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A pilot study to observe the progression of *Vyadhi Samprapti* in *Srotas* in the context of Hypothyroidism

Research Article

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Abstract

In chronic conditions, the progression of *samprapti* (pathogenesis) of Hypothyroidism in various *Srotasas* (Body Channels) can be observed due to the lack of *Nidanparivarjanam* (restraining of etiological factor) and *Shuddha-Chikitsa* (Comprehensive treatment). Assessment of the progression of the pathogenesis of Hypothyroidism in the *Srotasas* would help to decide the treatment plan for Hypothyroidism according to the stage of the disease, which prevents the further progression of the disease and drug dependency. Objectives: Observe the progression of the pathogenesis of Hypothyroidism in the *Srotasas* by assessing signs and symptoms of the *Dhatupradoshaja Vikara* (diseases due to vitiation of *dhatu*) along with their severity. Methods: In a cross-sectional study, 50 patients with chronicity of hypothyroidism for more than 1 year and on therapy were selected randomly and categorized into 5 groups, according to their chronicity. A separate case proforma was designed to focus on the assessment of the progression of the pathogenesis in patients of Hypothyroidism. The signs and symptoms described as *Dhatupradoshaja Vikara,* chronicity of hypothyroidism, findings of Thyroid Function Test (total serum thyroid-stimulating hormone, serum, total serum triiodothyronine, total serum thyroxine,) and drug dosage were recorded in each patient. The data was subjected to statistical tests. Results: It is observed that the extent of signs and symptoms of *Dhatupradoshaja Vikaras* increased with the chronicity of Hypothyroidism in study participants. Progression of *Samprapti* of hypothyroidism in further *Srotasa* was observed in patients with chronicity of Hypothyroidism, especially in individuals with *Avar Agni* (weak state of digestive and metabolic factors). It is observed that in the study participant drug dosages were escalated with chronicity and *Avara Agnibala* (weak state of *Agni*). *Rasadhatu* and *Rasavaha Srotas* along with *Medodhatu* and *Medovaha Srotas* are priorly and predominantly get vitiated in the *Samprapti* while other *Dhatus* and *Dhatuvaha Srotasa* are involved in *Samprapti* over the period. Conclusion: It can be concluded that the *vyadhi samprapti* of Hypothyroidism progresses in further *Srotasa* with the chronicity of hypothyroidism.

Key Words: *Dhatupradoshaj Vikar, Dhatu-parinamam, Dhatuvaha Srotasa,* Hypothyroidism.

Introduction

Hypothyroidism is a common endocrine disorder due to the deficiency of thyroid hormone. Lack of thyroid hormone or resistance of the body tissue to thyroid hormone concerning metabolic demand results in a disorder called hypothyroidism. According to a previous study conducted in eight urban cities in India, the prevalence rate of hypothyroidism was high and found to be 10%. "(1)".

Conventional treatment for hypothyroidism involves the daily use of the synthetic thyroid hormone. This oral medication restores adequate hormone levels, reversing the signs and symptoms of hypothyroidism "(2)". The aim is to reduce the symptoms, avoid short-term complications and improve or maintain the quality of life with minimal interference and with the least inconvenience to the patient "(3)".

Approximately 5% to 10% of patients continue to have symptoms of hypothyroidism, despite normal TSH (thyroid-stimulating hormone) and FT4 (free thyroxine) levels "(4)". Previous studies suggest the TSH level within the reference range is not a sufficiently optimal marker of adequate thyroid hormone replacement therapy in hypothyroid patients "(5)". The presence of residual symptoms and other hypothyroidism manifestations in patients treated for hypothyroidism indicates the inability of LT4 (Levothyroxine) monotherapy to restore truly normal thyroid physiology "(6)". Previous studies underline the limitation of Levothyroxine substitution therapy to normalize QOL (Quality of life) "(7)" and complete restoration of neurocognitive functioning, and psychological well-being "(8,9)".

