Journal of Psychiatric Research 172 (2024) 1–8

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/jpsychires

Early-onset obsessive-compulsive disorder: Sociodemographic and clinical characterization of a large outpatient cohort

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ARTICLE INFO

Keywords:
Obsessive-compulsive disorder
Early onset
OCD subtypes
Age at onset

ABSTRACT

Introduction: Obsessive-compulsive disorder (OCD) is a prevalent and disabling condition characterized by a wide variety of phenotypic expressions. Several studies have reinforced the hypothesis of OCD heterogeneity by proposing subtypes based on predominant symptomatology, course, and comorbidities. Early-onset OCD (EO) could be considered a neurodevelopmental subtype of OCD, with evidence of distinct neurocircuits supporting disease progression. To deepen the heterogeneous nature of the disorder, we analyzed sociodemographic and clinical differences between the EO and late-onset (LO) subtypes in a large outpatient cohort.

Methods: Two hundred and eighty-four patients diagnosed with OCD were consecutively recruited from the OCD Tertiary Clinic at Luigi Sacco University Hospital in Milan. Sociodemographic and clinical variables were analyzed for the entire sample and compared between the two subgroups (EO, age <18 years [n = 117,41.2 %]; LO: late-onset, age ≥18 years [n = 167, 58.8 %]).

Results: The EO group showed a higher frequency of male gender (65 % vs 42.5 %, $p < .001$), and a higher prevalence of Tic and Tourette disorders (9.4 % vs 0 %, $p < .001$) compared to the LO group. Additionally, in the EO subgroup, a longer duration of untreated illness was observed (9.01 ± 9.88 vs 4.81 ± 7.12; $p < .001$), along with a lower presence of insight (13.8 % vs. 7.5 %, $p < .05$).

Conclusions: The early-onset OCD subtype highlights a more severe clinical profile compared to the LO group. Exploring distinct manifestations and developmental trajectories of OCD can contribute to a better definition of homogeneous subtypes, useful for defining targeted therapeutic strategies for treatment.

1. Introduction

Obsessive-compulsive disorder (OCD) is a complex and disabling condition with a frequent chronic course, often presenting in comorbidity with other psychiatric disorders (Hofmeijer-Sevink et al., 2013; Lochner et al., 2014). The lifetime prevalence is around 2.5 % in the general population, with equal gender distribution, except for the higher rates in males shown during childhood and in females during adulthood (Mathes et al., 2019; Benatti et al., 2020). Characterized by recurrent obsessive thoughts and compulsive behaviors, OCD can significantly impact patients' quality of life, affecting their social and occupational functioning (Hollander et al., 2010).

According to available international guidelines, the first-line treatment (i.e., SSRI) for OCD consists of pharmacotherapy and cognitive-behavioral treatment; however, up to 50–60 % of patients do not respond or only partially respond to first-line treatments (Skapinakis et al., 2016; Thamby and Jaisoorya, 2019), and this may be related to the extreme heterogeneity of the disorder.

To date, several useful subtyping methods have been proposed to identify more homogeneous OCD subgroups to understand the complexities of the disorder (Leckman et al., 2010), and evidence suggested that age of onset could represent an important subtyping scheme for reliably distinguishing OCD populations (Taylor, 2011; Dell'Osso et al., 2016).

Research in the field reported that OCD has a bimodal age at onset; one peak in childhood (9–11 years), and one peak in adulthood (Delorme et al., 2005; de Mathis et al., 2013). Though there has been a debate about what should be the cutoff for defining early onset OCD

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https://doi.org/10.1016/j.jpsychires.2024.02.009
Received 30 November 2023; Received in revised form 16 January 2024; Accepted 1 February 2024
Available online 2 February 2024
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(EO; Taylor, 2011), a cutoff of 18 years looks promising and has been utilized in previous studies (Butwicka and Gmitrowicz, 2010; Katerberg et al., 2010; Kichuk et al., 2013).

EO patients are reliably differentiated from those with late-onset (LO) in terms of multiple etiologic and phenotypic factors, showing a higher prevalence in males (Stewart et al., 2004; Torresan et al., 2013), higher levels of genetic heritability (Bolton et al., 2007; Narayanaswamy et al., 2012), higher comorbidity rates with other neurodevelopmental diseases such as tics and Tourette's syndrome (De Mathis et al., 2008; Janowitz et al., 2009; Taylor, 2011), poorer treatment responses (Ravi Kishore et al., 2004; Van Roessel et al., 2023), and a higher overall OCD severity scores (Taylor, 2011; Anholt et al., 2014).

Regarding treatment, EO patients require therapy regimens with multiple drugs compared to LO OCD patients (Fontenelle et al., 2003), who often respond favorably to treatment (Erzegovesi et al., 2001), with evidence of short-term therapeutic responses to clomipramine and selective serotonin reuptake inhibitors (Rosario-Campos et al., 2001). Furthermore, the prognosis of EO patients turned out to be more unfavorable than LO patients (Jakubovski et al., 2013).

