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Psychopathology in children from families with blood disorders: a cross-national study

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Abstract *Background* This study examines the prevalence of psychiatric disorders in affected and in unaffected siblings from families with haemophilia or β -thalassaemia. *Method* Based on data derived from a cross-sectional and multi-centre study into the resilience of 115 families with blood disorders. Sociodemographic and developmental data were collected from the parent using a standardised and semi-structured interview, and medical data were elicited from the attending clinician. The children's psychopathology was assessed with the Schedule for Affective Disorders and Schizophrenia (K-SADS). *Results* Children with β -

thalassaemia were twice as likely to receive a diagnosis of psychiatric disorder and more likely to show a higher degree of impairment of general functioning than haemophilic boys or unaffected children from families with blood disorders. Clinical severity of haemophilia or β -thalassaemia was not associated with significant differences in prevalence of child psychiatric disorders or impairment. Mothers' evaluation of their relationship with their child as 'less than easy' predicted psychopathology. *Conclusions* The high prevalence of psychopathology in children with β -thalassaemia reported in this study suggests that specific blood disorders have differential impact on affected children. This difference may be related to medical therapy advances in haemophilia so that haemophilic boys can lead an almost normal life.

Key words psychopathology – haemophilia – β -thalassaemia

Introduction

Children with either haemophilia or β -thalassaemia are often exposed to considerable acute and chronic stress. Both haemophilia and β -thalassaemia are hereditary diseases, the first being transmitted as a sex-related characteristic from the mother as a carrier, to the son as

a sufferer. Whereas β -thalassaemia is inherited through both parents, who are symptomless carriers in a Mendelian recessive manner and can affect children of both sexes. These genetic differences may give rise to differential impact on parental behaviour and attitudes towards the sick child. They are both chronic and life-threatening conditions, the first being treated with Factors VIII or IX replacement and the second, with the

worst prognosis, with frequent blood transfusions and chelation therapy [34].

With the introduction of preventative and home treatment, older children and in the case of younger children, the parents, are trained to infuse concentrates of factor VIII or IX intravenously, or the iron chelating agent desferrioxamine subcutaneously. This requires compliance and continuous supervision, and the child is exposed on a regular basis to needle pricks. In addition, thalassaemic children require regular blood transfusions. Any consequent distress in the child can have repercussions for the functioning of the whole family.

Clinicians and researchers reported parental overprotection of children with β -thalassaemia [27], but in a thorough research review "the clinically reported tendency of parental overprotection and overindulgence was not confirmed by studies" of haemophilic individuals [4].

Most of the studies of haemophilic boys reported scores on measures of mood and behaviour to be within the normal range [7, 8, 18], although some reported that the boys might display anxiety, phobic states, transient depression as well as dangerously accident-prone behaviour [20, 23, 12]. Surprisingly few or no differences have been found between haemophilic boys with HIV positive and those with HIV negative sero-status [9, 22, 25]. However, in one study of haemophilic boys, 28% had a clinical diagnosis of attention deficit hyperactivity disorder of whom 53% received treatment with methylphenidate [22].

In a study of thalassaemic children 54% (31/57) fulfilled DSM-III-R criteria for psychiatric disorders, of whom one quarter of children were diagnosed with oppositional defiant disorder [1].

So far only two published studies have used direct semi-structured interviews to assess children with haemophilia [3]. In the first, anxiety disorders were reported in five of 17 interviewed children with haemophilia and HIV negative sero-status (29%); in four of six interviewed children with HIV positive sero-status (67%); and in six of 31 (19%) interviewed healthy controls. The second study found no significant differences between groups of children with haemophilia and HIV negative or positive sero-status and controls [33]. Altogether only three of 64 children with haemophilia (4.7%) were diagnosed as conduct disordered, and no psychiatric diagnosis was made in the control group.

In addition, there has been an almost complete neglect of studies of siblings of haemophilic boys despite related research showing that such siblings may be at a higher risk [29, 32]. In a study of siblings of thalassaemic patients [17], DSM-III-R disorders were present in 30/71 (42%) with mainly a higher rate of oppositional defiant disorder compared with controls.

