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The role of gender in a large international OCD sample: A Report from the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS) Network

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ABSTRACT

Introduction: Obsessive-compulsive disorder (OCD) is characterized by a range of phenotypic expressions. Gender may be a relevant factor in mediating the disorder's heterogeneity. The aim of the present report was to explore a large multisite clinical sample of OCD patients, hypothesizing existing demographic, geographical and clinical differences between male and female patients with OCD.

Methods: Socio-demographic and clinical variables of 491 adult OCD outpatients recruited in the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS) network were investigated with a retrospective analysis on a previously gathered set of data from eleven countries worldwide. Patients were assessed through

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structured clinical interviews, the Yale- Brown Obsessive-Compulsive Scale (Y-BOCS), the Montgomery-Asberg Depression Rating Scale (MADRS) and the Self-rating Depression Scale (SDS).
Results: Among females, adult onset (>18 years old) was significantly over-represented (67% vs. 33%, $p < 0.005$), and females showed a significantly older age at illness onset compared with males (20.85 ± 10.76 vs. 17.71 ± 8.96 years, $p < 0.005$). Females also had a significantly lower education level than males (13.09 ± 4.02 vs. 13.98 ± 3.85 years; $p < 0.05$), a significantly higher rate of being married (50.8% vs. 33.5%; $p < 0.001$) and a higher rate of living with a partner (47.5% vs. 37.6%; $p < 0.001$) than males. Nonetheless, no significant gender differences emerged in terms of the severity of OCD symptoms nor in the severity of comorbid depressive symptoms. No predictive effect of gender was found for Y-BOCS, MADRS and SDS severity.
Discussion/Conclusions.: Our findings showed significant differences between genders in OCD. A sexually dimorphic pattern of genetic susceptibility may have a crucial role to OCD clinical heterogeneity, potentially requiring different specific therapeutic strategies. Further research is warranted to validate gender as an important determinant of the heterogeneity in OCD.

1. Introduction

Obsessive-compulsive disorder (OCD) is characterized by largely variable phenotypic expressions. Moreover, it often occurs with comorbid conditions, with the most common being anxiety, mood and other OC-spectrum disorders [1,2]. Previous findings suggested that gender may be a relevant factor in mediating this heterogeneity [3].

Despite more than 50% of subjects reporting the onset of the disease in late adolescence/early adulthood [4,5] when considering the role of gender, a younger age of onset with greater symptom severity was found in males [3,6,7]. In terms of clinical differences between male and female patients with OCD, a significantly different expression of obsessions and compulsions phenotype were found across genders [3,7]. For example, females were more likely to report obsessions associated with contamination belief or aggressive concerns, while males usually reported blasphemous thoughts [7]. An early study by Drummond [8] found that for patients hospitalized with profound, refractory OCD, being female predicted a better response. However, a subsequent paper from the same Centre failed to show any advantage for women [9]. Besides, gender seems to play a role in the onset of OCD comorbidities, although the available data are discordant. Males with OCD seem to be more vulnerable to social phobia, tic disorders, alcohol use disorders, compulsive Internet use and sexual disorders [10] whereas females with OCD seem more likely to present with eating disorders, specific phobias, trichotillomania, skin picking and compulsive buying [7]. On the other hand, some results showed an association between female gender and alcohol use disorders, anxiety and mood disorders [4]. In conclusion, conflicting data regarding OCD patterns and gender exist. As a complement to those findings and to evaluate the extent of gender differences for those with OCD at a global level, we conducted a post-hoc analysis of international multisite cross-sectional data from the ICOCS network. We aimed to examine the correlates of demographic, geographical and clinical differences between male and female patients with OCD.

2. Methods

The sample included 491 adult outpatients with a DSM-IV-TR OCD diagnosis [11] at different stages of treatment were recruited in the International College of Obsessive-Compulsive Spectrum Disorders (ICOCS) network between 2008 and 2010 [5,12–14]. The network included a multisite collaborative teams of OCD experts spanning academic and tertiary clinics from across the globe, including the Americas (Canada, the United States, and Mexico), Africa (Libya and South Africa), Europe (Spain, Italy, Turkey, Bulgaria, the United Kingdom) and the Middle East (Israel). Local institutional review boards approved the protocol. Patients provided written informed consent to use their anonymized data.

The sociodemographic measures included: age, gender, years of education, marital status, professional status, age of OCD onset, psychopharmacological therapy, presence of monotherapy vs augmentation. Comorbidity of associated mood, tic and anxiety disorders (e.g., major depression, generalized anxiety disorder) was assessed using a Structured Clinical Interview based on the DSM–IV criteria (SCID–I and –II) [15,16]. Medical comorbidities were elicited by clinician interview.