In addition to these clinical features, recent neurobiological differences have also been evidenced in subtypes of OCD based on onset age (Boedhoe et al., 2017; Kim et al., 2020; Jurng et al., 2021), suggesting distinct pathophysiological mechanisms in early- and late-onset OCD groups. In particular, a study by Park et al. (2023) showed that OCD patients with EO had significantly greater cortical gyrification than those with LO in frontoparietal and cingulate regions. Moreover in another study, a lower regional cerebral blood flow in the left anterior cingulate cortex and in the right thalamus was found in the EO group compared to LO OCD (Busatto et al., 2001).

From this perspective, EO might be considered a neurodevelopmental subtype of OCD, suggesting that distinct neurocircuit pathways underlie the disorder's progression (Burchi and Pallanti, 2019), therefore distinguishing features between EO and LO for early diagnosis, the development of targeted interventions, and personalized treatment strategies for individuals remains crucial.

In this context, given the conflicting literature regarding the existence of an OCD subtype associated with the age of onset, the aim of the present study was to explore potential differences from sociodemographic, clinical, and pharmacological perspectives among adult patients with EO and LO in a large outpatient cohort from an OCD tertiary clinic.

2. Method

Two hundred and eighty-four patients with a DSM-5 primary diagnosis of OCD of any age and gender were consecutively recruited at the OCD tertiary clinic, ASST Fatebenefratelli Sacco, Milano, Italy from January 2021 to October 2023. Recruited patients belonged to the group of consecutive OCD patients attending the clinic during the overmentioned period and willing to participate in the study. Exclusion criteria were: individuals below 18 years or above 70 years of age; significant cognitive impairment or intellectual disabilities; inability to provide informed consent for the study participation.

Diagnoses were obtained through the administration of a clinically structured interview based on DSM-5 criteria (APA, 2013).

Patients were assessed on the following dimensions: (a) patient's main socio-demographic features (i.e., age, gender, occupation, years of education, and marital status); (b) clinical history (i.e., age at OCD onset, duration of illness, duration of untreated illness (DUI), age at first psychopharmacological treatment, positive psychiatric family history and type, presence of current psychiatric comorbidities and types, presence of at least one significant trait of co-occurring obsessive-compulsive personality disorder (OCPD), current substance use, obsession and compulsion phenotypes, suicide ideation and attempts lifetime; (c) psychometric assessment using the Structured clinical interview for DSM-5 disorders: clinician version (SCID-5-CV; First et al., 2015), the Structured clinical interview for DSM-5 personality disorders (SCID-5-PD; First et al., 2016), Yale-Brown Obsessive-Compulsive Scale (YBOCS; Goodman et al., 1989a; Goodman et al.,1989b), Clinical Global Impression-Severity (CGI-S; Guy, 1976), and Barratt Impulsiveness Scale (BIS-11; Patton et al., 1995); (d) pharmacological treatment (i.e., psychopharmacological therapy at the time of study inclusion and the first treatment). Additionally, the clinical variable "insight" was assessed using item 11 of Y-BOCS, where scores >2 indicated poor insight and scores ≤2 indicated good insight (Goodman et al., 1989).

Socio-demographic and clinical variables were collected for the whole sample and subsequently compared for the subgroups examined. For the purpose of the study, the whole sample was categorized into two groups with EO (<18 years) and LO (≥18 years), and their socio-demographic and clinical features were compared. Statistical analyses were performed with Pearson's chi-squared test for categorical variables and One-way ANOVA test for continuous variables. A Bonferroni-Holm procedure was used in the comparative analysis to reduce the risk of type 1 error due to the large number of tests analyzed. Next, the bivariate correlation between continuous variables of the study was estimated using Pearson's correlation for the whole sample. All analyses were performed using Statistical Package for the Social Sciences (SPSS) 26.0 software for Windows (SPSS Inc, Chicago, IL, USA). Statistical significance was set at $p < .05$.

The study was conducted in accordance with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008 (PMC2566407). Patients provided their written informed consent to participate in this study and for the use of their anonymized data for research purposes. No patients declined to share their data or refused participation in the study.

3. Results

The sample included 284 OCD outpatients recruited from the OCD Tertiary Clinic, ASST Fatebenefratelli Sacco, University Hospital, Milan. The whole sample showed a male rate of 51.8 % and a mean age of 39.38 ± 14.23 years. The mean years of education were 13.29 ± 2.87; half of the sample was employed, and 33.3 % was married. In terms of clinical features, the mean age at OCD onset was 22.29 ± 11.16 years, with a mean duration of illness and duration of untreated illness (DUI) of 16.74 ± 12.99 and 6.57 ± 8.61 years, respectively. The mean age at first psychopharmacological treatment was 28.82 ± 12.52 years. Additionally, the whole sample had a mean Y-BOCS score of 24.6 ± 7.33, 4.54 ± 1.19 on the CGI-S, and 63.63 ± 8.28 on the BIS-11. The main socio-demographic and clinical variables of the sample are reported in Table 1. All reported variables had a percentage of missing data ranging from 0 % to 14 %.

