**CHILDHOOD, ADOLESCENT AND ADULT AGE AT ONSET AND RELATED CLINICAL CORRELATES IN OBSESSIVE-COMPULSIVE DISORDER: A REPORT FROM THE INTERNATIONAL COLLEGE OF OBSESSIVE-COMPULSIVE DISORDERS**

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**Abstract**

**Objective**: Many studies suggest that age at onset (AAO) is an important factor for subtyping obsessive-compulsive disorder (OCD), with specific clinical differences between "juvenile-onset" and "adult-onset" patients. The present study aimed to assess the prevalence of different AAO groups and compare related socio-demographic and clinical features in a large sample of OCD.

**Methods:** 431 OCD outpatients from different psychiatric departments worldwide, participating to the “international college of obsessive-compulsive spectrum disorders” (ICOCS) network, were first categorized in groups with "childhood-onset" (≤12 years), "adolescent-onset" (13-17 years), and "adult-onset" (≥18 years), then in “pre-adult-onset” (<18 years) and "adult-onset" (≥18 years). Pearson Chi-squared tests for categorical variables and One-way analysis of variance (ANOVA) for continuous variables were performed for group comparison.

**Results:** Twenty-one % (n=92) of the sample was represented by patients with childhood-onset, while 36% (n=155) of the sample showed an adolescent-onset and 43% (n=184) an adult-onset. Patients with adult-onset showed a significant female prevalence compared with the other two subgroups (χ2=10.92, p<0.05).  Childhood- and adolescent-onset patients showed a significantly higher rate of treatment with cognitive behavioural therapy (CBT), compared to adult onset patients (χ2=11.5; p<.005). The pre-adult- vs adult-onset analysis confirmed previous results in terms of gender and CBT without showing additional significant differences.

**Conclusions:** Thepresent international multicenter study supports the notion that OCD onset occurs more frequently before adult age, with approximately 1 out of 5 patients showing childhood-onset. Pre-adult onset is associated with higher rate of CBT, while adult onset seems more prevalent in female patients.

**Key words**: Obsessive-compulsive disorder (OCD), age at onset (AAO).**Introduction**

Obsessive compulsive disorder (OCD) is an early onset and disabling condition, with a lifetime prevalence ranging between 1.5% and 3.5% in general population and an equal gender distribution (Ruscio et al., 2010).

Many studies suggest that age at onset (AAO) in OCD is an important factor for clinically subtyping OCD patients (Taylor, 2011) and it has been reported a bimodal distribution for AAO, with one peak at 12–14 years and another at 20–22 years (Grant et al., 2007). When compared to patients with generalized anxiety disorder and panic disorders, in fact, patients with OCD showed the earliest AAO, confirming the strong link between early onset, positive family history and genetic load in OCD (Mathews et al., 2012; Dell’Osso et al., 2013a)

Significant differences in clinical profile, including comorbidity patterns, have been observed among patients with "juvenile-onset" and "adult-onset" OCD (Sharma et al., 2015). Approximately one third to half of OCD patients report a childhood onset (Rasmussen and Eisen, 1990), characterized by a male preponderance (Tukel et al., 2005), a higher familial load (Nestadt et al., 2000; Rosario-Campos et al., 2005) and a higher comorbidity with tic disorders (Nakatani and Krebs, 2011).

The neurobiology of juvenile OCD has been extensively investigated and some cases showed a relationship with streptococcal infections (Fitzgerald et al., 1999). In particular, it has been suggested that OCD, in susceptible subjects, may be caused by an autoimmune response to streptococcal infections, with a biological mechanism similar to that associated with Sydenham's chorea (Arnold and Richter, 2001). As a consequence, children with abrupt onset or exacerbations of OCD and/or tic disorders, following streptococcal infections, have been described as affected by "pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections" (PANDAS) (Nicolini et al., 2015; Swedo et al., 2001).

On the other hand, the adult-onset phenotype has been less investigated as a distinct phenotype, and still there is no consensus about the definition of “adult-onset OCD”, ranging from 16 to 30 years (Grant et al., 2007; Lomax et al., 2009). In addition, some studies have used the term “late-onset OCD”, referring to an onset after 40 years (Frydman et al., 2014).

