

A PROSPECTIVE STUDY OF MEDICALLY UNEXPLAINED PHYSICAL SYMPTOMS IN DEPRESSIVE DISORDERSA. John Dinesh¹, S. Arun², Alok Pandey³, Siva Prakash B⁴, Gyaneshwar Sharma⁵**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: Physical symptoms in depression are highly prevalent and associated with substantial functional impairment. The prevalence of physical illness in psychiatric patients is higher than that in the general population. Both in developed & developing countries, very little attention is paid to the physical illness of psychiatric patients, which leads to a poorer outcome. Hence we decided to conduct this study and find out the effect of antidepressant treatment on somatic symptoms in depressive disorders. The study was conducted at Sri Venkateshwaraa medical college hospital & research center, Puducherry. Our study sample consisted of 72 consecutive new patients who fulfilled inclusion criteria and had consented to participate in the study. All new patients in the age group 18 to 60 years, who fulfill ICD-10-DCR (Diagnostic criteria for Research) criteria for the Depressive episode (F 32), recurrent depressive disorder (F33), Dysthymia (F 34.1), bipolar affective disorder, current episode depression (F 31.3) were included in our study. **MATERIALS AND METHODS:** A semi-structured proforma was used to collect socio demographic and clinical data from all the subjects included in the study. Enrolment of cases was done over a period of 6 months. All the subjects were rated on the Hamilton Depression Rating Scale (HDRS-17) to quantify the baseline severity of the depressive symptoms. Screenings for physical symptoms were done for all patients using the Patient Health Questionnaire (PHQ-15). The patients were classified into 4 groups based on physical complaints & co-morbid medical/ surgical diagnosis. HDRS-17 rating was recorded at baseline, 1 month & 6 months for the entire study sample. PHQ-15 scores were recorded at baseline, 1 month & 6 months after initiation of antidepressant treatment for all patients enrolled in the study. **RESULTS:** The study revealed the prevalence of medically unexplained physical symptoms in depressive disorders in patients attending our psychiatry OPD. The Results depicts the prevalence of physical pain symptoms in patients with depressive disorders. The reduction in HDRS-17 and PHQ-15 scores in 1month and 6 months shows the effect of antidepressant treatment in reducing both depressive symptoms and physical symptoms **CONCLUSION:** This study had been undertaken with intent to study the prevalence of unexplained physical symptoms and physical illnesses among patients with depressive disorders and to analyze the effect of antidepressant treatment on these unexplained physical symptoms.

KEYWORDS: Depression, physical symptoms, unexplained somatic symptoms.

INTRODUCTION: Despite increased awareness of depressive disorders, depression remains difficult to diagnose initially, and majority of the cases are diagnosed at subsequent consultations.¹ In approximately two third of the patients with depression, the clinical picture is dominated by physical symptoms.^{2,3} Approximately 20% of the patients in primary care present with clinically significant depressive symptoms.⁴

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Physical symptoms are present in more than half of all outpatients with depressive disorders. The importance of recognizing and evaluating physical symptoms has been heightened by recent evidence of the effectiveness of specific treatment strategies.^{5,6}

Physical symptoms increase the already marked burden and disability associated with depression⁷. An international study in 15 countries revealed that more than two-thirds of the depressed patients even in primary care present exclusively with physical symptoms⁸. The increased burden of physical symptoms in patients with depression leads to increased utilization of health care services and greater economic burden.^{5,7}

Depressive disorders are often accompanied by physical symptoms. In a significant proportion of patients, these symptoms are unexplained. Detection & treatment of depression may have a positive impact on these “medically unexplained” physical symptoms. In other depressive patients, physical symptoms could be indicators of co morbid non-psychiatric, medical/surgical illness.

For these reasons, thorough evaluation of physical symptoms in depression is of paramount importance. According to Gada & Shah (2004), somatic presentation of psychiatric disorders, particularly depressive disorder and anxiety disorder, is quite common⁹. Gada (1987) reported that 66% of his cases of depressive disorder presented only with physical symptoms, and 29% presented with both physical and psychological symptoms.¹⁰

Similar preponderance of somatic symptoms has been observed in Indian patients.^{11,12} Symptoms reported by more than 75% of these cases were weakness (96%), body ache (84%), and giddiness (83%), heaviness of head (80%), headache (79%), and abdominal pain (76%).¹³

According to Silverstone (2004), somatic presentation of depression is very common in general practice.¹⁴ Simon et al (1999) analyzed a World Health Organization study of “somatic symptoms in the presentation of depression” and found that of all the patients in 14 countries included in the survey who met the criteria for depression, 69% reported only somatic symptoms as the reason for their visit.¹⁵

The study concluded that patients with depression were more likely to report unexplained somatic symptoms than those without depression.

