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Attention deficit/hyperactivity disorder: burden of the disease according to subtypes in recently diagnosed children

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Introduction. Attention-Deficit/Hyperactivity Disorder (ADHD) is associated with deterioration of several dimensions of quality of life (QoL) and with the development of comorbid psychiatric disorders. The objective of the present study is to evaluate the burden of illness of ADHD subtypes in untreated newly diagnosed children in Spain.

Methods. We recruited 124 children (80 combined, 25 inattentive and 19 hyperactive-impulsive subtype) aged 6-12 years with untreated newly diagnosed Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) ADHD. We collected socio-demographic, clinical (Attention-Deficit/Hyperactivity Disorder Rating Scale [ADHD-RS], Conner's Parent Rating Scale-Revised: Short From [CPRS:R-S], Clinical Global Impression-Severity [CGI-S], Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version (K-SADS-PL), intelligence Quotient [IQ]), Quality of Life (QoL) (Child Health Questionnaire-Parent Form 50 [CHQ-PF50]), academic performance and health care resources utilization data. We investigated the correlations between ADHD symptom severity and QoL, academic performance and time from onset of symptoms to diagnosis.

Results. QoL of children with combined-type ADHD was rated as significantly worse in patients with predominance of hyperactivivity/impulsivity for most of the domains. Inattentive-type children also had worse ratings than patients with hyperactivity/impulsivity predominance in most of the domains. The ADHD Index of Conner's Parent Rating Scale-Revised: Short Form (CPRS-R:S) was significantly lower in hyperactive/impulsive patients. We found no differences across subtypes in IQ, academic performance and health care resources utilization. Higher ADHD symptom severity was associated to poor QoL.

Conclusions. Combined and inattentive subtypes are associated with greater disorder severity, more comorbid psychiatric disorders, and worse QoL than the subtype with hyperactivity/impulsivity predominance.

Key words:
Attention-deficit/hyperactivity disorder. Subtypes. Burden of illness. Inattentive. Combined.

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Trastorno por déficit de atención/hiperactividad: impacto de la enfermedad de acuerdo al subtipo en niños con diagnóstico reciente

Introducción. El trastorno por déficit de atención/hiperactividad (TDAH) se asocia con un deterioro en varias dimensiones de calidad de vida (QoL) y el desarrollo de trastornos psiquiátricos comórbidos. El objetivo del presente estudio es evaluar el impacto de la enfermedad de los subtipos de TDAH en niños con diagnóstico inicial y sin tratamiento en España.

Metodología. Reclutamos a 124 niños (80 de subtipo combinado, 25 inatento y 19 hiperactividad-impulsividad) entre 6 y 12 años de edad con nuevo diagnóstico de TDAH (Manual diagnóstico y estadístico de los trastornos mentales, 4.a ed [DSM-IV]) y sin tratar. Recogimos datos sociodemográficos y clínicos (Attention Deficit/Hyperactivity Disorder-Rating Scale [Escala de evaluación para el trastorno por déficit de atención/hiperactividad] [ADHD-RS], Conner's Parent Rating Scale-Revised: Short Form [Escala de evaluación de Conner, versión para los padres revisada: versión breve] [CPRS:R-S]; Impresión Clínica Global-Severidad [ICG-S], Kiddie Schedule of Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetie Version [Inventario Kiddie para los trastornos afectivos esquizofrenia para niños en edad escolar, versión actual y a lo largo de la vida] [K-SADS-PL] y coeficiente intelectual [CI]) de Qualite of Life [Calidad de vida] [Qol], Child Health Questionnaire-Parent Form 50 [Cuestionario de Salud Infantil, versión para los padres de 50 ítems] [CHQ-PF50], rendimiento académico y utilización de recursos sanitarios. Investigamos las correlaciones entre la gravedad del TDAH y QoL, rendimiento académico y tiempo transcurrido desde el inicio de los síntomas hasta el diagnóstico.

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Resultados. La QoL de niños con subtipo combinado de TDAH se valoró como significativamente peor que en pacientes con predominio de hiperactividad/impulsividad en la mayoría de los dominios. Los niños con subtipo inatento también puntuaron peor que los de predominio de hiperactividad/impulsividad en varios dominios. La puntuación de ADHD de la CPRS-R:S fue significativamente menor en los pacientes con predominio de hiperactividad/impulsividad. No encontramos diferencias entre los distintos subtipos respecto al coeficiente intelectual (CI), rendimiento académico y utilización de recursos sanitarios. Una mayor gravedad de los síntomas del TDAH se asoció con una peor QoL.

Conclusiones. Los subtipos combinado e inatento se asociaron con mayor gravedad del trastorno, más trastornos psiquiátricos comorbidos y peor QoL que el subtipo con predominio de hiperactividad/impulsividad.

Palabras clave:
Trastorno por déficit de atención/hiperactividad. Subtipos. Impacto de enfermedad. Inatentos. Combinados.

INTRODUCTION

Attention-Deficit/Hyperactivity Disorder (ADHD) is the most common psychiatric childhood disorder and one of the most prevalent chronic health conditions affecting school-aged children. Prevalence estimates vary according to the diagnostic criteria and the population studied. Prevalence among school-aged children is estimated to be between 3% and 12%[1,2].