Actually, there is no clear definition of AAO in OCD: in fact, some authors defined it as the beginning of the obsessive-compulsive symptoms, while others defined it as the age in which

patients began to display clinically significant distress or impairment associated with obsessions or compulsions that warrants a diagnosis of OCD (Albert et al., 2015; Rosario-Campos et al., 2001).

Furthermore, it needs to be mentioned that previous studies investigating AAO and clinical correlates in OCD have been mostly conducted with national samples, with potential cultural and geographic biases.

Therefore, the present multicenter, international study aimed to investigate AAO and clinical correlates in a large sample of OCD patients, recruited from the ICOCS network through a naturalistic database collecting patients’ socio-demographic and clinical variables. In particular, the purpose of the study was to categorize the sample according to AAO, exploring related prevalence, and to compare demographic and clinical features of patients with "childhood-onset" (≤12 years), "adolescent-onset" (13-17 years), and "adult-onset" (≥18 years).

**Methods**

The sample included 431 consecutive OCD outpatients of either gender and any age, afferent to different psychiatric departments worldwide, participating to the “International College of Obsessive-Compulsive Spectrum Disorders” (ICOCS) network. Details about involved centers and standard assessment procedures have been specified elsewhere (Dell’Osso et al., 2013b). After obtaining patients' written informed consent and approval from local Ethics Committee/Institutional Review Board for using patients' information for research purposes, socio-demographic and clinical variables were collected and included in a common web-database.  For the purposes of the present analyses, these included: age, gender, age of OCD onset, presence of current/past medical illnesses, current pharmacological and psychotherapeutic interventions, lifetime history of suicide attempts and hospitalizations, presence of comorbid psychiatric disorders and poly-comorbidity (i.e., >2 comorbid conditions), comorbid physical diseases, and OCD severity, measured through the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (Goodman et al., 1989). The latter was also assessed by means of a qualitative analysis, defining a ‘high severity of illness’ identified by a Y-BOCS score ≥24.

The AAO of OCD was defined as the beginning of distress and interference associated with obsessions and compulsions.

For the purpose of the study, patients were first categorized in three groups: patients with "childhood-onset" (≤12 years), "adolescent-onset" (13-17 years), and "adult-onset" (≥18 years); then in two additional groups: “pre-adult - onset” (<18 years) and "adult-onset" (≥18 years). The first categorization, in particular, has been already used in studies assessing AAO in patients with psychiatric disorders, including a recent study conducted with patients suffering from bipolar disorder (Holtzman et al., 2015).

Pearson Chi-squared tests for categorical variables and One-way analysis of variance (ANOVA) for continuous variables were performed to compare the subgroups. All analyses were two-tailed, used the .05 level of statistical significance and were performed using SPSS 22 for Windows software.

**Results**

Main demographic and clinical variables are reported in Table 1.

The sample was characterized by 57.3% of females, a mean age of 43.1±12.8 years and a mean age at onset of 19.2±10.01 years. Patients with a psychiatric comorbid disorder represented 23.4% of the whole sample, being tic disorder the most frequent (15.5%), while poly-comorbidity occurred in 4.8% of the total sample.

The whole sample was first divided in: patients with "childhood-onset" (n=92, 21% of the sample), "adolescent-onset" (n=155, 36% of the sample), and "adult-onset" (n=184, 43% of the sample).

Significant gender differences among the three different onset categories were observed, with a significant female preponderance in the adult onset subgroup (33.2% males vs 66.8% females; χ2=10.9, p<.005), while in the childhood- and adolescent onset-groups gender was equally distributed (childhood-onset group: 47.8% males vs 52.2% females; adolescent-onset group 49.7% males vs 51.3% females) (Figure 1a). A comparison of expected and observed values indicated no female over-representation in the single subgroups.