In our setting, we routinely encounter a large number of depressive patients with physical symptoms. We receive a substantial number of patients with unexplained physical symptoms from other departments. On thorough evaluation, many of these patients are found to have depressive disorders.

A review of literature indicates a paucity of Indian research data pertaining to this issue. Hence, this study has been undertaken in an attempt to contribute to the Indian research literature pertaining to physical symptoms in depressive patients.

AIMS AND OBJECTIVES:

1. To study the prevalence of physical symptoms & physical illnesses among patients with depressive disorders.
2. To study medically unexplained physical symptoms associated with depressive disorders.
3. To study the impact of antidepressant treatment on medically unexplained physical symptoms associated with depressive disorders.

MATERIALS AND METHODS:

Study design and Setting: This prospective study was carried out in Department of Psychiatry, Sri Venkateshwara medical College Hospital and Research center (SVMCH&RC), Puducherry, between May 2013 and April 2014. Our study sample consisted of 72 consecutive new patients who fulfilled the inclusion criteria and had consented to participate in the study. The study was approved by the institutional ethical committee.

Inclusion Criteria: All new patients in the age group 18 to 60 years, who fulfill ICD-10-DCR (Diagnostic criteria for Research) criteria for the following diagnoses:

1. Depressive episode (F 32).
2. Recurrent depressive disorder (F33).
3. Dysthymia (F 34.1).
4. Bipolar affective disorder, current episode depression (F 31.3).

PROCEDURE: All consecutive new patients attending the psychiatric outpatient department, SVMCH&RC either directly or referred from other clinical departments were screened for depressive disorders mentioned in the inclusion criteria. A comprehensive psychiatric assessment was done for all patients. The diagnosis were verified and confirmed by a consultant psychiatrist, based on International Classification of Diseases (ICD-10 DCR). Written informed consent (English or Tamil) was obtained from all the subjects and their key relatives. A semi-structured proforma was used to collect socio demographic and clinical data from all the subjects included in the study. Enrolment of cases was done over a period of 6 months.

All the subjects were rated on the Hamilton Depression Rating Scale (HDRS-17) to quantify the baseline severity of the depressive symptoms. The HDRS (also known as the Ham-D) is the most widely used clinician-administered depression assessment scale¹⁶. The original version contains 17 items (HDRS-17) pertaining to symptoms of depression experienced over the past week. The scale is used to assess severity of, and change in, depressive symptoms.¹⁷

Screenings for physical symptoms were done for all patients using the Patient Health Questionnaire (PHQ-15). PHQ-15 was translated into Tamil by a linguist and a psychiatrist. Inter-rater reliability of this translated version was found to be satisfactory. PHQ-15 is a self-report questionnaire with modules that assess various axis-I disorders.¹⁸

PHQ-15 is the somatic symptom module of the Patient Health Questionnaire. The PHQ-15 assesses current severity of 15 somatic complaints that have been demonstrated to be among the most common physical symptoms. PHQ-15 scores between 1 and 4 were considered as minimum severity, scores between 5 and 9 as low severity, scores between 10 and 14 as moderate severity, and scores between 15 and 30 were considered as high severity.¹⁸

All patients were subjected to standard physical examination & baseline laboratory investigations (Hemoglobin, complete blood counts, blood urea and creatinine, random blood sugar, liver function tests and thyroid function tests). Decisions regarding other necessary investigations were made as per the need of the individual patient.

All patients with physical symptoms were referred to the appropriate specialty departments for a complete & thorough physical evaluation & investigations. All medical/surgical diagnoses were recorded.

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The patients were classified into one of the following 4 groups based on physical complaints & co-morbid medical/ surgical diagnosis.

Group 1: Depressive patients without any physical complaints (a score of zero on PHQ-15).

