

Evidence for multidimensional resilience in adult patients with transfusion-dependent thalassemias: Is it more common than we think?

S. Y. Almahmoud,¹ K. G. Coifman,¹ G. S. Ross,² D. Kleinert² & P. Giardina²

¹Department of Psychological Sciences, Kent State University, Kent, Ohio, USA, and ²Department of Psychiatry, Weill/Cornell Medical Center, New York, New York USA

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SUMMARY

Background: Life expectancy of patients with transfusion-dependent thalassemias has increased with the development of improved treatment over the last few decades. However, β -thalassemia disorder still has considerable lifetime treatment demands and heightened risk of frequent complications due to transfusion-transmitted infections and iron overload, which may affect thalassaemic patients' functioning in different domains.

Objectives: The vast majority of published studies on thalassaemic patients have focused on children and adolescent functioning, and little research has examined adults. Hence, the current study was planned to examine the functioning and resilience of adult thalassaemic patients in a comprehensive way.

Methods: We examined multidimensional resilience and functioning across different domains (psychological adjustment, treatment adherence, social functioning and occupational functioning). We also examined demographic and medical variables that may relate to resilience and functioning. Participants were adult patients [$n = 38$; age $M = 31$ -63, standard deviation (SD) = 7.72; 72% female] with transfusion-dependent thalassaemia in treatment in a hospital in the northeastern United States.

Results: The results suggest that most adult thalassaemic patients tend to be resilient, demonstrating good functioning in four main domains: psychological adjustment, treatment adherence, social functioning and occupational functioning.

Conclusion: Despite the considerable demands of their illness, adult thalassaemic patients appeared to be adapting well, demonstrating evidence of multidimensional resilience.

Key words: adults, psychological functioning, resilience, treatment adherence, β -thalassaemia.

β -thalassemias (β -thalassaemia major, β -thalassaemia intermedia and β -thalassaemia minor) are inherited blood disorders characterised by abnormalities in the synthesis of the beta chains of haemoglobin (Modell & Darlison, 2008; Galanello & Origa, 2010). Most common in areas where malaria was or still is endemic (Weatherall & Clegg, 2001), the symptoms of β -thalassemias can range from severe anaemia demanding frequent and regular blood transfusions to no clinical symptoms at all (Weatherall & Clegg, 2001). Recent estimates suggest that approximately 100,000 patients are currently living with transfusion-dependent thalassemias across the globe. Although approximately 30,000 transfusion-dependent individuals are born annually, only 12% of those patients are transfused because of limited access to care. As a result, mortality rates can be quite high depending on the global region (Modell & Darlison, 2008). Until recently, the life expectancy of all patients with transfusion-dependent forms of the disorder was severely shortened due to specific disease-related factors as well as the consequences of lifelong blood transfusions (Cunningham *et al.*, 2004). However, over the last few decades, due mainly to improved iron chelation therapy and access to care in many regions, patients are living several decades longer (Jain *et al.*, 2013). As such, there is a new generation of adult patients with transfusion-dependent thalassemias, individuals who have had lifelong access to proper medical care and who are now living into the fourth, fifth and even sixth decade of life (Borgna-Pignatti *et al.*, 2005). Given the recency of these advancements, there is a relative paucity of information on the psychological consequences and implications of living with transfusion-dependent thalassemias into adulthood. As such, there is a clear need for comprehensive investigation of psychological functioning across multiple domains in adult patients with these disorders.

β -thalassaemia disorder has considerable lifetime treatment demands and frequent complications due to transfusion-transmitted infections and iron overload (Cunningham *et al.*, 2004). With a considerable increase in the life expectancy of thalassaemic patients, there is a corresponding risk for developing more complications and other, secondary disorders [e.g. osteoporosis, heart failure, human immunovirus

Correspondence: Shaima Y. Almahmoud, Department of Psychological Sciences, 276 Kent Hall, Kent State University, Kent, Ohio 44242, USA.

