

# Prevalence of Depression in Pre-Organ Transplantation Patients at King Chulalongkorn Memorial Hospital

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**Objective:** To study the prevalence of depression in pre-organ transplantation patients at the King Chulalongkorn Memorial Hospital.

**Materials and Methods:** The present study was a cross-sectional descriptive study. The data were collected from the pre-organ transplantation patients of heart, liver, kidney, and lungs, at the King Chulalongkorn Memorial Hospital. The demographic and clinical data questionnaire, the Patient Health Questionnaire-9 in Thai version (PHQ-9-T), the Generalized Anxiety Disorder-7 in Thai version (GAD-7-T), the Thai Mental State Exam (TMSE), and the Thai Alcohol Use Disorders Identification Test (AUDIT-T) were used. The prevalence of depression and other psychiatric problems in pre-organ transplantation patients were assessed. The relationship was then analyzed using chi-square and Pearson's correlation.

**Results:** One hundred ten pre-organ transplant patients participated in the present study. The mean age was 50.32±12.2 years old, with 73.6% male participants. Types of organ failure composed of liver (50.9%), heart (31.8%), kidney (16.4%), and lungs (0.9%). The prevalence of depression was 23.6% with mean PHQ-9 score of 5.56. Anxiety, cognitive impairment, alcohol, nicotine or other illicit substance use disorder appeared to be less prevalent in the present study cohort.

**Conclusion:** One in every five pre-organ transplantation patients were found to have depression. Suicide, anxiety, cognitive impairment, alcohol, and other illicit substance problems were also observed within the present study population but to a lesser extent. Therefore, the systematic pre-transplant psychiatric and psychosocial assessment are strongly recommended in Thai pre-organ transplantation patients.

**Keywords:** Depression; Psychiatric prevalence; Pre-organ transplantation patients

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Over the past decades, the solid organ transplantation cases have increased dramatically worldwide, including in Thailand<sup>(1)</sup>. The frequently operated organ transplantations in Thailand are kidney and liver, following by heart, and lung respectively<sup>(1)</sup>. Several international guidelines recommended a psychosocial evaluation during the pre-transplant period for all candidates along with the medical and surgical evaluation<sup>(2-5)</sup>.

These recommendations stemmed from previous studies that have found that the psychiatric illnesses are important predictive factors of the unfavorable post-transplant outcome involving the higher

morbidity and mortality rate<sup>(6)</sup>. Several psychiatric issues, such as depression and anxiety, are commonly observed during the pre-transplant period<sup>(7)</sup>. Other psychiatric syndromes observed in this population are cognitive impairment, and alcohol and illicit drug use<sup>(8-10)</sup>. Prior epidemiologic research reported the prevalence of depression, anxiety, cognitive, alcohol and illicit drug use at 24%, 50%, 25%, 15%, and 10% respectively<sup>(10-14)</sup>. Ongoing physical deterioration, individual psychological problems, social and family problems, as well as the prior psychiatric or substance abuse are likely the predisposing and precipitating causes of these psychiatric disorders occurring during the pre-transplant period<sup>(6)</sup>. Moreover, the study from Craig et al reported that pre-transplant depression and anxiety can persist for at least one year after surgery<sup>(15)</sup>. Despite the increasing numbers of solid organ transplant in Thailand, the information regarding the occurrence of psychiatric disorders within this pre-transplant patient group is lacking. Therefore, it is crucial for the transplant society in Thailand to explore the psychosocial data in this area. This preliminary data may enhance the awareness of the psychiatric disorders in the transplant candidates, support the development of an appropriate

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psychosocial care before the transplant, and expand the research study of the psychosocial factors in the transplant medicine in the country.

The present study aimed to explore the prevalence of depression and other psychiatric problems such as anxiety, cognitive impairment, alcohol use and illicit drug use disorder in pre-solid organ transplantation patients at King Chulalongkorn Memorial Hospital.

## Materials and Methods

The present study was a cross-sectional descriptive study focused on the pre-solid organ transplantation patients at the King Chulalongkorn Memorial Hospital. The sample size was calculated by the formula

$$N = \frac{Z^2 P(1-P)}{d^2}$$

$P=0.24$  (according to Mohamed et al)<sup>(11)</sup>

The calculated sample size was 71. Thus, in the present study, the authors planned to recruit at least 71 patients.

Inclusion criteria were 1) Thai solid organ transplant candidates at the King Chulalongkorn Memorial Hospital, 2) the age range was between 18 and 70 years old, 3) these patients were referred to the psychiatric inpatients or outpatients consultation service for pre-organ transplantation psychosocial evaluation, 4) the patients could provide consent for participation and communicate in the Thai language.

