

**PSYCHIATRIC COMORBIDITY IN TRANSFORMED MIGRAINE:  
PRESENTATION, TREATMENT, IMPACT AND OUTCOME**

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**INTRODUCTION**

Transformed migraine is one of the subtypes of chronic daily headache (CDH), and is similar to chronic migraine, described in the new International Headache Society (IHS) classification 2004.<sup>1</sup> The term CDH refers to the Headache disorders experienced 15 or more days a month and includes headaches associated with medication overuse.<sup>2,3</sup> CDH can be divided into primary and secondary varieties. Primary CDH is not related to a structural or systemic illness. It includes diseases such as Transformed migraine (TM). Chronic tension-type headache (CTTH), new daily persistent headache (NDPH), and hemicrania continua (HC). Secondary CDH has an identifiable underlying cause, including post-traumatic headache, cervical spine disorders, vascular disorders, nonvascular intracranial disorders and headaches associated with temporomandibular joint disorders, sinus infections, chronic meningitis, low and high intracranial pressure. In this

study we have adopted the 1996 definition of TM proposed by Silberstein and Lipton in preference to the new discredited 2004 IHS criteria for chronic migraine.

The association between migraine and psychiatric disorders has long been established. Several clinic-based<sup>4-6</sup> and population-based<sup>7-9</sup> studies have discussed the relationship. However psychiatric comorbidity in transformed migraine has seldom been discussed, and the effect on overall outcome has not been examined. Population based studies have shown that 4% to 5% of the general population has primary CDH.<sup>10</sup> Transformed migraine is the major cause of CDH and is associated with poor quality of life and greater medical and social expenses compared to episodic migraine.<sup>11,12</sup> CDH is most commonly transformed Migraine and is accompanied by high anxiety levels in most patients and with hysterical traits in some. These patients frequently have a coexisting depressive disorder.<sup>12</sup> The purpose of this study is to characterize psychiatric disorders accompanying TM in a tertiary headache center and to examine their impact on outcome.

## **Patients and Methods**

One hundred and thirty nine consecutive patients of Transformed Migraine (Defined by Silberstein Lipton criteria) attending a quaternary headache center were offered entry into the study. Their headache history was taken by a neurologist. Each patient had a diagnostic semi

structured psychiatric interview by a psychiatrist or psychologist, a Beck Depression Inventory (BDI), Migraine Disability Assessment Score (MIDAS), and a SF-36.

At 3, 6, and 12 months, headache frequency, intensity scores, BDI, MIDAS, and SF-36 scores were measured. MIDAS and SF-36 have been validated in previous headache studies and are sensitive to clinical change.<sup>13,14</sup> The BDI is a standardized test and also validated to diagnose the presence of depression.

The headache severity index was calculated by multiplying number of days with baseline headache by the baseline intensity and adding the number of days with a headache exacerbation multiplied by the exacerbation intensity and divided by 30 days. The data was then analyzed using SAS and regression analysis.

## **RESULTS**

Overall 82 subjects consented to the study. 69 were women (84%) and 13 were men (16%). With a mean age of  $39.7 \pm 13.2$  years. The mean age of onset of episodic migraine was  $18.6 \pm 11.5$  years and mean duration of daily headache was  $7.0 \pm 8.0$  years. Aura was present in 23 patients (28%) (16 visual, 1 sensory, and 6 mixed). 86.6% (71 Pts) of the study population over used acute treatment, with a mean duration of overuse of  $4.3 \pm 5.4$  years. The mean initial headache frequency was  $23.2 \pm 6.1$  days. At twelve months, the mean headache frequency decreased to

13.4±11.1 days. The mean initial baseline headache intensity was 5.7±2.0 out of 10, at twelve months, the mean baseline headache intensity decreased to 5.1±1.9. The baseline mean exacerbation headache frequency and intensity was 6.2±5.9 and 7.8±3.4, respectively. At twelve months the mean exacerbation headache frequency and intensity decreased to 4.0±4.2 and 7.6±1.8 respectively. The headache severity index was 6.5±1.5 at headache onset and 4.5±2.5 at 12 months ( $p<0.0001$  for difference, Dunnett's method for multiple comparisons).

