Living donor liver transplantation: risk factors associated with anxiety symptoms in an Egyptian sample: a prospective study

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Background
Living donor liver transplantation has become an established treatment for end-stage liver disease. It remains unclear whether the donation process is psychologically harmful or beneficial.

Aim
This prospective study investigated the rate of anxiety and its severity along 3 months of follow-up and to determine the associated possible risk factors after donation.

Patients and methods
A total of 65 potential donors were investigated using the General Health Questionnaire, the Structured Clinical Interview DSM-IV Axis I diagnosis (SCID-I), and the Eysenck Personality Questionnaire. Only 33 patients fulfilled the inclusion criteria (actual donors). Thus, they were assessed along three visits during the 3-month period using the Taylor Manifest Anxiety Scale.

Results
Data revealed that 24% of actual donors experienced anxiety symptoms at the end of first week after donation. The rate of anxiety declined over the consecutive visits, wherein almost 81.1% of the studied sample was anxiety-free at the last visit after 3 months. Linear regression analysis denoted that a higher risk for emergence of anxiety is associated with female sex, younger age, being married, having either preparatory or university education, being a housewife, engagement in managerial job, and the recipient being the donor's father. Moreover, donors who scored higher in neuroticism, psychoticism, and impulsivity were more prone to experience anxiety symptoms after donation.

Conclusion
Psychiatric assessment for living donor liver transplantation during the postdonation periods allows early identification of anxiety symptoms and recognition of the possible risk factors that may subject donors to experience anxiety after donation.

Keywords:
anxiety, living donors, neurotisim, personality

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Introduction

Over the last decades, liver transplantation has evolved into the treatment option of choice for a variety of patients with acute or chronic end-stage liver disease (ESLD) [1]. Living donor liver transplantation (LDLT) was developed in the late 1980s to overcome the shortage of deceased donor organs available and has been widespread since then [2]. The rapid growth of LDLT is attributable to continued improvement in recipient survival rate and a significant reduction in the mortality of recipients listed for liver transplantation [3]. In Egypt, there is a problem of endemic hepatitis C virus with a prevalence of 14.7% [4,5]. Hepatitis C ESLD is the main indication for liver transplantation and represents 89.8% of cases in Egypt [5].

In the absence of an Egyptian law that permits the use of deceased donor organ, living liver donation becomes the only hope for patients with ESLD [6,7].

Although the medical and surgical aspects of LDLT have been investigated to a large extent, few studies have focused on the psychological aspects and quality of life of living donors [8]. Assessing donors' mental health is vital for the potential serious mental health consequences after donation [9,10]. There are few studies that have evaluated both the preoperative and postoperative psychological status of liver donors and revealed that some donors have developed psychiatric morbidity, including depression, and anxiety or prolonged somatic symptoms [11–14]. A recent study by El Meteini *et al.* [5] in a sample of Egyptian hepatic donors revealed that 27% of their sample developed depressive symptoms immediately after surgery and they had recommended careful preoperative psychiatric assessment and postoperative monitoring of liver donors, which could decrease the future development of psychiatric morbidity. In contrast, other studies have reported that living liver donors were

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mostly psychologically normal during the postoperative period [15–18].

Psychiatric complications in living liver donors are still a controversial issue [19,20]. Thus, the aim of this study was to investigate the rate of anxiety and its severity along 3 months of follow-up and to determine the associated possible risk factors after donation in an Egyptian sample.

Patients and methods

Design and site of the study

It is a descriptive prospective longitudinal study. Donors were recruited from the inpatient wards of the Liver Transplantation Unit in Ain Shams University Specialized Hospital, Wadi El-Nil Hospital, and Egypt Air Hospital. They are located in Cairo and serve both urban and rural areas, including greater Cairo and other governorates as well.

Ethical consideration

Ethical approval for the study was granted by the Ain Shams University Ethical and Research Committee. Informed written consent was obtained from all participants, after they were informed about the details of the study. Patients were ensured about the confidentiality of information and they were free to withdraw at any time.