For the purpose of the study, the whole sample was first categorized into two OCD groups with EO and LO, and their socio-demographic and clinical features were subsequently compared. Specifically, 41.2 % of patients were classified as EO (n = 117), while 58.8 % were classified as LO (n = 167).

The EO group showed a significantly higher male proportion (65 % vs. 42.5 %; $p < .001$, see Fig. 1), a longer duration of untreated illness (9.04 ± 9.88 years vs. 4.81 ± 7.12 years, $p < .001$), and a lower mean age at first psychopharmacological treatment (22.71 ± 10.7 years vs 33.07 ± 11.95 years; $p < .001$; see Fig. 2) when compared to LO patients. Furthermore, in the EO group, lower rates of engagement or marital status (20.3 % vs. 42.5 %; $p < .05$) and employment status (35.6 % vs. 59.8 %; $p < .05$) were found.

In relation to lifetime comorbidities, a significant difference emerged; EO patients reported a higher prevalence of Tic and Tourette disorders before the onset of OCD compared to the LO group (9.4 % vs 0 %, $p < .05$). Conversely, the LO group reported a significantly higher prevalence of Anxiety disorders (15.6 % vs 6.8 %; $p < .05$).

Regarding psychiatric comorbidities that occurred post-OCD onset,

Table 1
Comparison of sociodemographic and clinical features between early and late-onset groups.