Tel.: +1 330 672 2184; fax: +1 330-672-3786; e-mail: salmahmo@kent.edu

(HIV), hypo/hyper-gonadism, diabetes, hepatitis and bacterial infections] (Cunningham *et al.*, 2004). Regular blood transfusions and iron chelation treatments are ideally initiated very early in life. Therefore, the lifelong treatment demands for transfusion-dependent forms of thalassemia are considerable (Khoury *et al.*, 2012; Jain *et al.*, 2013).

Given the only recent increases in patient lifespan, the relative absence of information on the lifelong psychological impact of such a demanding disease is particularly significant. Indeed, there is considerable research linking psychological functioning to adherence and patient self-management in other chronic illnesses (Kahana *et al.*, 2008), although this research is rarely extended to thalassemia populations. Considerable data suggests that psychiatric symptoms can interfere with treatment compliance, patient self-management and, ultimately, increased morbidity (De Groot *et al.*, 2001; Arrieta *et al.*, 2013; Kaur *et al.*, 2014). In addition, the vast majority of published research on transfusion-dependent thalassemias has focused exclusively on children and adolescents, with relatively few studies examining adults. Moreover, many of these studies suggest high rates of psychopathology due to the demands of the disorder and the extreme circumstances of this population (e.g. Sadowski *et al.*, 2002; Mikelli & Tsiantis, 2004; Cakaloz *et al.*, 2009; Jain *et al.*, 2013). In this investigation, our goal was to extend the considerable research conducted on children with thalassemias to individuals in adulthood as well as to integrate rigorous research methodology frequently applied to *other* highly stressed populations in the assessment of multidimensional resilience. Specifically, our goal was to examine the potential for multidimensional resilience in *adult patients* with transfusion-dependent thalassemias.

MULTIDIMENSIONAL RESILIENCE

It is increasingly evident that resilience is not simply the absence of psychopathology (Bonanno, 2004; Bonanno *et al.*, 2005). Indeed, there are now at least two decades of research on comparably stressed populations suggesting that *multidimensional* resilience or high levels of psychological functioning across multiple domains (e.g. interpersonal, occupational) during highly aversive conditions is more common than not (Luthar *et al.*, 2000; Bonanno, 2004; Bonanno *et al.*, 2010). In particular, the data suggest that anywhere from half to two-thirds of any given highly stressed population are functioning quite well. This has been evident in adult populations during infectious disease outbreaks [e.g. severe acute respiratory syndrome (SARS) epidemic; Bonanno *et al.*, 2008] and after terrorist attacks (9/11/01: Bonanno *et al.*, 2006) as well as during chronic stressors including chronic illness (Lam *et al.*, 2012). The present study has particularly demonstrated the importance of examining multiple indicators of psychopathology and functioning across multiple domains in order to complete thorough and rigorous assessments of the populations in question. For example, attempts to capture functioning more broadly by assessing the individual's

engagement in life's tasks including work, social relationships, as well as managing their health, provide a richer and deeper assessment of the potential for resilience (Zautra *et al.*, 2010). In addition, there is growing evidence suggesting that reliance exclusively on participant reports on a single index can be particularly limiting due largely to memory-related biases and/or demand characteristics that can emerge when reporting on aversive conditions or experiences (Schwarz & Clore, 1983; Jones & Johnston, 2011; Qin *et al.*, 2012; Wolf, 2012). Finally, the focus of dominant models of resilience and corresponding research has been on understanding resilience as an outcome rather than focusing on identifying resilient individuals (i.e. conceptualising resilience as a dispositional or trait-like construct that differentiates individuals). 'Resilience is an inferential construct that refers to good functioning in different domains during or following conditions that would be expected to disrupt the life of the individual' (Masten, 2001). Multidimensional resilience is a construct most effectively measured in a multidimensional way. These models largely suggest that *anyone* has the potential to be resilient and that typically, there are multiple factors and/or pathways leading to that outcome (Luthar *et al.*, 2000; Masten, 2001; Bonanno *et al.*, 2010).

IS THERE RESILIENCE IN THALASSEMIC PATIENTS?