We classified the 82 patients enrolled in the study into three categories of response to treatment, high, intermediate and low. High response was defined as a decrease in headache severity of 4.73 or greater. Intermediate response, based on severity change between 0.83 and 4.73 and low response, based on severity changes less than 0.83 on the 11 point VAS scale. Based on this response criteria 29 subjects had a high response, 36 an intermediate response and 17 a low response (Figure 1). Age can not predict outcome as patients with young age showed both type of response, high as well as low and patients with middle age group had intermediate response (Figure 2).

The highest change in headache severity index occurs with patients who had worst headache score at baseline, showed by Kruskal-Wallis test for non-parametric analysis. (Figure 3). The Beck Depression Inventory (BDI) scores varied widely with an initial range of 0-44, and it decreased gradually between six months but slightly increased at 12 months but all were still less than at baseline. (Figure 4). Patients with low BDI score at baseline had a good outcome (Figure

5). SF-36 results showed a varied response among its various sub-categories and was not a good predictor of outcome but was a good measurement of outcome.( Figure 6 ). The MIDAS scores were predominantly in Grade IV with 78% (n=58) scoring greater than 21 at the initial evaluation. A number of subjects improved to a Grade I-III at 3 and 6 months (Figures 7).

Most patients had psychiatric comorbidity, seventy-two patients (88%) had at least one Axis I diagnosis. The most common diagnostic groups were Adjustment Disorder (n=35), Depression (n=22), and Generalized Anxiety Disorder GAD (n=14) (Figure 8). In utilizing 3 categories of high/intermediate/low response, patients with Adjustment disorder showed low response in 55% of cases as compared to 38% in each of high and lintermediate response categories. 17% of Depressed patients showed high response, 33% intermediate and 18% low response. 11% of GAD patients showed high response, 18% intermediate and 12% low response, as compared to patients with no Axis 1 psychiatric disorder 22% showed high response, 8% intermediate and 6% low response.

## **DISCUSSION**

On Transformed Migraine patients had severe disability which profoundly affected their function and quality of life. Patients improved with treatment but still had significant pain, disability, and poor quality of life.

For chronic migraine (CM) the requirement that the daily headache must meet the criteria for migraine without aura each day remains a concern with the first revision of the new proposed IHS criteria, which captures only a small number of patients with TM, as even episodic migraine does not always meet IHS migraine criteria throughout the attack.<sup>1</sup> For that reason we adopted Silberstein and Lipton revised Criteria for transformed migraine, stating that patients should have daily or almost daily ( $\geq 15$  d/mon) head pain for  $\geq 1$  month with average headache duration  $\geq 4$  h/day with at least one of the following 1) history of episodic migraine meeting an IHS criteria 1.1 to 1.6. 2) history of increasing Headache frequency with decreasing severity of migrainous features or headache at one time meets IHS criteria for migraine but it doesn't meet criteria for new daily persistent headache or hemicrania continua and is not attributed to another disorder. Our study is consistent with other studies showing high prevalence of psychiatric comorbidity in Transformed Migraine.<sup>15</sup> Regardless of psychiatric comorbidity our patients severity and intensity of headache decreased by time as is indicated by Figure 3. Treatment outcome cannot be predicted based upon initial severity, depression, disability, or quality of life. We found no difference between drug-overusers and non overusers in outcome.<sup>16</sup> As most of our patients were drug overusers and the mean duration of their analgesic overuse was several years. Their final assessment scores varies widely and many of them improved regardless of their acute drug use.

Overall disability, physical health and social functioning are more impaired in TM than in many other chronic illness.<sup>17,18</sup> Our study showed some improvement in disability scores and total headache days which decreased from an average of 23.2 to 13.4 headache days per month.

