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**Dr. Aftabuddin khan**

Assistant Professor, Birbhum  
Vivekananda Homoeopathic  
Medical College and Hospital,  
BHMS, MD (Practice of  
Medicine), National Institute  
of Homoeopathy, Kolkata,  
West Bengal, India

**Dr. Sarfia Haque**

Assistant Professor, BHMS,  
MD (Homoeopathic  
Pharmacy), Birbhum  
Vivekananda Homoeopathic  
Medical College and Hospital,  
National Institute of  
Homoeopathy, Kolkata,  
West Bengal, India

**Corresponding Author:**

**Dr. Aftabuddin khan**

Assistant Professor, Birbhum  
Vivekananda Homoeopathic  
Medical College and Hospital,  
BHMS, MD (Practice of  
Medicine), National Institute  
of Homoeopathy, Kolkata,  
West Bengal, India

## Correlation of improvement in symptoms of depression and improvement in somatic manifestations of hypothyroidism with constitutional homoeopathic treatment

**Dr. Aftabuddin Khan and Dr. Sarfia Haque**

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### Abstract

**Background:** Hypothyroidism and Depression are common diseases. Independent studies on hypothyroidism and depression found constitutional homoeopathic treatment effective. A clinical study is required to establish the relationship between their responses to Homoeopathic treatment.

**Aim and Objectives:** To assess the correlation in the improvement of Depression with the improvement of somatic manifestations in cases of Hypothyroidism having associated Depression; to assess the improvement in Depression by utilizing HAM-D score and improvement in somatic manifestations of Hypothyroidism by utilizing Zulewski score.

**Materials and Methods:** A prospective clinical study was conducted at the National Institute of Homoeopathy on 30 patients having Depression associated with Hypothyroidism treated with constitutional homoeopathic medicine for 3 months. Depression and physical symptoms of hypothyroidism were assessed by the HAM-D scale and Zulewski scale respectively. The correlation between the two responses was analysed.

**Results:** After treatment, the mean decrease in HAM-D score was 8.96 and in Zulewski score was 3.70. The decrease in HAM-D and Zulewski score was statistically significant. ( $P < 0.01$  in both series). Pearson's correlation coefficient ( $r$ ): 0.736.

**Conclusion:** There is a strong partially positive correlation between improvement of Depression and improvement of somatic manifestations in Hypothyroidism patients having associated Depression with Constitutional Homoeopathic Treatment.

**Keywords:** Depression, hypothyroidism, constitutional homoeopathic treatment, ham-d score, zulewski score, correlation

### Introduction

Hypothyroidism is one of the endocrine disorders with which Depression is commonly associated <sup>[1]</sup>. There are many features that are common to both Hypothyroidism and Depression-like fatigue, weight gain, sleeplessness, low libido, decreased appetite and hair loss <sup>[2]</sup>.

Depression is a mental state of depressed mood characterized by feelings of sadness, despair, and discouragement. It ranges from feelings of gloominess to depression. In many ways, it resembles the grief and mourning that follows bereavement. Feeling of low esteem, guilt and self-reproach, withdrawal from interpersonal contact, and somatic symptoms such as eating and sleeping disturbances are also observed in such patients <sup>[3]</sup>. A major depressive episode is defined as a depressed mood on a daily basis for a minimum duration of 2 weeks. In DSM-V there are 9 criteria given, out of which 5 symptoms need to be present, in which depressed mood and loss of interest are must and these symptoms should not be due to any other medical condition <sup>[4]</sup>. Depression in diseased patients may be attributed to psychiatric trauma caused by disease coping, the disease phase itself, drugs used for recovery, or even coexisting at the time of diagnosis. Patients with heart disease suffer from depression (About 20% to 30%) to a varying degree <sup>[5]</sup>. Depression affects 25% of cancer patients, with the pancreas and oropharynx being the most common <sup>[5]</sup>. Depression is often linked with neurological disorders such as cerebrovascular illness, cerebral tumor, Parkinson's disease, dementia, Alzheimer's disease etc. <sup>[6, 7]</sup>. Among endocrine disorders depression affects 8% to 27% of people with diabetes <sup>[5]</sup>. Cushing's disease, Addison's disease, and hyperparathyroidism are also endocrine disorders that cause depression <sup>[8]</sup>.