	Early onset OCD n = 117 (41.2 %)	Late onset OCD n = 167 (58.8 %)	Total sample n = 284
Gender (m; f)	**76(65 %); 41 (35 %)****	**71(42.5 %); 96 (57.5 %)**	147(51.8 %); 137 (48.2 %)
Age (years; mean ± ds; min-max)	**35.4 ± 14.4***	**42.07 ± 13.53**	39.38 ± 14.23; (18–69)
Years of education (mean ± ds)	13.18 ± 2.78	13.37 ± 2.93	13.29 ± 2.87 8
Marital status (f, %)			
Engaged/Married (y/n)	**12(20.3 %); 47(79.7 %)***	**37(42.5 %); 50 (57.5 %)**	49 (33.6 %); 97 (66.4 %)
Age at OCD onset (years; mean ± ds; min-max)	**13.40 ± 3.37****	**28.52 ± 10.48**	22.29 ± 11.16; (5–62)
Age at first psychopharmacological treatment (years; mean ± ds)	**22.71 ± 10.7****	**33.07 ± 11.95**	28.82 ± 12.52
Duration of illness (years, mean ± ds)	**20.27 ± 13.98****	**14.24 ± 11.66**	16.74 ± 12.99
Duration of untreated illness (DUI; years, mean ± ds)	**9.04 ± 9.88****	**4.81 ± 7.12**	6.57 ± 8.61
Professional status (f, %)			
Worker	**21(35.6 %)***	**52(59.8 %)**	73(50 %)
Unemployed	22(37.3 %)	20(23 %)	42 (28.8 %)
Student	**13(22 %)***	**7(8 %)**	20(13.7 %)
Retired	3(5.1 %)	8(9.2 %)	11 (7.5 %)
Current Medical Comorbidity (y/n, f, %)	6(15 %); 34 (85 %)	15(28.3 %); 38(71.7 %)	21(22.6 %); 72 (77.4 %)
Psychiatric Comorbidity (y/n)	84(73 %); 31 (27 %)	103(62.8 %); 61(37.2 %)	187(67 %); 92(33 %)
Psychiatric Comorbidity pre-OCD onset (f, %)			
None	75(64.1 %)	97(58.1 %)	172(60.6 %)
Unipolar depression	5(4.3 %)	18(10.8 %)	23(8.1 %)
Bipolar disorder	3(2.6 %)	8(4.8 %)	11(3.9 %)
Anxiety disorders	**8(6.8 %)****	**26(15.6 %)**	34(12 %)
Psychotic disorders	1(0.9 %)	2(1.2 %)	3(1.1 %)
ICDs	2(1.8 %)	1(0.6 %)	3(1.1 %)
Eating disorders	4(3.4 %)	7(4.2 %)	11(3.9 %)
ADHD	2(1.7 %)	0(0 %)	2(0.7 %)
Tic and Tourette disorders	**11(9.4 %)****	**0(0 %)**	11(3.9 %)
Personality disorders	1(0.9 %)	4(2.4 %)	5 (1.8 %)
Polycomorbidities	5(4.3 %)	4(2.4 %)	9 (3.2 %)
Psychiatric Comorbidity post OCD onset (f, %)			
None	**37(32.2 %)***	**80(49.1 %)**	117(41.1 %)
Unipolar depression	31(27 %)	36(22.1 %)	67(24.1 %)
Bipolar disorder	13(11.3 %)	13(8 %)	26(9.4 %)
Anxiety disorders	9(7.8 %)	20(12.3 %)	29(10.4 %)
Psychotic disorders	2(1.7 %)	2(1.2 %)	4 (1.4 %)
ICDs	**3(2.6 %)***	**0(0 %)**	3 (1.1 %)
Eating disorders	2(1.7 %)	3(1.8 %)	5 (1.8 %)
ADHD	0(0 %)	1(0.6 %)	1 (0.4 %)
Tic and Tourette Disorders	**8(7 %)***	**1(0.6 %)**	9 (3.2 %)
Personality disorders	1(0.9 %)	2(1.2 %)	3 (1.1 %)
Polycomorbidities	9(7.8 %)	5(3.1 %)	14(5 %)
Positive family history (y/n, f, %)	70(61.4 %); 44(38.6 %)	102(63.7 %); 58(36.3 %)	172(62.8 %); 102 (37.2 %)
Type of family history (f, %)			
None	44(38.6 %)	57(35.6 %)	101(36.9 %)
Mood disorders	38(33.3 %)	55(34.4 %)	93(33.9 %)
Anxiety disorders	10(8.8 %)	25(15.6 %)	35(12.9 %)
Psychotic disorders	3(2.6 %)	6(3.8 %)	9(3.3 %)
ICDs	1(0.9 %)	1(0.6 %)	2 (0.7 %)
Eating disorders	1(0.9 %)	1(0.6 %)	2 (0.7 %)
Substance abuse	0(0 %)	1(0.6 %)	1 (0.4 %)
OCD spectrum	16(14 %)	12(7.5 %)	28(10.2 %)
Personality disorders	1(0.4 %)	2(1.3 %)	3(1.1 %)
Presence of OCPD traits (f, %)	22(44.9 %)	27(55.1 %)	49(19.4 %)
Current substance abuse (y/n, f, %)	7(12 %); 51 (88 %)	5(5.3 %); 89 (94.7 %)	12(7.9 %); 140(92.1 %)
Stress event lifetime (y/n, f, %)	9(33.3 %); 18 (66.7 %)	17(51.5 %); 16(48.5 %)	26(43.3 %); 34(56.7 %)
Suicide ideation lifetime (y/n, f, %)	5(29.4 %); 12 (70.6 %)	9(29 %); 22 (71 %)	14(29.2 %); 34(70.8 %)
Suicide attempts lifetime (y/n, f, %)	3(6.8 %); 41 (93.2 %)	3(5 %); 57 (95 %)	6(5.8 %); 98(94.2 %)
Obsession Phenotypes (f, %)			
Hoarding	0(0 %)	3(1.8 %)	3(1.1)
Pathological Doubt	18(15.4 %)	32(19.2 %)	50(17.6 %)
Symmetry	4(3.4 %)	4(2.4 %)	8(2.8 %)
Violence/Harm	11(9.4 %)	15(9 %)	26(9.2 %)
Sexual/Religion	7(6 %)	9(5.4 %)	16(5.6 %)
Somatic	5(4.3 %)	7(4.2 %)	12(4.2 %)
Contamination/Hygiene	19(16.2 %)	41(24.6 %)	60(21.1 %)
More phenotype	47(40.2 %)	45(26.9 %)	92(32.4 %)
Magical Thinking	3(2.6 %)	1(0.6 %)	4(1.4 %)
Other	3(2.6 %)	9(5.4 %)	12(4.2 %)
Compulsion Phenotypes (f, %)			
Washing and Cleaning	20(17.2 %)	36(22.6 %)	56(20.4 %)
Arranging	4(3.4 %)	10(6.3 %)	14(5.1 %)
Hoarding	1(0.9 %)	2(1.3 %)	3(1.1 %)
Counting	3(2.6 %)	0(0 %)	3 (1.1 %)
Repeating	9(7.8 %)	5(3.1 %)	14(5.1 %)
Avoidance	7(6 %)	14(8.8 %)	21 (7.6 %)
Checking	17(14.7 %)	33(20.8 %)	50(18.2 %)
More phenotypes	45(38.8 %)	48(30.2 %)	93(33.8 %)
other	9(7.8 %)	9(5.7 %)	18(6.5 %)
Presence of Insight (f; %)			
Good insight	100(86.2 %)	149(92.5 %)	249(89.9 %)
Poor insight	**16(13.8 %)***	**12(7.5 %)**	28(10.1 %)
Y-BOCS total scores	25.47 ± 7.17	23.98 ± 7.39	24.6 ± 7.33
Mild (9–15)	10(8.5 %)	23(14 %)	33(11.7 %)
Moderate (16–23)	24(20.5 %)	47(28.7 %)	71(25.3 %)
Severe (24–32)	66(56.4 %)	76(46.3 %)	142(50.5 %)
Extreme (33–40)	17(14.5 %)	18(11 %)	35(12.5 %)
CGI-S (mean ± ds)	4.68 ± 1.07	4.45 ± 1.26	4.54 ± 1.19
BIS-11 (total score, (mean ± ds)	62.38 ± 8.28	64.25 ± 8.67	63.63 ± 8.28