ADHD is frequently associated with the development of co-morbid psychiatric disorders, the most frequent being oppositional defiant and conduct disorders which could also influence its natural course and prognosis[3,4]. The disorder is also associated with broad impairment in several of the dimensions of Quality of Life (QoL), including academic performance, school behavior, peer relations, and family functioning[5,6].

The definition of the three DSM-IV ADHD subtypes in 1994 with predominance of inattentive deficit, hyperactive-impulsive, and combined inattentive/hyperactive-impulsive[7] was obtained from the debate on the defining features of ADHD, which has led to numerous revisions of the criteria for the disorder over the past 30 years. The DSM-IV field studies[8] and subsequent work in the community, including clinic-referred samples of persons[9-13] and nonreferred community samples[14-20] have consistently found that the different ADHD subtypes exhibit different patterns of impairment according to symptom dimensions.

Todd et al. (2002)[18] reported that the groups of individuals with ADHD subtype with predominance of attention deficit and combined subtype according to the DSM-IV criteria showed significant deficits in cognitive and achievement testing, worse grades, and increased use of special education resources compared with the primarily hyperactive-impulsive subtype and non-ADHD groups. Gadow et al. (2002)[15] found that subjects with the inattentive subtype were less academically proficient and socially adapted (although they were less likely to have behavior problems). Those subjects who had the combined subtype were the most behaviorally disruptive and those who were in the hyperactive/impulsive subtype also had problems with disruptive behavior, however, although they were less socially impaired. Graetz, Sawyer, Hazell, Arney, and Baghurst (2001)[17] reported more emotional and behavioral problems and lower psychosocial quality of life in all three ADHD subtypes compared with non-ADHD controls. Combined subtype rated more impaired than hyperactive-impulsive and inattentive subtypes on externalizing behavior problems, disruption to family activities, and symptom-specific impairments with schoolwork and peer-related activities. Those persons with predominance of inattentive subtype were rated as having lower self-esteem, more social and school-related problems, but fewer externalizing problems than those with predominance of the hyperactive-impulsive type.

Study objectives

The present study investigates several aspects of the disorder in order to assess the burden of illness of the different ADHD subtypes in a clinic-referred sample of untreated newly diagnosed children in Spain. The study design differs from previous ones because, in general, they include heterogeneous populations with newly diagnosed and previously diagnosed patients and the use of medication for ADHD, which represents a potential confounding factor regarding the burden of illness.

METHODS

This is a prospective, case-control study designed to evaluate the burden of illness in children with untreated newly diagnosed ADHD (case group) compared to two control groups (children with newly diagnosed asthma and healthy children). This paper reports the burden of illness exclusively in the different subtypes of children with ADHD.

Participants

One hundred and twenty four (124) children with ADHD were enrolled consecutively in 13 child and adolescent psychiatry or child neurology units in Spain from March 2003 to April 2004. Patients were eligible for the study if they were children and adolescents aged 6 to 12 years with untreated newly diagnosed DSM-IV ADHD, confirmed by the Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version

(K-SADS-PL)[21]. Since the study sample consisted of newly diagnosed patients, in order to assure the proper diagnosis of ADHD, a minimum severity score of 1.5 standard deviations above the norm for age and diagnostic subtype on the Attention Deficit/Hyperactivity Disorder-Rating Scale (ADHD-RS) was required[22]. Children with a history of bipolar I or II disorder, psychosis, mental retardation, previous or current serious medical conditions, comorbid asthma, or who had received pharmacological treatment for ADHD or asthma for more than 2 weeks prior to evaluation were excluded.

This study was approved by the Ethics Committee of each participating site and was conducted in accordance with the ethical principles of the Declaration of Helsinki and to Good Clinical Practice standards. After a full explanation of the study was given to each child and their parents or guardians, written informed consent was obtained from parents or guardians and assent was obtained from the child prior to their enrolment in the study.

Measures

Data collected included socio-demographic characteristics of the children and families, and clinical characteristics of the children, including: the ADHD Rating Scale (ADHD-RS) evaluated by the investigator, the Clinical Global Impression-Severity (CGI-S)[23] and the Conners' Parent Rating Scale-Revised: Short Form (CPRS-R:S)[24], which were also used to determine the disorder severity; the diagnostic interview K-SADS-PL to evaluate the presence of psychiatric comorbid disorders; and the Wechsler intelligence scale for children[25] to establish the Intelligence Quotient (IQ). In addition, parents rated their perception of the children's academic performance in comparison to their classmates using a 10 point Visual Analogical Scale (VAS). Health care resources utilization during the previous 6 months were obtained by a questionnaire about their visits to pediatrician, mental health services, emergency room, home assistance, hospitalizations, prescriptions, laboratory tests and accidents.