Unfortunately, research examining the potential for multidimensional resilience in patients with thalassemia is difficult to find as much of the research has focused particularly on capturing rates of psychological symptoms or dysfunction. Moreover, given the considerable focus on children with the disorder, relatively little is known about adults. For example, Sadowski *et al.* (2002) compared children with β -thalassemia and children with haemophilia, finding that thalassaemic children had higher rates of psychiatric disorders. The most frequent diagnoses were depressive and anxiety disorders. Consistent with these results, Cakaloz *et al.* (2009) compared 20 thalassaemic patients to 34 healthy children. The results indicated that the thalassaemic children showed a higher frequency of anxiety disorders (30.0%) and depression (15%). They also showed significantly greater problems in peer relationships and educational attainment in comparison to the healthy children. There are fewer studies of adult patients with thalassemia; however, the results have been relatively similar. For example, Messina *et al.* (2008) examined 147 young adult thalassaemic patients using a variety of assessments. The results suggested elevated somatisation and depression as well as some dispositional obsessive-compulsive tendencies. This finding is consistent with Mednick *et al.* (2010) and Yahia *et al.* (2013), whose research indicated higher rates of anxiety and depression among adult thalassaemic patients using varied methods. Moreover, Mednick *et al.* (2010) demonstrated that symptoms of anxiety and depression were associated with decreased self-reported adherence with treatment.

In contrast, there is some data suggesting that individuals with thalassemias are functioning comparably to healthy populations. For example, Zani *et al.* (1995) examined the psychological functioning and social behaviour of 90 adolescent thalassaemic patients and 100 healthy adolescents. The data suggested that thalassaemic patients were similar to healthy children in terms of psychological and social functioning. They also had better scores than controls on assessments of self-esteem and coping. On the other hand, Mikelli & Tsiantis (2004) examined 68 thalassaemic child patients and matched healthy controls, finding that thalassaemic patients experienced more depressive symptoms and lower quality of life. More recently, Zani & Prati (2015) demonstrated that *adults* with thalassaemia reported higher psycho-social functioning indicative of resilience. In related research examining subjective report of quality of life, thalassaemic patients (adults and children) reported lower quality of life or subjective well-being relative to healthy or normative samples (e.g. Sobota *et al.*, 2011; Khani *et al.*, 2012; Trachtenberg *et al.*, 2014).

In short, the majority of the research examining thalassaemic patients' functioning has been relatively mixed, some evidence suggesting elevated rates of pathology, other evidence suggesting normative functioning and some showing lower quality of life or well-being. In general, however, this literature is limited by the focus exclusively on symptoms (with heavy reliance on self-report indicators) *or* one index of functioning as well as the primary focus on mostly child/adolescent samples. Even in a few studies that have examined adults with thalassaemia, rather than a mere focus on adult patients, the focus has been on both adults and adolescents (e.g. Di Palma *et al.*, 1998; Yahia *et al.*, 2013). In sum, the extant research does not provide comprehensive information about patient functioning *across* domains and, as such, has yet to evaluate the likelihood of resilience in adult thalassaemic patients.

Given this considerable gap in the literature, the goal of the current study is to begin to better understand psychological adjustment in adults with transfusion-dependent thalassemias with more objective indicators of psychopathology and by examining comprehensive indicators of psychological functioning and the potential for multidimensional resilience in a small US sample. We specifically examined functioning in four domains: psychological adjustment, treatment adherence, social functioning and occupational functioning. When possible and appropriate, we statistically compared participants' rates and responses to normative populations or to other chronically ill samples to assess whether the sample was adapting to stress in a normative way. We also examined demographic and disease-related variables that can influence psychological functioning.

METHODS

Participants and procedure

The sample consisted of 38 adults with transfusion-dependent thalassemias (including Thalassaemia Major and Thalassaemia

Intermedia) in treatment at a large urban medical centre in the northeastern United States who were offered the opportunity to participate in the study by their physician. Patients who expressed interest in participating in the current study were approached directly by the researchers. The mean age of participants was 31.63 years, $SD = 7.72$. The sample was mostly female (72%) and Caucasian (81%). All the participants were treated with ongoing blood transfusions (at 2–3 week intervals) and iron chelation therapy (5–7 times per week).

