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Exploring Interleukin-6 ,CRP in cellphone addiction and depression: a case control study in the precincts of medical college

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ABSTRACT

Cellphone technology has tremendously grown in its market and uses in the last decade. But it's overutilization has led to the development of new problems also. Objectionable cellphone use can be accounted for in the form of technological addiction, which can develop depression, anxiety, and other health problems. Depression is the third leading cause of global disease burden if it continues; by 2030, it will become the leading cause of disease burden. Stress or addiction can lead to the development of psychiatric disorders or vice versa. These stressors lead to the neuroinflammatory response, resulting in an exaggerated response to subsequent pro-inflammatory challenges. Depression was diagnosed by Hamilton depression scale (HAMD) and cellphone addiction was evaluated by smartphone addition scale-short version (SPAS) and their serum sample was evaluated for IL-6 and CRP according to protocol. Overall Mean score of HAMD in cases was 12.21 and in controls was 4.68. Mean score of SPAS scale in cases and controls was (37.75, 17.43) respectively. Mean IL-6 levels of cases and controls (21.03±35.85, 11.07±13.61 pg/ml) respectively with the significance of (p=0.026). Higher levels of the systemic inflammatory biochemical marker IL-6 in cases are associated with depression. Smartphone addiction scores are in correlation with depression scores but not in association with interleukin-6 or CRP levels. Females of a young age are more prone to depression and smartphone addiction together. Early assessment and diagnosis could be helpful in preventing further more damage to social and mental vicinity of individuals. Inflammatory pathways may provide important new interpolation and anticipation targets for these ailments.

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INTRODUCTION

The most effective mode of information and communication technology in the present era is the mobile phone/smartphones, the use of which has grown tremendously in the past years. Current generations are thriving on cellphone/smartphone technology so much so that, even a toddler lullabies by parents have been replaced by a smartphone. Smartphone utilization and benefits are such enormous that the potential threat, lying just beneath this glorified instrument, has been masked. Objectionable

cellphone use can be accounted for in the form of technological addiction, which is now addressed by medical, educational and social society as well. This phone addiction can develop anxiety, irritability, sleep disturbances, shaking, insomnia, and even illusions (Hassanzadeh and Rezaei, 2011). Research of Thomee et al. concluded that problematic and excessive use of mobile phones is in association with anxiety, sleeplessness, depression, psychological misery, and unhealthy lifestyle (Thomée *et al.*, 2011). physical, bodily and emotional or mental problems have been reported from cell-phone abuse, including rigidity and muscle pain, fatigue, dryness, blurry vision, irritation, or ocular redness (Gutiérrez *et al.*, 2016).

Depression is the third prominent cause of worldwide disease burden, accounting for 4.3% of total disability-adjusted life years, in terms of public health significance. If the trend continues, by 2030, it will become the chief reason of disease burden (Pattanayak and Sagar, 2014). Individually, it affects the mental and emotional wellbeing, compromise with the overall quality of life and may intensify the risk of other medical ailments. It also adversely affects the job and family social life, it leads to product damage and economic burden (Pattanayak and Sagar, 2014). Depressive disorders can affect any person irrespective of age, gender or community residing in urban and rural areas or slums. National mental health survey reported a lifetime prevalence of 5.2% of depression in India (Gururaj *et al.*, 2016). Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), includes symptoms and the diagnosis of major clinical depression (MCD), behaviour addiction (internet abuse/ gambling). Besides these, smartphone addiction has also been in the queue to be added in DSM5 (Tolentino and Schmidt, 2018). Again depression not only causes excessive mental trauma but also intrudes upon vital biological processes just like termites eating inside a log, depression regulates inflammatory pathways, metabolism pathways, autonomic function, neuroendocrine regulation, sleep and appetite (Gold *et al.*, 2015). It has a cause and consequence relation with several noncommunicable diseases, substance abuse disorders and dietary disorders (Amudhan and Gopalkrishna, 2016). Stress or addiction in life can lead to the development of psychiatric disorders or vice versa. These stressors lead to the neurological and inflammatory responses, resulting in an exaggerated reaction to subsequent pro-inflammatory challenges. Both acute and chronic stressors are found in association with elevated peripheral biochemical markers of inflammation (Lurie, 2018).

