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The Degree of Multidimensional Severity of Alcohol Use Disorder among Treatment-Seeking Patients

Is There an Additive Effect of Parental Alcohol Use Disorder?

Ahmad-Nielsen, Emil B; Andersen, Nicolai Gundtoft; Andersen, Kjeld; Nielsen, Anette Søggaard; Mellentin, Angelina I

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Title page

Title: The degree of multi-dimensional severity of alcohol use disorder among treatment-seeking patients. Is there an additive effect of parental alcohol use disorder?

Running title: The additive effect and multi-dimensional addiction severity

Authors: Ahmad-Nielsen E.B.^{*, 1}, Andersen N.G.^{*, 1}, Andersen K.¹, Nielsen A.S.¹, Mellentin A.I.^{1,2}

* Shared first authorship

Affiliations:

¹ Unit for Clinical Alcohol Research, Unit for Psychiatric Research, Department of Clinical Research, University of Southern Denmark.

² Unit for Psychiatric Research, Institute of Regional Health Services Research, University of Southern Denmark, Aabenraa, Denmark.

Corresponding author: Nicolai Gundtoft Andersen

Postal address: Unit of Psychiatric Research, Department of Psychiatry, University Hospital, J. B. Winsløvsvej 18, 220 A, DK-5000 Odense C, Denmark.

Email: nicolaigundtoft@gmail.com

Phone: +4531314891

Keywords: alcohol use disorder, addiction severity, family history, outpatients

ABSTRACT

Background: The additive effect of parental alcohol use disorders (AUD) is conventionally defined as an increasing risk of the offspring developing AUD relative to family history negative (FHN), < family history positive with one parent (FHP1), < family history positive with two parents (FHP2). The few studies on the additive effect of parental AUD have focused on the risk of development of offspring AUD and not on the degree of multi-dimensional AUD addiction severity.

Aims: The aims of the present study were to examine the frequency of treatment-seeking outpatients exposed to FHP1 and FHP2 and whether addiction severity was impacted by the additive effect of parental AUD among AUD female and male offspring.

Methods: This cross-sectional study was based on 3361 consecutive treatment-seeking outpatients from 2006 to 2016, assessed by means of the European Addiction Severity Index (EUROP-ASI). The EUROP-ASI assessed multi-dimensional addiction severity, comprising alcohol and other drug use, somatic and psychiatric health status, family and other social status, economy and employment-related problems, and criminal status composite scores at treatment entry.

Results: Among females, 40.38% had FHP1 and 15.68% FHP2, whereas males had 40.90% FHP1 and 13.24% FHP2. No conventional additive effect was found on the composite scores among both genders. However, another type of synergistic additive effect, only manifesting with exposure to FHP2, was found for employment-related problems and psychiatric status composite scores among male offspring.

Conclusions: Exposure to parental AUD is strikingly high among treatment-seeking outpatients. Nonetheless, the additive effect has a modest impact on multi-dimensional addiction severity and is mostly related to psycho-social impairment among treatment-seeking male offspring.

Keywords: alcohol use disorder, addiction severity, family history, outpatients

1. Introduction

In Europe, Alcohol Use Disorders (AUD) are dichotomous constructs and defined as the harmful use or dependence of alcohol according to the International Classifications of Diseases, version 10 (ICD-10) (1). Harmful use of alcohol is characterized by a pattern of continued alcohol use that causes damage to physical and/or mental health, and alcohol dependence, a more severe condition, is characterized by a cluster of behavioral, cognitive, and physiological phenomena that develops because of repeated alcohol use and which typically include different constellations of symptoms. These symptoms include: cravings, lack of control over alcohol use, continued use despite harmful consequences, prioritizing alcohol use over other activities and obligations, increased tolerance to alcohol; and physiological withdrawal (1).

