therefore, they might succumb to peer pressure and use media excessively in order to fit in. Also, younger people tend to show more favorable views of technology, and they depend on SNSs to build

diploma had more social network addiction (55.8%). Also, social network addiction was more among students in schools or universities (56.1%) and less among self-employed people (34.4%). People with high scores on depression, anxiety, or stress subscales, were more likely to be addicted. Conversely, there was no addiction in more than 70% of people who have low scores on depression, anxiety, or stress, while as the severity of each subscale increased, the number of people with addiction also increased.

their self-esteem and identity (12,23). Furthermore, adolescents and young persons have lower executive functions (24). One of the aspects of executive function which is engaged in addictive behavior is impulse control. Evidence consistently suggests that adolescents have lower impulse control than adults, and adolescents engaged in addictive behavior have a lower level of impulse control than their non-addictive peers (25).

In the present study, social network addiction appeared to be more prevalent among participants with high scores on depression, anxiety, or stress subscales. Dieris-Hirche et al. (26) found that the prevalence of internet addiction among depressed people was 36% which is considerably high. Addictive behavior may deprive persons of enjoyable social lives and lead to their personal lives' negligence (27). In general, Individuals are striving to feel good. However, some individuals resort to SNS use as a shortcut to gain such feelings (28).

As shown earlier, evidence suggests a high association between SNSs usage and higher scores on depression symptoms and psychopathology (29). Furthermore, depressive disorder might predict the emergence of social network addiction (30). Our finding might align with repeatedly reported and reviewed comorbidity of addiction and psychiatric symptoms (31). Ko et al. (30) suggested a

bidirectional interaction between social network addiction and psychiatric disorder to combine both perspectives. On the one hand, excessive and maladaptive use of SNSs might be utilized to cope with psychiatric symptoms. On the other hand, social network addiction might also induce psychiatric pathology like alcoholism (32).

Some authors argue that internet addiction or social network addiction might be better explained as a result of a primary disorder (33), as our study showed that with an increase in depression, anxiety, or stress, social network addiction increased. However, we cannot certainly infer that social network addiction is a secondary disorder resulting from a primary disorder such as depression because other authors argue that social network addiction is a specific disorder. Therefore, although it is comorbid with other psychiatric disorders, it is a distinct disorder itself (34).

This might be important for clinical diagnosis and psychotherapy in patients with psychiatric disorders. For example, many epidemiological studies have revealed frequent co-occurrences (called dual diagnosis) of depression and addictive disorders (35). Dual diagnosis is associated with more significant functional impact, poorer treatment outcomes, and increased costs to society and the individual (36). Thus, the co-occurrence of social network addiction and other psychiatric disorders such as depression should be considered in treating social network addiction or other psychiatric patients.

Conclusion

The present study results revealed the prevalence of social network addiction among the Iranian population and its significant association with depression, anxiety, and stress. Hence, given the increase in the number of users, side effects arising from the excessive use of the social network sites, and its adverse effects on various aspects of health, especially mental health, it is necessary that clinicians and researchers identify it and take interventional attempts in order to reduce its aversive effects.

Acknowledgment

References

1. Moqbel M, Kock N. Unveiling the dark side of social networking sites: Personal and work-related consequences of social networking site addiction. Information management 2018; 55: 109-19.
2. Boyd D, Ellison N. Social network sites: definition, history, and scholarship. IEEE engineering management review 2010; 3: 16-31.
3. Ellison NB, Vitak J, Gray R, Lampe C. Cultivating social resources on social network sites: Facebook relationship maintenance behaviors and their role in social capital processes. J Comput Mediat Commun 2014; 19: 855-70.
4. Griffiths MD. Social networking addiction: Emerging themes and issues. J Addict Res Ther 2013; 4: 201-34.
5. Facebook. Company Info: Facebook Newsroom. [cited 2017]. Available from: https://newsroom.fb.com/company-info.
6. Ho SS, Lwin MO, Lee EW. Till logout do us part? Comparison of factors predicting excessive social network sites use and addiction between Singaporean adolescents and adults. Comput Human Behav 2017; 75: 632-42.
7. Durkee T, Kaess M, Carli V, Parzer P, Wasserman C, Floderus B, et al. Prevalence of pathological internet use among adolescents in Europe: demographic and social factors. Addiction 2012; 107: 2210-22.
8. Kuss DJ, Griffiths MD. Online social networking and addiction-a review of the psychological literature. Int J Environ Res Public Health 2011; 8: 3528-52.
9. Turel O, Romashkin A, Morrison KM. Health outcomes of information system use lifestyles among adolescents: videogame addiction, sleep curtailment and cardio-metabolic deficiencies. PloS One 2016; 11: 154-64.
10. Andreassen CS, Torsheim T, Brunborg GS, Pallesen S. Development of a Facebook addiction scale. Psychol Rep 2012; 110: 501-17.