The disease hypothyroidism as such is not described in classical Ayurvedic texts. It can be better

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understood with the help of principles of diagnosis and management of *Anukta-Vyadhi* (diseases that are not described in Ayurvedic classical text) "(10,11)". The concept of *Anukta* guides us to understand newly emerging diseases (12,13). In the last few years, much Ayurvedic research has been conducted to elaborate on the Ayurvedic perspective of etiopathogenesis and the management of hypothyroidism. According to the principle of *Anukta-Vyadhi* (14) and the available online medical research database, Hypothyroidism is mainly caused due to the vitiation of *Agni* (digestive and metabolic factor) and *Dhatwagni* (metabolic factor located at Dhatu) (15-19). The *Dhatwagnimandya* (weak metabolic factor located at dhatu), and *Sanga* in various *Srotas* (obstructive pathology at srotasa), (20-25) result in the impairment in process of *Dhatuparinaman* (sequential Dhatu formation process.). *Sam-Dhatus* (*Dhatus* associated with *Aam*) fail to perform their accustomed work and manifest the group of symptoms and further vitiate the *srotasas* (structural or functional channels) (26-30). *Rasavaha* and *Medovaha srotasa* are mainly involved in the pathogenesis. "(30 to 38)".

The presence of residue symptoms and limitation of treatment to restore normal thyroid physiology highlights the lack of *Shuddha-Chikitasa* (comprehensive treatment)"(39)" and the continuation of the progress of *Samprapti* "(40)". The symptomatology of Hypothyroidism includes the involvement of various *Srotasa* in *Samprapti* of disease.

Assessment of the progression of the pathogenesis of Hypothyroidism in the *Srotasa* would help to decide the treatment plan of the Hypothyroidism according to the stage of the disease, which prevents the further progression of the disease and drug dependency. Thus, this pilot study was planned to observe the progression of *Vyadhi Samprapti* of hypothyroidism in *Srotas* by assessing the presence of signs and symptoms of the *Dhatupradoshaja Vikara* (41) which can be considered as the symptoms of respective *Srotasdushti* (42) in patients.

Materials and Methods

Study Sites, IEC approval of the study-

The study was conducted in OPD and IPD of the, D. Y. Patil Ayurvedic Hospital, Nerul, Navi Mumbai, Maharashtra state. Approval was obtained from the institutional ethics committee (IEC) of D. Y. Patil Deemed to be the University School of Ayurveda, Nerul, Navi Mumbai.

Study Design

The pilot study was a cross-sectional observational study. A separate case proforma was designed to focus on the progression of Hypothyroidism in *Dhatuvaha srotasa.* The case proforma was validated by resource persons. The progression of Hypothyroidism in *Dhatuvaha srotasa* was assessed by the presence of signs and symptoms of the *Dhatupradoshaja Vikara* in patients. The signs and symptoms described as *Dhatupradoshaja vikara* in *Charak Samhita* "(41)", Chronicity of Hypothyroidism, findings of Thyroid Function Test, and current drug dosage in the patient were recorded in each patient.

Sample Size

The total sample size in the study was 50 patients. A total of 50 patients with Chronicity of Hypothyroidism for more than 1 year and on hormonal replacement therapy were selected randomly irrespective of, sex, religion, education, occupation, etc. Patients were categorized into 5 groups, according to their chronicity from 1 year to more than 20 years (Group I: Chronicity 1 to 5 years, Group II: Chronicity 6 to 10 years, Group III: Chronicity 11 to 15 years, Group IV: Chronicity 16 to 20 years, Group V: Chronicity more than20 years). 10 patients were included in each group.

Inclusion & Exclusion Criteria

Inclusion Criteria

Patients between 18-70 years of age, diagnosed with Hypothyroidism for more than 1 year, on hormonal replacement therapy, and ready to give written consent were enrolled in the study.

Exclusion Criteria

Patients of age below 18 years or above 70 years, not willing to register, Pregnant or lactating women, or a person suffering from psychological diseases, were excluded from the study. A person suffering from systemic diseases affecting multiple body systems (diabetes Mellitus, Hypertension, etc.) or any major/ minor illness in the last month at the time of the case study was also excluded.

Criteria for assessment

The signs and symptoms described as *Dhatupradoshaja Vikara* were recorded in case record form. It was assessed by adopting suitable scoring methods (eg. Visual Analogue Scale, mild-moderate-sever, etc.) and objective parameters by using appropriate clinical tools (e.g. Thyroid Function Tests, Current drug dosage of patients).