As regards past/present cognitive behavioral therapy (CBT) among the three subgroups, Chi squared test revealed a significantly decreasing proportion of patients on CBT across groups with increasing AAO. In particular, childhood- and adolescent-onset patients showed a significantly higher rate of treatment with CBT compared to adult-onset patients (childhood-onset: 51.6% on CBT, adolescent-onset: 47% on CBT, adult-onset 32.6% on CBT; χ2=11.5, p<.005) (Figure 1b).

No significant differences in terms of current/past treatment with psychiatric medications, lifetime number of suicide attempts, psychiatric hospitalizations, presence of comorbid psychiatric disorders, psychiatric poly-comorbidity and comorbid physical diseases were found

An ANOVA analysis controlling for gender as a covariate was also performed in order to assess differences in terms of OCD severity across groups, but no significant differences were found. The high-severity of illness category was similarly represented across the three subgroups, showing no significant differences.

When the total sample was divided in two subgroups, “pre-adult-onset”(n=247, 57.3% of the total sample) and "adult-onset"(n=184, 42.7% of the total sample), a significant gender difference was found, consistently with what previously reported (33,2% males vs 66,8% females; χ2=10.9, p<.001) (Table 2).
In terms of treatment, the pre-adult onset showed a significantly higher rate of patients on CBT compared to the adult-onset subgroup (48.8% vs 32.6%; χ2=11.5, p<.001).

No significant differences in terms of current/past treatment with psychiatric medications, past suicide attempts, past psychiatric hospitalization, comorbid psychiatric disorders, psychiatric poly-comorbidity, comorbid physical diseases and severity of illness were found.

**Discussion**

To authors’ knowledge, this is the first study investigating AAO differences in OCD through an international catchment perspective. In this respect, the geographic heterogeneity of the sample should have minimized the risk of possible socio-cultural bias and other conditioning factors related to a single catchment area.

From an epidemiologic point of view, the most relevant finding of this study is that the majority of the sample had a pre-adult-onset, with approximately 1 out of 5 patients showing a childhood-onset. Such finding confirms that OCD onset is even more common in young patients than previously thought (Piacentini et al., 1992). Our result on childhood onset is, moreover, consistent with the U.S. National Comorbidity Survey Replication by Kessler and colleagues, showing that about 20% of all OCD patients in the USA showed the first symptoms of the disorder since the age of 10 years or even earlier (Kessler et al., 2005 a,b).

The fact that OCD tends to show its onset more frequently in pre-adult age somehow challenges its current conceptualization as a disorder of the adult age in DSM-5 (APA, 2013), or would at least require a specification in that sense, stressing the need for care-continuity in these patients between child and adult psychiatrists, being likely the former ones those who should first screen for the disorder and start appropriate treatment.

The other noteworthy finding from the present study is represented by the higher female prevalence in the adult-onset subgroup. On one hand, in fact, OCD has been traditionally considered a condition with a similar gender prevalence. However, our result seems to be consistent with a recent Brazilian study that analyzed a large sample of OCD patients, dividing them in early-onset (<16 years-old), regular-onset (>16 but < 40 years-old), or late-onset OCD (>40 years-old) subgroups. Authors found that late-onset OCD was more likely to occur in females and that a significant rate of late-onset patients  had a history of recent pregnancy (Frydman et al., 2014).

With respect to early-onset OCD, some evidence suggests that androgens may play a crucial role in the onset and exacerbation of the disease, with several reports describing the successful treatment of obsessive–compulsive symptoms with anti-androgenic drugs (Eriksson, 2000, Weiss et al., 1995). In light of such findings, it has been hypothesized a different hormonal role for distinct subtypes of OCD, even though the precise mechanisms underlying this phenomenon are still unsettled (Fontenelle et al., 2003).

As regards the role of CBT in OCD patients, results from present study showed a higher rate of past/present treatment with CBT in patients with childhood- and adolescent-onset, compared to those with adult-onset. These results may be interpreted in different ways. Actually, it is not surprising that CBT was more used in childhood/adolescent-onset patients, such therapeutic approach being considered the first-line treatment in mild to moderate cases of paediatric OCD (NICE, 2005; Geller et al., 2012; Krebs et al., 2015), while medications tend to be reserved to more severe cases and/or to young people who fail to respond to CBT (Watson et al., 2008) and,, ultimately, to adult patients. On the other hand, it may be also speculated that adult patients with childhood/adolescent-onset and a likely consequent long duration of illness need CBT as sole or integrated therapy to obtain larger benefit (Albert et al., 2012).