Operational definition

Potential donors are individuals who are excluded as donors due to medical and/or psychiatric disorders and therefore are not subjected to surgery, and actual donors are the individuals who will be subjected to both the physical burden of a surgical procedure and the preoperative and postoperative psychological burdens [19].

Procedures

Predonation assessment

A total of 65 potential donors underwent detailed medical evaluation and the following questionnaires were applied:

(1) A designed questionnaire to determine the willingness to donate, to obtain information on the decision-making motivation, relation with the recipient, satisfaction about donation, and different psychodemographic data.
(2) The General Health Questionnaire[21], Arabic version [22], was used to assess possible psychiatric morbidity (those who obtained scores higher than the cutoff point 7 according to the Egyptian norms).
(3) High scorers on the General Health Questionnaire were further interviewed using the Structured Clinical Interview for DSM-IV Axis I diagnosis (SCID-I) [23]. We used the Arabic version [24]. Those with psychiatric diagnosis were exempted from donation.
(4) All participants were asked to complete the Eysenck Personality Questionnaire (EPQ) [25]. We used the Arabic version [26]. This is a simple self-report test designed to measure two major dimensions of personality: psychoticism (P)–neuroticism (N) and extraversion–introversion. It also includes a lie scale (L), which is regarded by Eysenck as a measure of 'faking good'. For illiterate people the test was read in colloquial formal Arabic.

During this recruitment phase, 65 participants were assessed and 31 were excluded. 11 recipients died before surgery and thus their donors were dismissed; five were excluded because of a history of substance abuse, bipolar disorder, and panic disorder; four were hesitant about donation; two declined on knowing that the recipient's chance for recovery was questionable; four were subjected to coercion by their families, thus putting them under pressure to donate; and five left the hospital on the night of the surgery after they declined their consent to donate without reasons. One donor refused to sign the consent. Thus, the current study included 33 actual donors who underwent the operation.

Postdonation assessment

Taylor's Manifest Anxiety Scale (TMAS) [27]: This scale is composed of 50 items to assess anxiety state. The total score indicates the severity of the anxiety state either absent or varied from mild to severe. We used the Arabic version. This was applied 1 week, 1 month, and 3 months after donation.

The total score indicates the severity of anxiety state (score of 0–16 is considered normal, 17–25 indicates mild anxiety, 25–36 indicates moderate anxiety, and scores above 36 indicates severe anxiety).

Statistical analysis

The data were statistically analyzed using the statistical package for the social sciences (SPSS software, version 17; SPSS Inc., Chicago, Illinois, USA). We used the suitable statistical parameters. For categorical variables we used the χ^2-test, and for noncategorical variables we used Student's *t*-test. We used the two-tailed *t*-test to compare changes across visits.

Pearson's correlation coefficient was used to determine the correlation between anxiety scores and personality traits. The logistic regression backward likelihood ratio technique was used to clarify the significant independent predictors of anxiety. *P*-value was used to determine the level of significance ($P<0.05$).

Results

Description of the donor

The age range of the sample recruited was 18–45 years, with a mean of 30.3 ± 7.12 years. The majority of the sample comprised men [23 (69.7%) male and 10 (30.3%) female]. Twenty of 33 (60.6%) donors were married; the majority of donors were living in a stable courtship. About 20 (60.5%) donors had received school education (primary, preparatory, secondary, and technical schools), ~4 (9%) were illiterate, and 10 (30.3%) were university graduates. Meanwhile, 66.7% of the donors were employed, 27.3%

were manual workers, 24.2% were employees, and 15.2% were employed in managerial jobs. An overall 21.2% were housewives and 12% were students. An overall 42.4% ($n = 14$) of the donors were volunteers, whereas 24.2% ($n = 8$) donated to their parents; the rest of the donors donated to their first or second degree relatives.

Assessment of anxiety across visits

Assessment of anxiety using TMAS revealed that in the first visit about 76% of donors were not anxious, whereas 24% of the donors had anxiety symptoms; of them, 12% had mild symptoms, 9% had moderate symptoms, and 3% had severe anxiety symptoms. Meanwhile, the mean score of anxiety did not change from the first visit (12.63 ± 10.02) to the second (12.33 ± 9.55); however, it reduced to 10.93 ± 8.53 at the last visit (Table 1).