Participants completed assessments indexing socio-demographic variables, disease-related factors, psychological symptoms, treatment adherence and social and occupational functioning. The depression, post-traumatic stress disorder (PTSD) and generalised anxiety disorder modules of the structured clinical interview (SCID) to assess Axis I disorders (DSM-IV-TR) were administered to all participants (First *et al.*, 2002) by a trained masters-level clinician. A treatment diary was used to measure adherence with iron chelation and ongoing psychological symptoms. Participants were administered the treatment diary questionnaires six times during consecutive transfusion appointments, approximately every 2–3 weeks, over a period of 12–18 weeks. In addition, adherence to treatment-related appointments over the previous 12-month period was indexed via their medical record. Participants were not offered any compensation and completed other tasks as part of a broader investigation about coping with thalassaemia. All participants signed an informed consent form. The study was approved by the appropriate institutional review boards governing human subjects research and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki (World Medical Association, 2013).

Socio-demographic, occupational and disease-related indicators

A questionnaire was used to index education, employment, financial status, race, ethnicity and age of participants.

Additional questionnaires administered to participants (and later confirmed in the medical record) assessed the specific diagnosis of thalassaemia, co-occurring disorders as well as type and frequency of iron chelation treatment. Eighty one percent of the participants had thalassaemia major, 16% thalassaemia intermedia and 3% Blackfan Diamond anaemia. As is typical in adults with this disease, most participants had additional health problems resulting from the complications of lifelong blood transfusions. The mean number of additional health problems was 3.51, $SD = 1.63$. The most common were osteoporosis, heart failure, HIV, hypo/hyper-gonadism and diabetes. Forty seven percent of participants were using subcutaneous iron chelation; 50% of them were using an oral iron chelator (e.g. Exjade; Piga *et al.*, 2006), and 1 participant (3%) had suspended chelation for medical reasons. Iron chelation therapy was prescribed by patient's physician between 5 and 7 times per week, $M = 5.83$ times ($SD = 1.61$).

Psychological functioning

Structured clinical interviews. Participants were interviewed by a masters-level clinical psychologist using the Structured Clinical Interview to Diagnose Disorders for the DSM-IV-TR (SCID; First *et al.*, 2002). Interviewers assessed current symptoms of major depressive disorder (MDD), generalised anxiety disorder (GAD) and PTSD. MDD and GAD are the two most common psychological disorders among thalassaemic patients (Khoury *et al.*, 2012; Jain *et al.*, 2013). In this sample and among thalassaemic patients in general, the risk for PTSD is also significant as many patients report traumatic events (e.g. from this sample: having experienced a heart attack). The SCID allowed for the assignment of both continuous symptom scores as well as diagnostic determinations for each module/disorder. For example, for the depression module, participants can get a continuous score ranging from 0 to 9 depending on which symptoms are evident as well as a determination of whether or not an individual meets the criteria for a diagnosis of current major depressive episode according to the DSM-IV-TR. Continuous scores are commonly used to capture greater variance and variability within populations, given the considerable evidence suggesting that as few as three symptoms for any given disorder can have a significant impact on functionality (Cuijpers & Smit, 2004; Bonanno *et al.*, 2005; Haller *et al.*, 2014). Interviews were videotaped in order to calculate the interviewer's reliability. Twenty five percent of the interviews were watched and coded by a separate interviewer in order to assess reliability at the symptom level ($\kappa = 0.96$).

Self-reported psychological symptoms. Current psychological symptoms were also assessed via the treatment diary at six consecutive blood transfusion appointments (approximately every 2–3 weeks, for a total of 12–18 consecutive weeks) using a combination of depression, anxiety and hostility scales from the symptom checklist (SCL-90-R; Derogatis, 1983). Ratings were aggregated across time to capture a more robust indication of symptoms. The checklist consists of 29 items that are scored on a 5-point Likert scale, indicating the extent to which the participants have felt 'distressed or bothered' during the past 7 days (0 = not at all; thru 4 = extremely). The items from these three scales were summed and averaged to form an estimate of self-reported psychological symptoms ($\alpha = 0.95$). Each participant's scores were averaged across all six-diary entries.