IL-6 is a small but multifunctional protein that can be released from many tissues and organs including blood cells, endothelium, epithelium, adipose tissue, astrocytes, microglia and neurons (Rossi *et al.*, 2015). IL-6 is chiefly branded as a pro-inflammatory cytokine, but it also has anti-inflammatory properties (Wolf *et al.*, 2014). Recent researches in both preclinical (Hodes *et al.*, 2014) and clinical models (Khandaker *et al.*, 2014) has suggested a functional role for IL-6 in the expansion of depression and potential for targeting it to treat depression in humans. N.L. Nishuty found significantly raised concentrations of serum IL-6 in Major depressive patients compared to control group (Nishuty *et al.*, 2019) there are also contrasting studies available with no significant relationships (Chen *et al.*, 2007; Becking *et al.*, 2013). Hence the present study was proposed with the aim to explore levels of IL-6, CRP marker together in smartphone-addicted and depressive adults in the arena of medical college.

MATERIALS AND METHODS

Study design

The present study was conducted in the Department of Biochemistry of Santosh Institute of Medical Sciences and Research, Ghaziabad with the collaboration of F.H medical college and hospital Etmadpur, Agra, and also it was ethically approved by the same authority. It was a case-control study conducted in January 2018-Dec 2019. The prime aim of this study was to evaluate serum IL-6 and CRP levels in both depression and smartphone-addicted individuals. Subgroup analyses were also performed to explore the effects of markers in the severity of depression. In addition, we also aimed to examine the gender differences in the expression of these proteins.

Participant population

In the present study, we observed data pertaining to patients diagnosed with depression and smartphone addiction together. The depression and smartphone addiction was assessed with the aid of widely used scales, Hamilton Depression Rating Scale (HAMD) and smartphone addiction scale – short version (SAS-SV) (Hamilton, 1960). Healthy controls were included if they were free of these above disorders. All of them were apparently healthy (not suffering from acute infections/fever). Total number of 75 cases and 75 controls data were included in the study.

The inclusion criteria were 1) adult patients $\geq$18 years of age irrespective of sex which were selected according to the protocol criteria of study design,

among the staff/students, residents of FH medical college and any patient's attendants coming in OPD of the medical college.2) Individuals with both depression and smartphone addiction, and not receiving any antipsychotics. The exclusion criteria were:1) Pregnant females, 2) Any drug abusers or alcoholics. Informed consent of every participant was taken.3) individuals with any of the following associated complications like acute or chronic infections, antidepressant or antipsychotic treatment, allergies, autoimmune disorders, systemic diseases and or immunomodulatory treatment.

Sample collection and measurements

Blood sampling for laboratory investigations was conducted, taking all necessary precautions. Fasting peripheral venous blood samples (5mL) without anticoagulants were collected by venipuncture. The sample serum was separated, stored into aliquots, and stored at -80°C in a deep refrigerator before laboratory assays. Serum levels of IL-6 were determined with ELISA kits (Diaclone, France) in accordance with the manufacturer's instructions. Serum CRP was measured by turbidimetry method on semiauto analyser chem7. The CRP sensitivity was 0.2mg/L.

Statistical analysis

The statistical analysis was performed using the SPSS 17.0 program (SPSS Inc., Chicago, IL, USA) in Windows 10 Ultimate. The statistical analysis of the data, including the application of tests for description and analytical parametric, with binary logistic regression tests, was performed. The independent t-test was used to compare the parametric variables between the genders. Pearson correlations were used to define the strength of the relationships between the examined variables. The statistical significance was set at $p < 0.05$

RESULTS AND DISCUSSION

Comparison between cases and controls

In total, 150 individuals were randomly included, in the study after inspecting and interrogating around 170 people. Those 20 person data was disqualified on the basis of exclusion criteria .75 cases and 75 controls were extracted for study. The qualification of cases was to have depression and smartphone addiction together irrespective of gender. Controls were simultaneously found during the process of cases subject's identification, as they did not have either of depression or smartphone addiction and were also apparently healthy.

T-test shows all variables are significant except CRP when equal variances are assumed (Table 1). The cases comprised 33 males and 42 females with a mean age of 21.68 years. Controls had 43 males and 32 females with mean 28.61 years. Age came out as a significant factor among both groups ($p< 0.001$). It was an unexpected finding. HAMD and SPAS scores are predefined and widely accepted scales, hence significant. Mean score of HAMD in cases was 12.21 and in controls was 4.68. Mean score of SPAS scale in cases and controls was (37.75, 17.43) respectively. IL-6 values are significant (p=0.026).Mean of cases and controls (21.03±35.85, 11.07±13.61 pg/ml).