Patients still had 1/3 of the month with pain along with substantial social mal-functioning and physical ill health after 12months follow up. Previous studies using the SF-36 in headache patients, showed that patients with TM had the worst pain profile. SF-36 scale scores were most severely reduced in patients with TM, followed by CTTH and episodic migraine.<sup>19</sup> Effective management of episodic migraine might prevent its progression to the more disabling TM.<sup>20</sup>

Overall 86.6% of our TM patients had a coexisting psychiatric disorder this is similar to the 90% that Verri et al found.<sup>21</sup> Most common were adjustment disorders, Depression and generalized anxiety disorders (Fig 8)

Overall outcome could not be predicted on initial severity and coexisting illnesses, but comorbid psychiatric diseases have important treatment implications. TM requires a combination of both pharmacological and behavioral treatment.<sup>22</sup> Psychiatric comorbidity demands that a comprehensive treatment approach is needed.

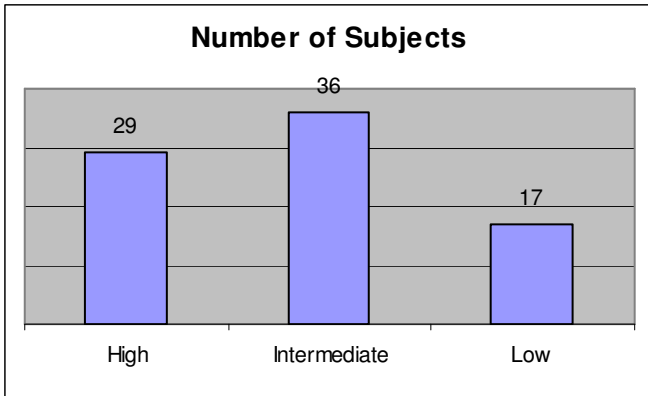
Depression can be a consequence of living with chronic, disabling headaches and may respond as headaches improve. However preexisting headache or anxiety may precipitate or exacerbate headache episodes in patients who are headache-prone. Headaches or affective distress may not improve until the comorbid psychopathology improves.<sup>23</sup> Our study supports the view that

combined psychologic and pharmacologic treatment need to be considered.<sup>24,25</sup> Relaxation or biofeedback training and short-term cognitive-behavioral therapy are particularly useful.

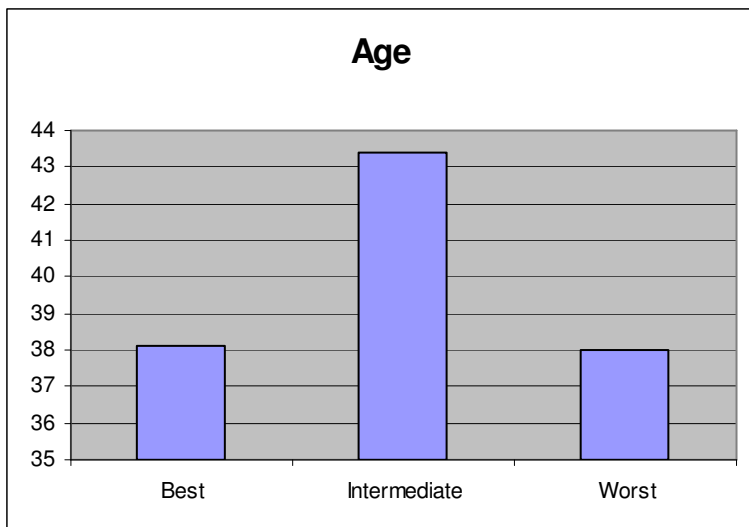
Cognitive-behavioral headache treatment may include focused attention on the specific psychological problems that precipitate or exacerbate headache episodes or interfere with the treatment compliance. The role of antidepressants in chronic headache with comorbid psychiatric illness, is supported by several studies.<sup>26</sup> We frequently use antidepressants combined with psychotherapies, such as stress management, behavior-relaxation therapy, biofeedback may be affective adjuvant treatment of transformed migraine.