Studies based on narrated accounts derived from clinical samples of thalassaemic subjects have reported that

the adolescents themselves felt that the illness did not affect their present life but frequently destroyed their plans for the future and their ability to enjoy life. They also have talked about premature death [10, 11]. Thalassaemic children and adolescents have also been described as being anxious and depressed, and overdependent on their parents. Anxiety about death has also been observed in younger subjects whereas thalassaemic adolescents may become socially isolated and non-compliant to treatment [15, 37]. Parents have also been reported as overprotective; displaying pathological or adaptive denial of the burden imposed by the illness and neglect of the healthy siblings needs [34]. The children's adjustment to the illness was also found to be related to the parental acceptance of the illness [14]. Similarly the children's poor psychiatric adjustment was correlated with impaired understanding of their illness [31].

■ Aims of current study

This study is part of a cross-sectional, multi-national and multi-centre study into the resilience of families with blood disorders. The intention was to compare prevalence rates of psychiatric disorders of affected and unaffected siblings from families with haemophilia or β -thalassaemia. The main hypotheses under investigation were:

- School age children and adolescents in families with haemophilia or β -thalassaemia will have more emotional and behavioural disturbance than physically healthy children in families with blood disorders.
- School age children and adolescents with β -thalassaemia will show an increased level of psychopathology in comparison to children with haemophilia or their siblings.

Method

■ Participants

Families with haemophilia or β -thalassaemia and school-aged children were recruited from the outpatients of the Royal Free and Whittington Hospitals, London, the 'Aghia Sophia' Children's Hospital, Athens and the Institute of internal medicine in Milan from 1994 to 1996. The entry criteria were that one family member was affected by haemophilia or β -thalassaemia, and that the family had at least one child of school age. The intention was to collect all affected children if possible. None of the eligible families in London refused participation in the study. In Athens, 98% of eligible families agreed to participate in the study and in Milan approximately 80% of eligible families agreed to participate. In total, 75 families with haemophilia and 40 families with

β -thalassaemia were interviewed. Altogether 33 families participated in Milan, 23 each in London and in Athens. Families with haemophilia were interviewed at all three centres; β -thalassaemia families were recruited only in London and Athens.

With limitation of resources the investigation was confined to maximum two children of school age per family. If there were more than two children in the relevant age range, the affected child and the sibling nearest in age were selected.

In all, 168 children in 115 families were assessed. The findings are presented for four groups of children: 1) 58 haemophilic boys, 2) 43 children whose father or sibling were affected with haemophilia, 3) 42 children with β -thalassaemia, and 4) their 25 unaffected siblings. Although the sibling groups and the group of children with β -thalassaemia contained both males and females, individuals in the haemophilia group were all males because of the sex-linked nature of their condition (Table 1).

Measures

The participants underwent a number of semi-structured interviews and tests. For the purpose of this paper only selected sociodemographic, medical data and data regarding the children's psychopathology are presented.

All interviews were originally developed in English

and translated into Greek and Italian. Accuracy of translation was checked by translating the measures back into English by another translator and comparing the translations with the original interview schedules and questionnaires.

Children's psychopathology was assessed using the Schedule for Affective Disorders and Schizophrenia for school-age Children (K-SADS), Present Episode Version [26] and the modified version of the Children's Global Assessment Scale [30] for the K-SADS. Altogether 157 children (93%) completed this interview: 57 haemophilic boys, 43 unaffected children from families with haemophilia, 38 children with β -thalassaemia and 19 of their unaffected siblings.

Sociodemographic data

Sociodemographic data were elicited from the parents by standardised questionnaires previously used [16]. These included questions regarding the parents' judgement of their own relationship with each individual child, of their child's relationship with siblings or peers, questions on parental concern about the children's behaviour or emotional state, and questions regarding previous contact with child guidance or other mental health professionals. Demographic data were incomplete for nine families.

Table 1 Children's demographic data

	Haemophilia families		Thalassaemia families	
	Children without haemophilia N = 43	Haemophilic boys N = 58	Children without β -thalassaemia N = 25	Children with β -thalassaemia N = 42
Mean age in years and months (SD)	11.3 (3.2)	11.8 (3.6)	12.1 (3-1)	13.2 (2.3)
Gender				
Boys	26 (60.0%)	58 (100.0%)	9 (36.0%)	20 (48.0%)
Girls	17 (40.0%)	-	16 (64.0%)	22 (53.0%)
Ethnicity				
European	39 (91.0%)	54 (93.0%)	24 (96.0%)	40 (95.0%)
Asian	4 (9.0%)	3 (5.0%)	1 (4.0%)	2 (5.0%)
Other	-	1 (2.0%)	-	-
Faith				
Roman Catholic	15 (35.0%)	28 (48.0%)	-	-
Greek Orthodox	14 (33.0%)	16 (28.0%)	23 (92.0%)	38 (90.0%)
Protestant	1 (2.0%)	4 (7.0%)	-	-
Muslim	1 (2.0%)	1 (2.0%)	2 (8.0%)	4 (10.0%)
Other	9 (21.0%)	5 (9.0%)	-	-
None	3 (7.0%)	4 (7.0%)	-	-
Schooling	N = 42	N = 56	N = 20	N = 36
None	-	5 (8.9%)	-	1 (2.8%)
Infant or junior	26 (61.9%)	31 (55.3%)	9 (45.0%)	6 (16.7%)
Secondary	15 (35.7%)	18 (32.0%)	11 (55.0%)	29 (80.6%)
Other	1 (2.4%)	2 (3.6%)	-	-

