Common cardiovascular non-communicable diseases in the parental generation across different anxiety disorders: A cross sectional study using pedigree analysis

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Abstract

Background: There is considerable overlap in the genetic and pathophysiological mechanisms of anxiety and cardiovascular disorders. **Aim:** We aimed to assess the occurrence rates of CNCDs (hypertension, myocardial infarction and stroke) in the parental generation of those with three anxiety disorders- generalized anxiety disorder (GAD), phobic disorder and panic disorder, using pedigree charting. **Methods:** This was a cross sectional study conducted on 100 patients with anxiety disorder- generalized anxiety disorder (n=48), panic disorder (n=26) and phobic disorder (n=26). Pedigree charting was done for parental generation and the analysis included 841 relatives. **Results:** The occurrence rate of CNCDs in anxiety disorders, in total was 28%, with parents (first degree relation) contributing 53.6% and siblings of parents (second degree relation) contributing 46.4% of it. While occurrence rate of hypertension was 19%, the rates for myocardial infarction and stroke were 6% and 3%, respectively. The occurrence rates of CNCDs in patients with GAD, panic disorder and phobic disorder were 29.17%, 23.08% and 30.77%, respectively. No significant difference was noted on the comparison of frequencies ($\chi2$ =1.23;p=12). **Conclusion:** About one-third of patients with anxiety disorders have at least one occurrence of CNCDs in the parental generation, with first- and second- generation pedigree contributing almost equally. Occurrence rates of hypertension are the commonest, followed by MI and stroke.
Keywords: Anxiety; cardiovascular diseases; hypertension; myocardial infarction; stroke; familial predisposition.

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INTRODUCTION

Commonest cardiovascular non-communicable diseases (CNCDs; myocardial infarction, stroke and hypertension) and anxiety disorders are complex entities that are determined by multiple gene-gene as well as gene-environment interactions, and also multiple genotypes. Both anxiety and these CNCDs have common risk factors too.[1-2] Also, there is a considerable overlap in the genetic and pathophysiological mechanisms of anxiety and cardiovascular disorders.[2] Different anxiety disorders have been shown to have a differential contribution to the risk of future cardiovascular disorders.[3-4] Examining the rates of CNCDs in the parental generation of those with different anxiety disorders will help us understand the level of predisposition, with respect to each of these disorders. The primary aim of the present study was to assess the occurrence rates of CNCDs (hypertension, myocardial infarction and stroke) in the parental generation of those

with three anxiety disorders- generalized anxiety disorder (GAD), phobic disorder and panic disorder, using pedigree charting. Assessing the distribution of occurrence between first degree and second degree relation was an ancillary aim of the study.

METHODOLOGY
This was a cross sectional study conducted at a tertiary care mental health institute.
Subjects
Probands: Subjects (n=100) with diagnostic criteria of anxiety disorder as per DSM-IV TR diagnosis were included. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) was used for diagnosis. A signed informed consent was obtained prior to inclusion. Age and gender matched subjects were recruited from the inpatient and the outpatient services. Only those subjects who were accompanied by reliable informants including themselves were considered eligible. Patients with mental retardation were excluded; no other comorbid psychiatric disorder was excluded.

Assessments
Anxiety disorder probands were screened with the Mini International Neuropsychiatric Interview screen (M.I.N.I screen) for co-morbid psychiatric disorders.[17] The patients' socio demographic and vascular risk factor profile were obtained through socio-demographic and risk factor questionnaire. Probands and reliable informants of probands with anxiety disorders were then interviewed so as to obtain a pedigree which was focused on the parental generation.

Pedigree Drawing
A pedigree was drawn as part of the initial ascertainment to determine whether a particular family is suitable for study. If the proband could not provide the information to draw the pedigree, another family member provided the data. At a minimum, the pedigree included the proband and his/her parents. The pedigree indicates the presence of bilineality. When a proband's relatives include affected individuals on both the mother's and the father's side, the family was said to be bilineal. The reliability of the pedigree charting was assessed by corroborating it between two available informants. When corroboration was not found, it was confirmed from a third informant.

Ethical considerations
The study had the approval of the Institute Ethics Committee. Written informed consent was obtained from all the subjects after explaining them fully about the procedures and then enrolled into the study. Confidentiality of all the information obtained was maintained and subjects had the right to withdraw the consent at any stage.

Statistical analysis
The data were suitably coded and extracted on a Microsoft excel spreadsheet. Frequencies were extracted. Comparison of frequencies between the disorder subgroups was done using Pearson χ^2 test.