The prevalence of AUD, according to ICD-10, is 7.5% in Europe (2), and it has been estimated, that approximately 20% of children in the general population are exposed to parental AUD (3, 4). It is well known that AUD have a tendency to accumulate in families (5, 6). The prevalence of adults with AUD and a family history of AUD range from 4-22% in the general population (3, 4, 7, 8) and from 47% to 56% among treatment-seeking AUD populations (9, 10). It has been hypothesized, that there may be an additive effect by exposure of parental AUD with an increasing risk of offspring developing AUD with family history negative (FHN) < family history positive with one parent (FHP1) < family history positive with two parents (FHP2). The current focus in the empirical literature evolves around studies based on the general population, either through survey- or register-based studies. Three population-based studies have investigated whether there is an additive parental effect on the risk of offspring developing AUD (4, 8, 11), and the studies suggest an at least two-fold increased risk when offspring is exposed to FHP1 (4, 8, 11) and four-fold increased risk when exposed to FHP2, when compared to FHN (8, 11). Overall, the studies

support an additive effect of parental AUD, though less clear, whereas female (8) or male (11) offspring is the most impacted by the effects.

While the development of AUD is a relatively specific concept following the diagnostic criteria and ending up in a dichotomous classification according to ICD-10 (1, 12), the severity of the disorder has somehow been harder to define. In general, severity has been a disputed concept with both narrow definitions, e.g. AUD symptom counts operationalised from a uni-dimensional scale using AUD diagnostic criteria (13, 14), and broader definitions operationalized with multi-dimensional scales, e.g. Addiction Severity Index (ASI) assessing seven or nine different areas that affect and/ or are affected by AUD (15, 16). The European adapted version (EUROP-ASI), consists of the following nine dimensions; alcohol and other drug use, psychiatric and somatic health status, family and social relations, economy and employment-related problems and criminal status (16). It is plausible that offspring may not just be more likely to develop AUD as a dichotomous classification concept, but that the additive effect may indeed impact the severity of the disorder. This may be true regarding operationalization with uni-dimensional scales and, in particular, multi-dimensional scales, given that the accumulation of genetic and environmental influences may manifest in several areas, worsening the overall addiction severity profile. An Australian register-based children-of-twins study investigated AUD severity defined in narrow terms in relation to the additive effect and found, that FHP2 fulfilled more diagnostic AUD criteria than FHP1. Hence, their study supported an additive effect on addiction severity (17), and indicates that not just the presence of AUD, but also the severity of AUD, may be impacted. In contrast to prior studies on the development of AUD (8, 11), no difference was found among genders.

With a linkage indicating an additive effect on the likelihood for offspring of AUD parents developing AUD, the number of studies concerning other indices of addictive

severity than symptom counts of the diagnostic criteria for AUD is lacking. Furthermore, no studies have examined the degree of addiction severity, neither within a narrow nor broad definition concerning the additive effect among treatment-seeking AUD populations. The degree of parental AUD exposure and AUD severity measured with a multi-dimensional measure is of crucial importance to estimate how congested and which areas are mostly affected when AUD offspring are seeking alcohol treatment.

1.1.Aims

The aims of the present study were: 1.) to estimate the frequency of treatment-seeking female and male patients exposed to FHP1 and FH2, and; 2.) to investigate whether multi-dimensional addiction severity was related to an additive effect of parental AUD among offspring entering outpatient treatment for AUD. Regarding the latter, we hypothesized greater severity, showing an additive effect of FHP branching into various areas of life at the time of admission into treatment.

2. Methods and Materials

2.1. Study setting

In Denmark, AUDs are mainly treated at outpatient municipal treatment facilities and only alcohol-related problems are addressed at these facilities. The public outpatient treatment is free of charge for the patient, open for self-referral and has available anonymity. If the patients either suffer from mainly illegal substance use disorders, have severe psychiatric co-morbidity (e.g. acute psychotic disorders), severe cognitive impairment (e.g. dementia) or terminal somatic illness, treatment takes place elsewhere (18).

2.2. Design and participants

This study was carried out as a cross-sectional study based on all 3647 consecutive patients during 2006-2016 seeking treatment for AUDs at the outpatient facility in Odense, Denmark. The data was derived from the database at the treatment facility, covering all patients who underwent pharmacological and psychosocial treatment for the AUD. All patients were required to fulfil an assessment interview at the start of treatment. Since patients may return to treatment several times, entry into the study sample was registered at the patients' first encounter with the outpatient treatment facility. 286 patients were excluded from the study due to lack of information on their gender or family history of AUD. Hence, 3361 patients remained.