Socio-economic status (SES) was determined by the Hollingshead Redlich two-factor method [13]. The main breadwinner's Hollingshead occupational codes were grouped according to three SES levels as follows: Lower Social Strata = 10–35; Middle Social Strata = 40–65, and Higher Social Strata = 70–90.

The great majority of parents (94%) were married or cohabiting. The sample included only six single parent families (5%) – four single mothers and two single fathers – and one couple who had separated (1%). The father was the main breadwinner in 98 families (88%), and the mother in 13 families (12%). Eighteen families (17%) were lower social strata, 64 families (60%) middle social strata, and 24 families upper social strata (23%).

The assessed children were between six and 18 years old with a mean age of 12 years (SD 3yrs–1mth). Children from haemophilic families were younger than children from families with β -thalassaemia (t -value 2.35, $p < 0.05$, Table 1). Children from haemophilic families were significantly younger in London ($F [154, 2] = 6.88$, $p < 0.01$), which was true both for unaffected children ($F [40, 2] = 3.47$) and for the group of haemophilic boys ($F [55, 2] = 3.78$, $p < 0.05$). Post hoc analyses showed for each comparison a significant difference between the haemophilic boys' mean age at London and at Athens (Tukey test $p < 0.05$). Thus more children from thalassaemic families (40/56) than from haemophilic families (33/98) attended secondary schools ($\chi^2 = 17.55$, $df = 1$, $p < 0.001$; OR = 4.9).

While children at Milan and Athens were almost exclusively of European or Mediterranean ethnicity, the ethnicity of the London sample included 10 Asian children and one Black Caribbean child. The cultural difference between the different centres was further reflected in the children's religious affiliation. Children in Athens were all Greek Orthodox and all but one child in Milan was Roman Catholic, whereas the London sample was heterogeneous.

Medical data

The physical description of patients was elicited by a medical data schedule developed for the purposes of this study, and the medical data were collected by the patients' haematologists.

Severity of haemophilia was determined according to typical medical procedures related to plasma factor level available in the blood: a factor level less than 1% was used to indicate severe haemophilia; 1% – 5% moderate haemophilia, and greater than 5% mild haemophilia. Evidence of joint damage, frequency of bleeds and school absence due to haemophilia was also examined.

Fifty-one boys (93%) had severe haemophilia and four had moderate haemophilia. Regular prophylactics

were given in 17 cases (31%). One third of haemophilic boys had undergone surgery (18/54) in their life, and there was clinical evidence for joint damage in 40% (21/52) of the boys. Seven haemophilic boys (13%) were HIV positive.

Severity of β -thalassaemia was determined according to medical procedures necessary, i.e. transfusion requirements and chelation therapy, and physical complications such as bone structure abnormalities, facial appearance, and growth failure. Fourteen children with β -thalassaemia (34%) had experienced at least one major complication due to their illness. Thirty-three children underwent various regimes of transfusion therapy (81%), and nearly all thalassaemic children (39/41, 95%) were treated with desferrioxamine.

In addition, attending clinicians were asked to rate the severity of any physical health problem for all children participating in the study on a four-point scale (no, mild, moderate or severe health problem). They rated the physical health as severely affected by their blood disorder for 80% of the thalassaemic children (33/41) but only five of 55 (9%) haemophilic boys ($\chi^2 = 47.13$, $df = 1$, $p < 0.001$; OR = 41.25).

The K-SADS

For the purpose of this study an abbreviated present episode version of the Schedule for Affective Disorders and Schizophrenia for school-age children [26] was employed in which the manic and the psychotic sections were excluded. On the basis of the information psychiatric diagnoses over the past 12 months were established. Additional items were included and combined with clinical observations in order to allow a diagnosis of Attention Deficit Hyperactivity Disorder. After instruction on the K-SADS interview format (supervised by IK), role-playing interviews were used followed by co-ratings of taped interviews.