Hypothyroidism, like hyperthyroidism, exhibits depression-like symptoms, most notably a depressive disposition and memory impairment. Depression and learning difficulties are present in patients with subclinical hypothyroidism [6].

Since the 19<sup>th</sup> century, hypothyroidism has been linked to neuropsychiatric disorders. But measurements and therapy of thyroid hormones were not yet available. As the result, the diagnosis was often taken purely on the basis of the distinctive symptomatology of long-term illness, which included lethargy, exhaustion, dementia, and psychosis in instances of extreme hypothyroidism [9, 10]. On this account, there is extensive research from the late nineteenth century on the behavioural and psychiatric effects of untreated hypothyroidism [11, 12]. The most detailed explanation of the symptomatology at the time was given by the Committee of the Clinical Society of London in a historical paper on 109 myxoedematous patients published in 1888 [2]. Mental disturbances were identified in many of the patients, ranging from irritability to melancholia and depression. "Delusions and hallucinations arise in about half of cases, primarily when the condition is advanced," according to the same article, marking the first mention of the connection between myxedema and hysteria, later described as "mad myxoedema" [13]. Shortly after, it was widely recognised that hypothyroidism would seriously impair brain activity, and a scientific finding was made that using dried thyroid formulations (thyroid siccatum) derived from sheep's thyroids produced excellent results for a variety of psychiatric disorders as well as cases of myxoedema and goitre [14].

Thyroid hormones have significant activity in the Systemic development of the brain, such as in neurogenesis, glial development, myelination, and dendritic cell proliferation [15]. It has been observed that dysfunction in the triiodothyronine (T<sub>3</sub>) hormone leads to defects in the morphology of brain cell microglia, which further leads to the development of psychological dysfunctions [2]. Mental diseases such as schizophrenia, bipolar disorder, anxiety and depression can be results of hypothyroidism or hyperthyroidism [16].

M Depression has been seen in 60% of hypothyroidism cases [17]. Women are more likely than men to have neuropsychiatric problems and have higher rates of depression and anxiety disorders [17]. Hypothyroidism was shown to be prevalent in 20.5 percent of those with major depressive disorder [18]. Clinically, hypothyroidism and depression have a lot in common. As a result, some scientists refer to depression as "brain hypothyroidism" [16]. There is proof that hypothyroidism affects both affective and psychic symptoms because it is related to depression [2]. Depression, cognitive impairment, apathy, and psychomotor slowing are all common symptoms of hypothyroid patients [2, 19]. "The diagnosis of subclinical or clinical hypothyroidism must be considered with a patient with depression," according to the American Association of Clinical Endocrinologists [20]. Indeed, depression is the most frequent of the different neuropsychiatric symptoms of thyroid disorders [21]. In depressed patients thyroid defects are characterised by elevated T4 levels, low T3, and elevated rT3, a blunted TSH reaction to TRH, positive anti-thyroid antibodies, and elevated TRH concentrations in the cerebrospinal fluid (CSF).

From research works available in Homoeopathy it was found that no clinical study was done yet to find the effect

of constitutional treatment in two co-existing illnesses "Hypothyroidism" and "Depression" in a patient. Several studies are available in homoeopathy which was conducted on hypothyroidism separately and on depression separately. The results of these studies showed the effectiveness of Homoeopathy [22-27]. A study was required to observe whether with Constitutional Homoeopathic Treatment there is any correlation between improvement of somatic manifestations of hypothyroidism and improvement in symptoms of depression in these two co-existing illnesses in a patient.

### Materials and Methods

This Prospective clinical study was carried out at the National Institute of Homoeopathy from November 2019 to April 2021. The sources of the samples were patients visiting the National Institute of Homoeopathy (NIH). Initially, 67 cases of hypothyroid were screened for the study out of whom 40 cases fulfilled the inclusion criteria (as given below). Of these 40, 10 cases were discontinued before the end of two months or did not have an investigation at the proper time; hence were taken as dropped out. The study was duly completed on the basis of the remaining 30 cases.