We used the 50-item parent version of the Child Health Questionnaire (CHQ-PF50)[6] to measure quality of life. This is a generic health status measure designed to record physical and psychosocial well-being of children ≥5 years of age. It assesses the child's physical and mental health and the mother's and father's perceptions of the extent to which problems in these areas interfere with peer and school activities, family activities, and the lives of mothers/fathers. The mothers/fathers were instructed to consider the 4-week period preceding the time when the questions on the questionnaire were answered. In accordance with the recommendations established in the Child Health Questionnaire (CHQ) manual, prior to the analysis of results, we transformed the raw score of each scale to a 0-100 scale, with higher scores indicating a better quality of life. Two summary scores (physical and psychosocial) were calculated. A physical or psychosocial summary score of 50 represents the mean for the general United States population. Ten points above/below reflects one Standard Deviation (SD) difference in either direction.

Data analysis

Summary statistics using number of observations, mean, Standard Deviation (SD), median, range and 95% confidence intervals were reported for quantitative variables, and absolute and relative frequencies for categorical variables. We analyzed comparisons among the three subtypes of ADHD using ANOVA for quantitative variables, and chi-square for categorical variables. We analyzed pairwise between-group comparisons using *t*-tests for quantitative variables and chi-square or Fisher tests for categorical variables. Duncan adjustment was applied in order to avoid chance significance when performing the different pairwise *t*-tests. Two-point differences in CHQ scores were considered «very small» differences, 5-point differences were «clinically and socially relevant»; 10-point differences were «moderate» and 20-point differences were considered to be «great» difference[6].

Pearson correlation coefficients were used to investigate the relationship between ADHD symptom severity as measured by the ADHD-RS and the following variables: QoL (CHQ physical and psychosocial summary scores, and scores for each domain subscale), academic performance and time from onset of symptoms to diagnosis, in the total population and also by ADHD subtype.

RESULTS

A total of 124 children with ADHD were included in the study: 80 (64.5%) presented the combined subtype, 25 (20.2%) had a predominance of attention deficit and 19 (15.3%) were predominantly hyperactive-impulsive.

The socio-demographic and clinical characteristics of the participants are summarized in tables 1 and 2. Mean ± SD age of the children was 9.1 ± 2 years, and 97 (78.2%) were male. We found no significant difference between the subtypes in socio-demographic characteristics. Mean ± SD time from onset of symptoms to diagnosis was 5.8 ± 2.3 years and no significant ($p = 0.8741$) differences among the different subtypes were observed. The ADHD-RS total score was significantly higher in the combined subtype than in the remaining two subtypes, and the ADHD Index of the CPRS-R:S was significantly lower in hyperactive patients. This indicates that the combined subtype was the most severe one, and the subtype with predominance of hyperactivity/impulsivity was the less severe subtype. Consistently with these results, the CGI score was higher in the combined subtype and lower in hyperactive patients, although no

Table 1 Socio-demographic characteristics of participants

	Combined (n=80)	Inattentive (n=25)	Hyperactive/impulsive (n=19)	Total (n=124)	p-value
Age (mean [SD])	9.0 (2.0)	9.7 (2.0)	8.6 (1.7)	9.1 (2.0)	0.1567**
Gender (n [%] of males)	63 (78.8)	19 (76.0)	15 (78.9)	97 (78.2)	0.9557***
Place of residence (n [%])					0.8683***
<10,000 inhab.	13 (16.3)	4 (16.0)	5 (26.3)	22 (17.7)	
10,000-100,000 inhab.	42 (52.5)	13 (52.0)	11 (57.9)	66 (53.2)	
>500,000 inhab.	25 (31.3)	8 (32.0)	3 (15.8)	36 (29.0)	
Educational level (n [%])					0.5978***
Kindergarten	2 (2.5)	–	1 (5.3)	3 (2.4)	
Elementary school	73 (91.2)	21 (84.0)	17 (89.5)	111 (89.5)	
Secondary school	5 (6.3)	4 (16.0)	1 (5.3)	10 (8.1)	
Family structure (n [%])					0.6225***
Both parents	64 (80.0)	20 (80.0)	17 (89.5)	101 (81.5)	
Other	16 (20.0)	5 (20.0)	2 (10.6)	23 (18.5)	
Occupational status of parents* (n [%])					0.3992***
Both parents unemployed	–	1 (4.0)	–	1 (0.8)	
One parent unemployed	3 (3.8)	1 (4.0)	1 (5.3)	5 (4.0)	

SD: standard deviation. *Homemakers are considered as employed. **Means analyzed using ANOVA. ***Frequencies analyzed using a chi-square test.