A consensus review of all psychopathology data was undertaken jointly by H.S. and I.K. (the latter being blind to any medical or demographic data) to ensure the diagnoses complied with DSM-IV criteria.

Global assessment of impairment

Overall impairment of child's functioning was determined using the Children's Global Assessment Scale (C-GAS, 30). The version used in this research was the variation (K-GAS) developed for the K-SADS [5] with scores ranging from 1 for the most impaired child to 9 for the highest functioning. Following the completion of the clinical assessment, the interviewer rated the level of functioning over the previous 12 months at the end of the interview.

Procedures

Parental and the children's consent were sought by the attending clinician before inclusion in the research. Both parents, or the one who was living with the child in case of disrupted families, were invited to participate. If only one parent attended, the interview was limited to this particular carer. Each subject underwent a series of semi-structured interviews and tests, which took about one and one half-hours for the children and about two hours for each adult. All self-rating questionnaires were read aloud to younger children and questions or statements were clarified, if requested.

Interviews of parents and children were conducted by psychologists, child psychiatrists and physicians who had undergone a training programme to ensure uniformity across centres. Training courses for semi-structured interviewing with reference to the Kiddie-SADS were held in London and in Milan. While parents and children were interviewed in parallel in London, this was not always feasible or practicable at other centres. Data collected at all three centres were reviewed in London.

Statistical procedures

For the purpose of this paper, univariate analyses of data were undertaken to examine differences between groups. Categorical data were subjected to chi-square tests, and confidence intervals and odds ratios were calculated where appropriate. Continuous data were analysed using student's t-test or analysis of variance

(ANOVA) where appropriate for assessing between group differences, and Tukey's post hoc test was used to examine the main effect of significant intergroup differences.

In order to examine the independent effects of the independent variables on the presence of any DSM-IV disorder over the year prior to the assessment, multivariate analyses were conducted using logistic regression. Backwards stepwise selection was used and the variables entered which were found to be significant in univariate analysis, with removal based on the probability of the Wald statistic.

Results

12-Month prevalence of DSM-IV diagnoses

Table 2 shows the 12-month prevalence of child psychiatric disorders for the four children's groups. Overall there was a significant difference in the prevalence of psychiatric disorders in the four different children's groups, and this difference was predominantly accounted for by a higher rate of anxiety disorders in the group of children with β -thalassaemia as compared to the other group.

DSM-IV disorders were significantly more likely in thalassaemic children compared to haemophilic boys ($\chi^2 = 4.33$, $df = 1$, $p < 0.05$) with an odds ratio of 2.76 (95% C.I.: 1.15-6.64), and also higher than in all 62 unaffected children ($\chi^2 = 5.56$, $df = 1$, $p < 0.05$) with an odds ratio of 3.09 (95% C.I.: 1.29-7.38).

Table 2 DSM-IV diagnoses over the year prior to the assessment

	Haemophilia families		β -Thalassaemia families	
	Children without haemophilia N = 43	Haemophilic boys N = 57	Children without thalassaemia N = 19	Children with thalassaemia N = 38
Major depressive disorder	4 (9.3%)	7 (12.3%)	2 (10.5%)	7 (18.4%)
General anxiety disorder	3 (7.0%)	5 (8.8%)	3 (15.8%)	5 (13.2%)
Separation anxiety disorder	4 (9.3%)	4 (7.0%)	—	7 (18.4%)
Panic disorder	—	—	—	1 (2.6%)
Social phobia	1 (2.3%)	—	—	—
Avoidant disorder	—	—	—	1 (2.6%)
Simple phobia	—	2 (3.5%)	—	2 (5.3%)
Oppositional defiant/Conduct disorder	1 (2.3%)	2 (3.5%)	—	3 (7.9%)
Attention deficit/Hyperactivity disorder	1 (2.3%)	3 (5.3%)	—	2 (5.3%)
Adjustment disorder	—	2 (3.5%)	1 (5.3%)	1 (2.6%)
Any Anxiety disorder*	6 (14%)	7 (12.3%)	3 (15.8%)	13 (34.2%)
Any Disruptive disorder	2 (4.7%)	5 (8.8%)	—	3 (7.9%)
Any DSM-IV disorder**	9 (20.9%)	14 (24.6%)	5 (26.3%)	18 (47.4%)

* $\chi^2 = 8.14$, $df = 3$, $p < 0.05$

** $\chi^2 = 8.37$, $df = 3$, $p < 0.05$

Anxiety disorders included general and separation anxiety disorders and panic disorder.