Subjective Criteria

Visual Analogue Scale (VAS) was used to assess the symptoms like *Angamarda* (Body pain), and *Rukparvanam* (Pain in the small joint/joints). *Dhatupradoshaja-Vikaras* of *Raktavaha* and *Mansavaha Srotosa* were assessed by the Presence or Absence of Symptoms of *Srotodushti*. The score was recorded for such symptoms as score 1 for Symptom present and 0 for Symptom Absent. *Dhatupradoshaja-Vikaras* of other *Srotasa* were assessed according to their severity or frequency or combinedly i.e., Score 0: No Symptoms present, score 1: Mild symptomatology, / Symptom present occasionally, score 2: Moderate symptomatology, / Symptom present frequently, score 3: Severe symptomatology/ Symptom present daily**.**

Objective Criteria

A thyroid Function Test was performed on every patient and the findings of Thyroid Function Tests were

noted. The current drug dosage of each patient was documented at the time of case taking.

Plan for Statistical Analysis

The study data generated and collected was put into statistical analysis to reach the results and conclusions. The demographic details were presented in the form of frequencies and percentages. The ordinal variables were presented in Median (Range) and continuous variables in Mean ± SD. The data were subjected to tests of significance. GraphPad InStat (www.graphpad.com) software was used for the statistical analysis of data. The relationship between the ordinal variables was assessed by Spearman Rank Correlation (Non – Parametric). Friedman Test (Non – Parametric ANOVA) (when data failed the normality test) was applied within the groups' comparison (intragroup comparison). Kruskal - Wallis Test (Non – Parametric ANOVA) was applied between the groups' comparison (inter-group comparison), and a P value < 0.05 is considered significant "(43)".

Observations and Results

Out of 50 patients with hypothyroidism enrolled in the study, the maximum number of patients was females i.e., 46 (92%) whereas only 04 (08%) males got enrolled. Out of 50 patients with hypothyroidism enrolled in the study, 18(39%) were in the 31 – 40 years of age group, 14(28%) patients were in the 41 – 50 years of age group, 8 (16%) patients were in the 21 – 30 years of age group, 5(10%) patients were in 51 – 60 years of age group, 4(08%) patients in 61 – 70 years of age group, whereas only 01(02%) patients were in the18 -20 years of age group.

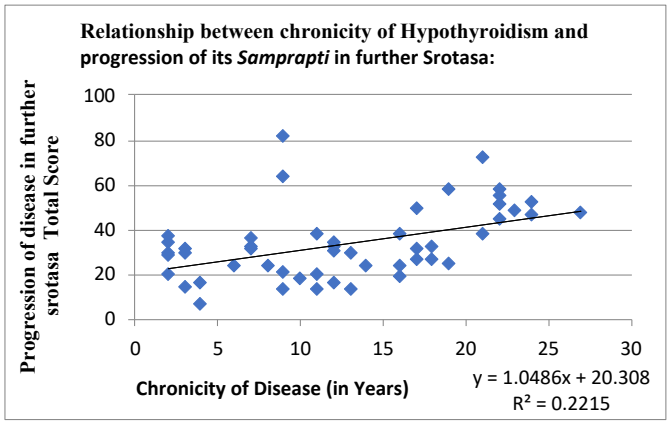
Out of the total of 50 patients, 35(70%) were working, 10 (20%) were housewives and 05 (10%) patients were students. Out of 50 patients enrolled in the study, 18 (36%) patients had *Vata–Pitta Prakriti,* 14 (28%) patients had *Kapha-Pitta Prakriti,* 06(12%) patients *had Kapha-Vata Prakriti*, 05(10%) had *Vata-Kapha Prakriti,* 05 (10%) patients had *Pitta–Kapha Prakriti*, 02 (04%) patients had *Pitta-Vata Prakriti.* The conventional method was adopted for the *Prakriti* examination "(44,45,46)". Out of 50 patients enrolled in study 37 (74%), patients were on a Mix diet whereas 13 (26%), patients were Vegetarian.