11. He Q, Turel O, Bechara A. Brain anatomy alterations associated with Social Networking Site (SNS) addiction. Scientific reports 2017; 7: 450-64.

12. Pelling EL, White KM. The theory of planned behavior applied to young people's use of social networking web sites. CyberPsychol Behav 2009; 12: 755-95.

13. Davenport SW, Bergman SM, Bergman JZ, Fearrington ME. Twitter versus Facebook: Exploring the role of narcissism in the motives and usage of different social media platforms. Comput Human Behav 2014; 32: 212-20.

14. Balakrishnan V, Shamim A. Malaysian Facebookers: Motives and addictive behaviours unraveled. Comput Human Behav 2013; 29: 1342-9.

15. SPSS I. Statistics, version 20. New York: Somers; 2012.

16. Henry JD, Crawford JR. The short-form version of the Depression Anxiety Stress Scales (DASS-21): Construct validity and normative data in a large non-clinical sample. Br J Clin Psychol 2005; 44: 227-39.

17. Asghari A, Saed F, Dibajnia P. Psychometric properties of the Depression Anxiety Stress Scales-21 (DASS-21) in a non-clinical Iranian sample. Int J Psychol 2008; 2: 82-102.

18. Poli R, Agrimi E. Internet addiction disorder: prevalence in an Italian student population. Nord J Psychiatry 2012; 66: 55-9.

19. Niemz K, Griffiths M, Banyard P. Prevalence of pathological Internet use among university students and correlations with self-esteem, the General Health Questionnaire (GHQ), and disinhibition. Cyberpsychol Behav 2005; 8: 562-70.

20. Pempek TA, Yermolayeva YA, Calvert SL. College students' social networking experiences on Facebook. J Appl Dev Psychol 2009; 30: 227-38.

21. Thompson SH, Lougheed E. Frazzled by Facebook? An exploratory study of gender differences in social network communication among undergraduate men and women. Coll Stud J 2012; 46: 88-99.

22. Larson RW. Toward a psychology of positive youth development. Am Psychologist 2000; 55: 170.

23. Davis KE. Young People's Digital Lives: The impact of interpersonal relationships and digital media use on adolescents' sense of identity. Harvard: Harvard University; 2011.

24. Prencipe A, Kesek A, Cohen J, Lamm C, Lewis MD, Zelazo PD. Development of hot and cool executive function during the transition to adolescence. J Exp Child Psychol 2011; 108: 621-37.

25. Dong G, Lu Q, Zhou H, Zhao X. Impulse inhibition in people with Internet addiction disorder: electrophysiological evidence from a Go/NoGo study. Neurosci Lett 2010; 485: 138-42.

26. Dieris-Hirche J, Bottel L, Bielefeld M, Steinbüchel T, Kehyayan A, Dieris B, et al. Media use and Internet addiction in adult depression: A case-control study. Comput Human Behav 2017; 68: 96-103.

27. Charlton JP. A factor-analytic investigation of computer 'addiction'and engagement. Br J Psychol 2002; 93: 329-44.

28. Wickel TM. Narcissism and social networking sites: the act of taking selfies. Elon journal of undergraduate research in communications 2015; 6(1): 5-12.

29. Carli V, Durkee T, Wasserman D, Hadlaczky G, Despalins R, Kramarz E, et al. The association between pathological internet use and comorbid psychopathology: A systematic review. Psychopathology 2013; 46: 1-13.

30. Ko C-H, Yen J-Y. The association between Internet addiction and psychiatric disorder: A review of the literature. Eur Psychiatry 2012; 27: 1-8.

31. Pani PP, Maremmani I, Trogu E, Gessa GL, Ruiz P, Akiskal HS. Delineating the psychic structure of substance abuse and addictions: should anxiety, mood and impulse-control dysregulation be included? J Affect Disord 2010; 122: 185-97.

32. Pettinati HM, O-Brien CP, Dundon WD. Current status of co-occurring mood and substance use disorders: A new therapeutic target. Focus 2015; 13: 356-62.

33. Shaffer HJ, Hall MN, Vander Bilt J. Computer addiction: A critical consideration. Am J Orthopsychiatry 2000; 70: 162.

34. Montag C, Bey K, Sha P, Li M, Chen YF, Liu WY, et al. Is it meaningful to distinguish between generalized and specific Internet addiction?. Asia Pac Psychiatry 2015; 7: 20-6.

35. Merikangas KR, He J-p, Burstein M, Swanson SA, Avenevoli S, Cui L, et al. Lifetime prevalence of mental disorders in US adolescents. J Am Acad Child Adolesc Psychiatry 2010; 49: 980-9.

36. Deady M, Teesson M, J Kay-Lambkin F. Treatments for co-occurring depression and substance use in young people: a systematic review. Curr Drug Res Rev 2014; 7: 3-17.