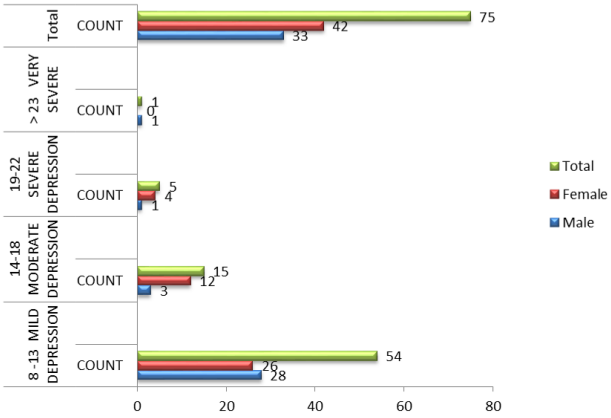

Figure 1: Gender tabulation according to severity of depression

Gender wise analysis between Cases

When independent sample test and a mean of parameters in males and females of cases were analysed, AGE factor was significant (p=0.004), Age of females was significantly less than males. IL-6 levels in males were very less (10.17±15.3), compared to females (29.57±44.35) and were significant (p= 0.019). In cases, females are found to be more depressed with the average HAMD score (12.62 ± 3.54) than males with an average score of (11.7± 3.4), but values were insignificant. SPAS and CRP were insignificant. Mean SPAS score in males and females (37.64±5.05, 37.83±5.13). Mean CRP in male and female is (2.65±2.90, 2.67±2.74) (Table 2).

Gender distribution according to the severity of depression

Overall, 54 cases are of mild depression, 15 of moderate, 5 cases of severe depression and only one person of very severe depression was found in this study. Mild depression is more in males 28 (84.8%), females were 26 (61%).In moderate depression, 12 females (28.6%) and three males (9.1%) were found. A severe type of depression had 4(9.5%) females and 1 (3%) male. Only one male of very severe depression was found in the study, as depicted in (Figure 1).

Table 1: 01 Comparison of cases and controls

		Levene's Test For Equality Of Variances	T-Test For Equality Of Means			
		Cases (75) Mean±SD	Control (75) Mean±SD	SIG. (2-TAILED)	Mean Difference	Std. Error Difference
Age(years)	Equal Variances Assumed	21.68 ± 2.32	28.61 ± 9.97	<.001**	6.93	1.18
HAMD (score)	Equal Variances Assumed	12.21±3.45	4.68 ± 2.08	<.001**	-7.53	0.47
IL-6 (pg/ml)	Equal Variances Assumed	21.03±35.85	11.06±13.61	.026*	-9.97	4.43
CRP	Equal Variances Assumed	2.66 ± 2.79	2.56 ± 4.41	0.866	-0.1	0.60
SPAS	Equal Variances Assumed	37.75 ± 5.06	17.43±6.84	<.001**	-20.32	0.98

*p < 0.05 significant ** p <0.001 highly significant

Table 2: Gender analysis

			Cases		T-Test For Equality Of Means		
			Male (33)	Female (42)	Sig. (2-Tailed)	Mean Difference	Std. Error Difference
Case	Age (years)	Equal Variances Assumed	22.55 ± 2.86	21.0 ± 1.50	.004**	1.55	0.51
	HAMD (score)	Equal Variances Assumed	11.70 ± 3.34	12.62 ± 3.53	0.254	-0.92	0.8
	SPAS (score)	Equal Variances Assumed	37.64 ± 5.05	37.83 ± 5.13	0.868	-0.2	1.19
	IL6 (pg/ml)	Equal Variances Assumed	10.17 ± 15.30	29.57± 44.35	0.019*	-19.4	8.08
	CRP	Equal Variances Assumed	2.65 ± 2.90	2.67± 2.74	0.975	-0.02	0.65