RESULTS
Socio-demographic characteristics: The sex distribution among the probands was 60 males and 40 females. The mean age was 29.77±6.38 years. The urban/rural status revealed that 64% belonged to rural area. The proportion of literacy (completed secondary education or more) was 43%. Informants were 37%- spouses, 27%- parents and 36%- siblings. About 42% had 2 informants and remaining had 1 informant.

Anxiety disorder probands: The distribution of type of anxiety disorder was as follows: generalized anxiety disorder (48%), panic disorder (26%) and phobic disorder (26%). There were 30% of probands who screened positive for a lifetime diagnosis of a secondary psychiatric illness, 15% nicotine dependence syndrome (NDS), 13% major depressive disorder (MDD) and 2% both NDS and MDD.

Family relatives: The number of proband parental generation relatives were 841. The mean age of proband parental generation relatives was 53.97 (SD 11.55).

Occurrence rates of CNCDs: Table 1 shows occurrence rates of hypertension, myocardial infarction and stroke in the parental generation probands with anxiety disorder. The occurrence rate of CNCDs in anxiety disorders, in total was 28%, with parents (first degree relation) contributing 53.6% and siblings of parents (second degree relation) contributing 46.4% of it. While occurrence rate of hypertension was 19%, the rates for myocardial infarction and stroke were 6% and 3%, respectively. The occurrence rates of CNCDs in patients with GAD, panic disorder and phobic disorder were 29.17%, 23.08% and 30.77%, respectively. No significant difference was noted on the comparison of frequencies ($\chi2=1.23;p=12$). Bilineality was seen in 4% of the entire sample and all such cases were seen for generalized anxiety disorder (table 1).

Table 1: Occurrence rates of hypertension, myocardial infarction and stroke in the parental generation probands with anxiety disorder (N=841)

	Father			Mother			Siblings of Father			Siblings of Mother			Total parental generation			First degree			Second degree			Total	Bilineality
	H	M	S	H	M	S	H	M	S	H	M	S	H	M	S	H	M	S	H	M	S		
Generalized Anxiety Disorder (n=48)	4	1	0	2	0	1	1	2	0	3	0	0	10	3	1	6	1	1	4	2	0	14 (29.17%)	4 (8.33%)
Panic Disorder (n=26)	1	0	0	1	0	0	1	0	1	1	0	1	4	0	2	2	0	0	2	0	2	6 (23.08%)	0
Phobic disorder (n=26)	2	0	0	2	1	0	0	1	0	1	1	0	5	3	0	4	1	0	1	2	0	8 (30.77%)	0
Total	7	1	0	5	1	1	2	3	1	5	1	1	19	6	3	12	2	1	7	4	2	28 (28%)	4 (4%)

H=Hypertension; M=Myocardial Infarction; S=Stroke

DISCUSSION

Our study results show that about 30% of patients with anxiety disorders have at least one occurrence of CNCDs in the parental generation, with first- and second-generation pedigree contributing almost equally. Hypertension was most commonly seen with occurrence rates of 19%, followed by MI and stroke (6% and 3%, respectively). Previously it was shown that anxiety symptoms or disorders may be independently associated with an increased risk (relative risk=1.41) of developing cardiovascular diseases and conversely about a fifth of patients with cardiovascular diseases have anxiety disoders.[3-4] Specifically, patients with GAD were shown to be more prone for developing adverse cardiovascular events.[4] Our study shows that there was no significant difference in the pattern of occurrence of CNCDs in parental generation across the three different anxiety disorders that were included. Several lines of experimental research demonstrates a strong relationship between stress and anxiety disorders. Structural changes in the limbic system and the corresponding neuroendocrinological changes that occur in response to underlie neurobiology of anxiety disorders.[5] Specifically, anxiety disorders represent a heightened cardiovascular stress responsivity.[3] Interestingly, studies have shown that family history of cardiovascular disease risk influences heightened stress responsivity.[6] Perhaps, this implies that anxiety disorders have a familial predisposition for a heightened cardiovascular stress responsivity. Our study results add strength to these implications. Moreover, common health behaviour mechanisms, apart from physiologic mechanisms (autonomic dysfunction, inflammation, endothelial dysfunction, changes in platelet aggregation) underlie the relationships between anxiety disorders and CNCDs.[3] Health behaviours, which are implicated in predisposing CNCDs and anxiety disorders,[3,7] have been noted to be similar across family generations.[8] All these factors together might have influenced our findings that about one-third of patients with anxiety disorders have a family history of CNCDs in parental generation.

CONCLUSION

About one-third of patients with anxiety disorders have at least one occurrence of CNCDs in the parental generation, with first- and second- generation pedigree contributing almost equally. Occurrence rates of hypertension are the commonest, followed by MI and stroke.

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