Notes: Values for categorical and continuous variables are expressed in percentages and mean ± SD, respectively. EO: age at OCD onset <18 years; LO: age at OCD onset ≥18; More phenotypes: presence of more than one obsession or compulsion phenotype; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale; CGI-S: Clinical Global Impression - severity; BIS-11: Barratt Impulsiveness Scale. Reported variables had a percentage of missing data ranging from 0 % to 14 %. Boldface indicates parameters with statistically significant differences between subgroups; **p < .001 *p < .05.

EO OCD patients showed higher rates of Impulse-Control Disorders (ICD) and Tic and Tourette disorders (2.6 % vs. 0 %; 7 % vs. 0.6 %; $p < .05$, respectively). Furthermore, a significantly higher proportion of LO OCD patients reported no psychiatric comorbidities following the onset of OCD compared to the EO group (49.1 % vs. 32.2 %; $p < .05$). No significant differences emerged in the psychometrics assessment for CGI-S (EO: 4.68 ± 1.07 vs. LO: 4.45 ± 1.26), BIS-11 (EO: 62.38 ± 8.28 vs. LO: 64.25 ± 8.67), and YBOCS score between groups (25.47 ± 7.17 vs. 23.98 ± 7.39).

Pearson's correlations showed that age at onset negatively correlated with DUI ($r = -0.262$, $p < .001$). A positive correlation was found between YBOCS scores and CGI-S ($r = 0.677$, $p < .001$; see Table 2).

As regards pharmacological treatment and potential differences

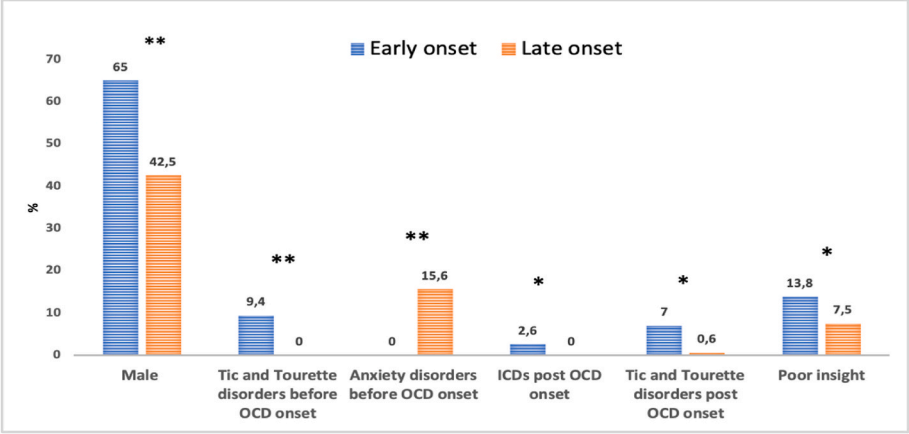

Fig. 1. Clinical characteristics between early versus late OCD onset.
Notes: OCD: Obsessive-compulsive disorder; ICDs: impulse control disorders. **p < .001 *p < .05.

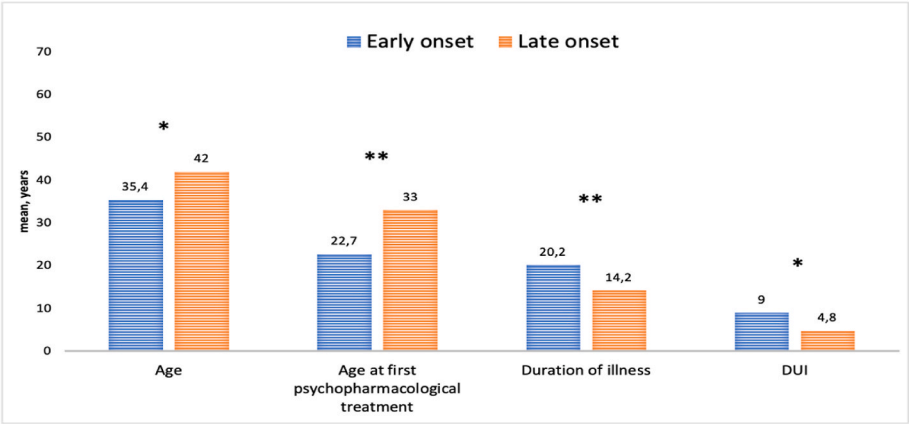

Fig. 2. Sociodemographic and clinical features between early versus late OCD onset.
Notes: DUI: duration of untreated illness. **p < .001 *p < .05.