The differences between the mean scores of the first and second visits and the first and third visits were not significant using the paired *t*-test, as displayed in Table 2.

Table 1 shows that the majority of donors were nonanxious throughout the follow-up visits. Only 12.1% had mild anxiety at the first visit. However, the rate declined in the subsequent two visits, reaching 6.1% at the last visit. Moreover, the incidence of moderate anxiety was as low as 9.1%; however, it increased to reach 12.1% in the subsequent visits. Fortunately, the only donor who had severe anxiety at the first and the second visit became nonanxious at the third visit denoting rather transient anxiety symptoms.

Personality assessment

As regards the subscales of the EPQ, there was a direct proportional relation between psychoticism (P), neuroticism (N), and impulsivity (I) scores with anxiety symptoms as measured using the TMAS. This relation was manifested almost similarly in the first and third visit. The extraversion scores did not show any correlation with anxiety (Table 3).

Risk factors

To evaluate the predictive value for the previously analyzed factors, we performed the linear regression analysis test. We used the presence of anxiety as detected using the TMAS as a dependent factor and the following variables, age, sex, marital status, education, occupation, relation to recipient, and EPQ scores.

Table 4 illustrates that the risk factors associated with the development of anxiety are as follows: female sex ($P = 0.00$), younger age group ($P = 0.012$), being married ($P = 0.00$), and having preparatory education ($P = 0.000$) rather than university education ($P = 0.038$). Housewives and those who were involved in managerial jobs were at a high risk ($P = 0.000$). Donors who donated to a father had high risk ($P < 0.00$) compared with those who donated to their sibs (0.137) or volunteers who were not related (0.244) to the recipient. High scorers on EPQ (e.g. psychoticism, neuroticism, and impulsivity) were also at risk of developing anxiety ($P = 0.000$). Other studied variables as shown in Table 4, were not found to predict the occurrence of anxiety in our donors.

Discussion

LDLT has now become an established solution for ESLD [11]. Living donors are considered a unique patient population in that they are healthy individuals who underwent a major surgical intervention for the favor of another person [28].

There is an ethical responsibility to define and understand the full range of risks (medical, psychological, social, and economic) with which the donor is confronted [29,30]. Understanding these risks will improve the predonation selection and the postdonation care of living donors [31,32].

The current study investigated the donors' anxiety state and the risk factors that may contribute to the development of their anxiety to enlighten the psychological problems to which donors may be exposed. We used TMAS to assess anxiety in donors 1 week after donation (visit 1) and then after 1 month (visit 2) and 3 months (visit 3). Despite the extensive preoperative psychological screening, 24% of our donors experienced anxiety symptoms after donation.

We reported almost similar rates recorded by Gökçe *et al*. [33], who found that 21.9% of donors in his study had displaced mild anxiety symptoms that did not necessitate any therapeutic approach.

A higher rate was reported by Lee *et al*. [34], who found that 44.5% of the donors had anxiety, which was centered around fear of pain or the postsurgical complication. In contrast, Trotter *et al*. [13] reported that only 0.5% had anxiety during the postoperative period. Other studies denoted the presence of anxiety in addition to depression, multiple somatic complaints, and psychosocial difficulties [31].

Differences in the above rates may be attributed to the use of different tools of assessment, time of assessment, support system, or sociocultural context.

In our study, follow up of the emerged anxiety symptoms revealed a decline in the rate of anxiety across visits, reaching about 18%, with mild to moderate severity at the final visit. The donors' condition did not necessitate pharmacotherapy, thus only supporting psychotherapy was used.