Treatment adherence

Iron chelation adherence. Participants indicated via the treatment diary on six consecutive occasions how frequently in the prior 2-week period they chelated (either subcutaneous or oral iron chelation). This questionnaire was administered six times, every 2–3 weeks, at each consecutive transfusion appointment, over a period of 12–18 weeks. Scores reflecting the percentage of adherence to prescribed iron chelation were calculated based on the number of reports of iron chelation over the diary relative to the number prescribed to that individual by their physician.

Treatment appointment adherence. Information was aggregated from the participants' medical records by the primary physician and a nurse practitioner. Reviewing these records provided information about participants' adherence to six routine medical tests (bone density scans, eye exams, hearing exams, oral glucose tolerance, electrocardiograms, and echocardiograms) over the previous 12-month period. These *same six tests* are prescribed to all adult patients with a transfusion-dependent treatment at this facility every year. Participants were each assigned a percentage of adherence with those six tests over the most recent 12-month period.

Social functioning

The social network index (SNI) measures the participants' social functioning in nine domains (a partner, parents, siblings, relatives, friends, workmates, schoolmates, members of groups without religious affiliations and members of religious groups). Participants were asked to rate the frequency of interactions with close others in each domain within the past 2-week period (e.g. 'Do you speak in person or on the phone with your parents at least once every 2 weeks?'; 'How many of your siblings do you speak with in person or on the phone at least once every 2 weeks?'). Scoring of the SNI produces a measure of social network diversity based on the presence or absence as well as degree of contact in each of the nine relationship domains over a 2-week period. For example, for the question about parents, the rating scale was none = 0, one parent = 1, two parents = 2 and three parents (including step-parents, biological parents and adoptive parents) = 3. The answers on each domain were recoded to 0 and 1. Zero denotes the absence of any kind of interaction or communication within a specific domain, and 1 denotes the presence of any kind of interaction and communication within a specific domain (Cohen *et al.*, 1997). The lowest score on this scale was 0, and the highest score on this scale was 9. High and low social network scores were generated based on a median split; scores larger than 4.5 were above the median (Rutledge *et al.*, 2008).

Data analytical strategy

Given the relative paucity of research that is conducted on adult thalassaemic patients examining different domains of functioning, our primary goal was to examine the prevalence of disorders and rates of functioning across the four main domains: psychological functioning, treatment adherence, social functioning and occupational functioning. In addition to examining these rates in our own sample, we also made statistical comparisons, when appropriate, to population prevalence rates (or the mean and standard deviation) from other samples.

Although comparison groups were carefully selected to match the methods and/or the population of the current study, there were times when the comparison was made with a sample from a different population or a sample using a different methodology. For example, when comparing the prevalence of disorders in our sample to normative populations, we selected prevalence

rates published from samples of normative adults in the United States in investigations that used a similar though not identical instrument (e.g. structured clinical interviews). Furthermore, when we compared our sample with other chronically ill populations, we selected patient samples with similar lifetime treatment demands, such as in the case of adult patients with sickle cell disease. In each circumstance, the nature and limitations for each comparison were made explicit so that the results could be interpreted appropriately. This statistical plan has its limitations, but it is an important step in beginning to understand how adult thalassaemic patients are functioning relative to other samples.

In each case, *t*-tests for independent samples or two-proportion *z*-tests were calculated using the statistical software MINITAB 17 (Minitab Inc., 2014). When the participant numbers in any subgroup were fewer than 10, *z*-test was not suitable to analyse the data. In such cases, analyses were conducted using Fisher's exact test. These procedures for population comparisons were based on common statistical conventions in studies focused on health and disease (e.g. Kirkwood & Stern, 2003; Kramer, 2012; Chen *et al.*, 2014; Lakhan & Ekundayo, 2015).

