Attention Deficit Hyperactivity Disorder and Tobacco Addiction: Clinical and Social Characteristics in a Large Sample of Tobacco Smokers

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ABSTRACT

Background: Several scientific studies indicate that Attention Deficit Hyperactivity Disorder (ADHD) is a risk factor for the development of pathological addiction, including Tobacco Use Disorder (TUD). Despite various hypotheses proposed to explain the reasons for this frequent comorbidity, the limited amount of research aimed at describing the characteristics of this population restricts our understanding of the nature of this relationship. Aims: The purpose of our descriptive and retrospective study is to examine the differences between a group of tobacco users with suspected ADHD and those without it, with respect to socio-demographic characteristics, factors related to tobacco addiction, alcohol consumption, past and current use of illicit substances, and comorbid psychiatric symptoms. Methods: A total of 1166 smokers who were referred to the Addiction Medicine Unit of the University Hospital in Verona between 2015 and 2021 were selected. Users for whom it was not possible to obtain all the necessary information were excluded from the sample. The remaining participants were divided into two groups based on their scores on an ADHD screening test. The group that scored negatively on the screening test (n = 964) was then compared to the group that scored positively on the same test (n = 114). Results: Statistically significant differences emerged between the two groups. Specifically, users in the positive group were found to be more likely to have the marital statuses of "Single" and "Separated/Divorced," as well as the occupational statuses of "Unemployed," "Student," "Teacher," "Housework," "Casual Worker," "Worker," and "Artisan/Trader." They also exhibited a higher level of nicotine addiction and reported an increase in smoking in the last 12 months. Furthermore, they had a history of both previous and current use of illicit substances and higher overall levels of anxious and depressive symptoms, regardless of gender. Conclusion: Several factors related to sociodemographic characteristics, smoking behavior, past and current use of illicit substances, and current levels of anxiety and depression could potentially mediate the relationship between ADHD and TUD. Clinicians involved in smoking cessation treatments should take comorbidity with adult ADHD into consideration.

Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is a neuropsychiatric condition characterized by deficits in attention, impulsivity, and hyperactivity.[1] Among neuropsychiatric conditions, ADHD is often considered one of the most prevalent,[2] affecting approximately 10% of children in the United States aged between 4 and 17 years.[3] Lower prevalence rates (4-7%) have been reported in epidemiological studies conducted in other countries,[4] likely due to differences in diagnostic methods, guidelines, and access to specialized care.[3] The syndromic spectrum of ADHD is frequently associated with impairments in various aspects of daily life, both during childhood [5,6] and adulthood.[7,8] While the disorder typically emerges in childhood, it often persists into adolescence and adulthood in many cases.[9-12] Longitudinal studies, for instance, have revealed that despite symptom reduction with age, a substantial percentage, ranging from 40 to 70%, continues to meet all diagnostic criteria for the condition throughout adulthood[12,13], leading to significant deficits in motivational processes.[14]

Among the main motivational disorders often encountered as comorbidities with ADHD, Tobacco Use Disorder (TUD) is likely the most common.[15-17] Recent evidence consistently supports a significant correlation between ADHD symptoms and smoking behavior. Specifically, it appears that ADHD is linked to an early onset of smoking, a more rapid progression to regular smoking, and early tobacco dependence.[18-21] The severity of tobacco dependence is also higher in individuals with ADHD compared to the general population. These empirical findings emerge from various studies that have investigated factors such as the number of cigarettes smoked,[15,16,22] the experience of tobacco abstinence,[23,24] the difficulty in quitting smoking,[25,26] and the scores obtained in standardized tests for assessing the intensity of dependence on tobacco. Examples of these tests include the modified version of the Fagerström Tolerance Questionnaire (mFTQ) [21] and the Wisconsin Inventory of Smoking Dependence Motives (WISDM).[27] Collectively, this evidence suggests that ADHD is a significant risk factor for the development of TUD,[18,21,28,29] independent of the influence of other comorbid conditions that may facilitate the transition to addiction.[30-32]

The theoretical models recently proposed to explain the association found in the literature between ADHD and TUD recognize the mediating influence of various classes of factors.[23,33,34] These factors include genetic factors, [23,35,36] psychological factors (e.g., impulsivity),[37,38] neurocognitive factors (e.g., sustained attention and working memory),[39,40] affective factors (e.g., emotional regulation),[41] and socio-environmental factors (e.g., socio-economic status).[42-44] The implications of these factors have led researchers to propose different hypotheses regarding the correlation between ADHD and TUD.

One of the main theories, often referred to as the "self-medication hypothesis",[34] is based on epidemiological studies,[15,45] systematic reviews,[30] and clinical drug trials.[46,47] It explains the association between ADHD and TUD by suggesting that smoking might have a reducing effect on ADHD symptoms [48-50] and other symptoms often present in comorbidities.[51-54] In particular, the hypothesis predicts that by improving the deficits in cholinergic neurotransmission [55] and dopaminergic neurotransmission [56,57] typically found in this population, nicotine could reduce ADHD symptoms (e.g., attention deficits and impulse control difficulties) and increase concentration and attentional capacities.[22,52,58-60] It may also improve other comorbid symptoms (e.g., anxious depressive problems and sleep disorders) by enhancing emotional regulation capacities and the quality of sleep.[51,52,61]