2.3. Assessment and assessment instruments

ICD-10 Diagnostic Criteria for Research (DCR-10: (1, 19)) and the European version of the Addiction Severity Index (EUROP-ASI: (15, 16)) comprise the foundation for the routine clinical assessment of patients' characteristics.

The DCR-10 was applied to assess the patients for harmful use of alcohol and dependence (AUD) according to the ICD-10 criteria (19).

The EUROP-ASI was used to collect information relating to parental AUD status (the parents should be biological or at least have adopted the treatment-seeking offspring, which is an exception and may occur in very few cases), sociodemographic characteristics and elaborate an addiction severity profile for each patient during the last 30 days (15, 16). The profile in the European version covers nine areas of the patient's life as described in the introduction (16). A composite score can be calculated in each area, based on the overall presence of problems within the specific area, and can range from 0 to 1, where 0 denotes no problems and 1 denotes severe problems in the specific area. The alcohol and other drug use

composite scores consist of items addressing the consumption pattern, alcohol- or drug-related problems, and perceived need for pharmacological and psycho-social treatment. The medical and psychiatric status composite scores consist of items addressing days with somatic and psychiatric symptoms, degree of concern about the symptoms and perceived importance of receiving relevant treatment. The family and other social status composite scores address whether there have been relational problems with family, friends, at work etc., and the perceived need of professional help to solve these problems. The economy and employment-related problems composite scores consist of items addressing the patients work status as well as work-related problems, degree of concerns and perceived need of counselling. Finally, the legal status composite score addresses whether the patient has been involved in criminal activities and perceived severity of the criminal activity (20).

All assessments were performed by the team of therapists in the facility with the aim of providing feedback to the patient, suggesting a treatment and collecting data for monitoring the quality at the organizational level of the facility. The therapists underwent training in psychiatric diseases and diagnostic procedures. To ensure the reliability of data collected by the therapists, training in the use of the instrument, and supervised test interviews, were conducted regularly during the time of sample collection.

2.4. Variables and analysis

For the analysis, the clinical database sample was divided into three subgroups based on family history for each gender: (1) No parental AUD, categorized as family history negative (FHN); (2) One parental AUD, categorized as family history positive 1 (FHP1) and (3) Two parental AUDs, categorized as family history positive 2 (FHP2). The degree of addiction severity was based on the nine composite scores from the EUROP-ASI.

For descriptive analyses of categorical or continuous data, cross tabulation models and Kruskal-Wallis rank models were used, respectively. The independent variable was family history divided by gender with dependent variables being the composite scores of the multi-dimensional addiction severity operationalized through EUROP-ASI. The selection of Kruskal-Wallis rank models, despite a large sample size, was due to marked deviations from a normal distribution as inspected visually by histograms and subsequently tested with the Shapiro-Wilk test.

A conventional definition of additive effect, i.e. the severity of AUDs would increase with higher FHP ($FHP2 > FHP1 > FHN$), were adopted for subsequent pairwise comparisons. While this more conventional definition was the highest order of additive effect, another unconventional synergistic additive effect approach was also employed. This approach followed the idea that the parent without an AUD-diagnosis could negate the effects of the affected, i.e. the difference in variables only became significant when both parents have AUD ($FHN = FHP1$ & $FHN \neq FHP2$ & $FHP1 \neq FHP2$). Dunn's Multiple Comparison Test were performed on significant Kruskal-Wallis rank models to examine how the groups differed. All analyses were conducted using STATA, version 15.

2.5. Ethics

The authors assert that all procedures contributing to this work comply 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. Formal ethical approval was not required for this study, in accordance with Danish legislation; however, the use of data from the database for research purposes was approved by the Danish Data Protection Agency (region of Southern Denmark, registration number: 2012-58-0018).