Group 2: Depressive patients without physical complaints (a score of zero on PHQ-15), who receive a co morbid medical/ surgical diagnosis.

Group 3: Depressive patients with physical complaints (a score of 1 to 30 on PHQ-15), who receive a co morbid medical/ surgical diagnosis.

Group 4: Depressive patients with physical complaints (a score of 1 to 30 on PHQ-15), who do not receive a co morbid medical/ surgical diagnosis. These patients were considered to have “medically unexplained physical symptoms.”

There were no patients in group 2 in the study sample. There were 2, 29 and 41 patients in group 1, 3 and 4 respectively. Antidepressant treatments for all patients were initiated in accordance with standard practice guidelines being followed in the Department of Psychiatry, SVMCH&RC. Patients in groups 1 & 4 received only antidepressant treatment. Patients in group 3 received appropriate medical/surgical treatment from the relevant department, in addition to antidepressant treatment.

Among the total study sample of 72 patients, only 60 patients attended follow-up for the entire study period of 6 months. Out of the 12 patients who did not attend follow-up at 6 months, 3 patients belong to group 3 and 9 patients to group 4. HDRS-17 rating was recorded at baseline, 1 month & 6 months for the entire study sample. PHQ-15 scores were recorded at baseline, 1 month & 6 months after initiation of antidepressant treatment for all patients enrolled in the study. The patients were clearly instructed about follow-up dates. Reminders were issued when required. Importance of strict drug compliance was emphasized to the patient and their key relative during each visit.

RESULTS: Of 72 patients inducted into the study, 60 completed 6 months of follow-up. patients in the study sample were predominantly between 26-32 years and 40-46 years of age, out of the 72 study sample 17 (24 %) were males and 55 (76 %) were females. Majority (76 %) of the patients in the study sample were married. Majority of the patients 56 (77.8 %) were from Tamilnadu state, while 16 (22.8 %) patients were from Pondicherry. It was observed that 49 (68.1 %) were from rural areas, and 23 (31.9 %) were from urban areas. It was observed that 54 (75 %) patients had a total duration of illness ranging between 1 & 12 months.

The duration of the current episode was between 1 and 12 months in 63 (87.5 %) patients. Sixty (83.3%) patients were experiencing their first depressive episode. Precipitating factors were present in 35 (48.6%) subjects, and absent in 37 (51.4%) subjects. Majority of the patients 58 (80.6 %) did not report active suicidal ideation, while 14 (19.4%) had active suicidal ideation. Seven (9.7%) patients had attempted suicide in the past.

The most common physical symptoms were trouble sleeping (97.2%), feeling tired or having low energy (97.2%) and feeling heart pound or race (68.5%). The least common symptom was pain

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or problems during sexual Intercourse (4.2%). There was a significant reduction in both HDRS-17 and PHQ-15 scores in group 4 which confirms the positive effect of antidepressant treatment on depressive symptoms and physical symptoms with medically unexplained physical symptoms.

Psychiatric diagnosis with ICD-10 code	Male (%)	Female (%)	Total (%) (n=72)
Mild depressive Episode (F32.0)	0	2 (100)	2 (2.7)
Moderate depressive Episode (F 32.1)	6 (17.1)	29 (82.8)	35 (48.6)
Severe depressive episode without psychotic symptoms (F32.2)	5 (35.7)	9 (64.2)	14 (19.4)
Dysthymia (F34.1)	4 (44.4)	5 (55.5)	9 (12.5)
Dysthymia, with mild depressive episode (F34.1, F 32.0)	0	2 (100)	2 (2.7)
Dysthymia, with moderate depressive episode (F34.1, F32.1)	0	1 (100)	1 (1.3)
Recurrent depressive disorder, current episode moderate (F33.1)	0	4 (100)	4 (5.5)
Recurrent depressive disorder, current episode severe without psychotic symptom (F33.3)	0	2 (100)	2 (2.7)
Bipolar affective disorder, current episode severe depression without psychotic symptoms (F34.1)	2 (66.6)	1 (33.3)	3 (4.1)

Table 1: Frequency distribution of psychiatric diagnosis

It was observed that 69 (95.8 %) patients had single psychiatric diagnosis (95.8 %), while 3 (4.1%) patients dual psychiatric diagnosis. Moderate depressive episode was the most frequent diagnosis [35 (48.6 %)]. The least common diagnosis was dysthymia with moderate depressive episode [1(1.3 %)].