While there is substantial evidence supporting this hypothesis, there are studies in the scientific literature that contradict it. For example, it has been observed that the alleviation of ADHD symptoms obtained after psychostimulant therapy does not provide the protective effect on the development of TUD as anticipated by the self-medication hypothesis.[62-65] Other studies have also demonstrated that ADHD symptoms are not reduced or are only marginally mitigated by smoking behavior,[47,66] nor are other symptoms present in comorbidity.[54] se results, possibly influenced by certain characteristics of the examined samples, such as the young age of the ADHD population and a high prevalence of females,[67] have led some researchers to restrict the explanatory validity of the self-medication hypothesis to understanding the maintenance, rather than the development, of TUD in the ADHD population.[34] . One example of this is the level of intensity of ADHD symptoms, which is often correlated with the severity of tobacco dependence.[19] Therefore, providing a detailed description of the characteristics of the ADHD smoking population could contribute to the formulation of more accurate hypotheses about the correlation between ADHD and TUD. Our study aims to identify the characteristics present in the population dealing with both TUD and suspected

ADHD in order to gain a better understanding of the nature of the relationship between these two disorders.

Materials And Methods

A database of 1166 smokers was analyzed. All data examined in this study were collected during the initial visit by a psychologist through a semi-structured interview, which investigated socio-demographic characteristics, factors related to tobacco addiction, alcohol consumption behavior, past and current use of illicit substances, and comorbid psychiatric symptoms. Data from 88 participants were excluded from the analysis due to incomplete information. The data from the remaining participants were divided into two groups based on the results obtained from the Adult ADHD Self-Report Scale (ASRS): one group that scored positively on the ASRS (positive ASRS group) and another group that scored negatively on the same screening test (negative ASRS group). A descriptive analysis was then conducted to assess statistically significant differences between the positive ASRS group (n = 114) and the negative group (n = 964).

PARTICIPANTS

Participants (n = 1078) were smokers who sought help to quit smoking from the addiction medicine service at the University Hospital of Verona between 2015 and 2021. After their initial visit, during which the data used in this study were collected, participants received individualized support to quit smoking from a medical specialist at the service, following a personalized treatment plan.

SOCIO-DEMOGRAPHIC CHARACTERISTICS

For each participant, information on sex, age, marital status (single, married/cohabiting, separated/divorced, widowed), level of education (primary/secondary school, high/professional school, degree), and employment status (unemployed, student, artisan/trader, homemaker, worker, employee, teacher, freelancer, manager, casual worker, retiree) was collected.

FACTORS RELATED TO TOBACCO ADDICTION

The smoking data collected during the first visit included the following: the average age of smoking onset, the intensity of nicotine dependence measured using the Fagerström Test for Nicotine Dependence (FTND) [68] (scores ranging from 0 to 10), the number of cigarettes smoked, previous attempts to quit smoking, the number of past attempts to quit smoking, the duration of previous abstinence (< 1 month, 1-3 months, 4-6 months, > 6 months), cohabitation with smokers, smoking during pregnancy, cigarette consumption in the last 12 months (increased, decreased, or unchanged), and waking up at night motivated by the need to smoke.

ALCOHOL CONSUMPTION

Each participant reported their current alcohol consumption status, specifying whether it was occasional, habitual, or problematic, and whether they had experienced previous issues with alcohol.

PREVIOUS AND CURRENT USE OF ILLICIT SUBSTANCES

We investigated past and current use and abuse of various illicit substances, including heroin, cocaine, and cannabis.

COMORBID PSYCHIATRIC SYMPTOMS

The possible presence of anxiety, depressive, and ADHD symptoms was assessed for each participant using standardized self-rating tests, including the Adult ADHD Self-Report Scale (ASRS) [69], the Self-rating Anxiety Scale (SAS) [70] and the Self-rating Depression Scale (SDS).[71] Further analysis was conducted to evaluate differences between male and female samples for anxious and depressive symptoms.

MEASURENTS

Different countries have used FTND to assess the intensity of physical addiction to nicotine.[72] The questionnaire consists of 6 questions that allow specialists to examine various aspects of smoking dependence, assigning a variable score from 0 to 3 points for each question. The final score (ranging from 0 to 10) enables specialists to classify nicotine dependence according to its intensity. In the present study, it was decided to follow the indications contained in the guidelines of the European Network for Smoking and Tobacco [73] for the classification of the level of nicotine addiction intensity: a score of 0-3 indicates the absence or presence of low addiction, a score of 4-6 indicates a presence of moderate dependence, while a score of 7-10 indicates a state of high dependence.

Usually, the SAS and the SDS are self-administered tests commonly used to evaluate the presence of anxiety and depressive symptoms, respectively. Both SAS and SDS are 4-point Likert scales consisting of 20 items related to the psycho-somatic state of the past week.[74,75] For both tests, four distinct scoring groups were adopted to assess the intensity of symptomatology. Specifically, for the SAS, the following criteria have been adopted: a score of 22-44 indicate no anxiety symptoms; a score of 45-59 indicate mild anxiety symptoms; a score of 60-74 indicate moderate symptoms; while, a score of 75-80 indicate high anxiety symptoms.

On the other hand, for the SDS, the following criteria have been employed: a score of 20-49 indicate no depressive symptoms; a score of 50-59 indicate mild depressive symptoms; a score of 60-69 indicate moderate depressive symptoms; while a score of 70-80 indicate high depressive symptoms.