Table 2 Clinical characteristics of participants

	Combined (n=80)	Inattentive (n=25)	Hyperactive/impulsive (n=19)	Total (n=124)	p-value
Time from onset of symptoms to diagnosis					
Mean (SD)	5.9 (2.3)	5.7 (2.1)	5.7 (2.2)	5.8 (2.3)	0.8741*
Median (range)	5 (2–12)	6 (2–10)	5 (3–10)	5 (2–12)	
ADHD-RS total score (mean [SD])	39.3 (6.4)	34.7 (8.2)	34.1 (7.2)	37.6 (7.2)	0.0017*
	Pairwise t-tests: inattentive vs combined p=0.0050; hyperactive vs combined p=0.0051				
ADHD index of CPRS-R:S (mean [SD])	27.1 (4.4)	26.6 (4.5)	20.1 (6.8)	26.0 (5.4)	<0.0001*
	Pairwise t-tests: inattentive vs hyperactive p<0.0001; hyperactive vs combined p<0.0001				
CGI-S score (mean [SD])	4.5 (0.8)	4.4 (0.8)	4.0 (1.1)	4.4 (0.8)	0.0755*
Psychiatric comorbidities (K-SADS-PL) [n (%)]					
Behavioral disorders	30 (37.5)	7 (28.0)	1 (5.3)	34 (27.4)	0.0473**
		Pairwise t-tests: hyperactive vs combined p=0.0115			
Oppositional defiant disorder	26 (32.5)	7 (28.0)	1 (5.3)	34 (27.4)	0.0584**
Anxiety disorders	26 (32.5)	3 (12.0)	1 (5.3)	34 (27.4)	0.0873**
Affective disorders	3 (3.8)	–	–	3 (2.4)	0.6114**
Intelligence Quotient (IQ) (mean [SD])	102.1 (16.3)	103.9 (13.0)	97.3 (14.0)	101.7 (15.4)	0.3496*
Academic performance VAS (mean [SD])	3.9 (2.2)	3.5 (1.9)	4.3 (1.9)	3.9 (2.1)	0.4989*

SD: standard deviation; ADHD-RS: Attention-Deficit/Hyperactivity Disorder Rating Scale; CPRS-R:S: Conners' Parent Rating Scale-Revised: Short Form; CGI-S: Clinical Global Impression-Severity; K-SADS-PL: Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version; VAS: Visual Analogue Scale. *Means analyzed using ANOVA. ** Frequencies analyzed using a chi-square test.

significant differences were found. Almost one third of the patients had comorbid behavioral disorders. Oppositional defiant disorder was the most frequent psychiatric co-morbid condition (27.4% of patients). Children with combined ADHD had a higher rate of comorbid behavioral disorders than did both hyperactive and inattentive patients, but we only found significant differences between combined and hyperactive subtypes. One fourth of the patients had anxiety disorders. These disorders were more frequently present in the combined subtype, although no significant differences were found. Affective disorders were rare in this population of children with newly diagnosed ADHD. The father's/mother's perception of the children's academic performance in comparison to their classmates measured using a 10 point Visual Analogical Scale (VAS) was below average (table 2). We found no significant differences across the subtypes in the intelligence quotient or the academic performance.

Parent-reported scores on the CHQ are summarized in figure 1. The quality of life of children with combined ADHD was rated worse than that of hyperactive/impulsive patients for most of the domains. The greatest differences were found for role/social-physical limitations (mean difference [95% CI]: −20.05 [−33.04, −7.07]; p=0.0028) and family activities (−17.79 [−29.0, −6.55]; p=0.0022). These differences were considered to be clinically and socially relevant as they were outside the range −5 to 5 points[19]. Statistically significant differences were also seen for parent impact-time (−14.81 [−25.48, −4.15]; p=0.0069), parent impact-emotional (−13.32 [−22.5, −14.12]; p=0.0049), behavior (-12.01 [−20.21, −3.82]; p=0.0044), role/social limitations-emotional/behavioral limitations (−9.37 [−16.61, −2.14]; p=0.0116), and mental health (−9.68 [−16.23, −3.14]; p=0.0041). The psychosocial summary score was also significantly lower in patients with combined subtype compared to hyperactive patients (−6.78 [−10.48, −3.09]; p=0.0004).

The quality of life of patients with predominance of attention deficit (inattentive patients) was also rated worse than that of hyperactive patients for several domains. Inattentive patients showed significantly lower scores than hyperactive patients for parent impact-emotional (mean difference: −19.42 [−30.38, −8.46]; p=0.0006), role/social limitations-physical (mean difference: −15.93 [−31.42, −0.44]; p=0.0439) and parent impact-time (−15.74 [−28.46, −3.03]; p=0.0157). The difference for parent impact-emotional was clinically and socially relevant. The psychosocial summary score was also significantly lower in inattentive than in hyperactive patients (−6.00 [−10.40, −1.61]; p=0.0078). No differences in quality of life between inattentive and combined subtypes were detected.

The health care resources most frequently utilized by the patients during the previous 6 months were mental health services (82.5% of patients with the combined subtype, 88% of inattentive patients, and 78.9 of hyperactive patients) and pediatrics departments (68.6% of combined, 68% of inattentive, and 68.4% of hyperactive patients). More than half of the patients were prescribed at least one treatment during the previous 6 months (55% of combined, 40% of inattentive, and 52.6% of hyperactive patients) and about one third were subjected to complementary tests (33.9% of combined, 28% of inattentive and 42.1% of hyperactive patients). No differences among the different subtypes in regards to health care resource utilization were found.