The patients who were unable to comprehend, communicate, or tolerate the psychiatric evaluation due to the limitation of their physical conditions or states such as unconsciousness, encephalopathy, delirium, dementia, severe dyspnea, sepsis, intubation, and severe substance intoxication or withdrawal were excluded.

The present study was approved by the Research Ethics Committee of the Faculty of Medicine, Chulalongkorn University (COA 477/2019). Data were collected between August 2019 and June 2020. Each participant was informed about the research objectives and details before giving the written informed consent to participate in the present research.

The research questionnaires comprised of three parts:

1) Demographic and clinical data included gender, age, weight, height, body mass index, marital status, occupation, physical illnesses, duration of illnesses, types and causes of solid organ failure, and past psychiatric history.

2) Assessment of the psychiatric disorders; The researchers assessed the depression by using the

Patient Health Questionnaire-9 Thai version (PHQ-9-T), anxiety by the Generalized Anxiety Disorder-7 scale-Thai version (GAD-7-T), and cognitive function by the Thai Mental State Exam (TMSE).

The PHQ-9 is a clinical screening tool for depression that was developed by Kroenke et al<sup>(16)</sup>. It was later translated and validated in Thai language by Lotrakul et al and it demonstrated a good validity and reliability<sup>(17)</sup>. The cut-off point score for major depression was 9 or greater with the sensitivity at 88% and specificity at 88%. The PHQ-9 differentiates severity of depression to mild (5 to 9), moderate (10 to 14), moderate to severe (15 to 19), and severe (20 to 27). Suicidal ideation is defined as present if participants score 1 to 3 on question number 9.

The GAD-7 is a screening tool for anxiety which was developed by Spitzer et al<sup>(18)</sup>. The cut-off point score for generalized anxiety disorder was 10 or above with 89% sensitivity and 82% specificity.

The TMSE is commonly used for cognitive function assessment in Thailand<sup>(19)</sup>. The cut-off point score for cognitive impairment is 23 or below.

3) Assessment of the substance use disorder. The researchers assessed the alcohol use problem with the Thai Alcohol Use Disorders Identification Test (AUDIT-T)<sup>(20)</sup>. This is the screening tool for alcohol addiction that was translated and validated into Thai version by Silpakit et al<sup>(20)</sup>. It was shown to have a high internal consistency reliability with a Cronbach's alpha of 0.83, as well as a good test-retest reliability index ( $r=0.86$ )<sup>(21-23)</sup>. Tobacco and other illicit drug uses were assessed by the formal psychiatric interview during the psychosocial transplant evaluation process.

## Statistical analysis

Statistical data were analyzed by the IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). The researchers reported the prevalence of depression and other psychiatric problem such as anxiety, cognitive function, alcohol, and illicit drug use, in frequency and percentage. Data were shown as mean  $\pm$  standard deviation (SD). Pearson's correlation was used to assess relationship between the quantitative variables and the depression (PHQ-9 score). The chi-square test was used to compare the depression (PHQ-9 positive) with the qualitative variables. A p-value of less than 0.05 was considered statistically significant.

## Results

One hundred ten pre-organ transplantation patients were included into the present study. Most of

the participants were male (n=81, 73.6%). The mean age was 50.32±12.2 years old. Most of the research participants were married, with a university degree. Up to 77% of the participants had been diagnosed with the organ specific illnesses for more than two years but had mostly been in the transplant evaluation process for less than three months. The organ failure subtypes recruited into the present study were liver (50.9%), heart (31.8%), kidney (16.4%), and lungs (0.9%). Ninety percent of the patients did not have previous history of psychiatric illness. The demographic and clinical characteristics are shown in the Table 1.