OCD illness severity was assessed by the Yale-Brown Obsessive Compulsive Scale (Y-BOCS); severity of OCD was also assessed by means of a qualitative analysis on Y-BOCS scores, differentiating "mild" OCD (range 9–15), "moderate" OCD (range 16–23), "severe" OCD (range 24–32) and "extreme" OCD (range 33–40) [17,18]. Severity of comorbid depressive symptoms was assessed using the Montgomery-Asberg Depression Rating Scale (MADRS) [19]. Interference with work/school, social life/leisure activities, and family life/home responsibilities was measured with the Sheehan Disability Scale (SDS) [20].

Statistical analyses were performed with Pearson's chi-squared test for categorical variables and ANOVA test for the continuous variables to explore gender differences. A linear regression was used to test whether Y-BOCS, MADRS and SDS severity could be predicted by gender. All analyses were performed using Statistical Package for the Social Sciences (SPSS) 25.0 software for Windows (SPSS Inc., Chicago, IL, USA). Statistical significance was set at $p < 0.05$.

3. Results

The sample included 60.5% females, mean age 38.56 ± 12.86 years. Patients were geographically distributed as follows: 217 (44.2%) from Europe (22% from Italy, 8.1% from Spain, 6.7% from United Kingdom, 4.9% from Turkey, 2.4% from Bulgaria); 115 (23.4%) from the Americas (14.1% from Canada, 7.7% from Mexico and 1.6% from USA); 100 (20.4%) from Africa (20.2% from South Africa and 0.2% from Libya) and 59 (12%) from Middle East (Israel).

For the purpose of the study the whole sample was divided into two subgroups based on sex. Comparison of socio-demographic and clinical variables between female and male samples are provided in Tables 1 and 2.

With respect to geographical differences among clinics involved in the ICOCS network, a significant difference by gender distribution emerged (see Table 3). Specifically, Americas showed significantly higher rates of female OCD patients compared to male OCDs (30.3% vs. 12.9%; $p < 0.001$, Fig. 1). However, no significant differences in gender rates emerged for Europe, Africa and the Middle East.

In the female group adult onset (>18 years old) was found to be significantly more represented (67% vs. 33%, $p < 0.005$; Fig. 2), showing a significantly older age at onset when compared with male patients (20.85 ± 10.76 vs. 17.71 ± 8.96 years, $p < 0.005$). No significant difference emerged neither in the severity of symptoms assessed through the Y-BOCS (22.32 ± 7.36 vs. 21.9 ± 7.26) nor in the severity of comorbid depressive symptoms, assessed through the MADRS and the SDS (Table 2). Furthermore, no predictive effect of gender was found for Y-BOCS, MADRS and SDS severity with linear regression ($b = 0.416$, $t = 0.577$ $p = 0.564$; $b = -1.220$, $t = -1.300$ $p = 0.194$; $b = 0.300$, $t = 0.363$

Table 1
Comparison of socio-demographic variables between female and male samples.

	Females	Males	Total sample
Gender	297 (60.5%)	194 (39.5.%)	491
Age	**40.28 ± 13.39****	**36.18 ± 11.72**	38.56 ± 12.86
Years of education	**13.09 ± 4.02***	**13.98 ± 3.85**	13.46 ± 3.97
Marital status			
Single	103 (40.2%)	110 (61.5%)	213 (49%)
Married	**130 (50.8%)****	**60 (33.5%)**	190 (43.7%)
Divorced	18 (7%)	7 (3.9%)	25 (5.7%)
Widow/er	5 (2%)	1 (0.6%)	6 (1.4%)
Professional status			
Worker	130 (50.4%)	101 (54%)	231 (51.9%)
Unemployed	73 (28.3%)	38 (20.3%)	111 (24.9%)
Student	37 (14.3%)	35 (18.7%)	72 (16.2%)
Retired	18 (7%)	13 (7%)	31 (7%)
Living			
Alone	40 (13.5%)	40 (20.6%)	80 (16.3%)
With spouse	**141 (47.5%)****	**63 (37.6%)**	204 (41.5%)
With parents	63 (21.2%)	73 (37.6%)	136 (27.7%)
Nursing home	53 (17.8%)	18 (9.3%)	71 (14.5%)

Notes: Values for categorical and continuous variables are expressed in percentages and mean ± SD, respectively. Reported variables had a percentage of missing data ranging from 2% to 12%. Boldface indicates parameters with statistically significant differences between the two subgroups; $^{**}p < 0.005$ $^{*}p < 0.05$.