Table 2
Correlations table for continuous examined variables.

		Age at OCD onset	Y-BOCS	CGI-S	BIS-11	Years of education	DUI (years)	Duration of illness (years)
Age at OCD onset	Pearson Correlation	1						
	Sig. (2-tailed)							
Y-BOCS	Pearson Correlation	−0,1	1					
	Sig. (2-tailed)	0,094						
CGI-S	Pearson Correlation	−0,03	,677**	1				
	Sig. (2-tailed)	0,645	0					
BIS-11	Pearson Correlation	−0,158	−0,341	−0,375	1			
	Sig. (2-tailed)	0,462	0,103	0,078				
Years of education	Pearson Correlation	−0,081	0,013	−0,013	0,169	1		
	Sig. (2-tailed)	0,275	0,865	0,876	0,463			
DUI (years)	Pearson Correlation	-,262**	0,081	0,118	0,155	0,083	1	
	Sig. (2-tailed)	0	0,177	0,069	0,469	0,264		
Duration of illness (years)	Pearson Correlation	-,304**	0,058	−0,008	0,024	0,1	,628**	1
	Sig. (2-tailed)	0	0,337	0,904	0,912	0,181	0	

Notes: OCD: Obsessive-compulsive disorders; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale; CGI-S: Clinical Global Impression - severity; BIS-11: Barratt Impulsiveness Scale; DUI: Duration of untreated illness. **p < .001.

between groups, in the whole sample, a higher prevalence of monotherapy exclusively with antidepressants (Ads) was reported as the first pharmacological treatment (63.6 %), which decreased at the time of study inclusion (28.2 %, see Table 3).

When stratified by age at onset, significant differences between OCD groups emerged. As the first treatment, the LO group reported significantly higher rates of polytherapy with ADs and benzodiazepines (BDZ; 15.5 vs. 2.7 %; p < .001) compared to the EO group. Furthermore, higher rates of polytherapy with AD and second-generation antipsychotics (SGA; 10.9 % vs. 4.5 %; p < .001), polytherapy with first-generation antipsychotics (FGA) and BDZ (5.5 % vs. 0.6 %; p < .001), and monotherapy with SGA (6.4 % vs. 0 %; p < .001) were found in the EO group. Contrariwise, no significant differences in terms of psychopharmacological prescription were observed between subgroups at the

Table 3
Focus on pharmacological treatment and differences between groups of age at onset.

Variables	Early onset OCD n = 117 (41.2 %)	Late onset OCD n = 167 (58.8 %)	Total sample n = 284
First pharmacological therapy (f, %)			
Monotherapy with ADs	70(63.6 %)	98(63.6 %)	164 (63.6 %)
Polytherapy with AD + MS	2(1.8 %)	5(3.2 %)	7 (2.7 %)
Polytherapy with AD + SGA	**12(10.9 %)****	**7(4.5 %)**	19 (7.6 %)
Polytherapy with AD + FGA	0(0 %)	2(1.3 %)	2 (0.8 %)
Polytherapy with 2 Ads	0(0 %)	2(1.3 %)	2 (0.8 %)
Polytherapy with AD + BDZ	**3(2.7 %)****	**24(15.5 %)**	27 (10.2 %)
Polytherapy with AD + AP + MS	0(0 %)	3(1.9 %)	3 (1.1 %)
Polytherapy with AD + AP + BDZ	2(1.8 %)	3(1.9 %)	5 (1.9 %)
BDZ	2(1.8 %)	4(2.6 %)	6 (2.3 %)
Polytherapy with AD + MS + FGA + SGA	1(0.9 %)	0(0 %)	1(0.4 %)
Polytherapy with FGA + SGA	2(1.8 %)	0(0 %)	9 (3.4 %)
Polytherapy with FGA + BDZ	**6(5.5 %)****	**1(0.6 %)**	2 (0.8 %)
Monotherapy with SGA	**7(6.4 %)****	**0(0 %)**	7 (2.7 %)
Monotherapy with FGA	0(0 %)	3(1.9 %)	7 (2.7 %)
Polytherapy with AD + MS + BDZ	2(1.8 %)	0(0 %)	3(1.1 %)
Pharmacological therapy at the time of study inclusion (f, %)			
Monotherapy with ADs	26(24.1 %)	48(32.2 %)	74 (28.2 %)
Polytherapy with AD + MS	1(9.2 %)	10(6.4 %)	11 (7.7 %)
Polytherapy with AD + SGA	30(27.8 %)	34(22 %)	64 (25.4 %)
Polytherapy with AD + FGA	4(3.7 %)	4(2.6 %)	8 (3 %)
Polytherapy with 2 ADs	3(2.8 %)	2(1.3 %)	5 (1.9 %)
Polytherapy with AD + BDZ	12(11.1 %)	15(9.8 %)	27 (10.3 %)
BDZ	4(3.8 %)	7(4.5 %)	11 (4.2 %)
Polytherapy with AD + AP + MS	6(5.5 %)	13(5.4 %)	19 (7.2 %)
Polytherapy with AD + FGA + SGA + BDZ	2(10.8 %)	2(1.3 %)	4(1.5 %)
Polytherapy with AD + MS + BDZ	0(0 %)	1(0.6 %)	1(0.4 %)
Polytherapy with AD + FGA + MS + BDZ	0(0 %)	3(1.9 %)	3(1.1 %)
Polytherapy with MS + SGA + FGA + BDZ	2(1.9 %)	1(0.6 %)	3 (1.1 %)
Polytherapy with FGA + SGA	1(0.9 %)	5(3.2 %)	6(2.3 %)
Monotherapy with SGA	1(0.9 %)	2(1.3 %)	3 (1.1 %)
Polytherapy with AD + SGA + BDZ	2(1,9 %)	2(1.3 %)	4(1.5 %)
Polytherapy with AD + SGA + MS	0(0 %)	2(1.3 %)	2(0.8 %)