RESULTS

Occupational functioning

Based on the participants' reports, our sample was generally highly educated with high levels of employment. Sixty-five percent of participants were college-educated as compared to 17% of adults between 25 and 54 years per U.S. Census Bureau (2013, Table 3). A test of our sample versus U.S. Census age-matched population averages yielded significant results, $z = 4.04$, $p < 0.0001$, suggesting that thalassaemic adults in our sample were significantly more likely to be college-educated. In addition, 65% of participants in our sample were employed. When statistically compared to other samples of chronically ill adults, the results suggested that adult patients with thalassaemia had significantly higher rates of employment. For example, we compared our sample to van Campen & Cardol's (2009) investigation of adults with mixed chronic illness and physical disability (e.g. people with motor, hearing or visual disabilities). Only 9% were employed when individuals had both chronic illness and disability, and 37% were employed when individuals had chronic illness without physical disabilities. When compared with our sample, the results were ($z = 7.30$, $p < 0.0001$) and ($z = 3.68$, $p < 0.0001$), respectively, suggesting that adult patients in our sample were significantly more likely to be employed. Although convincing, it is unclear if patients in these groups had similar physical impairments to our sample; as such, the results should be interpreted with caution.

Psychological functioning

Structured clinical interview results indicated that 8, 5 and 3% of the participants were diagnosed with MDD, GAD or PTSD,

respectively. The rates of pathology based on the SCID in our sample were compared to the rates gathered through large-scale epidemiological research in the United States with age-matched adults using Fisher's exact test. For example, Kessler *et al.* (2012) found that approximately 5.6% of US adults (age 18–74) meet diagnostic threshold for MDD, 6.2% meet for GAD and 8.0 % of people meet for PTSD. The comparison of rates in our sample to those from Kessler *et al.* (2012) suggested that patients in our sample were no more likely than average US citizens to be diagnosed with MDD, $p = 0.47$, GAD, $p = 1.00$, and PTSD, $p = 0.36$. It is important to note that in the Kessler *et al.* study, a different structured diagnostic interview was used (i.e. CIDI: Composite International Diagnostic Interview), and this methodological difference could have accounted for these results in addition to our substantially smaller sample. As such, these comparisons should be interpreted with caution.

In separate analyses, we compared the rate of MDD in our sample to rates documented in other samples with comparable chronic illness. For example, we compared the published rates of MDD in adult patients with sickle cell disease (Levenson *et al.*, 2008) and found that the rates of MDD in our sample were statistically lower, $p = 0.008$. However, it should be noted that Levenson *et al.* relied on established clinical cut-offs in a self-reported symptom questionnaire (i.e. PHQ: Patient Health Questionnaire) rather than diagnostic clinical interview, and questionnaires often overestimate the prevalence of disorders (Andrews *et al.*, 2006; Ben-Zeev & Young, 2010). However, other samples of patients with chronic illnesses also generally show higher rates of depression (e.g. chronic pain; Zhu *et al.*, 2014; Poole *et al.*, 2009; COPD; Zhang *et al.*, 2011).

In order to be more inclusive, we also considered clinically significant yet below diagnostic threshold indicators of pathology (typically greater than three symptoms of one disorder; e.g. Bonanno *et al.*, 2005). With this inclusive approach, the rates for MDD (14%), GAD (8%) and PTSD (24%) were higher. Mean continuous symptom scores for MDD, GAD and PTSD were $M = 1.17$ ($SD = 1.68$), $M = 0.47$ ($SD = 1.63$), $M = .47$ ($SD = 1.63$), respectively. Rates of sub-threshold symptoms based on the SCID in our sample were compared to rates gathered through large-scale epidemiological research. Fisher's exact test was used to get the *p*-value. For example, Carter *et al.* (2001) found that approximately 4.2% of respondents presented with sub-threshold symptoms of GAD, $p = 0.21$. This comparison suggested that the rate of patients with sub-threshold symptoms of GAD in our sample was no different than the rate in Carter *et al.* (2001). It is important to note that a different structured diagnostic interview (i.e. CIDI: Composite International Diagnostic Interview) was used in this study and that it was conducted on a German population. In contrast, McLaughlin *et al.* (2015) found that approximately 1.8% of participants had three symptoms of PTSD. This comparison suggested that the rate of patients with sub-threshold symptoms of PTSD was higher in our sample, $p < 0.0001$. This comparison should be interpreted with caution because McLaughlin *et al.* (2015) used sub-threshold DSM-5 PTSD symptoms.