In terms of severity of illness, no differences were found across onset subgroups, implying that severity of OCD does not seem to worsen when the disorder starts earlier. Similar results have been obtained by Fontenelle and colleagues, whose hypothesis was that the differences in clinical presentation and in the initial treatment steps of early-onset vs late onset-patients may not result in significant differences in terms of final treatment response in a naturalistic setting (Fontenelle et al., 2003).

With respect to psychiatric comorbidity, in our sample, we found no significant association between presence of comorbidity and AAO; interestingly, general psychiatric comorbidity rates appeared to account for approximately one fourth of the total sample, being lower compared to other studies (Ruscio et al., 2010) and potentially explaining the lack of significant associations, particularly for tic disorders. However, this result of similar comorbidity rates between OCD patients with different AAO is consistent with a previous study comparing patients with early vs late onset OCD and showing no difference in such regard (Grant et al., 2007).

The findings reported in the present study should be interpreted in light of some limitations. The first one is the possible presence of recall bias, since in most cases the AAO was retrospectively determined. In addition, it needs to be taken into account that centers participating to the ICOCS network and database have well-established expertise in the field of diagnosis and treatment of OCD and it may be speculated that patients attending such services may have shown higher severity of illness and, therefore, do not necessary reflect the clinical conditions of patients usually observed elsewhere. Furthermore, the severity of illness was measured through the Y-BOCS with other instruments assessing disability and quality of like potentially showing different results across different groups. Finally, reported data may only apply to patients seeking treatment, such population being not necessarily representative of the entire population of OCD patients.

Further research is required to confirm present epidemiologic results and further explore the clinical features of OCD associated with different AAO.

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Please insert here any collaborator who contributed to data collection**REFERENCES**

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**TABLES AND FIGURES
Table 1.** Main epidemiological and clinical variables of the childhood-, adolescent- and adult-onset subgroups.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | TOTAL SAMPLEN=431 | CHILDHOOD-ONSET (≤12 years)N=92 | ADOLESCENT-ONSET (13-17 years)N=155 | ADULT-ONSET (≥18 years)N=184 |
| GENDER (M:F) | 182 (42%):249 (58%) | 44(47.8%):48(52.2%) | 77(49.7%):78(50.3%) | 61(33.2%):123(66.8%)\* |
| MEAN AGE ± SD (years) | 43.1 ± 12.8 | 39.1±13.6 | 39.7±10.8 | 47.9±12.5 |
| MEAN YBOCS SCORE ± SD | 20.6 ± 9.1 | 20.6±9.4 | 20.4±8.9 | 20.7±9.4 |
| HIGH SEVERITY OF ILLNESS (YBOCS≥24) (Y:N) | 175(40.6%):231(53.5%) | 36(39.1%):52(56.5%) | 60(38.7%):89(57.4%) | 79(42.9%):90(48.9%) |
| PSYCHIATRIC COMORBIDITY (Y:N) |  101(23.4%):330(76.5%) |  30(32.6%):62(67.4%) | 37(23.8%):118(76.2%) | 34(18.4%):150(81.6%) |
| PSYCHIATRIC POLY-COMORBIDITY (Y:N) | 21(4.8%):410(95.2%) |  3(3.2%):89(96.7%) | 9(5.8%):146(94.2%) | 9(4.9%):175(95.1%) |
| PSYCHIATRIC MEDICATION (Y:N) | 297(88.4%):39(11.6%) | 60(83.3%):12(16.7%) | 116(87.2%):17(12.8%) | 121(92.4%):10(7.6%) |
| CBT (Y:N) | 176(41.9%):244(58.1%) | 47(51.6%):44(48.4%) | 71(47%):80(53%) | 58(32.6%):120(67.4%)\* |
| LIFETIME SUICIDE ATTEMPTS (Y:N) | 62(14.6%):363(85.4%) | 15(16.9%):74(83.1%) | 26(16.9%):128(83.1%) | 21(11.5%):161(88.5%) |
| LIFETIME PSYCHIATRIC HOSPITALIZATIONS (Y:N) | 79(18.7%):342(81.3%) | 18(20%):72(80%) | 26(17.2%):125(82.8%) | 35(19.4%):145(80.6%) |
| MEDICAL COMORBIDITY (Y:N) | 82(20%):327(80%) | 16(18.6%):70(81.4%) | 26(17.8%):120(82.2%) | 40(22.6%):137(77.4%) |