Patients with hypothyroidism of any aetiology having depression with Hamilton Depression Rating Scale (HAM-D) score above 7 and who score above 5 on Zulewski scale taken under consideration [5, 8]. In addition to this patient having serum TSH > 4.0 µU/mL, T3 <64 ng/dl or within 64 to 175 ng/dl, T4 < .0.8 ng/dl or within 0.8 to 2.0 ng/dl are included with written consent. Patients below 20 years of age, who are pregnant, taking psychiatric medicines or taking medicine for hypothyroid from modern or another system of medicine were excluded. Patients having malignancy or any terminal illness and scoring >18 on the HAM-D scale were also excluded.

Detailed case taking of each and every case having problems related to hypothyroidism was done along with relevant clinical examination. After that Scoring for depression using the HAM-D scale and Scoring for hypothyroidism using the Zulewski scale [5, 8]. Relevant investigation procedure was done as per the need of the case. Evaluation of symptoms was done as per homoeopathic philosophy and framing the totality in accordance with Organon of Medicine. Selection of medicine was done in consultation with Homoeopathic Materia Medica and therapeutics based on Organon of Medicine. Observation of responses of the patients was done through symptoms and signs and relevant investigation, and assessing the response by scoring scale (HAM-D and Zulewski) [7, 28]. Follow-up was done on regular basis as per the need of the patient for at least 3 months to ascertain whether there is a progressive improvement.

The assessment of the outcome of the treatment was done by the changes that occur in the scoring. Depression was assessed by using the HAM-D scale [9]. Depression was graded; as follows – Score 0 to 7 (normal limits), 8 to 13 (mild depression), 14 to 18 (moderate depression), 19 to 22 (severe depression), and score 23 and above (very severe depression). Somatic manifestations of hypothyroidism were assessed using the score by the Zulewski scale [7]. This Scale ranges from 0 to 12; and scores are graded as euthyroid (below 3), intermediate (3 to 5), and hypothyroid (above 5) [18]. Thirty (30) cases of hypothyroidism associated

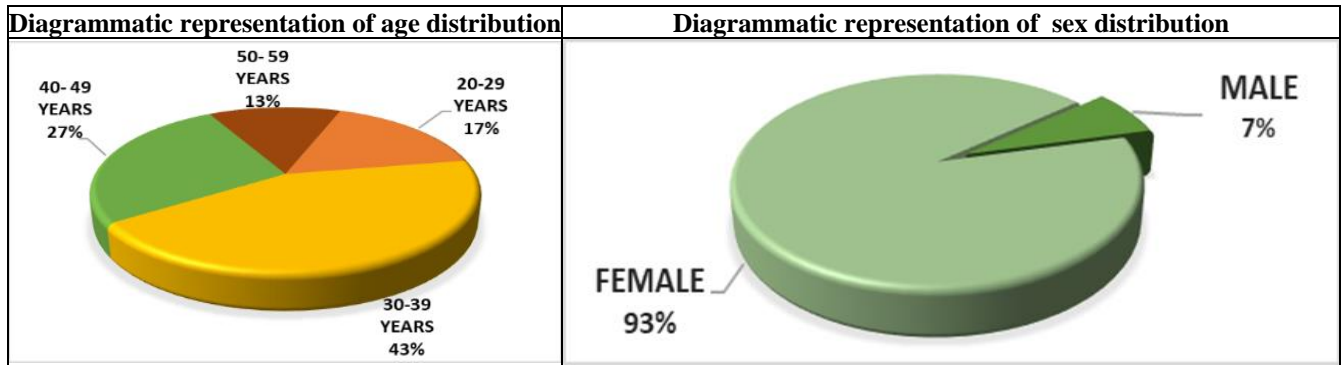
with depression were assessed for the outcome of treatment by using the scoring scale. Analysis was done to assess the correlation in the improvement of depression with the improvement of somatic manifestations in cases of hypothyroidism having associated with depression with the help of pictographic and other standard statistical methods [29, 30]. Data was analysed from a descriptive and inferential point of view. Further ‘Paired t-test’ has been done to analyse the response of medicines administered from ‘0’ to ‘3’ months and Pearson’s correlation coefficient was used to find out the correlation between the improvement of depression with the improvement of somatic manifestations in cases of hypothyroidism having associated depression.

Microsoft Office Excel 2013 sheet was utilised when required [31].