In addition, self-reported psychological symptoms were assessed in six time points during the diary period. Each participant's scores were averaged across all six-diary entries. The mean was $M = 0.52$, $SD = 0.52$. These data were compared with two normative community populations. For example, in a normative sample of married adults or adults who were living with their romantic partners ($n = 60$; mean age = 33.4, $SD = 9.08$, 64% female: Bonanno *et al.*, 1998), mean scores on this same version of the SCL-90 were $M = 0.61$, $SD = 0.46$. The result of an independent samples *t*-test indicated no significant differences between our sample of thalassaemic patients and this sample $t(96) = -0.90$, $p = 0.37$. Furthermore, we compared our sample to a normative sample of healthy young adults ($n = 225$; mean age = 21, $SD = 5.90$, 66% female) to data collected in our laboratory using this same indicator. The mean for the young adult sample was $M = 0.61$, $SD = 0.54$, and the *t*-test result was also non-significant, $t(261) = -0.96$, $p = 0.34$. The results of the two comparisons suggested that the thalassaemic patients were not reporting more psychological symptoms than two healthy adult samples using identical instruments. However, the circumstances of data collection were decidedly different, and it may have influenced our findings; as such, the results should be interpreted with caution.

Treatment adherence

The mean reported at chelation therapy adherence in our sample was 84.45%, $SD = 21.11$, which is lower than the other thalassaemic samples using chelation (e.g. Trachtenberg *et al.*, 2011: $t(115) = 2.14$, $p = 0.035$; $t(222) = 5.97$, $p < 0.001$ for deferoxamine and deferasirox, respectively). Although the sample size of thalassaemic patients in Trachtenberg *et al.* (2011) is relatively large, the sample was not restricted to adults and included a rather considerable proportion of children and adolescents. Studies have consistently showed that chelation adherence is higher in children who have parents that share treatment responsibility (e.g. Treadwell *et al.*, 2005). Indeed, prior to our data, there have been no studies that measure chelation adherence exclusively in adults with thalassemia. In addition, mean annual adherence with routine medical tests was 67.22%, $SD = 25.81$. Across both indicators, adherence for this sample was relatively high when we compared it to other chronic illnesses. For example, Teach *et al.* (1998) found adherence rates of 43% for patients with sickle cell anaemia (see also, Bezie *et al.* (2006) reported 64.5% compliance in patients with diabetes; Zullig *et al.* (2013) reported 54.9% treatment adherence in patients with cancer having solid tumour malignancy). Given the dramatic differences in adherence demands, formal statistical comparisons were not appropriate, and as a result, our interpretation is limited.

Social functioning

Participants reported social functioning in nine types of social relationships including a partner, parents, siblings, relatives,

friends, workmates, schoolmates, members of groups without religious affiliations and members of religious groups. The lowest score on this scale was 0, and the highest score on this scale was 9. High and low social network scores were generated based on a median split; scores larger than 4.5 were above the median (Rutledge *et al.*, 2008). Approximately 95% of patients in our sample reported scores in the upper half of the scale (i.e. above the median, or 4.5), resulting in a 'high' social network index score ($M = 4.3$, $SD = 0.70$). This reflects that there was generally frequent contact with supportive others across most relationship domains. When compared to other samples with chronic illness using Fisher's exact test, our data suggested that participants had relatively strong social networks and interpersonal relationships. For example, Rutledge *et al.* (2008) used the same index of social network and found that only 70% of adult patients with myocardial ischaemia had a high social network index (i.e. above the median) score, significantly lower than that of our sample, $p < 0.0001$.