*p < 0.05 significant ** p <0.001 highly significant

Table 3: Multiple Comparisons

Tukey Hsd Series	Dependent Variable	(I) HAMD	(J) HAMD	Mean Difference (I-J)	Std. Error	Sig.
Cases	Age	8-13 Mild Depression	Moderate Depression	-1.659*	0.656	.036*
			Severe Depression	0.607	1.051	0.832
		14-18 Moderate Depression	Mild Depression	1.659*	0.656	.036*
			Severe Depression	2.267	1.161	0.132
		19-22 Severe Depression	Mild Depression	-0.607	1.051	0.832
			Moderate Depression	-2.267	1.161	0.132
	IL6	8-13 Mild Depression	Moderate Depression	-11.177	9.863	0.497
			Severe Depression	-53.097*	15.798	.004**
		14-18 Moderate Depression	Mild Depression	11.177	9.863	0.497
			Severe Depression	-41.920*	17.452	.049*
		19-22 Severe Depression	Mild Depression	53.097*	15.798	.004**
			Moderate Depression	41.920*	17.452	.049*
	SPAS	8 -13 Mild Depression	Moderate Depression	1.207	1.371	0.654
			Severe Depression	-7.393*	2.196	.003**
		14-18 Moderate Depression	Mild Depression	-1.207	1.371	0.654
			Severe Depression	-8.600*	2.425	.002**
		19-22 Severe Depression	Mild Depression	7.393*	2.196	.003**
			Moderate Depression	8.600*	2.425	.002**
	CRP	8 -13 Mild Depression	Moderate Depression	-0.15381	0.83096	0.981
			Severe Depression	0.12419	1.33089	0.995
		14-18 Moderate Depression	Mild Depression	0.15381	0.83096	0.981
			Severe Depression	0.278	1.47022	0.98
		19-22 Severe Depression	Mild Depression	-0.12419	1.33089	0.995
			Moderate Depression	-0.278	1.47022	0.98

Table 4: Independent Samples Test On Gender BasisAmong Cases And Controls

Gender			T-Test For Equality Of Means				
			T	DF	Sig. (2-Tailed)	Mean Difference	Std. Error Difference
Males	Age	Equal Variances Assumed	3.369	74	.001**	5.455	1.619
	HAMD	Equal Variances Assumed	-12.022	74	<.001**	-7.464	0.621
	SPAS	Equal Variances Assumed	-15.253	74	<.001**	-20.66	1.354
	CRP	Equal Variances Assumed	-1.361	74	0.178	-0.7902	0.58054
	IL6	Equal Variances Assumed	-0.25	74	0.803	-0.766	3.05893
Females	Age	Equal Variances Assumed	4.796	72	<.001**	8.438	1.759
	HAMD	Equal Variances Assumed	-10.54	72	<.001**	-7.338	0.697
	SPAS	Equal Variances Assumed	-13.53	72	<.001**	-19.802	1.463
	CRP	Equal Variances Assumed	0.775	72	0.441	0.83018	1.07058
	IL6	Equal Variances Assumed	-1.976	72	.032*	-16.2701	8.233155

*p value significant <0.05 * *p value highly significant <0.001

Subgroup analysis of serum IL-6, I and CRP levels in different levels of depression

(Table 3) is depicting multiple comparisons by Tukey HSD. The significant age difference between mild and moderate depression was found (p=0.036). Significant difference between IL-6 values was found between mild and severe depression (p=0.004). IL-6 was also significantly different between moderate and severe depression groups (p=0.049). CRP levels were insignificant. SPAS scores were significantly different between mild, moderate and severe depression. This is a very important finding.

Gender wise comparison cases vs controls

(Table 4) depicts t-test between cases and controls among different genders. In male's age, HAMD, SPAS category are significant. Mean age in controls (28±8.94 years) and cases (22.55±2.86 years), this is depicting depression and smartphone addiction is more in younger males. In females, all parameters were significant between cases and controls, except CRP. This is another important finding in our study. AGE and HAMD score were highly significant (p<0.001). Average Age in controls (29.44±11.3 years) and in cases was (21±1.5 years), here also depression is trending towards younger females. Mean of IL-6 in controls (13.3±16.06 pg/ml) were lower than cases (29.57±44.35 pg/ml) and significant in females, indicating the presence of inflammation in depression and addiction. Overall IL-6 of both genders is more in cases than controls and significant.

Table 5: Correlations

Series			Age	SPAS	HAMD	CRP	IL6
cases	Age	Pearson Correlation	1	0.07	0.098	-0.005	-0.128
		Sig. (2-Tailed)	-	0.55	0.403	0.966	0.273
		N	75	75	75	75	75
	SPAS	Pearson Correlation	0.07	1	.262*	-0.184	0.13
		Sig. (2-Tailed)	0.55	-	0.023	0.113	0.268
		N	75	75	75	75	75
	HAMD	Pearson Correlation	0.098	.262*	1	0.105	.247*
		Sig. (2-Tailed)	0.403	0.023	-	0.369	0.032
		N	75	75	75	75	75
	CRP	Pearson Correlation	-0.005	-0.184	0.105	1	-0.084
		Sig. (2-Tailed)	0.966	0.113	0.369	-	0.474
		N	75	75	75	75	75
	IL6	Pearson Correlation	-0.128	0.13	.247*	-0.084	1
		Sig. (2-Tailed)	0.273	0.268	0.032	0.474	-
		N	75	75	75	75	75

*. Correlation Is Significant At The 0.05 Level (2-Tailed).
**. Correlation Is Significant At The 0.01 Level (2-Tailed).