Pearson correlation coefficients between ADHD symptom severity (ADHD-RS) and academic performance, duration of symptoms and quality of life (CHQ-PF50) are shown in table 3. In the combined subtype, higher ADHD symptom severity was associated with a poor QoL for the psychosocial summary score, and the domain subscales parent impact-time, behavior, general health perceptions and parent impact - emotional. Both in the hyperactive/impulsivity and the inattentive subtypes, greater ADHD symptom severity was associated with worse behavior and bodily pain/discomfort. All these associations between symptom severity and QoL were moderate, ranging from 19% to 50%. However, hyperactive/impulsive patients showed a moderately high association (50%) between greater symptom severity and better perception of their general health, the opposite to what we would have expected. In inattentive subtype, a longer time from the onset of symptoms to diagnosis of ADHD was associated with higher ADHD symptom severity at the time of diagnosis. No significant associations between ADHD symptom severity and academic performance were found.

CONCLUSIONS

Consistent with most of the clinic-based studies[9,10,15,22], the present study found that the combined subtype (64.5%) was more frequent than both the inattentive (20.2%) and hyperactive-impulsive (15.3%) subtypes. The consecutive enrolment of ADHD patients reflects the prevalence of the different subtypes in our sample.

Even though no significant differences were observed among subtypes in the mean time from onset of symptoms to diagnosis, both the total group as well as the different subtypes had almost a 6 year mean time from onset of symptoms to diagnosis. This represents a patent delay in the time to diagnosis and explains the important impact observed on each group. We found no significant differences among subtypes in gender and age in this study, although there was a trend toward a greater proportion of females and older subjects with the inattentive subtype, while hyperactive/impulsive patients tended to be younger, as reported in previous clinic-referred studies[9,13]. The DSM-IV field trials[8] reported similar results yet found significant differences. Our failure to find significant differences between groups may have been due to the small sample size of both inattentive and hyperactive/impulsive groups. Although previous studies have found greater social adversity among

combined subtypes[9,12], our study did not find differences between the groups.

Regarding quality of life, our results suggest than in many areas, the fathers and mothers of children with combined ADHD perceived that their children's health problems significantly interfere with the lives of the children, mothers and fathers and families, in a greater extent than in hyperactive-impulsive patients. The parents of inattentive patients also perceived greater interference in some of these areas compared to hyperactive-impulsive patients, especially in parent impact (emotional and time consuming), indicating that hyperactive-impulsive symptoms could be better tolerated and less frustrating according to the cultural context. We found no differences between inattentive and combined subtypes.