DISCUSSION

Contrary to some prior research on psychological adjustment and functioning in thalassaemic patients, the findings of this study suggest that most adult thalassaemic patients tend to show evidence of multidimensional resilience across four main domains: psychological adjustment, treatment adherence, occupational functioning and social functioning. Statistical comparisons of these patients with normative populations and/or other chronically ill samples suggested relatively high functioning despite the increased stress of their illness. For example, there were normative rates of psychopathology. The rates of MDD, GAD and PTSD in our sample were not significantly different than the rates of psychopathology in US adults (Kessler *et al.*, 2012) and were lower than some other samples with comparable chronic illnesses (e.g. sickle cell: Trachtenberg *et al.*, 2011). Furthermore, patients' self-reported distress was not significantly different from healthy samples (Bonanno *et al.*, 1998; Papa & Bonanno, 2008). Moreover, our data suggest that patients were largely financially independent, employed and well educated. In particular, the rates of education were considerably higher than population rates (U.S. Census Bureau, 2013, Table 3). They also had higher rates of employment when compared to people with chronic illness with or without physical disabilities (van Campen & Cardol, 2009) and comparable or higher treatment adherence than other patients with chronic illness (e.g. sickle cell: Teach *et al.*, 1998). Finally, the vast majority of patients reported excellent support networks and interpersonal relationships with others, which appeared to be relatively higher than the reports of patients with other chronic disorders (Rutledge *et al.*, 2008).

Clinical implications and future research

The literature has largely assumed that patients with thalassaemias have high rates of psychopathology and consequently low functioning. In contrast, this study suggests that adults may

be functioning well in multiple domains of life. Given the data collected in this study, it is possible that adult patients may benefit from resources that provide them with opportunities to be more productive and to pursue advanced education or improved employment. Given the increasing likelihood that adult patients will live with this disorder for decades, increased resources will facilitate a richer and more meaningful life. Finally, it is imperative that these findings be tested in future research on larger, perhaps more globally diverse, samples. The high-functioning patients in this sample could be unique to patients in the urban United States and not generalisable to patients receiving comparable treatment in other areas of the globe. The data of the current study clearly indicate that this research should be replicated with a larger sample, employing a case-control design. Future research should also continue to use multiple methods when assessing domains of functioning so as to ensure that the variability is not masked or limited by only indexing psychopathology.

Limitations

There were several limitations to this study. Transfusion-dependent thalassemias are rare in the United States. Therefore, the main limitation was the small sample size. Furthermore, the findings were based on cross-sectional data that did not have a healthy control group. For that reason, we could not predict long-term functioning and compare thalassaemic patients' functioning in different domains with a control group from the current study. However, we used objective indicators as well as self-report assessments to measure psychological functioning and treatment adherence, which gave a highly valid and comprehensive understanding of patient functioning. In addition, statistical comparisons with other populations were used to

interpret this data in a way that suggests important and meaningful differences and ultimately reinforces that adult patients in this sample were functioning very well across domains. These analyses were an important first step, and although we carefully selected comparison groups that tightly matched the current study, these findings must be interpreted with caution.

CONCLUSION

Thalassaemic patients appeared to be adapting well to the stress of their illness. Patients showed low rates of depression, anxiety and PTSD; low reports of psychological symptoms/distress; high treatment adherence; high social functioning; and high rates of employment, all suggestive of multidimensional resilience. These findings are consistent with the broader literature on resilience in other highly stressed samples and suggest that resilience is more common in adult patients with thalassaemia than often suggested in the literature. Future research should continue to assess adults with transfusion-dependent thalassaemias as they progress further in life, using multiple assessment methods across domains of adjustment in order to continue to inform our understanding of psychological functioning in patients with this disorder.

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K. C., G. R., D. K. and P. G. designed this research and completed all data collection. S. A. analysed the data. S. A. and K. C. wrote the paper.

CONFLICT OF INTEREST

The authors have no competing interests.

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