# A STUDY OF PANIC PATIENTS WITH AND WITHOUT DEPRESSION

## K. SRINIVASAN & IBY NEERAKAL

## **ABSTRACT**

In a sample of 94 panic patients, 43 patients (45.7%) had comorbid depression. In majority of patients, the comorbid depression was severe enough to be diagnosed as major depression. Panic patients with depression were more severely functionally impaired and had more generalized anxiety symptoms as compared to pure panic patients. There were no significant differences between panic patients with primary and secondary depression on any of the clinical variables. Findings from the present study are in agreement with earlier studies in that panic disorder comorbid with depression is a much more severe illness than pure panic disorder.

Key words: Panic disorder, depression

There is considerable co-morbidity between panic disorder and depression (Fawcett & Krawitz, 1983; Klerman, 1988; Leckman et al., 1983; Munjack & Moss, 1983). Studies suggest that about 40-60% of panic disorder patients in treatment settings have co-morbid depression (Brier et al., 1984; Sheehan et al., 1981). Noyes (1990) observed that the prevalence of depression in panic patients depended largely on whether the depression was primary or secondary. It is also reported that panic disorder and depression covary over time (Uhde et al., 1985) with temporal independence between the occurrence of panic disorder and depressive episodes (Bowen & Kohout, 1979; Brier et al., 1984; Raskin et al., 1982).

Several studies have reported that comorbidity of panic and depression results in a condition with greater symptom severity, inadequate treatment response and poorer outcome than pure panic disorder (Brier et al.,1984; Clancy et al.,1979; Keller et al.,1993; Noyes et al.,1990; Van Valkenburg et al.,1984;

Vollrath & Angst, 1989; Walker et al., 2000). Panic patients with a history of major depression had greater levels of past impairment, longer duration of panic disorder, more severe anxiety and depression as compared to patients with pure panic disorder (Brier et al., 1984; Lesser et al., 1988). Panic disorder comorbid with depression is also associated with a higher risk of suicide (Johnson et al., 1990; Warshaw et al., 2000). However, some studies have not found any difference between pure panic disorder and panic disorder with secondary depression on various clinical variables such as age of onset, duration of illness, sucididal attempt and severity of anxiety (Buller et al., 1986; Clancy et al., 1979; Delay et al.,1981).

Community based studies too have found a strong comorbidity between panic disorder and depression (Merikangas et al., 1996; Roy Byrne et al., 2000; Thompson et al., 1989). Comorbidity was associated with greater symptom severity, persistence of symptoms, role impairment and a

# PANIC DISORDER AND DEPRESSION

higher risk for suicide (Roy Byrne et al., 2000).

Research has also focussed on the nature of depression associated with panic disorder. Cassano et al. (1989) suggested that depression is a complication of panic disorder and is more like a demoralization reaction. However, others found that depressive symptoms accomanying panic disorder were severe enough to warrant a diagnosis of major depression (Brier et al., 1984; Reich et al., 1993). Most studies report no significant difference in the pattern of depressive symptoms between primary and secondary depression (Brier et al., 1984; Roy Byrne et al., 2000), while some have noted an excess of endogenous depressive symptoms in those with primary depression (Buller et al., 1986).

In summary, panic disorder comorbid with depression is a much more severe illness compared to pure panic disorder. However, some of the studies mentioned above have certain limitations such as a failure to distinguish between primary and secondary depression and not comparing other comorbid anxiety syndromes to both disorders. In addition, it is important to consider lifetime morbidity as panic disorder and major depression can occur temporally independent of each other. In the present study, we compared the pure panic disorder group to panic disorder comorbid with depression on various demographic and clinical variables.

#### **MATERIAL AND METHOD**

Subject: The present report is part of a larger study on phenomenology of panic attacks (Iby & Srinivasan,2002). A consecutive series of adult patients presenting with panic attacks to the outpatient psychiatric clinic of the department of psychiatry, St., John's Medical College Hospital were evaluated for the purpose of the study. Subjects with psychotic disorder and/ or substance abuse disorders were excluded from the study. All subjects, who consented to participate in the study, underwent physical examination and laboratory investigations including a thyroid profile. The study was

conducted over a one- year period from December 1998 until December 1999.