Pearson correlations

(Table 5) is depicting the correlation between the parameters of case series.HAMD was found in correlation with IL-6 (p= 0.032) and SPAS (p=0.023).

This study was conducted to explore the relation of inflammatory markers (interleukin-6 and CRP) in smartphone-addicted and depressed individuals. The study gave many astonishing results; firstly mean age was significantly different in cases and controls. Age was significant between males and females of cases also. Age of males (22.55 years) was more than females (21years). It was also found significant between mild depression (54 cases) cases and moderate (15 cases) depression. Also, on separate gender analysis, age was significant between cases and controls. Thus to our knowledge, we believe to be first in reporting, age as a significant factor for smartphone addiction and depression both. Our study also indicated that younger females are tending to get addicted to smartphone and eventually in depression. Inconsistent with our findings, a study by Per Hoguland also suggested that anxiety, sleeplessness and burnout were specifically severe and prevalent in younger females. Men of middle age group have a higher occurrence of mental ill-health compared to other age groups of men, with the lowest severity and prevalence in the age span 60–69 years (Höglund *et al.*, 2020).

Some contrasting, studies by Strodal and associates suggested that there was a negligible gender difference in depression scores and in prevalence rates of depression and both were found to increase constantly with age in both genders (Stordal *et al.*, 2001). While discussing the severity of depression,

maximum cases in our study fall in the group of mild depression with age (21.4years). Highest age of the subject was found in moderate depression (23.07) and age was lower in severe (20.8) and very severe (20.0) groups. Age factor was significant (p=0.058) particularly, the significant age difference between mild and moderate depression was found (p=0.036)

In accordance with our study, Csibi S research findings showed that the (20–34 years) age group had the maximum score on the problematic smartphone usage scale, next was those aged between 3–11 years and then those aged 35–50 years. The lowest scores were for those aged 11–19 years and those over 50 years of age (Csibi *et al.*, 2019).

These findings are establishing our facts that the younger generation is more vulnerable to depression and smartphone addiction. Possible reasons for a younger generation to get addicted could be their leisure time, lazy behaviour and no target for life or education achievements, lack of parents, teacher control or ignorance could also be the factor of their falling prey to this type of addiction and depression.

In this study, we found 33 males and 42 females in cases category clearly depicting females were more depressed. The score of female depression was more than males but was statistically insignificant. It was documented by M Kockler that women in the overall population suffered from more depressive symptoms than men and had more hunger disturbance and joylessness (Kockler and Heun, 2002).

The phrase ”gender gap” is frequently used in economic, income, social or political issues between men and women but the best-documented gender gap include a mood disorder/ depression. Women tend to develop depression twice as likely as men. They also have higher amounts of seasonal affective disorder, depressive signs in bipolar disorder, and dysthymia (chronic depression). The hormonal changes that accompany menstruation or any kind of sexual or child abuse can be explanation for women being vulnerable to depression. Some experts believe in equal development and frequency in reference to develop depression, but women are more likely to be diagnosed with this disorder because men do not share their feelings. Depression shows up in dissimilarly in men as in substance abuse or violent behaviour (Harvard Health Publishing, 2011).

In this study, we found biochemical associations and statistical association with cases (depressed and addicted to a smartphone). It was statistically proved by having a correlation of HAMD with SPAS, and HAMD in relation with IL-6 marker, thus proving the indirect relation of smartphone addiction and IL-6.

Interleukin-6 levels were found to be significant between cases and controls (p = 0.026), indicating rising levels of inflammation together with depression and addiction. IL-6 levels were significantly different between males and females (p=0.019*) in case category, with females levels on the higher side.

IL-6 levels were also significant between groups (p=0.011) of the severity of depression. Significant differences of IL-6 between mild and moderate depression and moderate and severe depression found, which is indicating inflammation relation with levels of depression. Significant difference between IL-6 values was found between mild and severe depression (p=0.004). IL-6 was found an insignificant difference among moderate and severe depression groups (p=0.049).

Study of Yoshimura showed that 51 MDD patients, plasma IL-6 levels were elevated during the acute state of MDD compared to controls, similar to our findings (Yoshimura *et al.*, 2009).