From the 110 transplant candidates, 26 of them (23.6%) scored 9 or above on the PHQ-9-T, which could be implied of reaching the major depressive disorder diagnosis. Most of the patients (n=57, 51.8%) had no depression and 27 patients (24.5%) had mild depressive symptoms. It should be noted that 10 participants (9.1%) reported current suicidal ideation in the item #9 of PHQ-9-T. Using the cut-off point at 10 or greater of GAD-7-T, four out of 110 patients (3.6%) were screened to have a significant anxiety with additional 7.3% who reported mild anxiety. Nine patients (8.3%) scored on TMSE at 23 or less indicating to be in the cognitive impairment state. Five out of 110 patients scored in the range of having medium to likely addictive risk of alcohol used in past year using the AUDIT-T assessment. Per an interview, 15 participants (13.6%) had previously used illicit drugs. One of them was a current user. In the present study, current users refer to participants who are actively using illicit drug up until the day of the interview. Twelve of them were cannabis users, followed by three of amphetamine, two of kratom, and one hypnotic drug abuser. Table 2 summarizes the prevalent data of each specific psychiatric disorders in the pre-organ transplantation candidates. When classified by the type of organ failure as shown in Table 3, heart transplant candidates had the highest percentage of depression (25.7%), followed by liver (23.2%) and kidney (16.7%). Anxiety showed different frequency between the organ subtypes as well, which liver were found to have the highest anxiety percentage of 12.5%.

The positive correlation between the PHQ-9-T score and the other factors including the GAD-7-T score, age, level of education, TMSE score, and AUDIT-T score were analyzed using the Pearson correlation coefficient as shown in Table 4. There was only a significant correlation between the PHQ-9-T and the GAD-7-T score (p=0.01). There was no relationship between qualitative variables such

**Table 1.** Demographic and clinical characteristics of pre-organ transplantation patients

Characteristics	n (%)
<b>Sex</b>	
Male	81 (73.6)
Female	29 (26.4)
<b>Age (years); mean±SD</b>	
<20	2 (1.8)
21 to 40	20 (18.2)
41 to 60	71 (64.5)
>60	17 (15.5)
<b>Status</b>	
Single	16 (14.5)
Married	83 (75.5)
Divorced	8 (7.3)
Widow	3 (2.7)
<b>Religion</b>	
Buddhist	105 (95.5)
Christian	3 (2.7)
Islam	2 (1.8)
<b>Level of education; mean±SD</b>	
Primary School (<6 years)	19 (17.3)
Secondary School (7 to 12 years)	31 (28.2)
University (>13 years)	60 (54.5)
<b>Incomes</b>	
<5,000 Baht/month	35 (31.8)
5,001 to 15,000 Baht/month	12 (89.1)
>15,000 Baht/month	63 (57.3)
<b>Duration of sickness</b>	
<6 months	10 (9.1)
6 months to 2 years	15 (13.6)
>2 years	85 (77.3)
<b>Duration in transplantation process</b>	
<3 months	72 (65.5)
3 to 6 months	23 (20.9)
>6 months	15 (13.6)
<b>Organ</b>	
Heart	35 (31.8)
Lungs	1 (0.9)
Liver	56 (50.9)
Kidney	18 (16.4)
<b>History of psychiatric illness</b>	
None	99 (90.0)
Depression	3 (2.7)
Anxiety	1 (0.9)
Substance	1 (0.9)
Other	6 (5.5)

SD=standard deviation

**Table 2.** The prevalence of depression, anxiety, cognitive impairment, alcohol use, tobacco use, and other illicit substance use in 110 pre-organ transplant patients

Parameter	n (%)
PHQ-9	
Negative (<9)	84 (76.4)
Positive (≥9)	26 (23.6)
PHQ-9 score; mean	5.56
PHQ-9 severity	
No depression (<5)	57 (51.8)
Mild (5 to 8)	27 (24.5)
Moderate (9 to 14)	20 (18.2)
Moderate Severe (15 to 19)	4 (3.6)
Severe (20 to 27)	2 (1.8)
Suicidal ideation	
Negative	100 (90.9)
Positive	10 (9.1)
GAD-7 positive for anxiety (≥10)	4 (3.6)
GAD-7 severity	
No Anxiety (<5)	87 (79.1)
Mild (5 to 9)	19 (17.3)
Moderate (10 to 14)	1 (0.9)
Severe (≥15)	3 (2.7)
TMSE	
Positive for cognitive impairment (≤23)	9 (8.2)
Negative for cognitive impairment (>23)	101 (91.8)
AUDIT	
AUDIT positive for at risk (≥8)	5 (4.5)
• Low risk (<7)	105 (95.5)
• Medium risk (8 to 15)	2 (1.8)
• High risk (16 to 19)	1 (0.9)
• Likely addictive (≥20)	2 (1.8)
Current smoking	
No	53 (48.2)
Yes	5 (4.5)
Used to	52 (47.3)
Illicit drug use	
No	94 (85.5)
Current use	1 (0.9)
Previously use	15 (13.6)
Illicit drug use classified by organ	
Heart (n=35)	4 (11.4)
Lungs (n=1)	0 (0.0)
Liver (n=56)	8 (14.3)
Kidney (n=18)	4 (22.2)
Illicit drug type	
Cannabis	12 (66.7)
Amphetamine	3 (16.7)
Kratom	2 (11.1)
Hypnotic drug	1 (5.6)

PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; TMSE=Thai Mental State Exam; AUDIT=Alcohol Use Disorders Identification Test

**Table 3.** Prevalence of depression, anxiety, and cognitive impairment classified by organ

Parameter	n (%)
Depression (PHQ-9 ≥9)	
Heart (n=35)	9 (25.7)
Lungs (n=1)	1 (100)
Liver (n=56)	13 (23.2)
Kidney (n=18)	3 (16.7)
Anxiety (GAD-7 ≥10)	
Heart (n=35)	2 (5.7)
Lungs (n=1)	0 (0.0)
Liver (n=56)	2 (12.5)
Kidney (n=18)	0 (0.0)
Cognitive impairment (TMSE ≤23)	
Heart (n=35)	3 (8.6)
Lungs (n=1)	0 (0.0)
Liver (n=56)	6 (10.7)
Kidney (n=18)	0 (0.0)

PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; TMSE=Thai Mental State Exam

**Table 4.** Pearson's correlation between PHQ-9-T score and other variable factors

Variable factors	Depression (PHQ-9 score)	
	Pearson's correlation coefficient	p-value
Age	-0.044	0.647
Previous smoking (pack-years)	0.143	0.289
Level of education (years)	-0.006	0.954
GAD-7 score	0.761	0.01*
TMSE score	0.889	0.889
AUDIT score	0.153	0.111

PHQ-9=Patient Health Questionnaire-9; GAD-7=Generalized Anxiety Disorder-7; TMSE=Thai Mental State Exam; AUDIT=Alcohol Use Disorders Identification Test

\* Correlate to significant at 0.05

as gender, religion, marital status, occupation, type of organ, and duration of transplant process, and depression (PHQ-9 positive) using chi-square.

## Discussion

The prevalence of depression among the pre-organ transplantation patients at the King Chulalongkorn Memorial Hospital is 23.6%. These patients scored in the moderate to severe range of depression severity in the PHQ-9-T. Additionally, 9.1% of this population reported to have suicidal ideation. These findings should prompt the transplant

team to further evaluate and manage the clinical depression during the pre-transplant period. In the present study, depression rate was higher in heart and liver candidates.

Prior systematic review by Mohamed et al reported the prevalence of depression in liver transplantation candidate at 24%<sup>(11)</sup>, and the study by Guimaro et al in 2008<sup>(24)</sup> found the prevalence of depression in liver transplantation candidates at 17%. Similarly, Delibasic et al reported the prevalence of depression in heart transplant candidates at 20.9%<sup>(25)</sup>. The depression prevalence of the kidney candidate appeared to be lower in the study of Müller et al in 2015<sup>(26)</sup>. The prevalence of depression of all organ subtypes in the present study was in an approximate range of the studies mentioned above<sup>(6)</sup>. Srifuengfung et al in 2017<sup>(27)</sup> conducted a cross-sectional study to search for a prevalence of depression in kidney transplant recipients at Maharaj Nakorn Chiang Mai University Hospital, Thailand and reported the depression prevalence at 12.9%, which was slightly lower to our finding at 16.7% of depression in the kidney group. On the contrary, the depression rate in Thai transplant patients was nearly nine times higher when compared to the depression prevalence in the Thai general population. According to the Thai Ministry of public health report in 2020<sup>(28)</sup>, the prevalence of depression in Thai population was only 2.48%. This may imply that pre-organ transplantation patients have a tendency to develop depression more than the general population. The explanatory factors of higher rate of depression in this population are multifactorial. For example, worsening symptoms from progressive organ failure, lower level of personal control, lack of emotional support, loss of routine and occupational role, and decreased quality of life can all lead to the clinical depression<sup>(15,29)</sup>. Therefore, the literature suggest that depression during the pre-transplantation period should be timely detected as it is associated with non-adherence to immunosuppressant medication, graft loss, and increased mortality rate after the transplant<sup>(30-32)</sup>. If the depression was suspected or screened, the psychiatry or psychology consultation is recommended for further comprehensive mental health evaluation and management.

The Pearson's correlation analysis demonstrated a positive correlation between depression and anxiety score (correlation coefficient 0.761,  $p=0.01$ ). This finding is relevant to the meta-analysis conducted by Jacobson et al<sup>(33)</sup>. Although the present study found no statistically significant relationship among Depression

(PHQ-9 score) and other factors such as age, previous smoking history, level of Education, TMSE score, and AUDIT score.