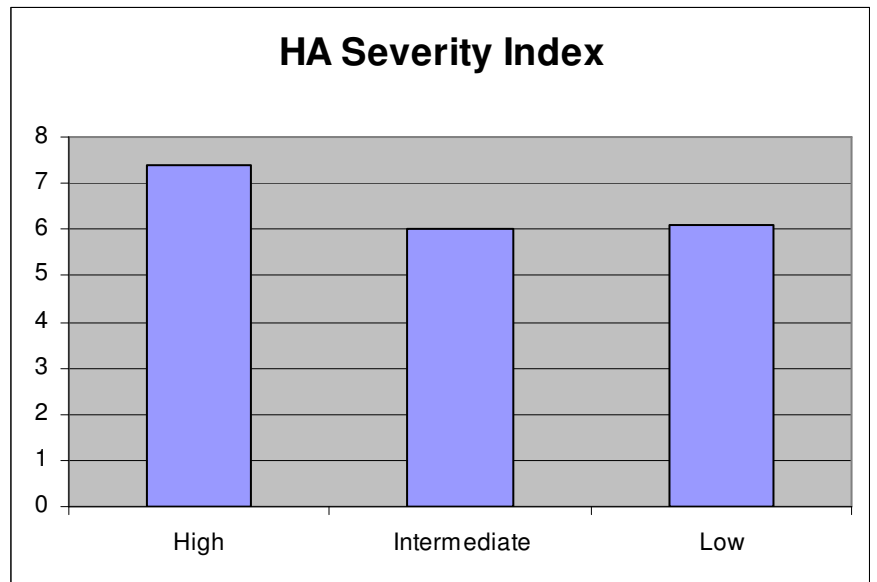
**Fig 1:** Based on response criteria describes in methods, 29 subjects showed high response, 36 intermediate response and 17 low response



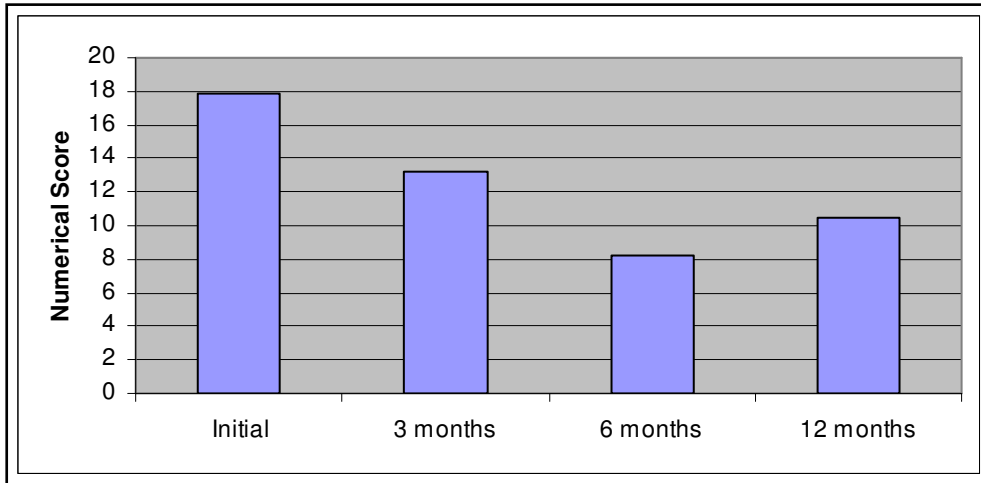
**FIGURE 2:** Age can not predict outcome as patients with young age showed both type of response high as well as low and patients with middle age group had an intermediate response



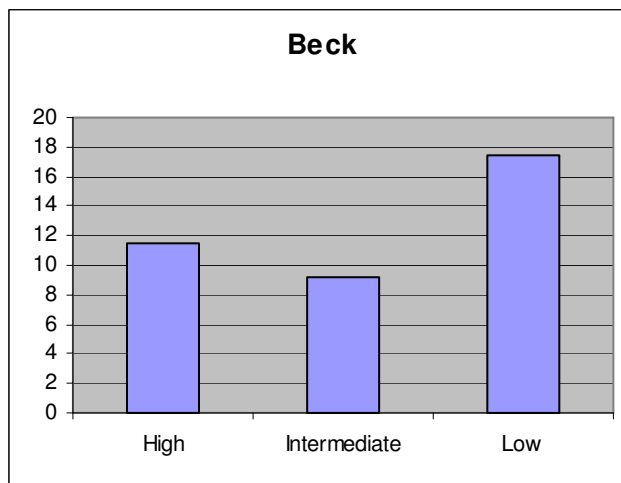
**FIGURE 3:** The Kruskal-Wallis test for non-parametric analysis of this data demonstrated the highest change in headache severity index occurs with patients who had worst headache score at baseline