Clinical Assessment:

Relationship between chronicity of hypothyroidism and progression of its *Samprapti* in further Srotasa:

The average chronicity of diseases in years in 50 patients was 12 (02 – 27) years whereas the average Total Score of progression of *Samprapti* of hypothyroidism in further *Srotasa* was 31 (07 – 81). There was a moderately positive correlation between the chronicity of disease and progression of *Samprapti* of Hypothyroidism in further *Srotasa* (Spearman r = 0.4696) which was statistically significant too (p = 0.0006).

Graph 1: Relationship between chronicity of Hypothyroidism and progression of its *Samprapti* in further Srotasa

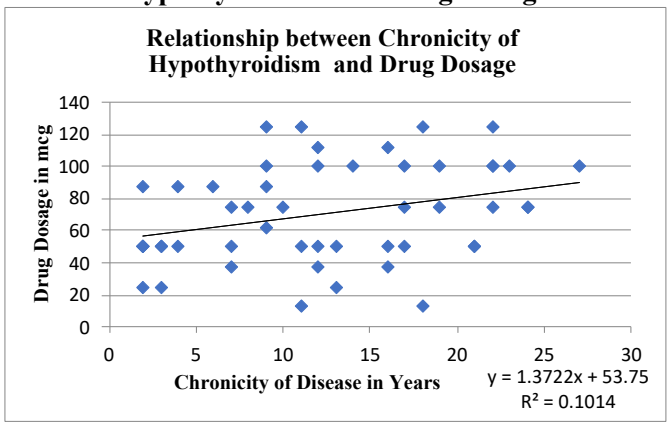


The signs and symptoms of *Dhatupradoshaja Vikaras* observed in the patients increased with the chronicity of Hypothyroidism indicating the *Samprapti* progressed in further *Srotasa* with chronicity of Hypothyroidism.

Relationship between chronicity of Hypothyroidism and Drug Dosage:

The average chronicity (in years) in 50 patients of Hypothyroidism was 12 (02 – 27) years whereas the average drug dosage was 75 (12.5 – 125). There was a moderately positive correlation between chronicity of disease and Drug Dosage (Spearman r = 0.3246) which was statistically significant too (p = 0.0231)

Graph 2: Relationship between Chronicity of Hypothyroidism and Drug Dosage

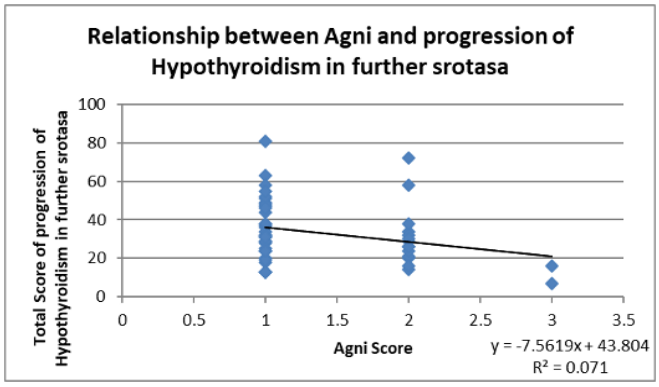


The drug dosage escalated with chronicity of Hypothyroidism.

Relationship between *Agni* and Progression of *Samprapti* of Hypothyroidism in further *Srotasa*:

The average score of *Agni* in 50 patients was 01 (01 – 03) whereas the average *Dhatugatawastha* total Score was 31 (07 – 81). There was a moderately negative correlation between the Jatharagni score and the total score of progression of *Samprapti* of Hypothyroidism in further *Srotasa's* (Spearman r = -0.2591) which was not statistically significant (p = 0.0693).

Graph 3: Relationship between Agni and progression of Samprapti of Hypothyroidism in further srotasa

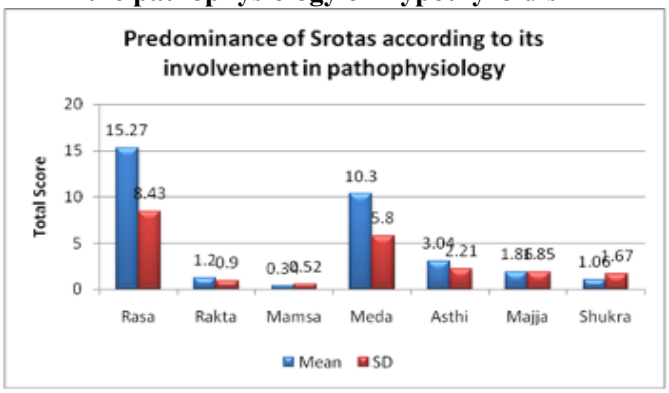


The *Samprapti* of Hypothyroidism progressed in further *Srotasa* in person with *Avar Agni Bala* (weak state of *Agni*).