**Results and Discussion**

In this study 30 cases of Hypothyroidism having associated Depression were studied in which 93% (28) cases were females and 7% (2) cases were males. The age distribution of this illness was found between the age group of 20-59 years but it was found that 43% (13) cases were found between the age group of 30-39 years. 90% (27) cases were from the rural area. The study revealed that females are more affected.

**Table 1:** Distribution of patients based upon socio-demographic characteristics (n=30)



Amongst 17 symptoms of Depression present on the HAM-D scale ‘Depressed mood’ was present in every case and no case was reported with an ‘Insight’ related issue. Most of the cases presented with ‘Anxiety’ in 96.66% (29) cases and ‘Insomnia’ related problems in 86.66% (26) cases. Very few cases were associated with ‘Weight loss’ 3.33% (1), ‘Retardation’ 10% (3), and ‘Hypochondriasis’ (4). After

treatment most improvement was seen in five symptoms related to ‘Suicide’ e.g. suicidal thoughts (61.9%), ‘Feeling of guilt’ (59.1%), ‘Insomnia middle’ (53.8%), ‘Somatic symptoms Gastrointestinal’ (53.8%) and ‘Depressed mood’ (50%). The least improvement was observed in ‘Genital Symptoms’ (7.1%), ‘Anxiety Psychic’ (27.6%) and ‘Insomnia delayed’ (28.5%).

**Table 2:** Comparison of the number of cases showing the presence of the different symptoms of HAM-D scale before and after treatment (n=30)

Sl. No.	Symptoms	No. of Cases		
		Before Treatment	After Treatment	Decrease
1.	Depressed mood	30	15	15 (50.0%)
2.	Anxiety Psychic	29	21	8 (27.6%)
3.	Insomnia middle	26	12	14 (53.8%)
4.	Anxiety Somatic	26	17	9 (34.6%)
5.	Somatic Symptoms Gastrointestinal	26	12	14 (53.8%)
6.	Somatic Symptoms General	24	13	11 (45.8%)
7.	Feeling of Guilt	22	9	13 (59.1%)
8.	Agitation	22	12	10 (45.4%)
9.	Suicide	21	8	13 (61.9%)
10.	Insomnia Initial	21	13	8 (38.1%)
11.	Work And Interests	20	12	8 (40.0%)
12.	Genital Symptoms	14	13	1 (7.1%)
13.	Insomnia delayed	7	5	2 (28.5%)
14.	Hypochondriasis	4	1	3 (75.0%)
15.	Retardation	3	0	3 (100%)
16.	Weight Loss	1	1	0 (0%)
17.	Insight	0	0	-

Symptoms of Depression which showed marked improvement were ‘Depressed mood’, ‘Insomnia middle’, and ‘Suicide’ related symptoms. Symptoms of depression which showed less improvement were ‘Anxiety somatic’, ‘Anxiety psychic’, ‘Insomnia initial’, ‘Insomnia delayed’ and ‘Genital symptoms’

Amongst 12 signs and symptoms of Hypothyroidism

present on the Zulewski Clinical Scoring Scale ‘Cold skin’ covered the highest number of cases (90%). Symptoms like ‘Constipation’ (86.7%), ‘Dry skin’ (83.3%), ‘Paraesthesia’ (76.7%) and ‘Hoarseness’ (63.3%) were covered by the majority of cases. Sign ‘Delayed ankle reflex’ was not found in any patient whereas ‘Coarse skin’ was found only in 1 case. After Constitutional Homoeopathic Treatment

marked improvement was noticed in ‘Constipation’ (88.5%), ‘Cold skin’ (81.5%), and ‘Diminished sweating’ (81.8%). Very good improvement was noticed in