Notes: OCD: Obsessive-compulsive disorders; AD: antidepressant therapy; AP: antipsychotics; BDZ: benzodiazepine; FGA: first-generation antipsychotic; SGA: second-generation antipsychotics; MS: mood stabilizers. Reported variables had a percentage of missing data ranging from 0 % to 14 %. Boldface indicates parameters with statistically significant differences between subgroups; **$p < .001$ *$p < .05$.

time of study inclusion (see Table 3).

4. Discussion

Our study aimed to further investigate the clinical characteristics of OCD, comparing EO and LO. Differences were found in terms of gender prevalence, longer duration of illness as well as DUI, worse social impairment, and different comorbidities before and after OCD onset. Moreover, some differences concerning the first pharmacological treatment emerged.

First, we found an association between male gender and EO OCD. The literature presents contradictory results on this topic. Some Authors who used empirically-defined age at disease onset cut off, failed to demonstrate an association between age and EO OCD (Rosario-Campos et al., 2001; Millet et al., 2004; Janowitz et al., 2009). Conversely, others found a positive association (Fontenelle et al., 2003; Mancebo et al., 2008; Grover et al., 2018; Benatti et al., 2022). To explain male gender prevalence in the EO group, a possible role of androgens in promoting the development of OCD has been hypothesized (Altemus et al., 1999). Moreover, various case series have documented an effective management of obsessive-compulsive symptoms with anti-androgenic medications (Casas et al., 1986; Eriksson, 2000; Nomani et al., 2020). However, further investigation is needed to clarify better the role of hormones in affecting OCD course.

Our study found that EO patients have lower rates of employment and engaged/married marital status compared to LO subjects. Moreover male patients, who are more frequently affected by EO OCD, as reported above, tend to display higher rates of unemployment and to be single more frequently than women (Lensi et al., 1996; Bogetto et al., 1999; Karadağ et al., 2006; Jaisoorya et al., 2009; Torresan et al., 2009), who generally have a higher age at onset (Torresan et al., 2013; Benatti et al., 2020). The pronounced global impairment observed in patients with EO OCD (Fontenelle et al., 2003; Albert et al., 2015) suggests the presence of a more severe subtype of OCD, potentially as the result of neurodevelopmental alterations (Burchi and Pallanti, 2019; Grassi et al., 2021.). In our sample, patients with EO OCD exhibited higher rates of comorbidities with neurodevelopmental disorders, including tics and Tourette's syndrome, both preceding and following OCD onset, compared to patients with LO OCD. Although a comprehensive meta-analysis by Taylor (2011) supported the association between EO OCD and these disorders, some discrepancies exist in the literature, with Douglass et al. (1995) providing alternative findings. Notably, Sobin et al. (2000) reported that in their study, these comorbidities only manifested before the onset of OCD. These neurodevelopmental conditions, characterized by repetitive behaviors (Miguel et al., 1995), a high familial prevalence (Ferrão et al., 2009), an early onset, and a potential shared pathogenesis involving basal ganglia alterations (Rapoport, 1990), exhibit similarities with EO OCD. Higher rates of comorbidities in patients with EO OCD compared to LO OCD are supported by neuroimaging studies showing that individuals with EO OCD are more likely to display alterations in the striatum (caudate and putamen) and distinct patterns of brain activation than those with adult-onset OCD (Rosenberg and Keshavan, 1998; Busatto et al., 2001). Consequently, it has been postulated that EO OCD might be regarded as a neurodevelopmental disorder with a genetic vulnerability (Deng et al., 2022) predisposing individuals to the development of other neurodevelopmental disorders.