Disruptive disorders comprised oppositional defiant/conduct and attention deficit/hyperactivity disorders

There was no significant difference between the subgroups of haemophilic boys and of unaffected children from haemophilic families, and the unaffected siblings of thalassaemic children had a similar rate of psychopathology as those two other groups.

Only two of the seven haemophilic boys who were HIV positive had major psychopathology warranting a DSM-IV diagnosis namely major depressive disorder, which occurred together with a separation anxiety disorder in one of these two boys.

Overall, major depression (20/157, 13%), general anxiety (16/157, 10%) and separation anxiety disorder (15/157, 10%) occurred most frequently, and other anxiety disorders were diagnosed often as comorbid conditions in particular in thalassaemic children (Table 2).

While in the subgroup of siblings of thalassaemic children no behavioural disorder was diagnosed, thalassaemic children had the highest rate of conduct disorder (8%). Attention Deficit Hyperactivity Disorder (ADHD) was diagnosed in three haemophilic boys (5%) and in one unaffected child from a haemophilia family (2%). In these two subgroups there was no comorbidity between the two behavioural disorders whereas the only two Thalassaemic children with ADHD had also comorbid Conduct Disorders.

In general, girls were twice as likely as boys to have anxiety disorders (29.5% versus 13.6%), ($\chi^2 = 4.68$, $df=1$, $p < 0.05$), and no behavioural disorder was diagnosed in girls (0/47 vs. 10/110, Fisher's Exact Test, $p < 0.05$). In the case of haemophilic families, no significant difference either in general psychopathology or in the rate of specific psychiatric disorders in children was found between cohorts at the three different centres. Similar analyses could not be undertaken for β -thalassaemia as such data were only collected in two centres.

Comorbidity and impairment

Unaffected children were less likely to receive two or more coexisting DSM-IV (7%) diagnoses than those with blood disorders (15%), but this difference was not significant (Table 3).

Comparison of the level of general functioning over the year before the assessment (K-GAS) revealed significant differences between the different subgroups (Table 3). Thalassaemic children were more severely impaired than their unaffected siblings (t -value 2.29, $p < 0.05$) and also than haemophilic boys (t -value 2.00, $p < 0.05$). While the comparison of the mean K-GAS between haemophilic boys and unaffected children from haemophilic families did not yield any significant difference, haemophilic boys were significantly more likely to show moderate or severe impairment rather than mild impairment than unaffected children from haemophilic families ($\chi^2 = 7.15$, $df = 2$, $p < 0.05$).

Severity of blood disorder, clinicians' rating of severity of physical problem and psychopathology

Severity of haemophilia or β -thalassaemia was not significantly related to presence of psychopathology or level of impairment.

However, the clinicians' ratings of the severity of any physical problem proved important. Of the children whose physical health problems were judged as severe, 45% (17/38) were found to have at least one DSM-IV psychiatric disorder as compared to only 24% of the residual children (29/119; $\chi^2 = 4.83$, $df = 1$, $p < 0.05$; odds ratio 2.51; 95% C. I.: 1.17, 5.39).

Children with severe physical health problems were significantly more likely to receive a diagnosis of anxiety disorder than the other children ($\chi^2 = 4.63$, $df = 1$, $p < 0.05$). The prevalence rate for any anxiety disorder

Table 3 Comorbidity and severity of impairment of overall functioning over the year prior to the baseline assessment

	Haemophilia families		β -Thalassaemia families	
	Children without haemophilia N = 43	Haemophilic boys N = 57	Children without β -thalassaemia N = 19	Children with β -thalassaemia N = 38
Comorbidity				
No DSM-IV child psychiatric disorder	34 (79%)	43 (75%)	14 (74%)	20 (52%)
One DSM-IV child psychiatric disorder	6 (14%)	7 (12%)	4 (21%)	11 (29%)
Two or more DSM-IV disorders	3 (7%)	7 (12%)	1 (5%)	7 (18%)
Overall level of general functioning				
No impairment (8 or 9)	34 (79%)	43 (75%)	14 (74%)	20 (53%)
Mild impairment (= 7)	5 (12%)	4 (7%)	4 (21%)	9 (24%)
Moderate and severe impairment (< 7)	4 (9%)	10 (18%)	1 (5%)	9 (24%)
Mean K-GAS (SD)*	8.16 (1.11)	7.95 (1.22)	8.11 (0.94)	7.45 (1.18)