The reduction in the rate of anxiety with time was also reported by Schulz *et al*. [35], who described a reduction in anxiety symptoms in his donors 6 months after surgery compared with that during the preoperative period. The improvement in the recipient's condition may constitute a psychological benefit for donors [36]. Another advantage for donors could be a reduction in the caregiver burden after successful transplantation as well as relief from emotional strain because a person close to them is

Table 1 Mean and frequency of anxiety along the donors visits

Taylor's Manifest Anxiety Scale	Visit 1 (1 week) [*N* (%)]	Visit 2 (1 month) [*N* (%)]	Visit 3 (3 months) [*N* (%)]
Mean ± SD	12.63 ± 10.02	12.33 ± 9.55	10.93 ± 8.53
Nonanxious	25 (75.8)	26 (78.8)	27 (81.8)
Mild	4 (12.1)	2 (6.1)	2 (6.1)
Moderate	3 (9.1)	4 (12.1)	4 (12.1)
Severe	1 (3.0)	1 (3.0)	0 (0)

Table 2 Comparison in the level of anxiety across visits

	Paired differences						
			95% confidence interval of the difference				
Paired samples	Mean	SD	Lower	Upper	*t*	*d.f.*	Significance (two-tailed)
Pair 1							
TMAS in V1–TMAS in V2	1.30	6.19	−1.89	2.49	0.281	32	0.780
Pair 2							
TMAS in V1–TMAS in V3	1.15	7.32	−2.44	2.74	0.119	32	0.906

The paired sample, which compared TMAS in different visits as Pair 1 is comparison between the first and second visit, Pair 2 is comparison between the first and the third visit.
TMAS, Taylor's Manifest Anxiety Scale.

Table 3 Correlation between personality trait assessment and anxiety scores

EPQ	Manifest anxiety scale in visit 1	Manifest anxiety scale in visit 2
Psychoticism		
Pearson's correlation	0.391*	0.424*
Significance (two-tailed)	0.025	0.014
Neuroticism		
Pearson's correlation	0.534**	0.658**
Significance (two-tailed)	0.001	0.000
Impulsivity		
Pearson's correlation	0.580**	0.641**
Significance (two-tailed)	0.000	0.000
Extraversion		
Pearson's correlation	−0.227	−0.217
Significance (two-tailed)	0.204	0.225

EPQ, Eysenck Personality Questionnaire.
*Significant.
**Highly Significant.

no longer exposed to an acutely life-threatening situation [37].

Donors who had lower self-esteem or who reflected ambivalence toward donation may have long-standing anxious mood after donation [38]. In contrast other researchers documented that donors are less likely to experience anxiety during the postdonation period, suggesting that the transplantation leads to positive psychological consequences for them [14,32,39,40].

Risk factors associated with anxiety symptoms

To investigate the risk factors associated with anxiety symptoms in donors after LDLT, we performed linear regression analysis; we used the presence of anxiety by scores of TMAS as dependent variable and the following variables, age, sex, education, occupation, marital status relation to recipients, and EPQ scores.

Demographic risk factors

Female sex was associated with a higher risk of developing anxiety. This could be explained by more stress and responsibilities toward their home or inability to perform their home duties with the same efficacy and taking care of their children during the first few months after donation. Nearly similar results were reported previously by Jin *et al.* [20], who explained that women are more prone to anxiety probably due to their different sex roles.

Our findings are in accordance with a previous research, which reported that younger age donors were at risk of experiencing anxiety. It was found that donors under the age of 55 years subjected to health-related stressors had a greater risk of developing anxiety, whereas donors between 55 and 60 years of age were found to have significantly better mental health. In addition, another study showed that donors older than 40 years scored higher in social functioning and good mental health than those younger than 40 years who were more liable to suffer from anxiety symptoms [17, 41].

The current study declared that married donors were at a higher risk of experiencing anxiety symptoms probably due to their fear of inability to fulfill their family commitments.