Predominance of involvement of Srotas in the pathophysiology of Hypothyroidism

The difference among *Sroto-Dushti* in 50 patients was statistically significant ($p < 0.0001$).

Graph 4: Predominance of involvement of Srotas in the pathophysiology of Hypothyroidism

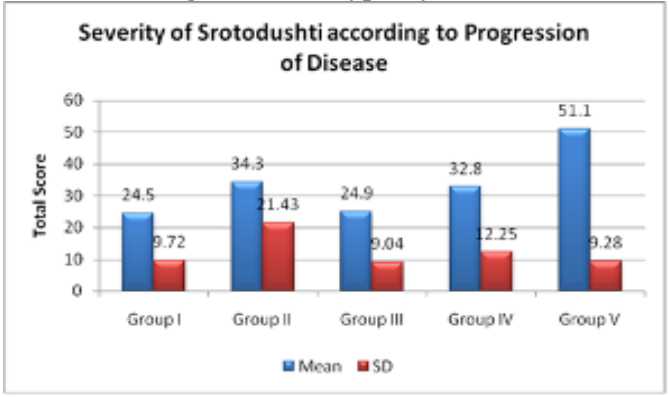


In the study, significant *Dushti* was observed in *Rasavaha* and *Medovaha Srotasa* followed by *Asthivaha Srotasa.*

Severity of *Srotodushti* according to Progression of Hypothyroidism

The severity of *Srotodushti* according to the progression of the disease was statistically significant ($p = 0.0009$).

Graph no – 5: Severity of *Srotodushti* according to Progression of Hypothyroidism



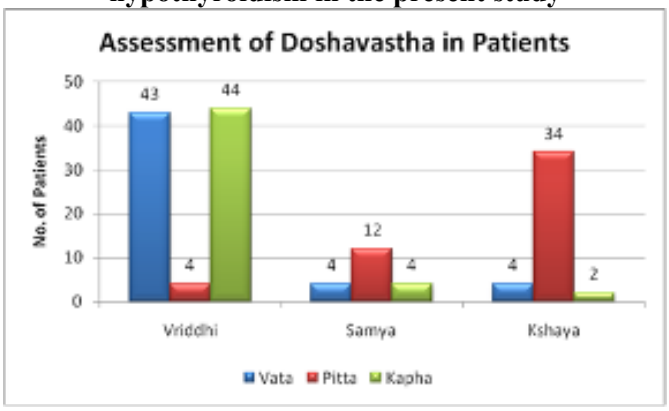
The severity of Srotodushti increased with the progression of the disease.

***Doshavastha* in Patients of hypothyroidism in the present study:**

Out of 50 patients, 43 (86%) patients showed *Vata-vriddhi*, 4 (08%) *Vata-samyaavastha,* and 4(08%) *Vata-kshaya*. Out of 50 patients, 44 (88%) patients showed *Kapha-vriddhi*, 4 (08%) *Kapha-samyaavastha,* and (04%) *Vata-kshaya*. Out of 50 patients, 4 (08%) patients showed *Pitta-vriddhi*, 12 (24%) *Pitta-samyaavastha*, and 34(68%) *Pitta-kshaya*.