* $F(153,3) = 2.95$, $p < 0.05$

over the year before the assessment was 32% (12/38) for children whose physical health problems were judged as severe compared to 14% (17/119) for the other children (odds ratio 2.77, 95% C.I.: 1.18, 6.51). Children with severe physical health problems had a significantly lower mean K-GAS (7.5, SD 1.1), which relates to a higher degree of impairment of overall functioning than the other children (8.0, SD 1.2, t -value 2.35, $p < 0.05$).

■ Parental reports of concern, of consulting health professionals, and of their relationship with their child in relation to psychopathology

Only four children (2%) had been seen at a child guidance clinic during the past year, and 15 children (10%) had ever attended their GPs or mental health professionals because of emotional or behavioural disturbance of which 6 (43%) were diagnosed with at least one DSM-IV psychiatric disorder in this study.

Few parents were concerned about their children's behaviour or emotional state (8/157, 5%), and there was no significant association between the history of consulting a health professional because of the child's emotional problems or parental reports of being concerned about their child's emotional state and psychopathology.

However, mothers' evaluation of their relationship with their child over the previous year was derived from the socio-demographic interview. The mothers' evaluation about the mother-child relationship was significantly related to psychopathology. Nine of 57 (16%) children whose mothers reported an 'easy' relationship with the child over the past year had a psychiatric disorder, but 34 of 93 children (37%) whose mother judged their relationship as 'less than easy' showed significant psychopathology (odds ratio 3.07, 95% C.I.: 1.34, 7.03; $\chi^2 = 4.32$, $df = 1$, $p < 0.05$).

■ Multivariate analysis

A stepwise logistic regression was performed in order to explore predictors of psychopathology. The dependent variable was identified DSM-IV psychiatric disorder. The categorical variables which were found to be significantly associated with psychopathology when using univariate analyses, were entered, namely 1) β -thalassaemia as present or absent, 2) haemophilia as present or absent, 3) clinicians' rating of severity of physical health problem (severe or not severe), 4) mother's evaluation of relationship (easy or less than easy), and 5) gender. In addition, 6) centre as categorical variable (Milan, London, Athens) and 7) age as continuous variable were entered to control for any age or cultural effects not found to be significant in univariate analyses.

Two variables predicted significantly DSM-IV psychiatric disorders: mothers' judgement of their relationship with their child as 'less than easy' (Wald 5.70, $df = 1$, $p < 0.05$) with an odds ratio of 1.67 (95% C.I.: 1.10, 2.55) and having β -thalassaemia (Wald 4.86, $df = 1$, $p < 0.05$) with an odds ratio of 1.59 (95% C.I.: 1.05, 2.39). The model accounted for 69.8% of the overall outcome ($\chi^2 = 12.93$, $df = 2$, $p < 0.005$).

Discussion

■ Literature comments

Generally, most of the previous studies reported in the literature were beset by a variety of methodological problems, were not controlled, and used narrated clinical material which although helpful for clinical purposes cannot be considered as evidence based (or conclusive). More recent research indicates that children with β -thalassaemia show a higher rate of psychiatric disorders than do children with other chronic diseases. This is true as well for the current study; the most frequent diagnoses are depression and anxiety followed by psychosomatic and conduct disorders [34]. Some of the earlier descriptive studies report that children in preschool and primary school age are anxious, show psychosomatic symptoms and are frequently over-dependent on their parents [14, 19]. Adolescents reported as showing difficulties in their relationship with peers are socially isolated and show depressive reactions. This latter group also present with problems of treatment compliance [21].

■ Prevalence of psychiatric disorders in affected and unaffected children from families with β -thalassaemia or haemophilia

Most of the children studied were not diagnosed as suffering a DSM-IV child psychiatric disorder. However, children with the respective blood disorder showed a higher degree of comorbidity and impairment in overall functioning than unaffected children from families with β -thalassaemia or haemophilia. Furthermore, in this study being affected by β -thalassaemia was significantly associated with the presence of DSM-IV psychiatric disorder in school-age children. Both groups of unaffected children and haemophilic boys showed slightly higher rates of internalising disorders compared to prevalence rates one would expect from epidemiological community surveys [2, 24].

