

## RESEARCH ARTICLE

## AN INVESTIGATION OF DEPRESSION IN GREEK THALASSAEMIC TEENAGERS

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**Abstract**

**Objective:** To explore characteristics of today's Greek teenagers with thalassaemia, a hereditary disease, associated with the possibility of developing depression. **Material and methods:** Study sample consisted of 74 thalassaemic teenagers. Data collection was conducted using the "Children Depression Inventory" (CDI) and a questionnaire on teenage thalassaemic patients' characteristics (socio-demographic; health condition) **Results:** In study thalassaemic teenagers, CDI Cronbach's alpha was found to be 0.82. Most (65/74; 87%) had an average CDI score of 8. The vast majority (68/74) of study's thalassaemic teenagers reported no body image changing. School absenteeism had a remarkable impact of 12% ( $sr^2=0.12$ ) on emotional mood of teenage thalassaemics. Relation of thalassaemic teenagers with their treating doctors and their mother's workload interpreted 7% ( $sr^2=0.07$ ) and 7% ( $sr^2=0.07$ ) of CDI score, respectively. **Conclusions:** CDI proved to be reliable in Greek thalassaemic teenagers; and used for the first time to investigate their risk of developing depression. Only minimal depression was experienced by most teenage thalassaemics. Ranked in the order of importance, frequent school absenteeism, followed by poor relation with treating doctors as well as their working mother (caregiver) limited time for their care due to high workload, may deteriorate their emotional mood. It would be useful to plan actions to further reduce the small risk of developing depression as part of their healthy life.

**Keywords:** depression, thalassaemia, teenagers

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## Introduction

Depression is a mental disorder that appears as a disorder in the mood, thinking and in the body with depressive mood, loss of interest or pleasure in most of everyday activities, reduced vitality, feelings of guilt, disappointment, despair, loneliness, self-doubt or low self-esteem, sleeping disorders or eating disorders and problems in focusing<sup>1</sup>. Major depression is a frequent, severe and relapsing disorder that is connected with lower functionality, quality of life, medical morbidity and mortality<sup>2</sup>. It is believed that in the year 2030 depression could be one of the major causes of illness globally, with a percentage of total handicap corresponding to 6%.<sup>3</sup> It often starts from childhood and can become chronic or relapsing and eventually preventing the patient from performing daily activities and even drive the patient suicidal. It is estimated that every year about one million lives are lost due to suicide. This corresponds to 3,000 deaths daily. Depression attacks about 5-10% of adolescents and 10-15% of adults<sup>4</sup>. Depression concerns all countries with percentages that vary between 8% and 12%. Despite the cultural differences, it can arise in any cultural background.<sup>5</sup>

In case depression starts in childhood, the consequences go far in time concerning adult life. The patients, incapable of receiving proper education, will face problems in career finding and difficulties in personal life<sup>6</sup>. If they become parents, their children will also face problems in health, development and education,<sup>7</sup> even in their mental health.<sup>8</sup> Depression is a serious mental health in

children and adolescents. It is discovered in 0.3% of children of pre-school age and to 2% of children of school age and 4-8% of adolescents. Sadness is found to be present in 0.6-1.7% of children and 1.6-8% of adolescents. In childhood, boys and girls have the same possibility to develop depression, while during adolescence girls are twice more prone to the risk of developing depression, in comparison with the boys of the same age.<sup>9</sup>

After an episode of depression, they recover within nine months on average. If it is a serious episode, it can become chronic in 10% of cases. In case of melancholy, the disorder can last three years on average.<sup>9</sup> When depression starts in childhood, the risk of being ongoing in teenage years rises to 60-70%, while 20-40% are at risk of developing bipolar disorder within five years.<sup>10</sup> When the depression episode passes, children may show low self-esteem, high-risk behaviour, sub-clinical symptoms of depression, problems in personal relationships and in their functionality, in general<sup>11</sup>. In 30-50% of children, depression can be accompanied with melancholy or stress and in 20-30% with substance abuse<sup>10</sup>. They often face problems within their family as in many cases they have parents who are also depressed, as depression tends to manifest within the same family.<sup>12</sup>