A validated questionnaire commonly used to assess symptoms indicative of a possible ADHD condition, based on the diagnostic criteria of the DSM-IV, is the ASRS.[76] It is divided into two parts (Part A and Part B), with Part A comprising 6 questions and Part B comprising 12 questions. Participants respond by choosing one of five possible choices (never, rarely, sometimes, often, very often). Scores equal to or greater than 6 in Part A of the ASRS indicate a positive result on the screening test and suggest the possible presence of ADHD. The test has good sensitivity (68.7%), specificity (99.5%), and accuracy (97.9%) in assessing the presence of ADHD,[77] although these properties tend to decrease in the presence of a substance use disorder.[78]

STATISTICAL ANALYSIS

The statistical analysis was performed using analysis of variance (ANOVA), as well as chi-square, Fisher"s exact, and Kruskal-Wallis tests with v.17.0. ©Statistics and Data Science software. "Analysis of Variance serves as a generalization of Student"s t-test and is employed when comparing three or more data sets.[79] The chi-square is a non-parametric test typically used with categorical variables and large sample sizes to compare the distribution of two or more independent variables with respect to a theoretical distribution (ibidem). Similarly, Fisher"s exact test is a non-parametric test used for analyzing categorical variables with small sample sizes. Finally, the Kruskal-Wallis test is used as an alternative to ANOVA to compare the medians (instead of the means) of different populations.

Results

SOCIO-DEMOGRAPHIC CHARACTERISTICS

Sex. In the general sample, males are more prevalent than females, constituting 58.4% and 41.6% of the total, respectively. Concerning the ASRS screening test, males are also more numerous in the ASRS negative group compared to the ASRS

positive group, accounting for 58.8% and 55.3%, respectively. However, this higher prevalence is not statistically significant (p-value = 0.483).

Age. The average age of the entire sample is 50.3 years. In the negative ASRS group, the average age is higher than in the positive ASRS group (50.8 vs. 46.0). However, these differences are not statistically significant (p-value = 0.491).

Marital status. In the overall sample, 54.6% were married or cohabiting, 23.7% were single, 17.2% were separated or divorced, and 4.5% were widowed. Regarding the negative and positive ASRS groups, the statistical analysis revealed significant differences (p-value = 0.003). There was a higher prevalence in the positive ASRS group compared to the negative ASRS group for the "single" category (33.3% vs. 22.6%) and the "separated/divorced" category (19.3% vs. 17.0%). Conversely, the negative ASRS group had higher percentages than the positive ASRS group for the "married/cohabiting" category (55.4% vs. 47.4%) and the "widowed" category (5.0% vs. 0.0%).

Education. : In the overall sample, the most prevalent education category is "high/professional school" (45.2%), followed by "primary/secondary school" (36.0%) and "degree" (18.8%). However, the differences observed between the negative and positive ASRS groups are statistically insignificant (p-value = 0.982).

Employment. Regarding the employment variable, the most represented categories are "employee" (28.7%), "freelance" (17.8%), and "other work" (16.5%). The following categories are below: "worker" (9.2%), "unemployed" (8.3%), "retiree" (5.9%), "artisan/trader" (4.2%), "manager" (2.8%), "housework" (2.3%), "student" (1.9%), "teacher" (1.8%), and "casual worker" (0.6%). For this variable, the differences found between the negative and positive ASRS groups are statistically significant (p-value = 0.014). In detail, the most represented categories in the positive ASRS group compared to the negative one are "unemployed" (11.5% vs. 7.9%), "student" (6.2% vs. 1.4%), "teacher" (3.5% vs. 1.6%), "housework" (3.5% vs. 2.1%), "casual worker" (1.8% vs. 0.4%), "worker" (9.7% vs. 9.1%), and "artisan/trader" (4.4% vs. 4.2%).

	Negative ASRS group		Positive ASRS group		Total		p-value*
	N	%	N	%	N	%	
SOCIO-DEMOGRAPHIC CHARACTERISTICS							
Sex							
males	567	58.8	63	55.3	630	58.4	0.483[1]
females	397	41.2	51	44.7	448	41.6	
Average age ± sd	50.8±12.3		46±12.9		50.3±12.5		0.491[2]
Marital status							
single	217	22.6	38	33.3	255	23.7	0.003[1]
married/cohabiting	533	55.4	54	47.4	587	54.6	
separated/divorced	163	17.0	22	19.3	185	17.2	
widower	48	5.0	0	0.0	48	4.5	
Education							
primary/secondary school	347	36.0	41	36.0	388	36.0	0.982[1]
high/professional school	436	45.3	51	44.7	487	45.2	
degree	180	18.7	22	19.3	202	18.8	
Employment							
unemployed	75	7.9	13	11.5	88	8.3	0.014[4]
student	13	1.4	7	6.2	20	1.9	
artisan/trader	40	4.2	5	4.4	45	4.2	
housework	20	2.1	4	3.5	24	2.3	
worker	86	9.1	11	9.7	97	9.2	
employee	274	29	30	26.5	304	28.7	
teacher	15	1.6	4	3.5	19	1.8	
freelancer	173	18.3	15	13.3	188	17.8	
manager	28	3	2	1.8	30	2.8	
casual worker	4	0.4	2	1.8	6	0.6	
retiree	57	6	5	4.4	62	5.9	
other work	160	16.9	15	13.3	175	16.5	

Table 1 summarizes the results related to the socio-demographic characteristics of the two analyzed groups. 1 Fisher"s exact; 2 ANOVA (one-way); 3 Kruskal-Wallis equality-of-populations rank test; 4 Chi-square.