Physical illnesses with ICD code	Frequency	% (n=72)
Hypothyroidism (K03.9)	13	18.0
Iron deficiency anaemia (D50.9)	5	6.9
Primary hypertension (I10.0)	4	5.5
Polycystic ovarian syndrome (E28.2)	4	5.5
Dyspepsia (K30.0)	3	4.1
Diabetes mellitus (E14.9)	3	4.1
Chronic gastritis, Unspecified (K29.5)	2	2.7
Acne vulgaris (L70.0)	2	2.7

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Low back pain (M54.5)	1	1.3
Primary infertility (N97.0)	1	1.3
Periarthritis shoulder (M75.0)	1	1.3
Chronic sinusitis, Unspecified (E03.9)	1	1.3
Irritable bowel syndrome without diarrhoea (K58.9)	1	1.3

Table 2: Frequency distribution of comorbid physical illnesses

Among 72 patients, 29 (40.2%) patients had co morbid physical illnesses along with psychiatric diagnosis. Of these, 17 (23.6%) patients had single co morbid physical illness, and 12 (16.6%) patients had dual physical diagnoses. The most common co morbid physical illness was hypothyroidism 13 (18.0%) and the second commonest was iron deficiency anemia 5 (6.9%)

We analyzed the severity of depressive symptoms at baseline, 1 month and 6 months for all study sample and found that there was reduction of HDRS-17 scores at 1 month and 6 months from baseline for all patients. The mean HDRS scores at baseline, 1 month and 6 month were 16.67 ± 5.52 , 9.08 ± 2.47 and 2.50 ± 1.03 respectively.

We analyzed the PHQ-15 Scores at baseline, 1 month and 6th month for the entire study sample and recorded a mean score of 8.15 ± 3.91 at baseline which reduced to 5.18 ± 2.61 at the end of 1 month. This score dropped further at 6 months to 1.50 ± 1.57 in the study sample. Since we found that there were reductions in both HDRS-17 and PHQ-15 scores at 1 month and 6 months from baseline scores, we wanted to know whether these reductions were statistically significant.

The paired' test was used to study the reduction of both the scores between baseline and 1 month, 1 month and 6th month and baseline and 6th month. All the comparison between months showed that the reduction of scores was statistically significant ($p < 0.001$). This statistical significance confirms the effectiveness of antidepressant treatment on depressive symptoms and physical symptoms.

We analyzed the reduction of HDRS-17 scores at baseline, 1 month and 6 months exclusively for group 4 patients as they had medically unexplained physical symptoms. We found that there was reduction of HDRS-17 scores at 1 month and 6 months from baseline scores. The mean HDRS scores at baseline, 1 month and 6th month were 16.76 ± 5.97 , 16.06 ± 5.34 , 8.34 ± 2.11 respectively.

We analyzed the PHQ-15 scores at baseline, 1 month and 6th month for group 4 patients and recorded a mean score of 7.66 ± 3.6 at baseline which reduced to 7.06 ± 3.71 at the end of 1 month. This score dropped further at 6 months to 4.31 ± 2.52 in the study sample. Since we found that there were reductions in both HDRS-17 and PHQ-15 scores at 1 month and 6 months from baseline scores, we wanted to study whether these reductions were statistically significant.

The paired' test was used to study the reduction of both the scores between baseline and 1 month, 1 month and 6th month and baseline and 6th month. All the comparison between months showed that the reduction of scores was statistically significant ($p < 0.001$). This statistically significant 'p' value again confirms the positive effect of antidepressant treatment on depressive symptoms and physical symptoms in group 4 patients with medically unexplained physical symptoms.

We also compared the reduction of HDRS-17 and PHQ-15 scores between groups 3 and 4. We wanted to find out whether the reduction of scores was similar or different between the groups.

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We found that the reduction of HDRS-17 scores was similar in both the groups 3 & 4 as the 'p' value was not significant. But when reduction of PHQ-15 scores between groups 3 & 4 were analyzed, we found that reduction of scores between (baseline & 6 months) and (1st month and 6th month) were statistically significant. Which means that the reduction of PHQ-15 scores between groups 3 & 4 were not similar.