Table 2
Comparison of clinical variables between female and male samples.

	Females	Males	Total sample
Age at OCD onset (years)	**20.85 ± 10.76****	**17.71 ± 8.96**	19.53 ± 10.15
Late onset (>18 years)	**126 (67%)****	**62 (33%)**	188 (45.7%)
Medical Comorbidity	50 (54.9%)	41 (45.1%)	91 (20.8%)
Psychiatric Comorbidity	140 (57.6%)	103 (42.4%)	243 (55.9%)
Polycomorbidities	38 (56.7%)	29 (43.3%)	67 (14.9%)
Tic disorder	36 (49.3%)	37(50.7%)	73 (17.6%)
Psychopharmacological therapy	182 (58.7%)	128 (41.3%)	310 (87.8%)
Monotherapy vs augmentation	97 (60.6%) vs 85 (56.7%)	63 (39.4%) vs 65 (43.3%)	160 (51.6%) vs 150 (48.4%)
Psychiatric hospitalization	46 (54.1%)	39 (45.9%)	85 (18.8%)
CBT	137 (60.1%)	91 (39.9%)	228 (46.4%)
Y-BOCS total scores	22.32 ± 7.36	21.9 ± 7.26	22.16 ± 7.32
Mild (9–15)	36 (53.7%)	31 (46.3%)	67 (13.6%)
Moderate (16–23)	110 (65.1%)	59 (34.9%)	169 (34.4%)
Severe (24–32)	88 (58.7%)	62 (41.3%)	150 (30.5%)
Extreme (33–40)	28 (68.3%)	13 (31.7%)	41 (8.4%)
MADRS score	13.13 ± 8.56	14.35 ± 8.37	13.57 ± 8.50
SDS score	16.98 ± 7.79	16.68 ± 7.96	16.87 ± 7.85

Notes: Values for categorical and continuous variables are expressed in percentages and mean ± SD, respectively. OCD: Obsessive-Compulsive Disorder; Polycomorbidities: co-occurrence of at least two comorbid psychiatric conditions other than OCD; CBT: Cognitive behavioral therapy; Y-BOCS: Yale–Brown Obsessive Compulsive Scale; MADRS: Montgomery-Asberg Depression Rating Scale; SDS: Self-rating Depression Scale.
Reported variables had a percentage of missing data ranging from 2% to 12%. Boldface indicates parameters with statistically significant differences between the two subgroups; $^{**}p < 0.005$ $^{*}p < 0.05$.

$p = 0.717$, respectively; see Table 4). Lastly, no significant differences in terms of psychiatric comorbidity and presence of poly-comorbidities, pharmacological or psychological treatment and presence of tic disorder were found. Regarding years of education, the female group showed a significantly lower duration of education compared to male subgroup (13.09 ± 4.02 vs. 13.98 ± 3.85 years; $p < 0.05$). Moreover, in the female group a significantly higher rate of being married (50.8% vs- 33.5%; $p < 0.001$) and a higher presence of living with spouse (47.5% vs. 37.6%; $p < 0.001$) emerged compared to males. No significant difference emerged regarding professional status between groups.

4. Discussion

In the present report, clinical correlates of gender differences in OCD disorder were examined. To the authors' knowledge, this is the first study analyzing gender differences in an international multisite OCD adult outpatient population.

We found that compared to males, females with OCD 1) had a lower level of education, 2) were more commonly married or living with partners, and 3) had a later age of onset of OCD. And finally, we found a higher female:male ratio in the Americas compared to other study sites (Europe, Africa and Israel).

Consistently with previous findings [3,5,21], OCD female patients showed a significantly higher age of psychopathological onset when compared to the males. In particular, in the female group the adult onset (>18 years old) was found to be significantly more represented. Previous studies showed a younger age at OCD onset with greater symptom severity in males compared to females [3,6,7]. Nonetheless, in our study no significant differences in the severity of OCD symptoms assessed by the Yale-Brown obsessive compulsive scale was found. In addition, no difference in the severity of comorbid depressive symptoms and no predictive effect of gender for Y-BOCS, MADRS and SDS severity were found.