It is estimated that 80% of underage who run away from home suffer from depression. The surge of depression in minors results in a higher risk of suicide, substance abuse, premature sexual experimentation, pregnancy in adolescents, depression during

adulthood, criminal behaviour and youth criminality<sup>11</sup>. Suicide consists of one of the major causes of death in adolescents in developed countries.<sup>13</sup> It is common in groups with low social and economical status, which have health problems<sup>14</sup>. In girls, it is found a higher risk of depression symptoms than in boys<sup>15</sup>. Differences in the socio-economic status of individuals (in the case of children, their parents status), reflect differences on their health condition. However, correlation between appearance of depression and socio-economic status is not linear in adolescents<sup>15</sup> as opposed to that in adults<sup>16</sup>. Factors such as income, profession, education, and severity of symptoms complicate the understanding of the correlation. Most studies conducted in adolescents showed that at least one of the factors of low socio-economic status as reported by parents or family is associated with the risk of developing symptoms of depression.<sup>15</sup> In addition to socio-economic status, the development of depression in teenage years is affected by other social factors such as place of parents' origin, financial difficulties, parents' unemployment, and single-parent families.<sup>17</sup> As yet socio-economic differences between genders have not been thoroughly studied and thus researchers cannot come to conclusion regarding how depression develops.<sup>18</sup>

In Greece, adoption, financing, co-ordination and application of politics concerning the mental health of children and adolescents are under-reporting at national and regional and level.<sup>19</sup> Stigmatisation of children and adolescents with mental disorders continues to exist.<sup>19</sup> A recent Greek study, conducted in 2015, showed that almost 6% of adolescents had developed depression episodes and 17% had

experienced depression symptoms. Only 17% of adolescents with depression had visited a specialist within the previous year. It was also found that the development of stress disorder, the use of substances, female sex, older age, the presence of a sibling and divorce or parental split were the factors mostly related with the development of depression.<sup>20</sup> In a 2010 study, showed a high percentage of depression symptoms (up to 26%)<sup>21</sup> among high-school pupils.

In children, management of depression most often consists of short-term psychotherapies in combination with medicine treatments.<sup>22</sup> An earlier Greek study, conducted almost 45 years ago, found that about 50% of Greek children with thalassaemia had developed abnormal emotional responses, with depression disorder being the most frequent response. A study performed in Egypt in 2009<sup>23</sup> found that about 90% of the 100 children who were examined had developed depression with 20% being severely depressed while showing poor performance in cognitive tests as they were three times more depressed than the controls. In India, a 2007 study<sup>24</sup> in children with thalassaemia showed a high rate (62%) of depression. A 2006 Iranian study investigated 250 children with thalassaemia showed that 22% developed severe depression. A 2011 case-control study from Egypt<sup>25</sup> found that 97% of adolescents with thalassaemia showed mild to severe depression. A Greek study, conducted 12 years ago,<sup>26</sup> found that 68 adolescents with thalassaemia participating in the study reported high levels of depression. On the other hand, a 2009 Italian study<sup>27</sup> in Italy found low levels of depression in study's 28 paediatric patients with

thalassaemia, even though three of them (10%) had high levels of depression.

The goal of the present study is to investigate the possibility of depression among teenagers with thalassaemia today. The objective of the study was to assess whether the features (socio-demographic, health condition) of today's Greek teenagers with thalassaemia were associated with the potential development of depression.

### Material-Method

The established "Children's Depression Inventory" (CDI)<sup>28,29</sup> was distributed to Greek teenage thalassaemics to complete. The CDI was easy to be completed by the participants within 10-20 min. It consisted of 27 three-point Likert scale questions (0=symptom absence; 1=minor symptom presence; 2=intense symptom presence) regarding a wide range of depression symptoms. Total score may range from 0 to 54. CDI has been adapted and validated in Greek paediatric population showing good reliability.<sup>30,31</sup> In study's teenage thalassaemics, the reliability of CDI was assessed using Cronbach's alpha that needed to be above 0.70 in order for CDI to be suitable for use for research purposes at least.<sup>32</sup> Study's thalassaemic teenagers were also invited to fill in an *ad hoc* questionnaire regarding their features such as socio-demographic characteristics and health condition.

Descriptive analysis was performed. Multiple regression analysis was also carried out in order to explore the impact of teenage thalassaemics' features on their CDI score. The decision for applying multiple regression analysis was tested. The decision was deemed right as long as residuals were normal.