Clinical assessments: Patients were asked to maintain a panic diary for 2 weeks. All subjects were then evaluated using the following:

- a) Composite International Diagnostic Interview (CIDI) (Robins et al., 1988) was used to generate lifetime psychiatric diagnosis according to DSM-IV criteria. CIDI has been used in India (Sartorius et al., 1993) and one of the authors (I N) was trained in its administration. For the purpose of the present study, the sample of patients with panic disorder was initially subdivided according to presence or absence of comorbid depression. Patients with comorbid depression were further classified into primary depressive and secondary depressive groups. Primary depression was defined as occurring before or in the same year as the onset of panic attacks. Secondary depression refers to depression occurring clearly at least one year after the onset of panic attacks. (Buller et al., 1986). In addition, we also included in our diagnostic scheme other comorbid anxiety disorders as per DSM-IV criteria.
- b) Panic symptoms checklist. This checklist consisted of symptoms commonly reported by panic patients. A list of 26 symptoms was developed from a literature review of published studies on the phenomenology of panic attacks. This list also included 13 symptoms described under DSM-IV criteria for panic attack. Symptoms were scored as present or absent.
- c) Panic disorder severity scale (Shear et al.,1997). This scale assesses the severity of panic disorder and associated symptoms along seven dimensions. The scoring is based on the patient's response (0-4) on each item with the last one month as the reference period. In the present study, the composite score obtained by averaging the scores on the seven items as a measure of severity of panic attacks were compared across the diagnostic groups
- d) The Global Assessment Scale (Endicott et al., 1976). In the present study, Global assessment scale (GAS) was used for evaluating the overall functioning of a subject.

#### K.SRINIVASAN & IBY NEERAKAL

TABLE 1
SOCIODEMOGRAPHIC VARIABLES AMONG THE THREE DIAGNOSTIC GROUPS

Variables	Panic attacks without Depression (n≈51)	Primary depression with Panic attacks (n=30)	Panic disorder with Secondary depression (n=13)
Sex			
Male	28(54.9%)	11(36.7%)	6(46.2%)
Female	23(45.1%)	19(63.3%)	7(53.8%)
Age(Years)	34.2±11.5	34.5±9.8	37.1±8.7
Marital Status			
Married	35(68.6%)	19(63.3%)	11(84.6%)
Single	15(29.4%)	9(30.0%)	2(15.4%)
Widowed/divorced	1(2.0%)	2(6.7%)	0 (0%)
Residence	,		
Urban	37(72.5%)	22(73.3%)	9 (69.2%)
Rural	14(27.5%)	8(26.7%)	4 (30.8%)

No significant difference among groups (One way ANOVA, Chi-square statistics)

TABLE 2
CLINICAL VARIABLES AMONG THE THREE DIAGNOSTIC GROUPS

Variables	Panic disorder without Depression (n=51)	Primary depression with Panic attacks (n=30)	Panic disorder with Secondary depression (n=13)
Duration of panic disorder (in weeks)	227.7±402.8	337.9±338.9	461.1± 323.0
Panic severity score	11.8± 5.7	13.6±6.8	14.7±4.8
Number of panic symptoms	12.0± 3.4	12.7±5.2	14.0±4.2
GAS score	67.3± 4.3	60.5±6.7	57.3±9.9*
Phobia+	24(47.1%)	13(43.3%)	6(46.2%)
Generalized Anxiety	5(9.8%)	12(40%)	6(46.2%)**

<sup>\*</sup> Significant at p<.05, df=2.91; \*\* Significant at p<.05, df=2

Statistical Analysis: Chi square tests were used to compare binary demographic and clinical variables among the three diagnostic groups of pure panic disorder, primary depression with panic attacks and panic disorder with secondary depression. One way analysis of variance followed by the Newman- Keuls test was done for comparisons of duration of panic disorder, mean number of panic symptoms, mean scores on panic disorder severity scale and mean scores on the GAS across diagnostic groups.