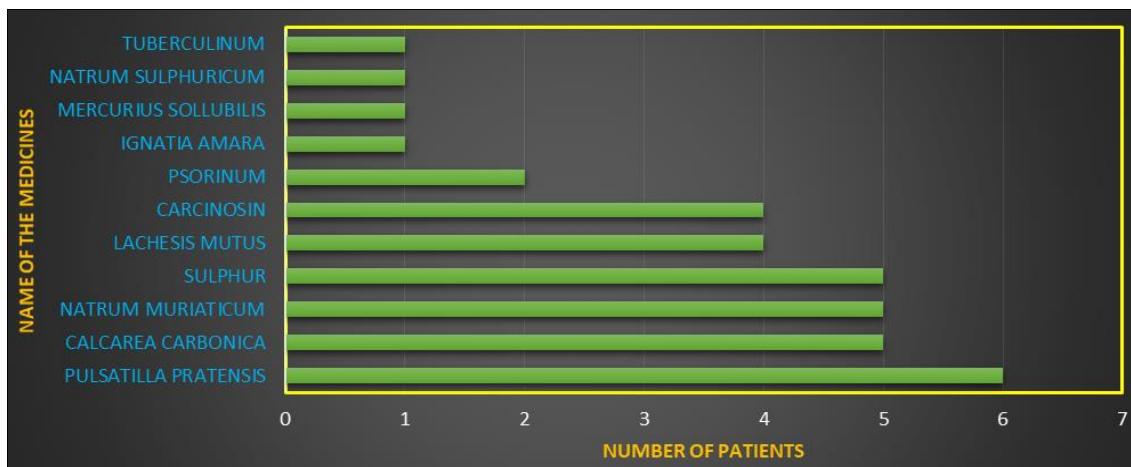
‘Hoarseness’ (68.4%), ‘Slow movement’ (66.7%), ‘Impairment of hearing’ (58.3%) and ‘Dry skin’ (56%).

**Table 3:** Comparison of the number of cases showing the presence of the different symptoms and physical signs in the Zulewski scale before and after treatment (n=30)

SN	Symptoms and signs	No. of Cases		
		Before Treatment	After Treatment	Decrease
1.	Cold skin	27	5	22 (81.5%)
2.	constipation	26	3	23 (88.5%)
3.	Dry skin	25	11	14 (56%)
4.	Paraesthesia	23	14	9 (39.1%)
5.	Hoarseness	19	6	13 (68.4%)
6.	Weight increase	17	11	6 (35.3%)
7.	Periorbital puffiness	15	10	5 (33.3%)
8.	Impairment of hearing	12	5	7 (58.3%)
9.	Diminished sweating	11	2	9 (81.8%)
10.	Slow movements	9	3	6 (66.7%)
11.	Coarse skin	1	1	0 (0%)
12.	Delayed ankle reflex	0	0	-

Total eleven (11) Homoeopathic medicines were used in all 30 cases. The most frequently prescribed medicine was Pulsatilla Pratensis (6 cases); followed by Calcarea Carbonica, Natrum Muriaticum, and Sulphur (5 cases each); Lachesis Mutus and Carcinosis (4 cases each). In every patient, treatment was continued for 3 months and the same medicines were continued for the whole duration of the

study, with the exception of 5 cases (Case No. 2, 4, 5, 11, 28). For these 5 cases, initially, the drugs prescribed were: Lachesis Mutus, Sulphur, Pulsatilla Pratensis, Lachesis Mutus, and Natrum Muriaticum; which were changed to Calcarea Carbonica, Calcarea Carbonica, Sulphur, Ignatia Amara and Lachesis Mutus respectively.



**Fig 1:** Bar diagram showing Frequency of Medicines

In this study before treatment in all the 30 cases, the initial value of the HAM-D score varied from 9 to 18, with a mean value of 15.30. After Constitutional Homoeopathic Treatment for 3 months, the HAM-D score varied from 0 to 12, with a mean value of 6.33. Out of 30 cases, 29 showed a decrease in value and one case showed no improvement. It was found that the difference in HAM-D scores before and

after Constitutional Homoeopathic Treatment varied from 4 to 14 with a mean decrease of 8.97. Paired t-Test was conducted to evaluate the extent of the decrease of the score (HAM-D), and it was found that  $p < 0.01$  (actually  $< 0.001$ ). This indicated that the improvement in HAM-D score by use of Constitutional Homoeopathic Treatment was statistically highly significant.