Psychiatric diagnosis	HDRS-17 - Baseline	HDRS-17 - 1 month	HDRS-17 - 6 months
BPAD-current episode severe depression without psychotic symptoms (n=3)	22.67 ± 0.94	12.3 ± 1.8	4.00 ± 0
Mild depressive episode (n=2)	11 ± 0	7 ± 0	2 ± 0
Moderate depressive episode (n=35)	14.9 ± 3.1	8.8 ± 1.95	2.64 ± 0.97
Severe depressive episode without psychotic symptoms (n=14)	24.3 ± 3.6	11.2 ± 2.8	1.83 ± 1.06
Dysthymia (n=9)	11.7 ± 1.3	7.6 ± 1.1	3.25 ± 0.82
Dysthymia with mild depressive episode (n=2)	13.0 ± 0.0	7 ± 0	2 ± 0
Dysthymia with moderate depressive episode (n=1)	12.0 ± 0.0	9 ± 0	0
RDD with current episode moderate depression (n=4)	12.5 ± 0.5	6.5 ± 0.5	2 ± 0
RDD with current episode severe depression without psychotic symptoms (n=2)	26.0 ± 0.0	10 ± 0	2 ± 0

Table 3: Average HDRS-17 scores for various psychiatric diagnoses

Psychiatric diagnosis	PHQ-15 - Baseline	PHQ-15 - 1 month	PHQ-15 - 6 months
BPAD-current episode severe depression without psychotic symptoms (n=3)	4.67 ± 0.94	2.33 ± 0.47	0
Mild depressive episode (n=2)	4 ± 0	2 ± 0	0
Moderate depressive episode (n=35)	9.45 ± 3.64	6.08 ± 2.46	2.14 ± 1.55
Severe depressive episode without psychotic symptoms (n=14)	8.14 ± 3.44	4.85 ± 2.16	1.16 ± 1.86
Dysthymia (n=9)	5.22 ± 3.64	3.88 ± 2.88	1.25 ± 0.82
Dysthymia with mild depressive episode (n=2)	4 ± 0	3 ± 0	0
Dysthymia with moderate depressive episode (n=1)	11 ± 0	8 ± 0	0
RDD with current episode moderate depression (n=4)	11.5 ± 0.5	6.5 ± 1.5	1.5 ± 0.5

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RDD with current episode severe depression without psychotic symptoms (n=2)	4 ± 0	3 ± 0	0
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Table 4: Average PHQ-15 scores for various psychiatric diagnoses

As the tables 3 and 4 indicate, baseline HDRS-17 scores were high for two diagnoses (Severe depressive episode without psychotic symptoms & RDD with current episode severe depression without psychotic symptoms). The lowest score was for mild depressive episode. Patients with RDD with current episode moderate depression & moderate depressive episode had the highest baseline PHQ-15 scores.

DISCUSSION: The salient findings of our study were:

- Most frequent depressive diagnosis observed was moderate depressive episode.
- Statistically significant reduction of both depressive and physical symptoms was noticed after initiation of antidepressant treatment.
- Antidepressant treatment produced a similar fall in depressive symptoms irrespective of presence or absence of comorbid physical illness.
- Reduction in physical symptoms was similar in depressive patients with or without comorbid physical illnesses.

The majority of the subjects in our study was female 55 (76%), married 55 (76%) and belonged to rural areas. The age range of the subjects was 18-60 years (34.6 ± 10.6 years). The female predominance in our study is in concordance with similar studies in the past. Malzberg (1929) found the percentage of women to be (63.1%) while Lundquist (1945) reported 61.5% incidence in women.^{19,20} In our study 55 (76%) of the study subjects were married and majority belonged to rural areas. In the study by Venkoba Rao (1966), 22 out of 30 subjects were married.²¹ According to Brooke (1959), married depressive patients have been shown to have good prognosis.²²

In our study, we studied the prevalence of physical symptoms among all the subjects at baseline irrespective of their groups. Majority of the patients (97.2%) reported low energy and trouble sleeping. Painful physical symptoms such as pain in arms, legs or joints (41.4%) and back pain (30%) were also reported by the patients. It is noteworthy that, in our study, all patients in group 4 reported sleep disturbance (100%) and feeling tired (100%).