FACTORS RELATED TO TOBACCO ADDICTION
Onset of smoking age. When considering the entire sample, the average age at which smoking began is 16.9 years for all participants. The same average age is observed in both the negative and positive ASRS groups, with no statistically significant differences (p-value = 0.687).

Scores of FTND. Referring to the total sample, 48.8% of users obtained a score of 4-6 on the FTND (indicating moderate nicotine addiction), while a a percentage of 35.5% reported a score of 7-10 (indicating high nicotine addiction), and 15.7% obtained a score of 0-3 (indicating absence/low addiction). Significant statistically differences (p-value = 0.045) were found between the negative and positive ASRS groups. The positive ASRS group had a higher representation of high nicotine addiction (44.7%) compared to the negative ASRS group (34.4%), and conversely, it was also more representative of moderate (49.2%) and absence/low addiction conditions (16.4%) than the positive group (45.6% and 9.6%, respectively).

Number of cigarettes smoked. The average number of daily cigarettes smoked by each user in our study is 20. This same number of cigarettes emerged in the negative and positive ASRS groups. Statistically significant differences (p-value = 0.045) are only evident in the interquartile range, with the positive ASRS group showing a greater fluctuation around the average number of daily cigarettes smoked (17-30) compared to the negative ASRS group (15-25).

Previous attempts to quit smoking, number of attempts, and duration of past abstinence. Out of the 1077 users in our database, for whom it was possible to obtain this data, 81.4% reported having attempted to quit smoking at least once before seeking our services. Regarding the duration of abstinence, 64.6% of users stated that they had achieved total abstinence lasting less than 6 months, while 35.4% had achieved abstinence from smoking lasting longer than 6 months. There were no significant differences between the negative and positive ASRS groups in terms of previous attempts to quit smoking (p-value = 0.702), number of

attempts (p-value = 0.310), and duration of past abstinence (p-value = 0.978). These results closely resemble those of the general sample.

Cohabitation with smokers. Among the smokers in our sample, 63.3% reported not living with another smoker. Small differences were observed between the negative ASRS group (63.8%) and the positive ASRS group (58.8%), although these differences were not statistically significant (p-value = 0.305).

Smoking in pregnancy. Of the 448 female users in our sample, 64.7% reported not smoking during pregnancy. Non-significant differences (p-value = 0.537) were observed in the comparison between the negative and positive ASRS groups. The positive ASRS group had a slightly higher prevalence of

smoking during pregnancy (39.2%) compared to the negative ASRS group (33.8%).

Cigarette consumption in the last 12 months. Among the users in our sample, 56.6% reported no change in their smoking behavior over the past year, while 28.1% reported an increase, and 15.3% reported a decrease. Statistically significant differences (p-value = 0.015) were found between the negative and positive ASRS groups. Specifically, in the negative ASRS group, 26.8% reported an increase in smoking compared to 39.5% in the positive ASRS group. In terms of decreased smoking, 15.9% of the negative ASRS group reported a decrease compared to 10.5% in the positive ASRS group. Additionally, 57.4% of the negative ASRS group and 50.0% of the positive ASRS group reported no change in consumption over the last year.

	Negative ASRS group		Positive ASRS group		Total		*p*-value*
	N	%	N	%	N	%	
FACTORS RELATED TO TOBACCO ADDICTION							
Average onset of smoking age ± sd	16.9±3.9		17±4.1		16.9±4		0.687[2]
FTND scores							
absence/low addiction	158	16.4	11	9.6	169	15.7	
moderate addiction	474	49.2	52	45.6	526	48.8	0.045[1]
high addiction	332	34.4	51	44.7	382	35.5	
Average number of cigarettes smoked (25°-75°)	20 (15-25)		20 (17-30)		20 (15-25)		0.045[3]
Previous attempts to quit smoking							
no	181	18.8	19	16.7	200	18.6	0.702[1]
yes	782	81.2	95	83.3	877	81.4	
Average number of past attempts to quit smoking (25°-75°)	1 (1-2)		1 (1-3)		1 (1-2)		0.5922[3]
Duration of previous abstinence							
< 1 month	398	41.3	46	40.7	444	41.2	
1-3 months	149	15.5	17	15	166	15.4	0.978[1]
4-6 months	76	7.9	10	8.9	86	8	
> 6 months	341	35.4	40	35.4	381	35.4	
Cohabitation with smokers							
no	615	63.8	67	58.8	682	63.3	0.305[1]
yes	367	35.4	53	42.4	420	36.2	
Smoking in pregnancy (n = 448)							
no	259	65.2	31	60.8	290	64.7	0.537[1]
yes	138	34.8	20	39.2	158	35.3	
Cigarette consumption in the last 12 months							
increased	258	26.8	45	39.5	303	28.1	
decreased	153	15.9	12	10.5	165	15.3	0.015[1]
unchanged	553	57.4	57	50	610	56.6	

Table 2 summarizes the results related to the tobacco addiction factors of the two analyzed groups. (*) The data collected for the "Smoking home" and "Average number of gestures" variables pertain to a period of 3 years (2019-2021). 1 Fisher''s exact; 2 ANOVA (one-way); 3 Kruskal-Wallis equality-of-populations rank test; 4 Chi-square.