The conventional method was adopted for the examination of Doshavastha *"(47,48,49)"*

Graph no-6: *Doshavastha* in Patients of hypothyroidism in the present study

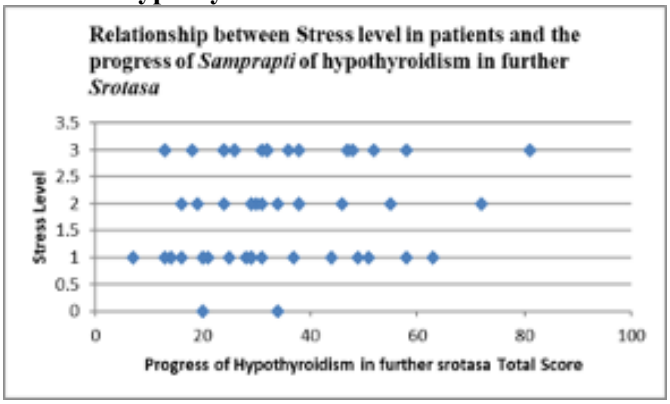


The status of *Dosha* in the *Samprapti* of Hypothyroidism in the present study was *Kapha-Vata Vridhhi* and *Pitta Kshaya*.

Relationship between Stress level in patients and the progress of *Samprapti* of hypothyroidism in further *Srotasa*:

The average score of progression of *Samprapti* of hypothyroidism in further *Srotasa's* in 50 patients was 31 (07 – 81) whereas the average stress level was 02 (00 – 03). There was a moderately positive correlation between the progression of *Samprapti* of Hypothyroidism in further *srotasa* and the total score of Stress level (Spearman r = 0.09786) which was not statistically significant ($p = 0.4990$).

Graph no 7: Relationship between Stress level in patients and the progress of *Samprapti* of hypothyroidism in further *Srotasa*



The *Samprapti* of Hypothyroidism was advanced in further *Srotasa* with increased stress level.

Discussion

Hypothyroidism is an *Anukta-Vyadhi* (a disease which is not explained in the *Ayurvedic* text) according to Ayurveda "(10-14)". It is mainly caused due to the vitiation of *Agni* (digestive and metabolic factor) and *Dhatwagni* (metabolic factor located at dhatu). The *Dhatwagnimandya* (weak metabolic factor located at dhatu), *Sanga* in various *Srotas* (obstructive pathology at srotasa), and impairment in the process of *Dhatuparinaman* (sequential Dhatu formation process.) play a pivotal role in the *samprapti* of Hypothyroidism. It results in the formation of *Sam-Dhatus* (*Dhatus* associated with *Aam*) which fail to perform their accustomed work and manifest the group of symptoms and further vitiate the *srotasa* (structural or functional channels). *Rasavaha* and *Medovaha srotasa* are mainly involved in the pathogenesis. (15-38)

According to contemporary science, Hypothyroidism is an endocrine disorder due to the deficiency of the thyroid hormone. The prevalence rate of hypothyroidism is high, affecting approximately one in 10 adults in the study population "(1)". The presence of residue symptoms and limitation of treatment to restore normal thyroid physiology (2-9) highlights the lack of comprehensive treatment (39) which failed to break the etiopathogenesis of the disease and hence leads to the progression of *vyadhi samprapti* ie etiopathogenesis of hypothyroidism. It results in the involvement of additional *Dhatu* and *Dhatuvaha sraotasa* in the pathogenesis of hypothyroidism "(40)".

The present study aimed to assess the progression of *samprapti* of hypothyroidism in *Srotas.* The progression of *samprapti* in further *Dhatuvaha Srotasa* was assessed by evaluating the presence of signs and symptoms of the *Dhatupradoshaja Vikara* (41) which can be considered as the symptoms of respective *Srotasdushti* (42) in patients. These findings along with other parameters analyzed to put forward the results.

In the present observational study, females were more in number than males, indicating female predominance in Hypothyroidism. The highest number of patients suffering from Hypothyroidism was predominantly from the middle age group i.e., 31-40 years and 41 to 50 years. In the present study prevalence of Hypothyroidism in working participants was more than in participants of other occupations. Workplace stress is one of the etiological factors which was present in the patients. Stress is a major etiological factor of vitiation of *Rasavaha Srotasa* "(50)" which is a predominant event in *Samprapti* of Hypothyroidism. The prevalence of Hypothyroidism was observed in the patients with a mixed diet or non-vegetarian patients more than in the patients with a completely vegetarian diet. A mixed diet or non-vegetarian food is heavy to digest or needs more time to digest resulting in *Agni-Mandya* (weak state of Agni). *Agni-Mandya* plays a pivotal role in the *Samprapti* of Hypothyroidism.