Only 3.6% of the patients in the present cohort scored 10 or more in the GAD-7-T reaching the generalized anxiety disorder diagnosis threshold, even if 17.3% appeared to have a mild level of anxiety. Relevant to the study of Craig et al in 2017, these patients may be at risk of developing a moderate to severe anxiety throughout the transplant process<sup>(15)</sup>. Up to 8.3% of the pre-transplant patients fell into the cognitive impairment state of TMSE. The liver candidates had the highest prevalence of cognitive impairment compared to other organ subtypes. Although the researchers had not found a statistical significant correlation between cognitive impairment and liver transplant candidates in the present study, it was recommended that a cognitive impairment should be done, especially in the liver patients<sup>(9)</sup>. It is well documented that hepatic encephalopathy affects a cognitive function of the individual<sup>(9)</sup>, which may impair the self-care ability of the transplant candidates.

In term of the substance use issues, the researchers found that almost half of the candidates (47.3%) used to smoke in the past but only 4.5% were active smoker. This rate was lower than in a 2017 study<sup>(34)</sup> that reported the prevalence of an active smokers at 24.2%<sup>(28)</sup>. Similar to the tobacco use, the rate of moderate to high alcohol use risk assessed by the AUDIT-T in the present study was 4.5%. Therefore, the six months rule of obtaining a substance abuse treatment then being abstinent from both tobacco and alcohol use should be applied<sup>(12)</sup>. One in every six to seven transplant patients in the present cohort previously had an illicit substance related problem. Most the substance misuse issues were reported in the liver transplantation candidates. This rate was lower than the prior study of Schneekloth et al in 2012 that reported a 35% prevalence of substance use disorder in the liver transplant patients<sup>(13)</sup>. The most common type of substance being used by the candidates in the present study was cannabis, followed by amphetamine, and kratom. This was in contrast to the study of U.K. liver transplant candidate in 2011 that showed the high rate of opioid, benzodiazepine, cannabis, and cocaine or barbiturate<sup>(35)</sup>. Despite a low rate of alcohol, tobacco, or other illicit drugs problems in the present study pre-transplant cohort, these issues could subsequently lead to the unfavorable post-transplant medical and psychiatric outcomes<sup>(36)</sup>. Therefore, a thorough interview regarding a substance



misuse history is recommended in all pre-transplant cases.

The first limitation of the present study is its small sample size. Although the researchers methodologically calculated the appropriate sample size for the study, a larger sample size for various organ subtypes may convey a more precise psychiatric prevalence. It needs to be mentioned that the present study had only one case of lung transplant candidate due to the limited lung transplant cases in the present study center. Secondly, the present study only explored the prevalence of depression in the pre-organ transplantation patients at King Chulalongkorn Memorial Hospital. Therefore, the generalizability of the finding to represent the true psychiatric prevalence of the pre-transplant patients in Thailand may be limited. The prevalence of depression and other psychiatric disorders reported in the present study covered only the pre-transplantation period. It would be interesting for a future research to search for the prevalence of these psychiatric issues after the transplant as well as to explore the causal relationship between the pre-transplant psychiatric problems and post-transplant clinical outcome in the Thai transplant patients.

## Conclusion

The present study reported 23.6% prevalence of depression and 9.1% prevalence of suicidal ideation in the pre-solid organ transplant candidates. Moreover, anxiety, cognitive impairment, as well as, alcohol, nicotine, or other illicit substance use were also observed. All these psychiatric problems may interfere with the appropriate health care behavior and medical compliance, which may associate with the poor peri or post-transplant outcomes. These initial findings may increase the awareness of the transplant centers in Thailand on the importance of a psychosocial evaluation and management during the pre-transplant period, which may further enhance a post-transplant outcome in each center in the future.

## What is already known on this topic?

Depression and other psychiatric issues such as anxiety, cognitive impairment, alcohol, and illicit drug use, are commonly found in the pre-organ transplantation patients. Previous studies from different countries found that these are important predictive factors of the unfavorable post-transplant outcome.

## What this study adds?

This is the first study of the prevalence of

depression and other psychiatric issues in pre-organ transplantation candidates in Thailand. The researchers reveal up to 23.6% of this patient population may be suffering from a clinical depression. Therefore, the implementation of a systematic psychosocial evaluation in pre-organ transplantation patients is recommended in all organ transplantation centers in Thailand.

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## Conflicts of interest

The authors, hereby, declare no conflict of interest.

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