The prevalence rates of psychiatric disorder for haemophilic boys in the current study were much higher than the prevalence reported by a similar study [33]. While their rates of behaviour disorders in haemophilic

boys are comparable with those in the present study, in contrast they did not diagnose any emotional disorder. Neither the present study nor the Thompson et al. study (1995) confirms the findings by Mayes et al. (1996) who reported clinically diagnosed Attention Deficit Disorder in 29% of haemophilic boys.

In the current study, Anxiety Disorders were diagnosed in 12% of all haemophilic boys. This prevalence rate is much lower than those reported by Bussing and Burket (1993).

It was surprising that there was little in the way of needle phobia reported. However, the presence and work over the last decade of a psychosocial input within the haematology departments has enabled the medical and nursing staff to contain the anxiety and offer access to early intervention to the children and their families, hence offering early preventative work.

The overall rate for psychiatric disorders for children with β -thalassaemia in the present study is slightly lower than that reported by Beratis (1993). However, there is one important difference: Beratis reports a very high rate (25%) of oppositional defiant disorder in thalassaemic children. In the present study, the higher overall rate of psychiatric disorders was mainly due to the high prevalence of anxiety disorders. In contrast, the prevalence of behaviour disorders was not significantly different from those found in the other three children's groups.

The present study indicates that siblings of children with β -thalassaemia show similar levels of psychopathology to affected and unaffected children from haemophilic families. Whereas the prevalence rates of anxiety disorders in the present study and in Labropoulou and Beratis' study (1995) are similar, the latter workers diagnosed oppositional defiant disorders in 14% of the siblings of thalassaemic children but none are reported in the current study. However, the latter study did not employ a standard semistructured interview and this could account for an overestimate.

Although many of the children in this study did not have a DSM-IV diagnosis, the general level of functioning over the year before the assessment showed moderate to severe impairment for both the haemophilic boys and those affected by β -thalassaemia. It is to be expected that although the effect of the chronic disorder may not be great enough to cause psychiatric psychopathology, it still may have a great impact on social adjustment and functioning due to the limitations associated with the illness such as reduced contact sports for haemophiliacs and the more cumbersome treatment with regular hospital admission for the thalassaemic group.

■ Cross-cultural differences

The current findings provided little evidence of cross-cultural differences in psychiatric psychopathology in

children in families with haemophilia. In β -thalassaemia, the numbers in one centre were insufficient for the purposes of statistical analyses.

■ Severity of physical problem and severity of blood disorder

Most studies of children with chronic physical illness do not report associations of behavioural psychopathology and the degree of severity of the physical illness. In the present study, clinicians rated the severity of any physical problem and associations with psychopathology were sought, but again the above conclusion was confirmed.

However, different illnesses are associated with different outcome [29], and the findings of the present study demonstrate this well in respect of two different blood disorders. Despite more general medical complications, the physical health problems of haemophilic boys were judged as far less severe than those of β -thalassaemic children. The specific complications and treatment regimes of each chronic physical illness seem to result in very specific stresses on the children and their families. Whereas with modern treatment methods haemophilic boys can live almost normal lives, children with β -thalassaemia need regular hospital admissions for blood transfusions and have a reduced life expectancy.

It is plausible that the significant difference in psychopathology is a result of overwhelming stress related to β -thalassaemia. However, about 50% of thalassaemic children cope well. Further, there were no within-group differences according to the degree of severity of the blood disorder or β -thalassaemia specific complications. Thus, general and specific protective and risk factors need to be explored further to inform intervention strategies in order to prevent emotional and behavioural disturbance.

■ Parental concern and child psychiatric service utilisation

Most strikingly, very few parents were concerned about their children's coping, behaviour or emotional state, which might explain in part the low rate of child mental health service utilisation over the year before the assessment. However, the rate of attendance at a child guidance clinic in this study is similar to those reported in community studies (2, 24), and most of the children diagnosed with DSM-IV psychiatric disorder whether associated with mild or more severe impairment did not receive any kind of mental health care. Since psychiatric disorders assessed by semi-structured interview of other clinical samples of children cannot be dismissed

as transitory [6], other explanations need to be considered. It is possible that parents allowed for emotional disturbance in the context of their children's physical illness normalising disturbance accordingly [36]. This in turn could have led to a significant number of children suffering secondary handicaps without adequate psychological or psychiatric treatment.