3. Results

3.1 *Sample characteristics*

Table 1 shows the sample characteristics of patients divided into parental history and by gender. Of the 3361 patients enrolled in this study, 1065 were female and 2296 were male. In the female patient group sample 468 (43.94%) were FHN, 430 (40.38%) were FHP1 and 167 (15.68%) were FHP2. In the male patients corresponding numbers were 1053 (45.86%), 939 (40.90%) and 304 (13.24%). Thus 56.06% of female and 54.14% of male patients were exposed to some degree of parental AUD.

Insert Table 1 here

The median age when seeking treatment was highest for FHN, followed by FHP1 and lowest for FHP2 among both genders. Similarly, continuing education, defined as any education beyond unskilled labourer, whether being a university degree or vocational education, and employment, defined as having received a pay-check within the last 30 days, followed the same pattern.

3.2 *Addiction severity*

Table 2, shows the multi-dimensional addiction severity, operationalized by means of the ASI composite scores.

For both genders, the only area showing a significant difference between the FHN, FNP1 and FHP2 groups was in relation to employment-related problems. For men, specifically, differences between the groups were also seen in psychiatric status and familial status composite scores. Interestingly, neither alcohol and other drug use, somatic status, economy, social nor criminal status differed between the groups. However, it is worth

noticing that among males, the social status was borderline significant as well as psychiatric status among female offspring, indicating a strong trend.

Insert Table 2 here

To examine how the groups differed from each other, that is, whether an effect was conventional additive or only manifesting with FHP2 (synergistic), Dunn's Multiple Comparison Test was applied on the significant Kruskal-Wallis rank models results. Among females, employment-related problems composite scores did not show an additive effect, neither conventional nor synergistic. Among males, none of the group differences manifested in a conventional additive manner, with family status not showing any additive effect. However, employment-related problems (Dunn's test: FHN-FHP1, $z = -0.467$, $p = 0.96$; FHP1-FHP2, $z = -2.40$, $p = 0.025$; FHN-FHP2, $z = -2.75$, $p = 0.009$), and psychiatric status (Dunn's test: FHN-FHP1, $z = -0.56$, $p = 0.86$; FHP1-FHP2, $z = -2.98$, $p = 0.004$; FHN-FHP2, $z = -3.41$, $p = 0.001$), demonstrated a synergistic effect with FHP2 on the composite scores, suggesting that a more severe addiction profile related to these indices may only manifest with two AUD parents.

4. Discussion

4.1 *General findings*

The main findings were: 1.) The prevalence of FHP was high; among females, 56% had FHP (40% FHP1 and 16% FHP2), and males 54% (41 % FHP1 and 13% FHP2), and; 2.) No conventional additive effect was found on the composite scores. However, another type of synergistic additive effect, only manifesting with exposure to FHP2, was found for employment-related problems and psychiatric status composite scores among male offspring.

4.2 Prevalence

Few and only general population-based studies have reported the prevalence of parental AUD according to the degree of exposure. However, the overall prevalence of FHP patients with AUD in this study corresponds with findings from other studies among treatment-seeking AUD out- and inpatients reporting FHP to be around 50% (9, 10). Nonetheless, when comparing this percentage with the general population studies, where data stems from either out- or inpatient hospital registers (3, 7) or surveys (4, 8), the difference is conspicuous. Usually, register-based population studies do not include data from alcohol treatment facilities, thus favouring selection of more severe cases that have been in contact with somatic or psychiatric hospitals and diagnosed with an AUD here. Nonetheless, it is worth noticing that some studies apply data from multiple sources, including relative new alcohol treatment registers as well as a wide range of administrative data that are not equivalent to AUD diagnoses based on diagnostic criteria registers. Even when applying many AUD proxy measures, it is not surprising that there is a much higher frequency of exposure to parental AUD among treatment samples than in the general population since AUD tends to aggregate in families. Further, to be registered as FHP, the parent(s) themselves also had to have been in contact with a hospital due to their AUD. Therefore, the likelihood of both a patient and their parent(s) to be included in the same setting would be diminished with a subsequent lower estimated prevalence of only AUD patients being FHP. Conversely, population-based surveys may be likely to exclude cases with a pronounced AUD addiction severity profile, as they may be too functionally impaired, therefore less likely to participate in a survey-study, and instead only include those with modest addiction severity. Accordingly, the two population-based survey-studies, having estimated the degree of exposure to parental AUD, have consistently found an FHP of 22% constituting approximately 19% FHP1 and 3% FHP2

(4, 8). Hence, although prevalence rates among the general population and clinical populations are highly relevant, rates from population studies are underestimating the strikingly high prevalence rates of exposure to FHP that physicians are going to encounter in a clinical setting.