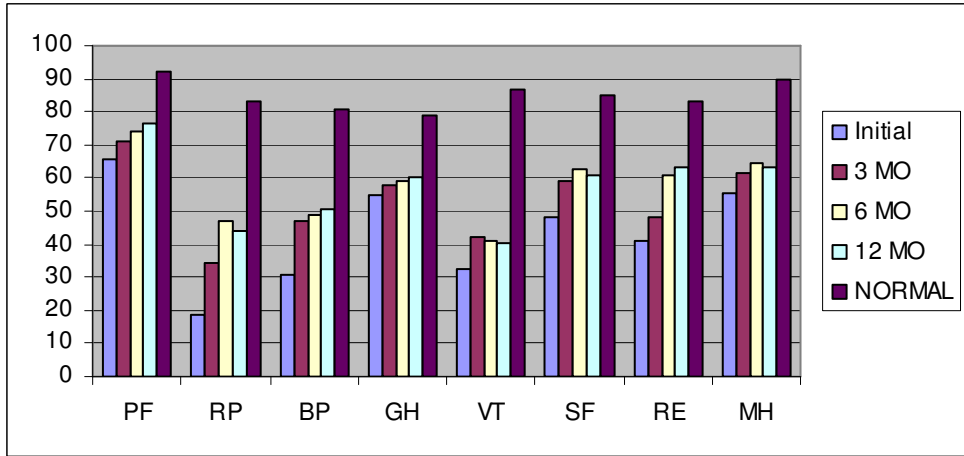
**FIGURE 4:** The Beck Depression Inventory (BDI) scores varied widely with an initial range of 0-44, and it decreased gradually till six months then slightly increased at 12 months but all patients were still less than baseline.



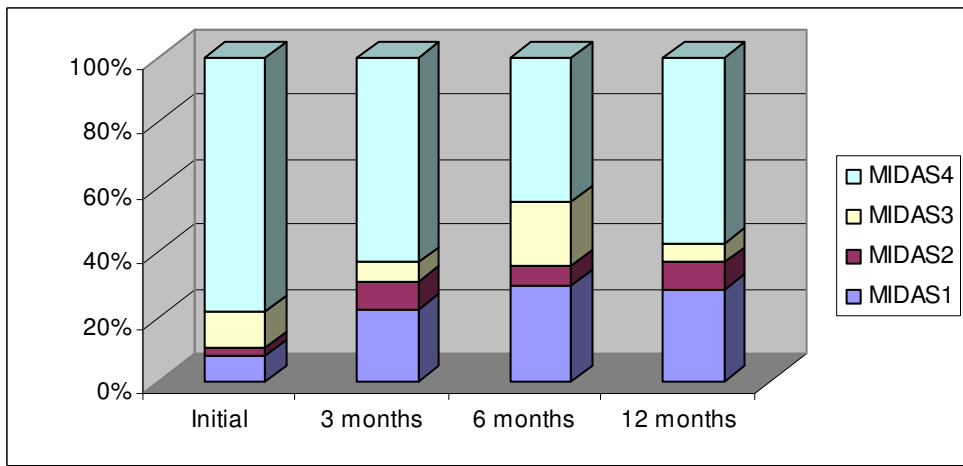
**FIGURE 5:** Patients with low BDI score at baseline showed good response at outcome