Residuals, considered to be independent with Durbin-Watson statistic values approaching 2, had a constant variance. Inexistence of (multi)collinearity was necessary in order for independent variables (teenage thalassaemic features) to be uncorrelated. Tolerance existed only if variance inflation of an independent value, explained by the remaining independent variables, was small. Collinearity was calculated using tolerance factor and variation inflation factor VIF. Collinearity was evident when tolerance factor values were less than 0.4 and VIF values were more than 2.5, while being considered to be possible when VIF value was more than 5. Collinearity was possible or severe when condition index values were greater than 15 or greater than 30, respectively. The coefficient of determination  $R^2$  represented the proportion of the variance in the dependent variable (CDI score) that is predictable from the independent variable percentage. An  $R^2$  of 1 indicated that the regression line perfectly fitted the data. The *F-test* of overall significance indicated whether a selected regression model provided a better fit than a *model* that contained no independent variables. Stepwise multiple regression was applied to select the subset of independent variables (thalassaemic teenager features) that could be useful for explaining the dependent variable (CDI score). The number of observations (teenage thalassaemic participants) needed to exceed the number of independent variables by 50. After the initial *ad hoc* grouping of thalassaemic teenager features, stepwise regression was used to rank order the theoretical importance of the variable to the model step-by-step. Contribution of independent variables to the model was explored

using standardised regression coefficient Beta. Comparison of each model variables was also made by testing semi-partial correlations of the variables. Results were presented as standardised regression coefficients Beta according to the equation:  $y = \text{Beta}_1 * x_1 + \text{Beta}_2 * x_2 + \dots + \text{Beta}_k * x_k$ , where  $y$  is the dependent variable (CDI score),  $x_{1,k}$  is the independent variable (feature),  $\text{Beta}_{1,k}$  is the standardised regression coefficient, in order for the interpretations to be based on the standard deviations of the variables. Coefficient Beta showed that the number of standard deviations may change the dependent variable to be interpreted when standard deviation of corresponding interpreting variable also changed by one unit given that the other interpreting variables remained unchanged. In the model, sensitivity of remaining coefficients Beta was tested by adding and removing the remaining independent variables using the rule of thumb which was that difference greater than 20% possibly implying interpretational confounding of variables.

The importance of impact for each independent  $x$  was tested by removing its impact in order for its contribution on interpreted-to-be dependent variable  $y$  to be found beyond the remaining independent variables by partialling out their impact. Regression of each independent variable  $x$  was carried out on the remaining independent variables. Then, residual of  $x$  was correlated to  $y$  and semi-partial coefficient ( $sr$ ) was computed. The coefficient  $sr$  indicated the variance of the dependent variable  $y$  that could be explained by the given independent variable  $x$ . Thus,  $sr$  indicated the impact of  $x$  on  $y$  that is additional to the impact of the remaining independent variables on

$y$ . The percentage of the impact of  $x$  (teenage thalassaemics' feature) on  $y$  (teenage thalassaemics' CDI score) was expressed as the square of semi-partial coefficient ( $sr^2$ ). Statistical analyses were performed using SPSS version 21. The  $p$ -values less than 0.05 were considered to be significant.

Approval for conducting the present research study was given by hospital authorities that monitored the research throughout the research period. Participation was on voluntary basis and participants could opt out any time they wished without any discriminatory consequence that may be negative for them. Questionnaire was distributed on an impersonalised basis and its anonymity ensured confidentiality and protection of personal data. The afore-mentioned procedure did not allow the possibility of participants' identification in the future by using valid methods of generalisation in less specific categories and of linear transformation. Consent on the part of thalassaemic teenagers and assent on the part of their parents were taken for granted as teenage thalassaemic participants voluntarily responded the questionnaire and gave it back without outside intervention.

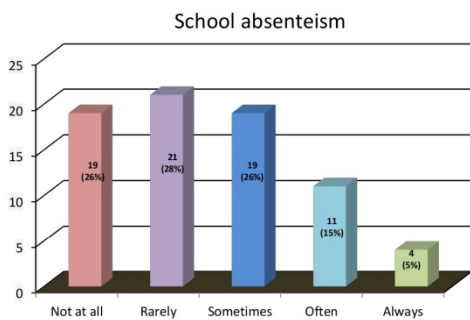
## Results

For CDI, Cronbach's alpha was found to be 0.82 corresponding to its excellent reliability in study's teenage thalassaemics far exceeding 0.70 that is suitable for research purposes. In total, 74 teenage thalassaemics participated in the study about their depression score and corresponded to 30% of the estimated number of today's thalassaemic teenagers in Greece.<sup>33</sup> Their number exceeded that of the

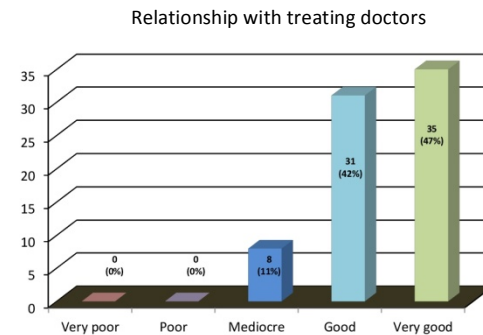
distributed CDI items by almost 50. The 33 (45%) were boys and the 41 (55%) were girls. Their median age was 14 years old. All of them were pupils with 31 (74%) attending high school. The 66 (90%) teenage thalassaemics did not report any complications, while 68 (92%) reported no change in their body image.