Present and prior findings indicate, that among patients with AUD the degree of “parental AUD exposure” is at least twice as high as in the general population. Indeed, this has also been reported by general population-based studies using inferential statistics and investigating on the additive effects of exposure to parental AUD where offspring have an at least two-fold increased risk of developing AUD when exposed to FHP1(4, 8, 11) and as high as five-fold increased risk when exposed to FHP2 (8, 11). However as already mentioned, AUD is according to diagnostic nomenclature such as ICD-10 and DSM-IV a categorical construct(1, 12), and doesn’t inform us about the degree of addiction severity. In the present study, we expected to find an additive effect related to broadly defined addiction severity and impacting several addiction-related areas. Contrary to our initial hypothesis, we did not find support for an additive effect on various addiction severity dimensions as no dimensions showed an additive effect among offspring’s in a conventional manner. Nonetheless, an additive effect manifesting when exposed to FHP2, hence synergistic, was found on two parameters for male offspring, suggesting that they may be more affected by double parental exposure to genetic and environmental influences. It is, however, interesting that the conventional additive effect doesn’t seem to impact other areas than the development of AUD (8, 11) and the AUD addiction severity in a more narrow sense (17), but not in a broader sense. This finding may be due to the fact that treatment-seeking patients with AUD have alcohol as the common severity denominator, equally burdening the patients with FHN and FHP, as indicated by no differences in the alcohol composite score, and the entire sample

may already be equally burdened on the addiction severity-related areas. In addition, although approximately 45% of the sample was not exposed to FHP, they may have been exposed to other adverse circumstances that increase their risk for developing AUD and impact their life negatively. For instance, both internalizing and other externalizing psychiatric pathology may increase the likelihood of the offspring to develop AUD (21-24). Further, when estimating medians in the data set, all but the alcohol composite score, are relatively low, suggesting that the present sample might not be severely impaired, and it is likely that other patterns may be found among treatment-seeking AUD inpatients.

Our finding of male offspring being more affected by FHP2 contrasts with one previous study that reported females being the most impacted by the additive effect concerning the development of AUD (8), but is in line with another study (11). Hence, our findings somehow extend this finding to multi-dimensional addiction severity, as treatment-seeking male offspring were the most impaired when exposed to FHP2 on both employment-related problems and psychiatric status. This finding is also in line with studies demonstrating males being generally more impaired than females when exposed to FHP (11, 25). Nonetheless, plenty of studies have also reported that female offspring were more impacted than males as well as no gender differences (3, 4, 17, 26).

4.5 Strengths and limitations

The strengths of the study are linked to the considerable size of the sample. Furthermore, the sample consisted of consecutive treatment-seeking patients and was assessed by means of the most used multi-dimensional assessment instrument in European treatment instances. The data were included in the clinical database over a decade and took place at one of the largest outpatient clinics for alcohol treatment in Denmark.

Limitations in the study need to be addressed. First, information on parental AUD was acquired through the patient and not the parent(s) themselves. The specificity of that kind of data is quite high (86-90%), while the sensitivity is lower (51-53%) (4), and a tendency towards underestimating the number of parents with AUD is, therefore, possible. Second, the outpatient setting might not be generalizable to a population where a more severe AUD profile is expected, e.g. inpatient setting, although the majority of AUD patients seeking treatment are treated as outpatients. Finally, the study does not incorporate length of exposure to alcoholic parents or exposure to an alcoholic pregnancy with the latter being a possible confounder.

5. Conclusion

Exposure to parental AUD is strikingly high among treatment-seeking outpatients. Nonetheless, the additive effect has a modest impact on multi-dimensional addiction severity and is mostly related to psycho-social status among treatment-seeking male offspring. Targeting these areas in alcohol treatment, as well as the involvement of other psychiatric and social instances, may be relevant to improve the recovery process.