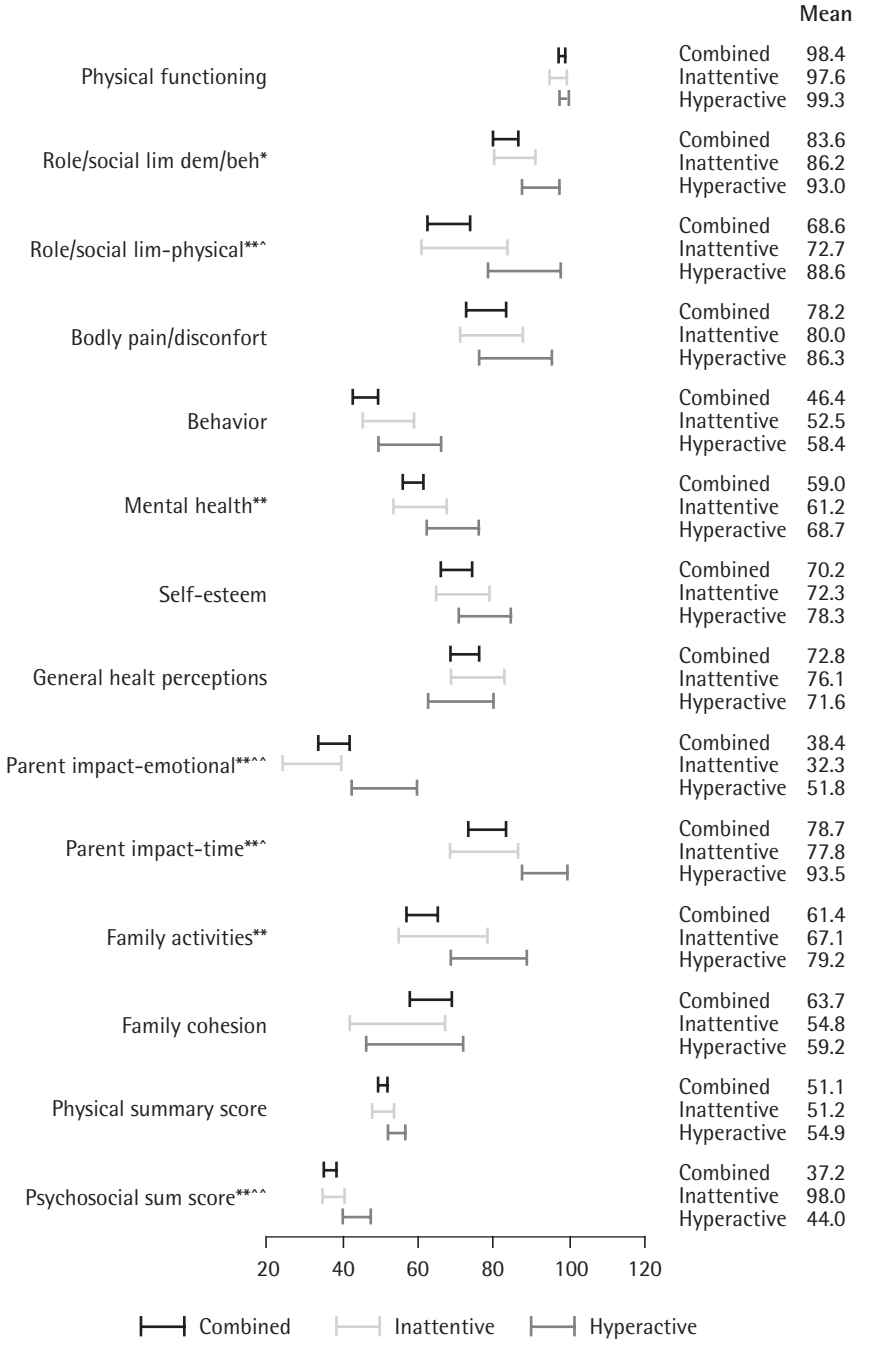

Figura 1 *95% confidence intervals for the mean scores on the Child Health Questionnaire (CHQ-PF50) of the different ADHD subtype. Lower scores indicate worse quality of life. Combined: N = 80; Inattentive: N = 25; Hyperactive: N = 19. Pairwise* t *tests: *hyperactive vs combined p < 0.05; **hyperactive vs combined p < 0.01; ^inattentive vs hyperactive p < 0.05; ^^inattentive vs hyperactive p < 0.01.*

Table 3 Correlation for each ADHD subtype between symptom severity (ADHD-RS) and academic performance, duration of symptoms and quality of life

	Subtipe			Total (n=124)
	Combined (n=80)	Inattentive (n=25)	Hyperactive/impulsive (n=19)	
Academic performance	–0.0745	0.0643	0.3730	0.0160
Time from onset of symptoms to diagnosis (years)	0.1269	0.4444*	0.4460	0.2460*
CHQ-PF50				
Physical summary score	–0.1538	–0.3341	0.2385	–0.1884*
Physical functioning	0.0954	0.0682	0.2904	0.1091
Role/social limitations-physical	–0.1663	–0.2782	0.0893	–0.2142*
Bodily pain/discomfort	–0.1186	–0.4073*	–0.4937*	–0.2560*
General health perceptions	–0.2719*	–0.1813	0.5044*	–0.1264
Psychosocial summary score	–0.3349*	–0.1392	–0.0006	–0.2776*
Role/social limitations-emotional/behavioral	–0.0152	–0.1554	0.0532	–0.0943
Behavior	–0.2983*	–0.4497*	–0.5027*	–0.4151*
Mental health	–0.1385	–0.0853	–0.0743	–0.1662
Self–esteem	–0.1991	0.0740	–0.0723	–0.1466
Parent impact-emotional	–0.2441*	–0.1580	0.3150	–0.1469
Parent impact-time	–0.3441*	0.1612	0.4359	–0.1758

* Pearson correlation is significant at the 0.05 level. Positive correlation indicates that both variables increase or decrease together, whereas negative correlation indicates that as one variable increases, so the other decreases, and vice versa. Academic performance measured using a 10 point Visual Analogical Scale (VAS).

Patients with the combined subtype were more limited in school work or activities with friends as a result of physical problems and limited family activities compared to hyperactive-impulsive patients. These differences were clinically and socially relevant. They also caused more limitations in parent's personal time, more parent emotional stress and worry as a result of their child's health. They had more behavioral problems and were more limited in school work or other daily activities as a result of emotional or behavioral problems than were hyperactive patients. As a result, patients with the combined subtype had worse psychosocial functioning compared to hyperactive-impulsive patients. Inattentive patients caused more emotional stress and worry for the parents as a result of their children's health (a clinically and socially relevant difference), were more limited in school work or activities with friends due to physical problems, and caused more limitations on their parents' personal time than did hyperactive patients. Therefore, they had worse psychosocial functioning compared to hyperactive-impulsive patients.

The overall pattern of impairment found for the ADHD subtypes in the present study is similar to that reported in previous studies[8,14,15,17,18,20]. In general, ADHD subtypes with higher levels of inattention (combined and inattentive) exhibit greater social and school-related impairments, whereas the subtypes high in hyperactivity-impulsivity (combined and hyperactive) display more externalizing behavioral problems. However, some studies observed a trend for greater behavioral problems among combined subtypes[14,20], as did our study. The main difference between the present study and other ones is the lack of differences between the combined and inattentive subtypes, in contrast to the results reported by Graetz, Sawyer, Hazell, Arney and Baghurst[17]. They found significantly more emotional problems, behavioral problems, limitations in school work or other daily activities as a result of emotional or behavioral problems, limitations in father's and mother's personal time and limitations in family activities in the combined subtype than in inattentive patients. Our failure to find significant differences between the combined and inattentive subtypes may have been due to the small sample size of the inattentive group. Studies evaluating nonreferred community samples[8,14,17,20] show consistently higher proportions of the inattentive subtype.