**Table 4:** Paired t-Test value for HAM-D score before and after treatment from ‘0’ to ‘3’ months

Mean HAM-D Score			Standard Deviation	Standard Error	t Value	p-Value
before	After	Decrease				
15.30	6.33	8.97	3.73	0.68	13.175	$< 0.01$ [ $9.06 \times 10^{-14}$ ]

Out of 30 cases, there were 7 (23%) with mild depression (1 male, 6 female). There were 23 (77%) cases with moderate depression (1male, 22 female). After treatment out of 23 cases with moderate depression, 13 became normal and 10 became mild. Out of 7 cases with mild depression, 5 became

normal, and 2 remained mild. One case out of the last two showed no change in score. In this study before treatment in all 30 castes, the initial value of the Zulewski score varied from 6 to 9 with a mean value of 7.10. After Constitutional Homoeopathic Treatment

for 3 months, the Zulewski score varied from 0 to 7 with a mean value of 3.4. Out of 30 cases, 29 showed improvement; one case showed an increase in the score indicating a worsening of the condition. It was found that the difference in Zulewski score before and after Constitutional Homoeopathic Treatment varied from (-) 1 to 6 with a mean decrease of 3.70.

Paired t-Test was conducted to evaluate the extent of the decrease in the score (Zulewski score), and it was found that  $p < 0.01$  (actually  $< 0.001$ ). This indicated that the improvement in Zulewski's score by use of Constitutional Homoeopathic Treatment was statistically highly significant.

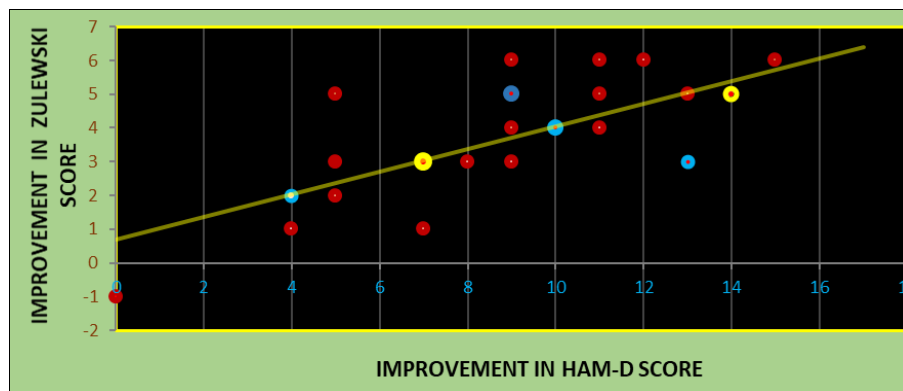
**Table 5:** Paired t-Test value for Zulewski score before and after treatment from '0' to '3' months

Mean Zulewski Score			Standard Deviation	Standard Error	't' value	'p' Value
Before	After	Decrease				
7.10	3.40	3.70	1.70	0.31	11.886	<0.01 (1.14 X 10 <sup>-12</sup> )

After completion of the study, data of both HAM-D score and Zulewski score was analysed and Pearson's correlation coefficient test was conducted. The Pearson's correlation coefficient test showed that there was a strong partially positive correlation as the r-value is  $> 0.7$ . In this study, the r-value is 0.736.

**Table 6:** Pearson's correlation coefficient between improvement in HAM-D score and improvement in Zulewski score after treatment (n=30)

	1	2
1. HAM-D score	1	-
2. Zulewski score	0.73626	1



**Fig 2:** Scatter diagram showing the relationship between improvement in HAM-D score and improvement in Zulewski score after treatment (n=30)

**Comment:** There are 4 blue bullets representing 2 cases each and 2 yellow bullets representing 3 cases each and 16 red bullets representing 1 each case.

**Conclusion**

Constitutional homoeopathic treatment showed marked improvement in symptoms of both depression and the somatic manifestation of hypothyroidism. There was no complication developed in any of the patients. Improvement occurred in both depression and somatic manifestations of hypothyroidism in 28 out of 30 cases. Paired t-test results on the series showed that the improvement in HAM-D Score for depression after 3 months was statistically highly significant ( $p < 0.01$ ). Paired t-test results on the series showed that the improvement in the Zulewski Score for somatic manifestations of hypothyroidism after 3 months was statistically highly significant ( $p < 0.01$ ). Correlation between improvement of depression and improvement of somatic manifestation of hypothyroidism in patients with hypothyroidism having associated depression was strong and partially positive. [Pearson's correlation coefficient (r) = 0.736]

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**Conflict of Interest**

Not available

**Financial Support**

Not available

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