#### **RESULTS**

The sample consisted of a consecutive

series of 99 adult patients of both sexes. Of the 99 participants, two patients did not have any psychiatric diagnosis on the CIDI interview and three individuals had a diagnosis of generalized anxiety disorder. These five patients were excluded. The remaining 94 patients formed the sample for the final analysis. In the first step, the sample was sub-divided into "panic disorder without depression" and "panic disorder with depression". In the second step, the panic group comorbid with depression was further subdivided into those with primary depression with panic attacks and those with panic disorder with secondary depression. Thus, in the final analysis the three diagnostic groups were those of panic

<sup>+</sup>Inclusive of simple phobia, social phobia and agoraphobia

# PANIC DISORDER AND DEPRESSION

disorder without depression (n=51), primary depression with panic attacks (n=30) and panic disorder with secondary depression (n=13). In the primary depressed group, 26 patients were currently depressed, while 4 had a past history of depression. One patient out of 13 in the secondary depressed group had a history of depression with 12 being currently depressed.

There were no significant differences in any of the socio-demographic variables among the three diagnostic group (Table 1). The various clinical features and associated psychiatric syndromes among the three diagnostic groups are presented in Table 2. The depressive group, both primary and secondary depression, had poorer overall functioning on GAS as compared to the panic disorder group without depression. Generalized anxiety disorder was significantly more frequent as a comorbid condition in both primary and secondary depression as compared to panic disorder without depression.

We also compared the nature of depression between the two depressive gorups. In both, primary and secondary depression, major depression was the most common psychiatric diagnosis. Twenty-eight patients (76.7%) in the primary depressed group had a diagnosis of major depression with the other two having dysthymic disorder. Eleven patients out of 13 (84.6%) in the secondary depressed had major depression.

# DISCUSSION

In the present report, we compared patients of panic disorder without depression and those with comorbid depression on various demographic and clinical variables. In agreement with earlier studies reported from the West, there is considerable comorbidity between panic disorder and depression. In our study, 43 patients (45.7%) with panic attacks had comorbid depression, which was of sufficient severity to be diagnosed as major depression according to DSM-IV cnteria. Among the depressed group, majority had primary depression as defined by the temporal occurrence of panic attacks and depression. The prevalence rate of depression in patients with panic disorder

depended largely on whether the associated depression was primary or secondary. In the present study, majority of panic subjects with comerbid depression had primary depression (69.8%), while secondary depression was diagnosed in only 30.2%. This is largely in agreement with findings from earlier studies (Noves, 1990).

Among the various demographic and clinical variables studied, there was a greater prevalence of concurrent generalized anxiety disorder in panic patients with depression (both primary & secondary depression) as compared to panic patients without depression. This is in keeping with findings from earlier reports (Cassano et al., 1989; Reich et al., 1993). In general, studies have also reported that panic patients with depression tend to have higher scores on measures of anxiety (Brief et al., 1984; Lesser et al., 1988). In a recent community based longitudinal study, it was found that most anxiety disorders are primary conditions and substantially increase the risk for later development of depression (Wittchen et al., 2000). Stein et al.(1990) observed that panic patients with comorbid social phobia are at an increased risk to develop depression. Thus, the presence of concurrent generalized anxiety may increase the risk of depression in panic patients.

However, like others, we did not find any difference between panic patients with and without depression on various indices of panic disorder such as severity of panic attacks, number of panic symptoms, duration of panic disorder and phobic severity (Buller et al., 1986; Clancy et al., 1979; Dealy et al., 1981; Lesser et al., 1988).

Panic patients without depression had a better overall functioning as indicated by the GAS score as compared to panic patients with depression. Both, clinic based (Clancy et al., 1978; Valkenburg et al., 1984; Vasile et al., 1997) and community studies (Roy Byrne et al., 2000) have consistently shown that panic disorder patients with comorbid depression are more functionally impaired that pure panic patietns. We did not find any difference in any of the clinical variables between the primary depressed group with panic

#### K.SRINIVASAN & IBY NEERAKAL

attacks and those panic patients with secondary depression. Thus, the overall seveiry of this specific comorbidity seems to be unaffected by the temporal relationship between panic diorder and depression (Brier et al., 1984; Roy Byrne et al., 2000).

The present study has certain limitations. It is a cross-sectional study based on patients seeking help from a tertiary care center. Longitudinal studies are needed to clarify the relationship between panic disorder and depression, as many panic patients ultimately experience an episode of depression (Gorman & Coplan, 1996). Thus, some of our pure panic disorder patients may develop depression later during the course of their illness.

In conclusion, using a structured psychiatric interview schedule, we found a considerable comorbidity between lifetime diagnosis of panic disorder and major depression in a clinic sample. Panic disorder comorbid with depression is a much more severe illness associated with a greater prevalence of generalized anxiety and poorer overall functioning as compared to pure panic disorder.