The rate of painful physical symptoms was higher with pain in limbs in (44%) and back pain in (34%) of patients compared to other groups. It was observed in our study that women reported more bodily distress, and more intense painful physical symptoms. This female preponderance is also reported by other similar studies.^{23,24}

There are various studies with similar findings with our observation in relation to the physical symptoms. Casper et al (1985) observed sleep disturbances as the commonest physical symptom in majority of their study subjects²⁵. This is reflected by the fact that sleep disturbance is listed among main symptoms of depression in both the leading systems of classification of psychiatric disorders.

In our study we also analyzed the frequency of individual psychiatric diagnosis. We found that 49% of our study sample suffered from major depressive episode and 19.4% suffered from severe

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depressive episode. In both these diagnosis there was female preponderance. We found that patients with severe depressive episode had highest baseline & 1st month HDRS scores. Patients with dysthymia had highest HDRS-17 scores at 6 months.

We observed highest PHQ-15 score at baseline in patients with RDD, current episode moderate depression. This means that patients with this diagnosis had more physical symptoms than other diagnosis. At 1 month, the mean scores were similar for patients with moderate depressive episode and RDD, current episode moderate depression. But at the end of 6 months patients with moderate depressive episode had higher physical symptoms score than other diagnoses.

Like previous studies our study also confirms that many physical symptoms are highly prevalent in patients with clinical depression.^{26,27} This study extends our understanding of physical symptoms in the presence of depression, by establishing a time course for improvement in individual symptoms with the treatment of depression. In our study, within the first month of antidepressant treatment a substantial proportion of depressed patients reported improvement in both their depressive and physical symptoms.

The burden of physical symptoms, as measured by PHQ-15, declined substantially during the first 4 weeks, and then continued to fall till the 6th month. Similarly, there was rapid initial improvement as well as continued gradual improvement in depressive symptoms over the entire 6 months of treatment. While there is substantial research literature demonstrating a strong cross-sectional association between physical symptoms and depression, there is lesser information about their longitudinal relationship.

Our study observed that improvement in depressive symptoms is associated with corresponding reduction in the associated physical symptoms. This in concordance with the findings of Greco et al (2004) and O'Malley et al (1999).^{28,29}

CONCLUSION: This study is an addition to the body of scientific literature on the prevalence of physical symptoms in depressive disorders.

This study showed that there was a statistically significant reduction in HDRS-17 and PHQ-15 scores after initiation of antidepressant therapy. In patients with unexplained physical symptoms, there was statistically significant reduction of physical symptoms with use of antidepressant medications.

The rate of reduction in HDRS-17 and PHQ-15 scores was similar in depressive patients with or without co morbid physical illness. This study has replicated earlier research reports on the favorable impact of antidepressant treatment on unexplained physical symptoms in patients with depressive disorders.

The fact that physical symptoms associated with depressive disorders frequently improve during the first month of antidepressant treatment in many patients is useful for the psychiatrist and primary care physician in counseling the depressed patient presenting with physical complaints.

Treating both the emotion and the physical symptoms associated with depression together is an important part of achieving remission. A majority of patients with depression initially seek treatment for the physical symptoms of depression rather than for their emotional symptoms. A treatment regimen that does not address physical symptoms and only focuses on core emotional symptoms could result in an incomplete remission and a poor prognosis for the patient.

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Limitations of our Study: Since the number of depressive patients without any physical complaints was very low, this group could not be meaningfully compared with other groups.

Even though we emphasized on strict drug compliance, we did not use any methods or instruments to verify (ensure) drug compliance of the patient. The fact that all the subjects were treated as outpatients contributed to this limitation.

Instead of ratings at baseline, 1 and 6 months, monthly assessments (scoring) of depressive and physical symptoms might have facilitated supervision of drug compliance and frequent monitoring of patient response.

Since depressive patients with co morbid physical illness were on treatment for both, the relative contributions of the antidepressant treatment and the medical treatment to improvement in depressive and physical symptoms could not be ascertained with confidence.

Suggestions for further Study: More studies of this kind need to be duplicated with larger sample size in our socio-cultural setting. The result of these studies will give patterns of somatic presentation in our population which will facilitate the effective management of such disorders.

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