The combined subtype appeared to be the most severe one, according to ADHD-RS scores and the CPRS-R:S, and the hyperactive/impulsive subtype seemed to be the mildest. A priori we could think that hyperactivity-impulsivity symptoms would be more obvious and hyperactive subtype patients would be diagnosed earlier. However, we found no significant differences among the subtypes for the time from onset of symptoms to diagnosis. Children with com-

bined ADHD had a higher rate of comorbid behavioral disorders than did hyperactive-impulsive patients. This finding is consistent with previous studies that reported higher rates of behavioral disorders in the combined subtype than in hyperactive patients[14,20]. However, these studies also found much lower rates of these disorders in inattentive patients compared to both combined and hyperactive subtypes that were not observed in our study, maybe due to the small sample size of the inattentive group.

As in the study performed by Klassen, Miller, and Fine[26], higher ADHD symptom severity was associated with poor QoL. Children with ADHD in our study showed an association between higher symptom severity and more behavioral problems, more bodily pain or discomfort, and more limitations in school work or activities with friends as a result of physical problems. In patients with the combined subtype, higher symptom severity was associated with more limitations on parent's personal time, more behavioral problems, a worst perception of general health, and more parents' emotional stress or worry as a result of their children's health. In both hyperactive and inattentive patients, greater ADHD symptom severity was associated with worst behavior and more bodily pain or discomfort in these patients. However, the association between greater symptom severity and better perception of their general health found in hyperactive patients is the opposite to what we would have expected.

As in previous studies[8,14,15,18,20], hyperactive/impulsive patients exhibited higher levels of academic performance than the other subtypes, although our study did not find significant differences. We found no differences among the subtypes in regards to IQ.

Children with ADHD had a substantial utilization of primary care, mental health and pharmacy services. We found no differences among the subtypes regarding the health care resources utilization in this study.

Limitations

The most important limitation of this study is that it mostly relied on information obtained from the mothers and fathers rather than from the patients themselves. It is possible that the children's perception of their health may have differed from that of their parents. There is evidence suggesting a difference in parents' and children's perceptions of child quality of life[27,28]. However, in the pediatric population, parent proxy tools are generally accepted as being a reliable measure of child health status. It may also be possible that parents may have incorrectly attributed their children's worse quality of life to the disease when, in fact, the impairment was caused by other factors. In this way, certain socio-demographic characteristics or comorbid conditions might be associated with worse functioning. However, the results presented here describe the parents' perception of the impact of ADHD. This may be considered as a key element to the physical, psychological and social functioning of children suffering from ADHD and their families.

Another important limitation is the difference between the sample sizes of the different subtypes. The reduced number of patients in the inattentive and hyperactive-impulsive subtypes may have resulted in lack of power in comparisons between groups. Although the present study does not represent the epidemiology of ADHD in Spain, as ADHD patients were enrolled consecutively, the proportions of the different subtypes found in this study represent the proportions present in a clinic-based population in Spain, and are consistent with the results of most epidemiological studies performed in clinic-based samples[9,10,16,22]. This is the first time that a clinic-based sample of newly diagnosed children who have not received any medication for ADHD is analyzed. The results are, therefore, very interesting and should be replicated in a sample with more homogeneous sizes of the different subtypes.

Clinical implications

The most relevant findings of this study are that in patients with newly diagnosed ADHD in Spain the combined subtype of ADHD, and the inattentive subtype to a lesser extent, are associated with a greater severity of the disorder, more comorbid psychiatric conditions, and a higher worse quality of life than the hyperactive-impulsive subtype. However, the mean time from onset of symptoms to diagnosis of 5.8 ± 2.3 years suggests that there is a lot of room for improvement in regards to earlier identification of children with ADHD in Spain. This diagnostic delay was present even though 83% of patients had visited mental health services and 75% had visited pediatricians. Therefore, parents consulted for their children's problems but it was not detected early enough. These results confirm the differences between ADHD subtypes reported by previous studies in other cultures and validate the clinical relevance of DSM-IV classification.