No significant differences in terms of psychiatric comorbidities, including tic disorders, and in comorbid depression severity emerged in the present sample. Previously other large multicentric studies did not show differences in terms of mood disorders and any anxiety disorder rates between genders [22]. Moreover, when comparing a sample of OCD patients in terms of gender differences, also Lochner and colleagues did not find significantly different tic disorders prevalence between males and females groups [23]. Previous reports from the ICOCS group highlighted lower general psychiatric comorbidity rates in the sample compared to other studies, potentially explaining the lack of significant associations [24]. Lastly no significant gender differences occurred in terms of pharmacological or psychological treatment, as also previously highlighted by the Spanish study of Labad and colleagues in 2008 [25]. These specific features need to be further investigated.

Consistently with several other authors [26–28], our results showed that women with OCD were more commonly married than men. In addition, we found a higher frequency of female patients living with partners compared to males, as previously highlighted by Sobin and colleagues [29]. One possible reason could be related to the earlier age at OCD onset among men, preventing stable relationships in those patients.

Regarding years of education, the female group showed a significantly lower duration of education compared to male subgroup. In this perspective, the current literature presented mixed results. Vander Stoep and colleagues attempted to quantify the societal burden of mental disorders in decreased educational attainment, estimating that as many as 46% of high school dropouts might be attributable to the negative effects of prior mental disorders [30]. Another study using data from the Australian National Survey of Mental Health and Wellbeing showed, contrary to our results, that male children with early-onset OCD had higher school dropout rates compared to OCD females and controls [31]. A possible explanation in the role of OCD gender differences and education levels may lie on age at OCD onset and DUI.

Lastly, our multisite results showed a significantly higher prevalence of females with OCD in Americas compared to males and no significantly gender differences in Europe, Africa and Israel.

When considering the role of gender, several studies with children OCD samples have identified a greater proportion of males [32–34], whereas some adult OCD samples find both equal distributions [35,36] or a greater proportion of females [37,38] across centres.

The above-mentioned results should be interpreted considering some methodological limitations. First, the cross-sectional nature of the study allowed only one time assessment. Secondly, some variables were obtained retrospectively, being susceptible to recall bias.

Table 3
Gender distribution of OCD sample recruited in the ICOCS network across the globe.

	Females		Males		Total sample	
Geographical area	**Europe** 118 (39.7%)		**Europe** 99 (51%)		**Europe** 217(44.2%)	
	Italy	59 (19.9%)	Italy	49 (25.3%)	Italy	108 (22%)
	Spain	19 (6.4%)	Spain	21 (10.8%)	Spain	40 (8.1%)
	Turkey	19 (6.4%)	Turkey	5 (2.6%)	Turkey	24 (4.9%)
	UK	13(4.4%)	UK	20 (10.3%)	UK	33 (6.7%)
	Bulgaria	8 (2,7%)	Bulgaria	4 (2,1%)	Bulgaria	12 (2.4%)
	Americas 90 (30.3%)**		**Americas 25 (12.9%)****		**Americas** 115 (23.4%)	
	Mexico	32 (10.8%)	Mexico	6 (3.1%)	Mexico	38 (7.7%)
	Canada	54 (18.2%)	Canada	15 (7.7%)	Canada	69 (14.1%)
	USA	4 3(1.3%)	USA	4 (2.1%)	USA	8 (1.6%)
	Africa 59 (19.9%)		**Africa** 41 (21.1%)		**Africa** 100 (20.4%)	
	South Africa	58 (19.5%)	South Africa	41(21.1%)	South Africa	99(20.2%)
	Libya	1 (0.3%)	Libya	0 (0%)	Libya	1(0.2%)
	Middle East		**Middle East**		**Middle East**	
	Israel	30 (10.1%)	Israel	29 (14.9%)	Israel	59 (12%)

Notes: Values for categorical variables are expressed in percentages. Boldface indicates parameters with statistically significant differences between the two subgroups; **p < 0.001 *p < 0.05.