ALCOHOL CONSUMPTION
Regarding the total sample of smokers, 81.2% reported consuming alcohol; among these, 63.2% had occasional consumption, 29.6% had habitual consumption, and 7.2% had problematic consumption. In total, 9.6% of the sample reported a history of problematic alcohol use. The differences observed in the negative and positive ASRS groups were not statistically significant for the variables "current alcohol consumption" (p-value = 0.128), "mode of current alcohol consumption" (p-value = 0.106), and "past alcohol problems" (p-value = 0.499). Specifically, the descriptive analysis revealed that 81.7% of the negative ASRS group and 75.4% of the positive ASRS group consume alcohol. Among these, 62.1% have occasional alcohol use in the negative ASRS group compared to 73.3% in the positive ASRS group; 30.3% have habitual use in the negative ASRS group compared to 23.3% in the positive group, while 7.6% have problematic use in the negative ASRS group compared to 3.5% in the positive group.

	Negative ASRS group		Positive ASRS group		Total		p-value*
	N	%	N	%	N	%	
ALCOHOL CONSUMPTION							
Current alcohol consumption							
no	176	18.3	28	24.6	204	18.9	0.128[1]
yes	788	81.7	86	75.4	874	81.1	
Mode of current alcohol consumption (n = 874)							
occasional	489	62.1	63	73.3	552	63.2	
habitual	239	30.3	20	23.3	259	29.6	0.106[1]
problematic	60	7.6	3	3.5	63	7.2	
Past alcohol problems (n = 1.078)							
no	874	90.7	101	88.6	975	90.4	0.499[1]
yes	90	9.3	13	11.4	103	9.6	

Table 3 summarizes the results related to the alcohol consumption of the two analyzed groups. 1 Fisher"s exact; 2 ANOVA (one-way); 3 Kruskal-Wallis equality-of-populations rank test; 4 Chi-square.

PREVIOUS AND CURRENT USE OF ILLICIT SUBSTANCES
Among the total sample, 8.7% reported previous use of illicit substances, including heroin, cocaine, or cannabis. The statistical analysis, however, indicates the presence of a marginally significant difference (p-value = 0.051) in this variable between the negative and positive ASRS groups, with percentages of 8.1% and 14.0%, respectively.

	Negative ASRS group		Positive ASRS group		Total		p-value*
	N	%	N	%	N	%	
PREVIOUS AND CURRENT USE OF ILLICIT SUBSTANCES							
no	886	91.9	98	86	984	91.3	0.051[1]
yes	78	8.1	16	14	94	8.7	

Table 4 summarizes the results related to the previous and current use of illicit substances of the two analyzed groups. 1 Fisher"s exact; 2 ANOVA (one-way); 3 Kruskal-Wallis equality-of-populations rank test; 4 Chi-square.

COMORBID PSYCHIATRIC SYMPTOMS
Anxiety symptoms. The analysis of the SAS yielded an average score of 44 for all users in our sample, with 51.4% reporting the absence of anxious symptoms. Conversely, 38.2%, 7.8%, and 2.6% reported mild, moderate, and high anxiety symptoms, respectively. Differences were also observed in these values when comparing scores by gender. For males, the average SAS score was 43, with 56.9% reporting the absence of anxiety symptoms. In contrast, for females, the average score was 46, with 43.8% reporting the absence of anxiety symptoms. Mild, moderate, and high anxiety symptoms were present in 33.7%, 6.8%, and 2.5% for males, and in 44.4%, 9.1%, and 2.7% for females, respectively. Regarding the statistical analysis conducted between the negative and positive ASRS groups, significant differences emerged in all the various dimensions of anxiety analyzed. Specifically, the positive ASRS group reported a SAS average score of 50, which was statistically higher (p-value < 0.001) than the average score of 44 reported by the negative ASRS group. The interquartile differences were also higher in the positive ASRS group (46-59) than in the negative one (38-50). Furthermore, the analysis

of anxiety symptom intensity (p-value < 0.001) highlighted a higher prevalence of mild and moderate anxiety symptoms in the positive ASRS group compared to the negative ASRS group (56.1% vs. 36.0%; 21.9% vs. 6.1%), while the negative ASRS group had a higher prevalence in the extremes of the anxious continuum, namely the presence of high symptoms (1.8% vs. 2.7%) and the absence of any symptoms (20.2% vs. 55.1%). Statistical significance also emerged when the differences in the two groups were analyzed by dividing the total sample according to gender (p-value < 0.001). In detail, the average SAS scores for males were 49 for the positive ASRS group and 41 for the negative one. Similarly, the same scores for females were 51 for the positive ASRS group and 45 for the negative one. The interquartile intervals also differed between the two groups: for males, the positive ASRS group obtained a higher interquartile score (44-59) compared to the

negative one (36-49). Likewise, for females, the positive ASRS group obtained a higher interquartile score (46-60) than the negative one (39-53). The distribution of anxiety symptom intensity also significantly differed between the two groups as a function of gender: for males, the absence of anxiety and the presence of severe anxiety symptoms were greater for the negative (60.4%; 2.8%) than the positive ASRS group (25.4%; 0.0%). Conversely, the presence of mild and moderate anxiety symptoms appeared higher in the positive (52.4%; 22.2%) than the negative ASRS group (31.6%; 5.1%). For the female gender, on the other hand, the percentage of absence of anxious symptoms was higher in the negative (47.6%) than the positive (13.7%) ASRS group; conversely, the presence of mild, moderate, and severe anxiety symptoms was higher in the positive (60.8%; 21.6%; 3.9%) than the negative ASRS group (42.3%; 7.6%; 2.5%).