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REFERENCES

1. Szatmari P. The epidemiology of attention deficit hyperactivity disorder. Child Adolesc Psychiatr Clin North Am 1992;1:361-71.
2. Brown RT, Freeman WS, Perrin JM, Stein MT, Amler RW, Feldman HM, et al. Prevalence and assessment of attention deficit/hyperactivity disorder in primary care settings. Pediatrics 2001;107:E43.
3. Cantwell DP. Attention deficit disorder: a review of the past 10 years. J Am Acad Child Adolesc Psychiatry 1996;35:978-87.
4. Burns GL, Walsh JA, Owen SM, Snell J. Internal validity of attention deficit hyperactivity disorder, oppositional defiant disorder and overt conduct disorder symptoms in young children: implications from teacher ratings for a dimensional approach to symptom validity. J Clin Child Psychol 1997; 26:266-75.
5. Landgraf JM, Abetz L. Functional status and well-being of children representing three cultural groups: initial self-reports using the CHQ-CF87. Psychol Health 1997;12:839-54.
6. Landgraf JM, Abetz L, Ware JE. The Child Health Questionnaire (CHQ): a user's manual. Boston: Health Institute, New England Medical Center, 1996.
7. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. Washington: American Psychiatric Association, 2000.
8. Lahey BB, Applegate B, McBurnett K, Biederman J, Greenhill L, Hynd GW, et al. DSM-IV field trials for attention deficit hyperactivity disorder in children and adolescents. Am J Psychiatry 1994;151:1673-85.
9. Eiraldi RB, Power TJ, Nezu CM. Patterns of comorbidity associated with subtypes of attention-deficit/hyperactivity disorder among 6 to 12 year-old children. J Am Acad Child Adolesc Psychiatry 1997;36:503-14.
10. Faraone SV, Biederman J, Weber W, Russell RL. Psychiatric, neuropsychological, and psychosocial features of DSM-IV subtypes of attention deficit/hyperactivity disorder: results from a clinically referred sample. J Am Acad Child Adolesc Psychiatry 1998; 37:185-93.
11. Lalonde J, Turgay A, Hudson JI. Attention-deficit hyperactivity disorder subtypes and comorbid disruptive behaviour disorders in a child and adolescent mental health clinic. Canad J Psychiatry 1998;43:623-8.
12. McBurnett K, Pfiffner LJ, Willcutt E, Tamm L, Lerner M, Ottolini YL, et al. Experimental cross-validation of DSM-IV types of attention-deficit/hyperactivity disorder. J Am Acad Child Adolesc Psychiatry 1999;38:17-24.
13. Morgan AE, Hynd GW, Riccio CA, Hall J. Validity of DSM-IV ADHD predominantly inattentive and combined types: relationship to previous DSM diagnoses/subtype differences. J Am Acad Child Adolesc Psychiatry 1996;35: 325-33.
14. Baumgaertel A, Wolraich ML, Dietrich M. Comparison of diagnostic criteria for attention deficit disorders in a German elementary school sample. J Am Acad Child Adolesc Psychiatry 1995;34:629-38.
15. Gadow KD, Nolan EE, Litcher L, Carlson GA, Panina N, Golovakha E, et al. Comparison of attention deficit/hyperactivity disorder symptom subtypes in Ukrainian schoolchildren. J Am Acad Child and Adolesc Psychiatry 2000;39: 1520-7.
16. Gaub M, Carlson CL. Behavioral characteristics of DSM-IV ADHD subtypes in a school-based population. J Abnorm Child Psychol 1997;25:103-11.
17. Graetz BW, Sawyer MG, Hazell PL, Arney F, Baghurst P. Validity of DSM-IV ADHD subtypes in a nationally representative sample of Australian children and adolescents. J Am Acad Child Adolesc Psychiatry 2001;40:1410-7.
18. Todd RD, Sitdhiraksa N, Reich W, Ji TH, Joyner CA, Heath AC, et al. Discrimination of DSM-IV and latent class attention-deficit/hyperactivity disorder subtypes by educational and cognitive performance in a population-based sample of child and adolescent twins. J Am Acad Child Adolesc Psychiatry 2002;41: 820-8.
19. Willcutt EG, Pennington BF, Chhabildas NA, Friedman MC, Alexander J. Psychiatric comorbidity associated with DSM-IV ADHD in a nonreferred sample of twins. J Am Acad Child Adolesc Psychiatry 1999;38:1355-62.
20. Wolraich ML, Hannah JN, Pinnock TY, Baumgaertel A, Brown J. Comparison of diagnostic criteria for attention-deficit hyperactivity disorder in a county-wide sample. J Am Acad Child Adolesc Psychiatry 1996;35:319-24.
21. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, et al. Schedule for affective disorders and schizophrenia for school-age children-present and lifetime version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 1997;36:980-8.
22. Du Paul GJ, Anastopoulos AD, Power TJ, Reid R, Ikeda MJ, Mcgoey KE. Parent ratings of attention-deficit/hyperactivity disorder symptoms: factor structure and normative data. J Psychopathol Behav Assess 1983;20:83-102.
23. National Institutes of Mental Health. Rating scales and assessment instruments for use in pediatric psychopharmacology research. Psychopharmacol Bull 1985;21:714-1124.
24. Conners CK. Conners' rating scales-revised, technical manual. Toronto: Multi-Health Systems, Inc, 1997.
25. Wechsler D. Wechsler Intelligence Scale for Children, 3rd ed. San Antonio: The Psychological Corporation, 1991.
26. Klassen AF, Miller A, Fine S. Health-related quality of life in children and adolescents who have a diagnosis of attention-deficit/hyperactivity disorder. Pediatrics 2004;114:e541-7.

27. Achenbach TM, McConaughy SH, Howell CT. Child/adolescent behavioral and emotional problems: implications of cross-informant correlations for situational specificity. Psycholog Bull 1987;101:213-32.

28. Sawyer M, Antoniou G, Toogood I, Rice M. A comparison of parent and adolescent reports describing the health-related quality of life of adolescents treated for cancer. Internat J Cancer 1999(Suppl. 12):39-45.