IL-6 was found to be correlated with a depression score of HAMD.IL-6 levels of females were significant between cases and controls but insignificant among males. CRP levels were higher in cases than controls, and were also raised in females as compared to males but were not found significant in the study.

It is possible that acute nerve-racking emotional event results in amplified levels of inflammatory markers such as IL-6 via stimulation created by nervous, endocrine and autonomic nervous system responding together, which we have discussed earlier is more in females thus explaining the IL-6 elevation. Cytokines can cross over the blood-brain barrier, thereby influencing many facets of mood disorder pathways and pathophysiology, including neurotransmitter mechamnism, neuroendocrine function, neural plasticity, and subsequently altering the activation of the brain and affecting emotion and behaviour. Some studies have found extraordinary raised levels of serum IL-6 in patients with depressive disorder, (Lu *et al.*, 2019). Since IL-6 induces synthesis of CRP in the liver, stress might be contributing to increasing levels of CRP via its effects on IL-6 levels. Acute stress also has the potential to induce peripheral blood mononuclear cells to migrate from the marginal pool resulting in an increased number of circulating cells. Thus, resulting in the acute increase in the number of cells producing. IL-6 may be responsible for the increase in inflammatory markers during times of trauma and stress. A fluctuation in plasma volume is another potential mechanism for stress-induced

upsurges in inflammatory responses. Acute negative emotions tend to stimulate reductions in plasma volume (Brummett *et al.*, 2010). On contrast to our study, among manic/mixed Bipolar Disorder patients, higher serum IL-6 levels were observed in males than female patients (Lu *et al.*, 2019).

SPAS scores were not found significant between males and female cases in our study, but females had a higher score of addcition towards the mobile phone.SPAS scores were significant between mild depression and severe depression cases. It was also significant between moderate and severe depression. SPAS were found in correlation with the HAMD score of cases.

However, no correlation was found between SPAS and any biochemical marker [IL-6, CRP]. SPAS scores were also significant categorically between severe and mild depression and severe and moderate depression; this is a remarkable finding as it is indicating that the severity of depression is also in a relationship with smartphone addiction.

Similar to our findings study of K Demirci, discovered that the Smartphone Addiction Scale scores of women were significantly advanced than those of males. Depression, anxiety and daytime dysfunction marks were higher in the high smartphone use group than in the low smartphone use group. Positive correlations were established between the Smartphone Addiction Scale scores and depression stages, anxiety levels, and some sleep quality scores (Demirci *et al.*, 2015).

On finding a correlation between the parameters in case series, we observed IL-6 was found in correlation with HAMD scores. Separately HAMD and SPAS scores are also in correlation (p=0.023) This is a very important finding of this study. Inconsistency with our study, a study by Fan et al. indicated that IL-6 levels are positively associated with Hamilton Depression Scale-17 scores for MDD patients (Ting *et al.*, 2020).

Limitations

While this study was strengthened by the combined analysis of biochemical, behavioural and psychological factors, but it had some limitations too. Many of the items required self-reporting hence limiting true reflection of data of health status. It was a hospital-based study and was not planned on a large scale, due to financial restrictions. Cofounders of depression were not studied in this study, which could make another research itself. Other biochemical parameters were not included, due to lack of resources. Depression, anxiety and high rates of comorbidity are significantly related to interconnected and co-occurring risk factors such as gender-based roles, stressors and negative life experiences and events were not discussed separately, nor evaluated in this study.

CONCLUSIONS

The present study has led us to countless important findings. Firstly IL-6 which was a key molecule of the study was found to be correlated with cases (p-value <0.05). Secondly, the age of males and females both is lesser in cases (22.55, 21) than controls (28, 29.44) respectively. Age factor was an important finding. Statistically, it was proven that depression cases are younger than healthy controls and this is an alarm to society, social worker, health workers, scientists who are directly or indirectly involved in constructing a culture.

In the present study, females are found to be more depressed with an average score (12.62 $\pm$ 3.54) than males with an average score of (11.7$\pm$ 3.4). Significant difference between IL-6 values was found between mild and severe depression (p=0.004). IL-6 was also significantly different between moderate and severe depression groups (p=0.049). Mild depression is more in males, whereas moderate and severe type is more in females. Overall, IL-6 values are significantly different with (p = 0.026). IL-6 and SPAS are in association with the HAMD scale of depression independently.

Younger females are more prone towards depression and smartphone addiction in our society. We strongly recommend studying depression and smartphone addiction together, especially in teenagers and adoloscents with all more possible biochemical markers. Extensive studies with different parameters cause's covariates should be taken as new targets of research.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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