In our study, comorbidity with Impulsive Control Disorder (ICDs) was also identified in patients with early-onset OCD, with onset subsequent to the initiation of EO OCD. In the literature, there are few studies on this matter; however, a low frequency of Impulse Control Disorders (ICD) has been reported in young patients with OCD, with the exception of grooming disorders (Grant et al., 2010). Additionally, it has been demonstrated that patients with EO OCD associated with ICD exhibit high rates of comorbidity with tic disorders (Nestadt et al., 2009). Dysfunction of the dopaminergic system has been hypothesized to underlie grooming ICDs and tic disorders (Leckman et al., 1997; Hemmings et al., 2006), as evidenced by positive responses to antipsychotics in both conditions (Dion et al., 2002; Scahill et al., 2003).

Regarding clinical data, we found that the EO group exhibited a longer duration of illness compared to LO OCD, according to the literature (Grant et al., 2007; De Luca et al., 2011). It has been demonstrated that in patients with EO OCD, prolonged duration of illness is correlated

with higher levels of disability (Dell'Osso et al., 2013 a). However, in our sample, a longer duration of illness was not associated with increased symptom severity in EO OCD patients. A comparable observation was made by Sobin et al. (2000), who, conversely, identified a correlation in patients with LO OCD.

While the duration of the disease in EO OCD patients apparently did not influence the symptomatology, the DUI could have clinical and pharmacological implications. In our investigation, patients in the EO group had a longer DUI than patients with LO OCD. This could be due to a more insidious onset of illness in EO OCD (Millet et al., 2004; Maina et al., 2008) or greater difficulty in attributing early-stage symptoms to a specific nosology category leading to delayed diagnosis and the introduction of appropriate treatment (Dell'Osso et al., 2013b). A protracted DUI may contribute to developmental impairment (Dell'Osso et al., 2010) and impair the response to treatment (Albert et al., 2019; Dell'Osso et al., 2019; Fineberg et al., 2019).

In this study, only in a minority of cases, ADs were not prescribed as a first pharmacological treatment for OCD, in line with available guidelines (NICE, 2005; APA, 2007; Bandelow et al., 2012) that recommend SSRIs or CBT as first-line treatments. The LO group reported significantly higher rates of polytherapy with ADs and benzodiazepine as the first pharmacological treatment, although the AD class was not specified. The efficacy of ADs, especially SSRIs, in patients with OCD is well-established (Skapinakis et al., 2016; Del Casale et al., 2019). Moreover, our findings revealed a significantly higher use of antipsychotic medications (FGA or SGA), as monotherapy or associated with BDZ, as the first pharmacological treatment in patients with EO OCD compared with LO OCD. The choice of antipsychotic therapy in patients with EO OCD may be attributed to the presence of comorbidities such as Tourette and tic disorders. Previous research has indicated that individuals with OCD and comorbid tic disorders exhibit a positive response to antidopaminergic pharmacotherapy (McDougle et al., 2000; Bloch et al., 2006). Furthermore, it has been demonstrated that individuals with early-onset obsessive-compulsive disorder may exhibit alterations in both the dopaminergic and serotonergic systems (Hesse et al., 2011; Lee et al., 2018).

Our results, however, should be considered in light of several limitations. First of all, the prevalence of EO and LO in OCD samples varies across the literature. Some studies used admixture analysis to test whether the bimodal distribution could be a better fit to separate patients based on age at disorder onset and found different cut-offs. The cut-off ranged from 15 years to 26 years (Delorme et al., 2005; De Luca et al., 2011; Albert et al., 2015), thus the allocation of individuals to each group varied among the studies, which led to differences in the clinical profiles of EO and LO patients. Secondly, our study's recruitment from a specialized OCD treatment center may limit generalizability. Additionally, the retrospective nature of our study introduces potential recall bias, including biases associated with earlier rather than later age-at-onset cases. Finally, an additional limitation arises from the challenge of accurately characterizing the degree of social and functional impairment in patients with OCD. Therefore, we used indirect measures of functioning, such as marital status and employment status, despite their limitations.

In conclusion, the study underlines the presence of diversified prescribing patterns for OCD. This variability may be influenced by the clinical complexity of patients, especially those with EO OCD, who often require multiple therapy regimens with different drugs to achieve response and remission (Fontenelle et al., 2003). The prescription of an appropriate first pharmacological therapy for OCD should, therefore, consider the age at symptoms onset in order to better personalize therapeutic strategies.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Nicolaja Girone: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Beatrice Benatti:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **Chiara Bucca:** Writing – original draft. **Niccolò Cassina:** Writing – original draft. **Matteo Vismara:** Writing – review & editing, Data curation. **Bernardo Dell'Osso:** Supervision, Conceptualization.

Declaration of competing interest

In the last three years, Prof. Dell'Osso has received lecture honoraria and grants from Angelini, Lundbeck, Janssen, Pfizer, Otzuka, Neuraxpharm, and Livanova.

In the last three years, Dr Benatti has received lecture honoraria from Angelini, Lundbeck, Janssen, Rovi.

The other authors have no conflicts to declare.

Acknowledgements

None.

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