1. Author Disclosure

Statement 1: Role of funding sources

This study did not receive any funding.

Statement 2: Conflict of interest

There is no conflict of interest to declare.

Statement 3: Ethical standards

The authors assert that all procedures contributing to this work comply 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.

Table 1. Sample characteristics divided by family history of AUD

	FHN	FHP1	FHP2	P-values
Female (n = 1065)				
Prevalence n(%)	468 (43.94)	430 (40.38)	167 (15.68)	
AUD				
Harmful use (%)	84 (18.14)	74 (17.49)	31 (18.56)	
Dependence (%)	379 (81.86) ^a	349 (82.51) ^a	136 (81.44) ^a	
Age ^a , years median (IQR)	51 (12)	47 (13)	42 (13)	0.0001
Continuing education ^a , n(%)	348 (74.68)	307 (71.73)	101 (60.48)	0.002
Employment ^a , n(%)	189 (40.65)	155 (36.30)	52 (31.14)	0.078
Cohabitant ^a , n(%)	202 (43.16)	196 (45.58)	79 (47.31)	0.60
Male (n = 2296)				
Prevalence n(%)	1053 (45.86)	939 (40.90)	304 (13.24)	
AUD				
Harmful use	162 (15.56)	133 (14.22)	38 (12.58)	
Dependence	879 (84.44) ^b	802 (85.78) ^a	264 (87.42) ^a	
Age ^a median(IQR)	48 (16)	43 (15)	40 (14)	0.0001
Continuing education ^a , n(%)	835 (79.37)	652 (69.51)	187 (61.72)	0.001
Employment ^b , n(%)	465 (44.58)	408 (43.68)	121 (40.47)	0.45
Cohabitant ^a , n(%)	479 (45.49)	401 (42.71)	138 (45.39)	0.42
<p>FHN: family history negative, FHP1: family history positive, one parent, FHP2: family history positive, both parents, ^a: at the time for treatment seeking. 0-10 patient entries missing, ^b: 11-25 patient entries missing, ^c: 26-40 patient entries missing.</p>				

Table 2. Calculated ASI Composite Scores divided by family history of AUD

	FHN	FHP1	FHP2	
ASI Composite Score, median (IQR)^a		Female (n = 1065)		P-value
Alcohol use	.71 (.35)	.68 (.36)	.69 (.27)	0.39
Other drug use	0 (.50)	0 (.24)	0 (.41)	0.71
Psychiatric status	.23 (.32)	.23 (.37)	.28 (.39)	0.064
Somatic status	.28 (.67)	.33 (.74)	.42 (.75)	0.13
Economy	.98 (1)	1 (1)	1 (1)	0.16
Employment-related problems	.083 (.58)	.22 (.66)	.33 (.75)	0.005
Family status	0 (.42)	0 (.44)	0 (.43)	0.43
Social status	0 (0)	0 (0)	0 (0)	0.51
Criminal status	0 (.20)	0 (.20)	0 (.20)	0.64
		Male (n = 2296)		
Alcohol use	.67 (.34)	.68 (.38)	.69 (.31)	0.45
Other drug use	0 (.35)	0 (.32)	0 (.35)	0.40
Psychiatric status	.11 (.32)	.11 (.34)	.19 (.41)	0.003 ^{UCAE}
Somatic status	.25 (.67)	.25 (.67)	.33 (.75)	0.19
Economy	.50 (1)	.50 (1)	.86 (1)	0.27

Employment-related problems	.17 (.58)	.17 (.67)	.33 (.67)	0.021 ^{UCAE}
Family status	0 (.046)	0 (.29)	0 (.31)	0.012
Social status	0 (0)	0 (0)	0 (0)	0.050
Criminal status	0 (.20)	0 (.20)	0 (.20)	0.87

FHN: family history negative, **FHP1:** family history positive, one parent, **FHP2:** family history positive, both parents, **CAE:** conventional additive effect, **UCAE:** only manifesting with FHP2, ^a: 0-10 patient entries missing ^b: 11-25 patient entries missing, ^c: 26-40 patient entries missing.

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