	Negative ASRS group		Positive ASRS group		Total		p-value*
	N	%	N	%	N	%	
PSYCHIATRIC COMORBIDITIES: ANXIETY SYMPTOMS							
SAS scores - total							
no symptoms	531	55.1	23	20.2	554	51.4	
mild symptoms	347	36	64	56.1	411	38.2	<0.001[1]
moderate symptoms	59	6.1	25	21.9	87	8	
high symptoms	26	2.7	2	1.8	28	2.6	
average SAS scores – total (25°-75°)	44 (38-50)		50 (46-59)		44 (38-51)		<0.0001[3]
SAS scores – males (n = 629)							
no symptoms	342	60.4	16	25.4	358	56.9	
mild symptoms	179	31.6	33	52.4	212	33.7	<0.001[1]
moderate symptoms	29	5.1	14	22.2	43	6.8	
high symptoms	16	2.8	0	0.0	16	2.5	
average SAS scores – males (25°-75°)	45 (39-53)		51 (46-60)		46 (39.5-53.5)		0.001[1]
SAS scores - females							
no symptoms	189	47.6	7	13.7	196	43.8	
mild symptoms	168	42.3	31	60.8	199	44.4	<0.001[1]
moderate symptoms	30	7.6	11	21.6	41	9.1	
high symptoms	10	2.5	2	3.9	12	2.7	
average SAS scores - females (25°-75°)	45 (39-53)		51 (46-60)		46 (39.5-53.5)		0.001[1]

Table 5 summarizes the results related to the anxiety simptoms of the two analyzed groups. 1 Fisher"s exact; 2 ANOVA (one-way); 3 Kruskal-Wallis equality-of-populations rank test; 4 Chi-square.

Depression symptoms. In the general sample, an average SDS score of 44 was found. The analysis of the distribution of depressive symptoms in the total sample revealed the following statistics: among users, 65.7% did not report any depressive symptoms, 22.7% reported mild symptoms, 9.3% showed moderate symptoms, and 2.3% reported

severe symptoms. When considering gender differences, the average SDS score was higher in the female group (46) than in the male one (43). In particular, 69.4% of the male group did not show any depressive symptoms based on the SDS scores, 20.9% showed mild symptoms, 8.6% reported moderate symptoms, while severe symptoms were

found in 1.1% of users. On the other hand, in the female group, 60.5% did not show any depressive symptoms, 25.2% had mild symptoms, 10.3% had moderate symptoms, while severe symptoms were found in 4% of users. The statistical analysis comparing the negative and positive ASRS groups highlighted a significant difference between the two groups: while the negative ASRS group scored an average SDS score of 44, the positive one reported an average score of 53.5 (p-value < 0.001). Significant differences also emerged when comparing the interquartile range of the positive (48-63) vs. negative ASRS group (36-51). Overall, the distribution of depressive symptoms appeared asymmetrical (p-value < 0.001): the absence of depressive symptoms was 69.3% for the negative ASRS group and 35.1% for the positive one; mild depressive symptoms were found in 21.7% of the negative ASRS group versus 31.6% of the positive group. The difference in the distribution of moderate depressive symptoms was more pronounced, with a percentage of 7.5% for the negative ASRS group and 24.6% for the positive one. Finally, the prevalence of severe symptoms was also significantly different, with the negative ASRS group at 1.6% and the positive one at 8.8%. Significant differences (p-value < 0.001) were also found when dividing the two groups according to

gender: for the ASRS negative group, the average SDS score for males was 43 (interquartile range: 36-50), while for the positive one, it was 53 (interquartile range: 45-61); conversely, for the ASRS negative group, the average SDS score for females was 45 (interquartile range: 39-54), while for the positive one, it was 55 (interquartile range: 48-66). For both male and female genders, the negative ASRS group had a higher percentage of users without any depressive symptoms (male: 72.7%; female: 64.5%) than the positive ASRS group (male: 39.7%; female: 29.4%). In contrast, the positive ASRS group reported higher percentages of users with depressive symptoms than the negative one for both male and female genders, with variable distributions according to the level of intensity of the symptoms: for the positive ASRS group, the percentage of mild, moderate, and severe depressive symptoms for the male gender was 30.2%, 25.4%, and 4.8%, respectively, while for the female one, it was 33.3%, 23.5%, and 13.7%, respectively. On the other hand, for the negative ASRS group, the percentage of mild, moderate, and severe depressive symptoms for the male gender was 19.9%, 6.7%, and 0.7%, respectively, while for the female one, it was 24.2%, 8.6%, and 2.8%, respectively.