The increase in the symptoms and signs of *Dhatupradoshaja Vikaras* with the chronicity of Hypothyroidism indicates the progress of *Samprapti* of Hypothyroidism in further *Dhatus* and *Dhatuvaha-srotasa. Samprapti* is a continuous process. The lack of proper management of disease and restrainment of etiological factors results in the involvement of further *Dhatus* and *Dhatuvaha-srotasa* in the pathogenesis that takes place over the period.

In the present study, participants who had a weak state of *Agni* (digestive and metabolism factors) showed the vitiation of Dhatus to a greater extent. This underlines the role of *Agnimandya* in the pathogenesis of hypothyroidism. It can be said that the hypothyroid person with a weak state of *Agni* is more susceptible to developing the progression of *Samprapti* of Hypothyroidism in further *Srotasa* earlier than the person with an intense state of *Agni.*

In the present study, the drug dosages were escalated with the chronicity of Hypothyroidism. Hypothyroidism is mainly caused due to *Jatharagni* and *Dhatwagni Mandya.* Long-standing *Agnimandya* is responsible for the *Dhatwagni-Mandya* "(51)" and leads to the progression of the *samprapti* of hypothyroidism. Thyroid hormone replacement therapy is aimed to maintain the need for body metabolism and overall functions of thyroid hormone. Hence, the drug dosage is also escalated as impairment of *Agni* and *Dhatwagni* increases with the chronicity of Hypothyroidism.

The conceptual study by Ayurvedic scholars suggested the status of Doshas in Hypothyroidism as *Kapha-Vata Vridhhi* (regression of Kapha-Vata) and *Pitta Kshaya* (diminished Pitta). The present observational study also supports this fact. The imbalance in the *Doshas* is due to the indulgence of etiological factors.

The status of Doshas in the *Samprapti* of Hypothyroidism is *Kapha-Vata Vridhhi* (regression of Kapha-Vata) and *Pitta Kshaya* (diminished Pitta). The major form of *Srotodushti* is *Sanga* (obstructive pathology*)*. As *Rasa Dhatu* has similar qualities to that of *Kapha-dosha* it affects *Rasadhatu* and *Rasavaha Srotasa* first. Afterward, it involves the *Medo-dhatu* in the *Samprapti* as it is *Kapha's* predominant *Sanga* type of *Samprapti.* The involvement of other *Dhatus* in Samprapti takes place over the period due to the disturbances in the sequential *Dhatu* formation process. So, in the present study, significant *Srotas-Dushti* was observed predominantly in *Rasavaha* and *Medovaha Srotasa* followed by *Asthivaha Srotasa.*

Dhatwagni-Mandya causes vitiation of the formation of the *Sthula Ansha* (gross part forming concerning body tissues and *Sukshma Ansha* (minute part acting as nutritive for further *dhatus*) at the time of *Dhatu* formation. this causes abnormalities in the process of sequential *Dhatu* formation. Vitiation of the *Sthula* part causes an increase in the severity of *Srotodushti Lakshana* of the concerned *Dhatu* while the vitiation in *Sukshma* part results in the progression of *Vyadhi* in further Dhatus. It results in an increase in the severity of *Srotodushti* with the chronicity of

hypothyroidism which indicates the progression of the *vyadhi samprapti* of hypothyroidism in further *srotasa.*

Rasavaha Srotads dushti (Vitiation) is the key element in the *Samprapti* of Hypothyroidism. *Chinta* (Stress) is one of the prime etiological factors of the vitiation of *Rasavaha Srotasa. Rasavaha Srotasa dushti* is a key event in *Samprapti* of Hypothyroidism. The presence of Stress in study participants indicates the continuous indulgence of etiological factors. It acts as one of the contributing factors for the progression of *Samprapti* of Hypothyroidism in further *Srotasa* "(50)".

Conclusion

The progression of *Samprapti* of *vyadhi* in further *srotasas* can be assessed by evaluating the presence of *Dhatupradoshaja vikar*. In the present study, it can be concluded that the *samprapti* of Hypothyroidism progress in further *Srotasa* with the chronicity of hypothyroidism.

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