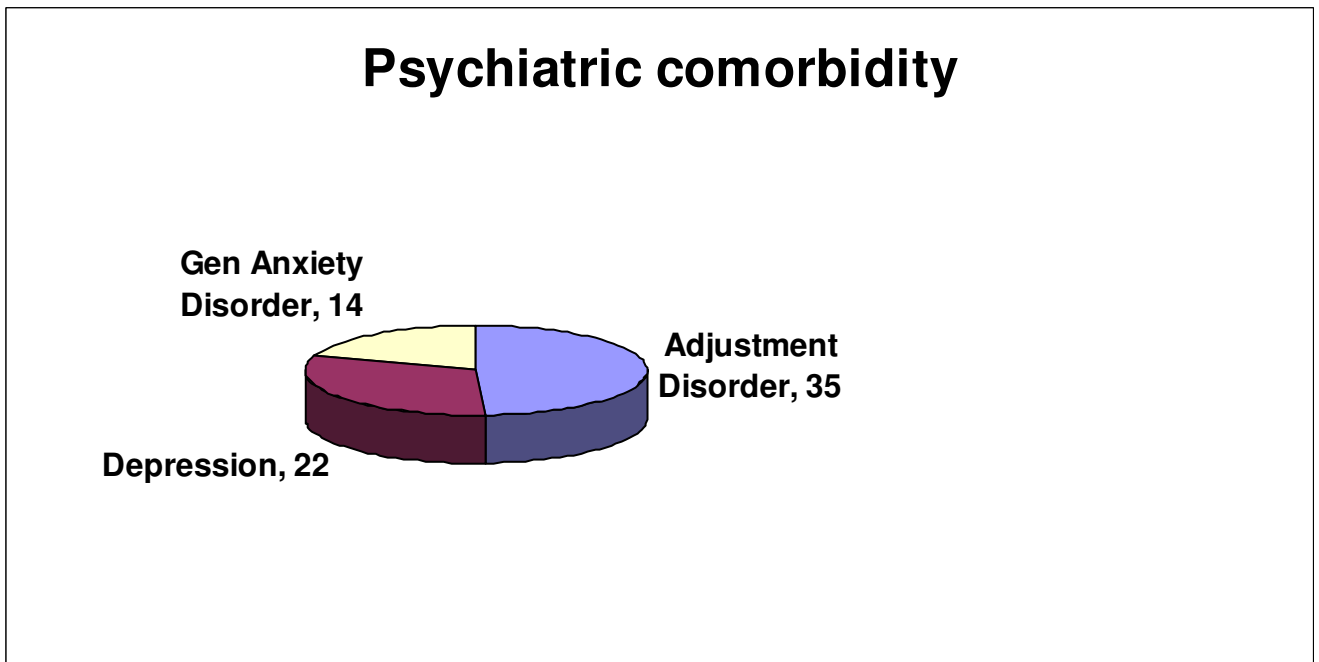
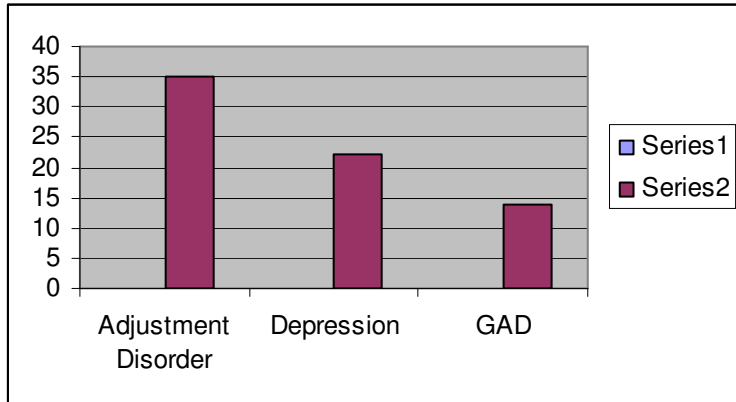
**FIGURE 6:** SF-36 Results, SF-36 results showed a varied response among its various sub-categories and was not a good predictor of outcome, but a good measurement of outcome.



**FIGURE 7:** The MIDAS scores were predominantly in Grade IV with 78% (n=58) scoring greater than 21 at the initial evaluation. The trend showed that a number of subjects improved to a Grade I-III at 3 and 6 months



**FIGURE 8:** seventy-two patients (88%) had at least one Axis I diagnosis. The most common diagnostic groups were Adjustment Disorder (n=35), Depression (n=22), and Generalized Anxiety Disorder GAD (n=14)





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