However, mothers' evaluation of their relationship with their child as being '*less than easy*' proved highly predictive of psychopathology, but relationship difficulties did not seem to contribute to a heightened perception of children's emotional disturbance. Thus, in families with blood disorders, clinicians should take parental reports of difficulties in their relationships with their children as indicators for screening emotional and behavioural disturbance.

Compliance and psychopathology

Two studies provide some useful information, one stresses the importance of identifying the subgroup of children with emotional and behavioural disturbance [8], finding that the higher the levels of behaviour and emotional difficulties rated by the boys' mothers, the lower were their sons' scores on the Medical Compliance Incomplete Stories Test. This indicates the likelihood of a lower compliance with medical treatment.

In the second study [1], preadolescent thalassaemic children with oppositional defiant disorder had higher serum ferritin levels, which was attributed to non-compliance with treatment. However, caution is warranted regarding conclusions that there is a wide specific link of a categorical psychiatric disorder associated with a medical disorder. This is especially true when there is a genetic basis, which could suggest a behavioural phenotype. This local finding merits explanation and replication.

With home treatment and increasing reliance on adolescent self-infusion of factor VIII or IX concentrate or desferroxamine, it seems imperative to seek ways of promoting healthy adaptation. This could contribute to the prospect of preventing unnecessary orthopaedic handicaps or premature deaths.

Self-help groups related to the patient and parents' associations mobilise support including free mobility benefits, free prescription and educational help all contribute to a more adaptive level of functioning in families with chronic blood disorders.

Limitations of this study

Tsiantis et al. [35] reported variations of psychopathology in adults in families with β -thalassaemia across different centres in different countries. However, in this

cross-sectional, multi-national and multi-centre study, only a few cultural differences were found between the centres. One explanation may relate to the size of the subgroups. Although the overall sample of both unaffected children and children with blood disorders is large, the respective subgroups of children at each centre were relatively small and this could inhibit the emergence of significant differences between the subgroups.

All children included in the current study had been living in a family where one member had a blood disorder. It is likely that an additional control group of children from families without physical illness matched for age and sex would have shown more differences in psychopathology.

Since unaffected children were from families with blood disorder themselves, they could not be matched for age and gender. Furthermore, the number of children with specific blood disorders differing in the degree of severity of haemophilia or β -thalassaemia could have been too small to yield significant within-group differences.

Conclusions

In conclusion, in the present study there is an increased one-year prevalence of DSM-IV psychiatric disorders in children with β -thalassaemia compared to haemophilic boys and unaffected children in families with blood disorders. Haemophilic boys were significantly more likely to show moderate or severe impairment of functioning than unaffected children from haemophilic families, but the overall prevalence of psychiatric disorder was not different from those of unaffected children.

Although children with haemophilia or β -thalassaemia are exposed to similar stressors requiring close medical supervision and continuous therapy, thalassaemic children regularly attend hospital for blood transfusions. This seems to be reflected in the higher prevalence of anxiety disorders in thalassaemic children indicating a higher risk of becoming overwhelmed by fears and a breakdown in coping.

Another difference between the conditions is the mode of transmission, which is different in the two conditions. In haemophilia only the mother is a symptomless carrier of the respective gene, while in β -thalassaemia both parents are carriers and thus there may be a differential impact of parental responses towards their affected child [34]. Hence it is possible that feelings of guilt, shame and social stigma are more severe amongst parents with thalassaemic children since both parents may feel responsible for transmitting the gene and this may affect their reactions to their sick child influencing his or her psychosocial development.

The findings of this study suggest that generalisations about children with chronic illness without physi-

cal handicap need careful re-examination – taking into consideration specific differences between related conditions, treatment advances and changes in life style or life expectancy.

Parent reports of relationship difficulties with their children seem to predict emotional and behavioural disturbance and should be followed up by the attending clinician with referral to child mental health services.

❖ Clinical Implications

- ❖ Children with β -thalassaemia are at high risk of suffering a psychiatric disorder
- ❖ Severity of β -thalassaemia or haemophilia does not predict behavioural psychopathology.
- ❖ Very few emotionally or behaviourally disturbed children from families with blood disorders were brought to the attention of mental health professionals.

❖ Limitations

- ❖ Unaffected children were from families with blood disorder themselves and could not be matched for age and gender.
- ❖ The sub-groups of children with or without blood disorders were often too small to support statistical exploration of within-group differences.
- ❖ The lack of a control group of children from families without physical illness precludes the exploration of differences between unaffected children from families with blood disorders and those from physically healthy families.

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