Moreover, we found that donors who received preparatory and secondary education had a statistically significantly higher risk of developing anxiety as they were mostly manual workers and they had excess worry about their physical ability to perform their jobs after donation. University graduate donors were preoccupied about their job performance, thus they were prone to anxiety. Similarly, previous studies by Schulz *et al.* [39] showed

Table 4 Risk factors correlated with anxiety

	Unstandardized coefficients				
Models	*B*	SE	Standardized coefficients (β)	*t*	Significance
Donor's age	−0.101	0.023	−0.072	−4.337	0.012
Female donors	6.599	0.423	−0.307	15.589	0.000*
Being married	−7.117	0.277	−0.452	−25.738	0.000*
Preparatory education	−33.146	1.128	−0.576	−29.372	0.000*
Managerial jobs	−4.259	0.272	−0.155	−15.653	0.000*
Housewife	38.693	0.932	1.603	41.516	0.000*
Donation to father	12.710	0.777	0.420	16.364	0.000*
EPQ psychoticism	1.966	0.122	0.531	16.161	0.000*
EPQ neuroticism	−2.077	0.103	−0.930	−20.095	0.000*
EPQ impulsivity	1.814	0.129	0.959	14.016	0.000*
University graduates	2.406	0.787	0.112	3.056	0.038*
Primary education	0.068	1.088	0.002	0.063	0.953
Employee	0.666	0.354	0.029	1.883	0.133
Donate to sibs	1.468	0.790	0.043	1.859	0.137
EPQ extraversion	0.170	0.110	0.139	1.545	0.197

EPQ, Eysenck Personality Questionnaire.
*Significant.

that donors with a graduate degree were at risk of developing anxiety postoperatively. They were more likely to have a professional occupation with more work-related responsibilities leading to more stressors. Moreover, working in a managerial position was significantly related to anxiety probably due to their over concern about time away from work that may negatively impact their career.

Relation to recipient

Donation to a family member suggested the strong cohesion in the Egyptian families. Our result highlighted that donation to fathers was statistically significantly related to anxiety, as they represent the source of security and support to their donors, and hence they were afraid of losing them or failing to help them to become better or survive. In Western communities, Erim *et al.* [40] found that adults donating to their parents demonstrated the highest mental burden. Surprisingly, 42% of the actual donors in our study were volunteers, and they were not at a higher risk of developing anxiety as was expected. According to Abdeldayem *et al.* [7], those volunteers may have higher religious and moral principles and beliefs, and hence for them donation held meaningful ethical aspects.

Personality traits

We found that obtaining high scores in neuroticism, psychoticism, and impulsivity were correlated to the development of anxiety. Individuals with high neuroticism have low activation thresholds and were unable to inhibit or control their emotional reactions and experienced negative effect in the face of very minor stressors; hence, they were more liable to develop anxiety [25].

In contrast, those with high psychoticism had tough-mindedness, suspiciousness, recklessness, hostility, anger, and impulsiveness that made them more prone to develop psychiatric illness under stress [25].

Donors who scored high in impulsivity automatically responded to donate to save their loved ones' life, and this might be conflicting with other family and work responsibilities. Despite that some authors emphasized the importance of studying personality traits before donation [42,43]. However, Hayashi *et al.* [37] stated that the psychological status of donors was not related to personality characteristics, but it is relevant to decision-making motivation. In contrast, our findings indicate the importance of assessing personality traits before donation; thus, the team can provide those vulnerable donors appropriate preoperative or postoperative psychological support.

Limitations

Our study is considered one of the fewest Egyptian studies that enlighten the importance of careful psychiatric assessment of LDLT and point out the most significant factors that may lead to the development of anxiety symptoms in living donors during the preoperative and postoperative periods. Previously related research studies focused on depression [5] and quality of life [44]. The current study was limited by the relatively small sample size and the short follow-up period. It seems necessary to follow-up donor to monitor anxiety symptoms and severity across a longer period. It would be beneficial to expand the study population and to focus on the decision-making process in the context of sociocultural background.

Conclusion

An overall 24% of donors had anxiety symptoms during the first visit; the rate was reduced to only 18% of mild and moderate severity 3 months after donation. Risk factors associated with emergence anxiety included being a female, younger age group, being married, having preparatory level education or university education, being a housewife, engagement in managerial job, donating to their fathers, and high scores in neuroticism, psychoticism, and impulsivity. Our findings pointed to the importance of detecting individuals at a high risk to enable donors to overcome distress created by donation. The study recommend psychiatric close monitoring of donors for a longer period and introducing professional

reassurance and coping strategy training in the protocol of LDLT in Egypt.

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Conflicts of interest

There are no conflicts of interest.

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