	Negative ASRS group		Positive ASRS group		Total		*p*-value*
	N	%	N	%	N	%	
PSYCHIATRIC COMORBIDITIES: DEPRESSIVE SYMPTOMS							
SDS scores - total							
no symptoms	668	69.3	40	35.1	708	65.7	
mild symptoms	209	21.7	36	31.6	245	22.7	
moderate symptoms	72	7.5	28	24.6	100	9.3	<0.001[1]
high symptoms	15	1.6	10	8.8	25	2.3	
Average SDS scores (25°-75°)	44 (36-51)		53.5 (48-63)		44 (38-53)		
SDS scores – males (n = 630)							
no symptoms	412	72.7	25	39.7	437	69.4	
mild symptoms	113	19.9	19	30.2	132	20.9	
moderate symptoms	38	6.7	16	25.4	54	8.6	<0.001[1]
high symptoms	4	0.7	3	4.8	7	1.1	
Average SDS scores - males (25°-75°)	43 (36-50)		53 (45-61)		43 (36-51)		
SDS scores - females							
no symptoms	256	64.5	15	29.4	271	60.5	
mild symptoms	96	24.2	17	33.3	113	25.2	
moderate symptoms	34	8.6	12	23.5	46	10.3	
high symptoms	11	2.8	7	13.7	18	4.0	<0.001[1]
Average SDS scores - females (25°-75°)	45 (39-54)		55 (48-66)		46 (39-54)		

Table 6 summarizes the results related to the depressive simptoms of the two analyzed groups. 1 Fisher"s exact; 2 ANOVA (one-way); 3 Kruskal-Wallis equality-of-populations rank test; 4 Chi-square.

Discussion

A neuropsychiatric disorder that can occur in preschool and persist into adulthood is ADHD.[8] Several studies have recently confirmed the presence of an association between ADHD and smoking.[80] For instance, the presence of ADHD has been linked to an increased risk of smoking during adolescence [81] and early adulthood,[18] along with a incresed number of cigarettes smoked compared to individuals without this diagnosis.[15,16,22] Furthermore, the number of cigarettes smoked appears to be directly proportional to the severity of ADHD symptoms.[19] Although this association is well-established in scientific literature, the underlying reasons for this relationship remain unclear. According to the "self-medication hypothesis",[34] smoking has been suggested as a coping strategy employed by people with ADHD to reduce certain symptoms of the disorder, particularly those related to inattention.[40,58-60,82] However, the presence of data that contradicts this hypothesis [62-65] prompts pts further investigation into the nature of the relationship between smoking and ADHD. Our study aims to contribute to this understanding by providing potentially valuable data.

In line with previous epidemiological studies that identify male gender as a risk factor for the development of ADHD [12] and TUD, our data corroborate this prediction. The percentage of male smokers in our sample was higher than that of female smokers. Moreover, the percentage of male users exhibiting suspected ADHD symptoms was also greater than that of female users with similar characteristics. While these statistics might have led us to hypothesize a higher prevalence of suspected ADHD among male smokers, our data did not confirm this assumption. There were no statistically significant differences between the group of male smokers with suspected ADHD and those without possible ADHD symptoms. Therefore, male gender appears to be a risk factor for both ADHD and TUD, but not for the comorbidity between the two disorders.

The variable "Average age" does not appear to be a predictive factor for the comorbidity between ADHD and TUD. Contrary to findings in other studies,[27] the difference in mean age, while observed in our study between the positive ASRS group and the negative ASRS group, did not reach clear statistical significance. However, different results were obtained regarding the variable "Marital status". Specifically, the percentages of singles and separated/divorced individuals in the group with suspected ADHD in our sample were statistically higher compared to those reported by the group without this potential issue. These findings could collectively suggest that individuals experiencing ADHD symptoms may face greater difficulties in maintaining stable romantic relationships over time, aligning with findings from other studies in the literature.[83]

Considering the data present in the literature,[84] one might have expected that the positive ASRS group in our sample would have lower education levels compared to the negative ASRS group. However, such evidence did not emerge in our study, as the differences in education levels between the two groups did not reach statistical significance. This lack of evidence gives rise to several possible explanations, one of which aligns with the aforementioned self-medication hypothesis. It is therefore plausible to hypothesize that individuals with ADHD symptoms, using smoking as a coping mechanism for their attention difficulties, manage to attain academic achievements on par with those of non-symptomatic individuals. However, the compensatory effect offered by smoking may not extend to the work environment. The observed differences in terms of occupation between the positive ASRS group and the negative group could be attributed to the potential impact of ADHD symptoms on employment opportunities or job performance, as indicated in the literature. [85]

Interesting insights into understanding the association between ADHD and TUD are revealed through the analysis of Tobacco Addiction Factors. Specifically, users with a positive ASRS score tend to smoke more cigarettes on average and exhibit a stronger nicotine addiction compared to those with a negative ASRS score. This finding aligns with established knowledge in the scientific literature.[18,19] However, what stands out as surprising is the absence of a clear difference in the age of onset of smoking behavior between the two groups, despite this being reported in many studies on the subject.[16,29,86] It is also intriguing that tobacco product consumption has seen a more significant increase in the positive ASRS group than in the negative ASRS group over the past 12 months. Considering the entire timeline of the pandemic, this finding could suggest that smoking is being employed as a coping mechanism to deal with emotional and relational distress during various phases of pandemic-related lockdowns.