For the interpretation of depression level of teenage thalassaemics, the selected model was statistically significant ( $F=10.7$ ;  $p<0.001$ ) and interpreted 31.5% ( $R^2=0.32$ ) of variance of depression

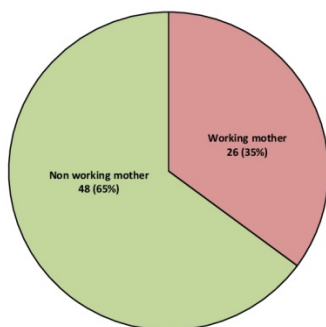
scoring (*Depression overall score*) =  $0.36*(School\ absenteeism) - 0.27*(Relation\ with\ treating\ doctors) - 0.27*(Mother's\ workload)$ . School absenteeism had a remarkable impact of 12% ( $sr^2=0.12$ ) on their emotional mood of teenage thalassaemics. The relation of thalassaemic teenagers with their treating doctors and their mother's workload interpreted 7% ( $sr^2=0.07$ ) and 7% ( $sr^2=0.07$ ) of the introduced independent variables' variance, respectively.



**Graph 1.** School absenteeism among 74 thalassaemic teenagers.



**Graph 2.** Relationship of 74 thalassaemic teenagers with their treating doctors.



**Graph 3.** Thalassaemic teenagers with non-working mothers and with working mothers

### Discussion

In general population, mental disorders are more prominent in adults than in adolescents.<sup>34</sup> By contrast, underage thalassaemics have historically been considered to be very vulnerable, developing mental disorders such as depression as they cannot have coping strategies, and thus being in need of psychological support.<sup>35</sup> It is of interest, though, that in the present study the vast majority (65/74; 87%) of teenage thalassaemic participants did not score high in CDI, with average score of 8, while only nine (13%) reported a tendency for depression. Our finding was in agreement with that of a recent study showing that

90% of the general paediatric population in Greece did not have increased depression level, with average score of 7.<sup>30</sup> To corroborate this, it was found that in developed countries depression rate ranged between 0% and 10% using CDI. In Antalya<sup>36</sup> one of the most developed Turkish regions, a zero percentage of depression was found among 20 children with thalassaemia, while in developed Italy<sup>27</sup> a percentage of 10% was found among their counterparts. On the contrary, in Iran<sup>37</sup> that is a developing country, 14% of thalassaemic aged 9-16 years old developed depression, thus being about 2.5 times higher than that (5.5%) in healthy subjects. In Thailand,<sup>38</sup> depression was found to affect 28% of underage patients with thalassaemia participating in the Thai study and scoring high (17.5) in CDI. It is worth to note that in Egypt<sup>23</sup> where the average age of those patients with thalassaemia was only 9.5 years old, 89% of children with thalassaemia experienced symptoms of depression with CDI score of 24.

Thalassaemics' cranio-facial features include larger cheekbones resulting in a rodent or "squirrel-like" face with a depressed nasal bridge and a protruding maxilla. In developed countries such as Greece, sufficient transfusions prevent young thalassaemics bones from changing, with deformations of the "squirrel-like" face not appearing.<sup>39</sup> As a consequence, nowadays thalassaemics do not face discriminations in developed countries, as opposed to the past,<sup>40</sup> when the changes in their body image were obvious and could not be easily handled resulting in their social isolation.<sup>12</sup> By contrast, in developing countries where transfusions are insufficient, thalassaemic adolescents were not satisfied with their image and themselves.<sup>41</sup>

As expected, the vast majority (68/74) of study's thalassaemic teenagers did not report changes in their body image. However, about 10% of them reporting changes in their body image had a high CDI score. That no significant correlation was found between depression scoring and body image perception<sup>42</sup> may have possibly been attributed to the rather small number of teenage thalassaemic participating in the study. On the other hand, excessive school absenteeism, poor relations with treating doctors and huge workload on the part of their mother (preventing her from spending enough time with her thalassaemic teenager), ranking in order of importance, were found to have a great impact on teenage thalassaemics' possibility of developing depression, explaining more than 30% of the likelihood.