# REFERENCES

Bowen, R.C.& Kohout, J. (1979) The relationship between agoraphobia and primary affective disorders. Canadian Journal of Psychiatry, 24,317-322.

Brier, A., Charney, D.S.& Heninger, G.R. (1984) Major depression in patients with agoraphobia and panic disorder. *Archives of General Psychiatry*, 41,1129-1135.

Buller, R., Maler, W. & Benkert, O. (1986) Clinical subtypes in panic disorder. Their descriptive and prospective validity. *Journal of Affective Disorders*, 11, 105-114.

Cassano, G.B., Perugi, G., Musetti, L.& Akiskal, H.P. (1989) The nature of depression presenting concomitantly with panic disorder. *Comprehensive Psychiatry*, 30,473–482.

Clancy, J., Noyes, R., Hoenk, P.R.& Slymen, D.J. (1978) Secondary depression in anxiety neurosis. *Journal of Nervous and Mental Disease*, 166,846-850.

Dealy, R.S., Ishoki, D.M., Avery, D.H., Wilson, L.G.& Dunner, D.L. (1979) Secondary depression in anxiety disorder. *Comprehensive Psychiatry*, 22,612-617.

Endicott, J., Spitzer, R.L., Fleiss, J.L. & Cohen, J. (1976) The global assessment scale: A procedure for measuring overall severity of psychiatric disturbances. Archives of General Psychiatry, 33,766-771.

Fawcett, J. & Krawitz, H.M. (1983) Anxiety syndromes and their relationship to depressive illness. *Journal of Clinical Psychiatry*, 44,8-11.

Gorman, J.M. & Coplan, J.D. (1996) Comorbidity of depression and panic disorder. *Journal of Clinical Psychiatry*, 57, 34-41.

**Iby,N.& Srinivasan,K.(2002)** A factor analytic study of panic symptoms. *Indian Journal of Psychiatry* (in press).

Johnson, J. Weissman, M.& Klerman, G.(1990) Panic disorder, comorbidity and suicide attempts. Archives of General Psychiatry, 47, 805-808.

Keller, M., Lavori, P., Goldenberg, I.M., Baker, L.A., Pollack, M.H., Sachs, G.S. & Rosenbaum, J.F. (1993) Influence of depression on the treatment of panic disorder with imipramine, alprazolam, and placebo. *Journal of Affective Disorders*, 28, 17-38.

Klerman, G.L. (1988) Overview of the Cross-National collaborative panic study. *Archives of General Psychiatry*, 45,407-412.

Leckman, J.F., Merikangas, K.P., Pauls, D.L., Prusoff, B.A. & Weissman, M.M. (1983) Anxiety disorders and depression: Contradictions

## PANIC DISORDER AND DEPRESSION

between family study data and DSM-III convention. American Journal of Psychiatry, 140,880-882.

Lesser, I.M., Rubin, R.T., Pecknold, J.C., Rifkin, A., Swinson, R.P., Lydlard, R.B., Burrows, G.D., Noyes, R. & Dupont, R.L. (1988) Secondary depression in panic disorder and agoraphobia. *Archives of General Psychiatry*, 45,437-443.

Merikangas, K.R., Angst, J., Eaton, W., Canino, G., Rubio-Stipec, M. Walker, H., Wittchen, H.U., Andrade, L., Essau, C., Whitaker, A., Kraemer, H., Robins, L.N. & Kupfer, D.J. (1996) Comorbidity and boundaries of affective disorders with anxiety disorders and substance misuse: results of an international task force. British Journal of Psychiatry, 168(supp:30), 58-67.

Munjack, D.J.& Moss, H.B. (1981) Affective disorder and alcoholism in families of agoraphobics. *Archives of General Psychiatry*, 38,869-871.

**Noyes,R.(1990)** The comorbidity and mortality of panic disorder. *Psychiatric Medicine*, 8, 41-66.

Noyes, R.,Reich, J., Christansen, J., Suelzer,M., Pfohi, B.& Coryell, W.A.(1990) Outcome of panic disorder. Relationship to diagnostic subtypes and comorbidity. *Archives of General Psychiatry*, 447, 809-818.