Values for categorical and continuous variables are expressed as N (%) and mean ± SD, respectively. Reported variables had a percentage of missing data ranging from 0% to 22%.

**Legenda:**

Y-BOCS: Yale-Brown Obsessive Compulsive Scale

CBT: Cognitive behavioral therapy

**Statistics:**\*= p<0.05

**Table 2.** Main epidemiological and clinical variables of the preadult and adult onset subgroups

|  |  |  |  |
| --- | --- | --- | --- |
|  | TOTAL SAMPLEN=431 | PRE-ADULT-ONSET (<18 years)N=247 | ADULT-ONSET (≥18 years)N=184 |
| GENDER (M:F) | 182 (42%):249 (58%) | 121(49%):126(51%) | 61(33.2%):123(66.8%)\*\* |
| MEAN AGE ± SD (years) | 43.1 ± 12.8 | 39.6±11.9 | 47.9±12.5 |
| MEAN YBOCS SCORE ± SD | 20.6 ± 9.1 | 20.6±8.9 | 20.6±9.3 |
| HIGH SEVERITY OF ILLNESS (YBOCS≥24) (Y:N) | 175(40.6%):231(53.5%) | 96(38.9%):141(57.1%) | 79(42.9%):90(48.9%) |
| PSYCHIATRIC COMORBIDITY (Y:N) |  101(23.4%):330(76.5%) |  67(27.1%):180(72.9%) | 34(18.4%):150(81.6%) |
| PSYCHIATRIC POLY-COMORBIDITY (Y:N) | 21(4.8%):410(95.2%) | 12(4.8%):235(95.2%) | 9(4.9%):175(95.1%) |
| PSYCHIATRIC MEDICATION (Y:N) | 297(88.4%):39(11.6%) | 176(85.9%):29(14.1%) | 121(92.4%):10(7.6%) |
| CBT (Y:N) | 176(41.9%):244(58.1%) | 118(48.8%):124(51.2%) | 58(32.6%):120(67.4%)\*\* |
| PAST SUICIDE ATTEMPTS (Y:N) | 62(14.6%):363(85.4%) | 41(16.9%):202(83.1%) | 21(11.5%):161(88.5%) |
| PAST PSYCHIATRIC HOSPITALIZATION (Y:N) | 79(18.7%):342(81.3%) | 44(18.3%):197(81.7%) | 35(19.4%):145(80.6%) |
| MEDICAL COMORBIDITY (Y:N) | 82(20%):327(80%) | 42(18.1%):190(81.9%) | 40(22.6%):137(77.4%) |

Values for categorical and continuous variables are expressed as N (%) and mean ± SD, respectively. Reported variables had a percentage of missing data ranging from 0% to 22%.

**Legenda:**

Y-BOCS: Yale-Brown Obsessive Compulsive Scale

CBT: Cognitive behavioral therapy

**Statistics:**

\*\*:p<0.01

**Figure 1a.** Gender differences across AAO subgroups of OCD patients

\*1

\*2

\*2

**Statistics**

**\*1:** p<.005, Χ2=10.9

**\*2:** p<.001, Χ2=10.9

**Figure 1b. Differences in treatment with CBT across onset subgroups of OCD patients.**

\*1

\*2

**Statistics**

**\*1:** p<.005, Χ2=11.5

**\*2:** p<.001, Χ2=11.5

**Legenda:**

 CBT= cognitive behavioral therapy