All children and adolescents with thalassaemia who participated in the present study were attending school, with more than 30% attending high school. The findings of the present study were in accordance with those of a previous Greek study showing that education of patients with thalassaemia was not affected by their illness.<sup>43</sup> By contrast, in Iraq, according to a recent study conducted in 2015,<sup>44</sup> 39% of patients with thalassaemia withdrew from their studies because of their illness. In addition, studies conducted in India<sup>45</sup> and Turkey<sup>46</sup> showed that the majority (60%) of children with thalassaemia had poor school performance as they were affected by frequent hospital admissions to undergo blood transfusions. In the present study, however, only 19 (25%) thalassaemic teenagers did not occasionally show up to class as they were living their life as being

healthy. The rate of their school absenteeism was compatible with that of the pupils in general population in Greece. A 2011 study, conducted in Greek schools, found absenteeism reaching up to 28%. It is of interest that nearly 60% (7/12) of teenage thalassaemics undergoing subcutaneous administration of chelators did not show up to class quite often, while nearly 60% (20/35) of those receiving oral chelation were only rarely absent. An explanation would be that many children with thalassaemia faced difficulties in adhering to subcutaneous administration resulting in frequent school absenteeism.<sup>47</sup> Therefore, subcutaneous chelation is recommended to be administered in the evening in order not hinder thalassaemic teenagers' activities for the rest of the day.<sup>48</sup>

In children with thalassaemia, school absenteeism has been found to highly affect them emotionally.<sup>49</sup> In an earlier study,<sup>50</sup> it was found that school absenteeism was associated with the occurrence of psychological problems, mainly depression. In the present study, 2/4 (50%) thalassaemic teenagers, who were absent consistently, had a high CDI score. In such cases, school absenteeism may serve as a remarkable indication ( $sr^2 = 0.12$ ) for the risk of emotional problems posed to thalassaemic pupils.

Treating doctors being under constant pressure may behave in a paternalistic way<sup>51,52</sup> requiring thalassaemic teenagers' adherence to therapy. In the paternalistic model, physicians were considered to be the powerful others, who made the decisions on behalf of the patient. Physicians were the only ones who knew what is right for their patients.

They were not obliged to justify their decisions,<sup>53</sup> while they provided poor information to their patients.<sup>54</sup> On the contrary, doctors showing empathy are able to communicate with their patients, thus resulting in better disease management.<sup>55</sup> In this study, the vast majority (66/74; 89%) of teenage thalassaemic patients claimed that they have good or very good relationship with their physicians reported that they maintained good to very good relationship with their physicians that seemed to improve ( $sr^2 = 0.07$ ) their emotional status.

Children can cope with their disease as long as it is well accepted by their family; therefore sick children's parents are invited to participate in the therapeutic relationship.<sup>56</sup> The finding that 80% of fathers and 75% of mothers of the 74 thalassaemic teenagers participating in the present study had lower levels of education may be responsible for their not received proper genetic counseling before giving birth to a thalassaemic child.<sup>57</sup> Genetic counseling has not been mandatory in Greece since 1980,<sup>58</sup> but in other countries with historical large numbers of thalassaemic patients such as Cyprus, Iran, Saudi Arabia, and Cyprus it is compulsory by law.<sup>59</sup>

A 1998 multi-centre study on thalassaemia, conducted in different countries,<sup>56</sup> found that in those countries thalassaemic children bonding with their family could mobilise coping mechanisms. In general, Greek mother are not actively supported by fathers in thalassaemic children therapies as the latter do not historically participate in actively in raising of children.<sup>56</sup> Mothers are considered to the main health caregiver for their thalassaemic children. It is not, therefore, surprising that the mother acting as the



main caregiver is the parent who may have a critical impact on her thalassaemic child coping with the disease.<sup>27</sup>

Most recently, a 2015 study<sup>60</sup> found the provided support to children with haemoglobinopathy by their parents reduced the occurrence of depression symptoms and is an important parameter of their treatment. In the present study, in 35% (26/74) of participants, thalassaemic teenager mother is a working mother. When mother is able to downsize the workload ( $sr^2 = -0.07$ ) and thus spend more time with her thalassaemic teenager, the latter's emotional mood improved.

## Conclusions

The present study has come into conclusions for the first time regarding the use of a psychometric tool

(CDI) for the investigation of depression in Greek thalassaemic teenagers and the factors affecting their CDI score. CDI proved to be reliable and contributed to the investigation of depression in study's thalassaemic teenagers. They found to be in good mood as they attend school without interruptions due to sick leave and had very good relationship and communicate with their treating doctor. Less workload on the part of their mother who took care of them also prevented them from feeling depressed. Based on the above conclusions for teenagers with hereditary diseases such as thalassaemia, it would be useful to plan actions to further reduce the small risk of developing depression as part of their healthy life.

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