Raskin, M., Peeke, H.V.S., Dickman, W.&. Pinsker, H. (1982) Panic and generalized arrxiety disorders: Developmental antecedents and precipitants. *Archives of General Psychiatry*, 39, 687-689.

Reich, J., Warshaw, M., Peterson, L.G., White, K., Keller, M., Lavari, P. & Yonker, K.A. (1993) Comorbidity of panic and major depressive disorder. *Journal of Psychiatric Research*, 27, 23-33.

Robins, L.N., Wing, J.K., Wittchen, H-U., Helzer, J.E., Babor, T.F., Burke, J., Farmer, A., Jablensky, A., Pickens, R., Regier, D.A., Sartorius, N. & Towle, L.H. (1988) The composite international diagnostic interview: an epidemiologic instrument suitable for use in conjunction with different diagnostic systems and in different cultures. Archives of General Psychiatry, 45, 1069-1077.

Roy-Byme, P., Stang, P., Wittchen, H-U., Ustun, B., Walters, E.E. & Kessler, R.C.(2000) Lifetime panic depression comorbidity in the National Comorbidity Survey. *British Journal of Psychiatry*, 176, 229-235.

Sartorius, N., Ustun, T.B., Costa e Silva, J.A., Goldberg, D. & Lecruiber, Y. (1993) An International study of psychological problems in primary care. *Archives of General Psychiatry*,50, 819-824.

Shear, M.K., Brown, T.A., Barlow, D.H., Money, R., Sholomskas, D.E., Woods, S.W., Gorman, J.M. & Papp, L.A.(1997) Multicenter collaborative panic disorder severity scale. *American Journal of Psychiatry*, 154,1571-1575.

Sheehan, D.V., Ballenger, J. & Jacobson, G.(1981) Relative efficacy of monoamineoxidase inhibitors and tricyclic antidepressants in the treatment of endogenous anxiety, In, Klein, D.F.& Rabkin, J.G.(Eds) Anxiety: New research and changing concepts, New York, Raven Press, 47-67.

Stein, M.B., Tancer, M.E., Gelenter, C.S., Vittone, B.J. & Uhde, T.W. (1990) Major depression with social phobia. *American Journal of Psychiatry*, 147, 637-639.

Thompson, A.H., Bland, R.C. & Orn, H.E.(1989) Relationship and chronology of depression, agoraphobia and panic disorder in general population. *Journal of Nervous and Mental Disease*, 177, 456-463.

## K.SRINIVASAN & IBY NEERAKAL

Uhde, T., Boulenger, J., Roy-Byrne, P., Geraci, M.F., Vittone, B.J. & Post, R.M.(1985) Longitudinal course of panic disorder: clinical and biological considerations. *Progress in Neuropsychophramacology and Biological Psychiatry*, 9,39-51.

Van Valkenburg, C., Akiskal, H.S., Puzantian, V. & Rosenthal, T.(1984) Anxious deppressive: clinical, family history and naturalistic outcome for persons with panic and major depressive disorder. *Journal of Affective Disorders*, 6,67-82.

Vollrath, M. & Angst, J.(1989) Outcome of panic and depression in a seven-year followup: results of the Zurich study. *Acta Psychiatrica Scandinavica*, 80,591-596.

Walker, E.A., Katon,W.J., Russo, J., Von, Korff, M., Lin, E., Simon, G., Bush, T., Ludman, E. & Unutzer, J.(2000) Predictors of outcome in a primary care depression trial. J. Gen. Intern Med, 15, 859-867.

Warshaw, M.G., Dolan, R.T., & Keller, M.B.(2000) Suicidal behaviour in patients with current or past panic disorder: five years of prospective data from the Harvard/Brown anxiety research program. American Journal of Psychiatry, 157,1876-1878.

Wittchen, H-U., Kessler, R.C., Pfister, H. & Lieb, M. (2000) Why do people with anxiety disorders become depressed? A prospective longitudinal community study. *Acta Psychiatrica Scandinavica*, 102(Suppl, 406), 14-23.

K.SRINIVASAN \*. D.P.M., M.D., Professor, IBY NEERAKAL, Lecturer, Department of Psychiatry, St. John's Medical College Hospital, Sarjapur Road, Bangalore-560034 (email: stjohnas@bir.vsnl.net.in).

<sup>\*</sup>Correspondence