While we expected similar results when analyzing the "Alcohol consumption" variable,[32] our study did not reveal significant differences between the positive ASRS group and the negative ASRS group. Several factors may contribute to this, including the

cultural context of our sample, which is more accepting of regular alcohol use even in non-clinical populations. However, a different pattern emerged concerning past disorders related to illicit substance use (cannabis, cocaine, heroin), where the positive ASRS group displayed a statistically higher percentage compared to the negative ASRS group. This finding is not surprising,[87] but it still lacks a clear explanation in the literature.[33] Drawing upon the gateway hypothesis,[88] it is conceivable that early exposure of the brain to the dopaminergic and acetylcholinergic effects of nicotine might enhance the subsequent reinforcement of other substances of abuse, potentially increasing the risk of developing addiction disorders later in life than the onset of TUD. Some recent studies seem to lend support to this hypothesis [33,89] offering a potential explanatory framework for the findings in our study.

Finally, with regard to the last group of variables we examined, related to the "Comorbid psychiatric symptoms" group, the data from our descriptive research reveal that, regardless of gender, users in the positive ASRS group display overall higher levels of anxiety and depression symptoms compared to those in the negative ASRS group. This finding aligns with other data in the literature that demonstrate a higher prevalence of affective symptoms in the ADHD population compared to the non-clinical population.[54,56] Despite the presence of such symptoms suggesting a self-medicating use of smoking,[52] the existence of studies predicting cigarette and alcohol consumption independently from anxious and depressive symptoms [32] encourages considering alternatives. What is surprising in our study is the unexpected gender difference observed between the two groups. While one might have expected a higher overall prevalence of anxious and depressive symptoms in the positive ASRS group compared to the negative one, our data revealed a higher prevalence of high-intensity anxious symptoms in the negative ASRS group compared to the positive one, which can be attributed to gender differences. This difference was explained by the absence of male users in the positive ASRS group who reported high-intensity anxious symptoms, a distinction that appears to be selective for this symptomatology. In contrast, when it comes to depressive symptoms, male users reported higher percentages of high-intensity symptomatology. One possible explanation that could be derived from this observation is that smoking may offer a greater anxiolytic effect in the male ADHD population than it does in the female ADHD population. If this hypothesis were correct, it could account for the discrepancies found in the literature regarding the self-medication hypothesis, prompting a differential analysis of the impact of smoking on the ADHD population based on gender.

What emerges from our study is that several factors related to sociodemographic characteristics, smoking behavior, previous and current use of illicit substances, and current levels of anxiety and depression could potentially influence the maintenance of TUD. At the current state of scientific knowledge, it is not clear how these factors may interact with each other, contributing to the persistence of tobacco dependence in the ADHD population. For instance, one hypothesis could be that ADHD symptoms, by contributing to difficulties in maintaining stable emotional relationships and steady employment, may elevate levels of anxiety and depression, thereby driving compulsive smoking as a means of self-medication. Simultaneously, it could be posited that a heightened sensitivity to the cognitive dimension of withdrawal symptoms[16,23,24] might render the ADHD smoker population more susceptible to developing anxious and depressive symptoms that disrupt equilibrium in their personal and professional lives. Alternatively, it could be proposed that difficulties in inhibiting maladaptive automatic responses [90,91] could predispose these individuals to develop and sustain high levels of dependence, irrespective of other factors related to emotional, familial, and occupational domains. Further research is warranted to elucidate the nature of this intricate relationship.

Conclusions

This study is not without limitations. Firstly, the retrospective nature of the study hinders the ability to select participants post hoc, making it challenging to control for potential moderating variables. Consequently, the obtained results might be influenced by variables not considered in our study. Secondly, the self-report nature of the administered questionnaires renders the results susceptible to biases associated with each user's subjective perspective. Some users might unconsciously underestimate or overestimate certain addiction, anxiety, or depression symptoms; they might intentionally provide incorrect answers to present a more socially acceptable self-image; they could exaggerate their level of distress to obtain the help they believe they need; or they might deny the presence of problems in areas investigated by the questionnaires that go beyond the objectives of nicotine cessation, which they sought the service for. The absence of psychophysiological measurements alongside the self-report data limits the validity of these responses. Thirdly, the users in our sample

were recruited to our service both before and during the pandemic crisis. Given the highly stressful nature of this event, many of the results emerging in the study might represent more of a psycho-emotional reaction confined to the onset of the pandemic rather than stable characteristics of the populations under study. Lastly, since the ASRS is not a diagnostic questionnaire but a screening tool, the users in our study who obtained a positive score might not truly have ADHD. In fact, none of the participants in the positive ASRS group had a previous diagnosis of ADHD. These significant limitations therefore prevent the extension of the results obtained from this group to the general population grappling with the disorder and, as such, they should be interpreted with caution. Although further studies are necessary to comprehend the characteristics of the population grappling with ADHD and TUD, a potential comorbidity with ADHD should be evaluated within smoking cessation pathways. The ASRS test, while not diagnostic, has demonstrated in our study its ability to differentiate a more intricate pattern of TUD due to its ease of use. A screening diagnosis could facilitate a diagnostic investigation and provide an opportunity for tailored treatments.

Conflicts of Interest Statement and Funding Statement

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