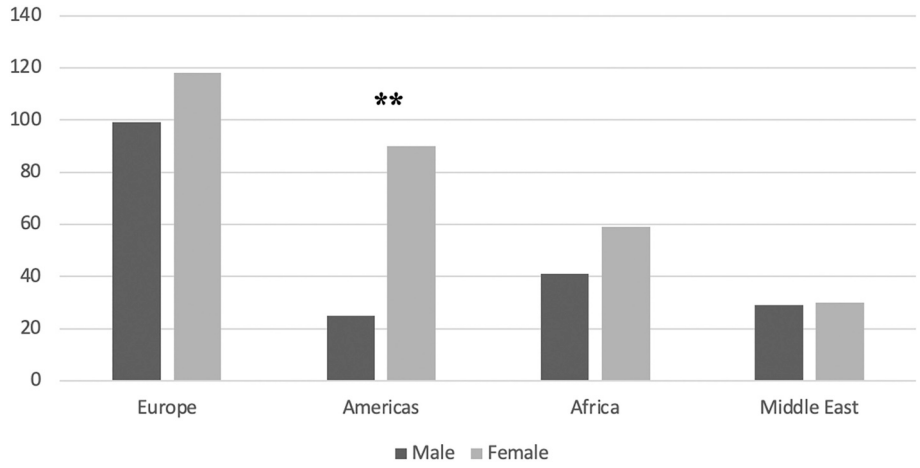

Fig. 1. Gender distribution of OCD sample recruited in the ICOCS network across the globe.
Notes: Boldface indicates parameters with statistically significant differences between the two subgroups; **$p < 0.001$.

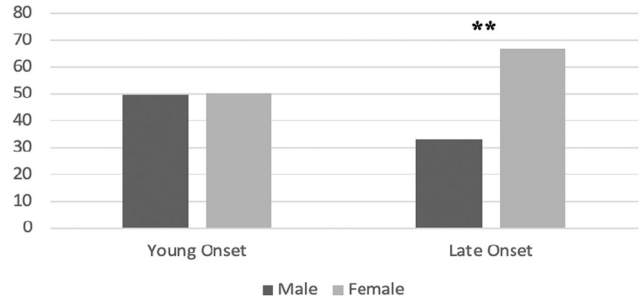

Fig. 2. Comparison of psychopathological onset between female and male OCD patients.
Notes: Boldface indicates parameters with statistically significant differences between the two subgroups; **$p < 0.005$.

Nevertheless, our findings suggest that gender is a fundamental contributor to OCD clinical heterogeneity potentially necessitating the establishment of specific therapeutic strategies. Future investigation may, therefore, benefit from a focus on gender diversified severity variables, such as suicidality, stressful life events or history of trauma and from a wider sample size and longer follow-up.

Table 4
Linear regression analysis of predictive effect of gender for Y-BOCS, MADRS and SDS severity.

Subscales	Predictor	Unstandardized Coefficients		Standardized Coefficients	t	p
		b	SE	*β*		
Y-BOCS	*Constant*	*21.489*	*1.216*		*17.672*	
	Gender	0.416	0.721	0.028	0.577	0.564
MADRS	*Constant*	*15.572*	*1.604*		*9.707*	
	Gender	−1.220	0.939	−0.060	−1.300	0.194
SDS	*Constant*	*16.387*	*1.395*		*11.750*	
	Gender	0.300	0.827	0.019	0.363	0.717

Notes: b: Regression coefficient; SE: standard error; Y-BOCS: Yale–Brown Obsessive Compulsive Scale; MADRS: Montgomery-Asberg Depression Rating Scale; SDS: Self-rating Depression Scale.

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Declaration of Competing Interest

- BB has received lecture honoraria from Lundbeck and Janssen.

- BDO has received lecture honoraria from Angelini, Janssen, Lundbeck, Livanova, Arcapharma, and Neuraxpharm.
- CR in the last 3 years, has served as a consultant for Epiodyne and received research grant support from Biohaven Pharmaceuticals and a stipend from APA Publishing for her role as Deputy Editor at The American Journal of Psychiatry.
- MVA has been on the advisory board of Allergan, Almatica, Brainsway, Lundbeck, Myriad Neuroscience, Otsuka, Purdue Pharma. He has received research support from Janssen-Ortho Inc., Purdue Pharma (Canada), the Canadian Foundation for Innovation, and Hamilton Aca- demic Health Sciences Organization (HAHSO).
- NF declares that in the past 3 years she has held research or networking grants from the ECNP, UK NIHR, EU H2020 (COST Action), University of Hertfordshire; she has accepted travel and/or hospitality expenses from the BAP, ECNP, RCPsych, CINP, International Forum of Mood and Anxiety Disorders, World Psychiatric Association, Indian Association for Biological Psychiatry, Sun; she has received payment from Taylor and Francis and Elsevier for editorial duties. In the past 3 years, she has accepted a paid speaking engagement in a webinar sponsored by Abbott. Previously, she has accepted paid speaking engagements in various industry-supported symposia and has recruited patients for various industry-sponsored studies in the field of OCD treatment. She leads an NHS treatment service for OCD. She holds Board membership for various registered charities linked to OCD. She gives expert advice on psychopharmacology to the UK MHRA.

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