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A SYSTEMATIC REVIEW OF HYPOTHYROIDISM AND ITS CORRELATION WITH THE AYURVEDIC PARADIGM: PATHOPHYSIOLOGY, DIAGNOSTIC CONCORDANCE, AND INTEGRATIVE MANAGEMENT STRATEGIES

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ABSTRACT

Background: Hypothyroidism, the most common endocrine disease in medical practice, which is caused by inadequate production of thyroid hormones, is an emerging global public health issue with diverse clinical presentations that have been reported.[1,2,45] However, the traditional Indian system of medicine, Ayurveda a unique ontological and physiological model for this relating to metabolic disorders, categorized under *Mandagni* (reduced digestive fire) and *Jatharagni* defect resulting in *Dhatvagni Vishama* (inadequate digestive fire that is imbalanced).[8,9,57] An organized investigation of the relationship between biomedical hypothyroidism and Ayurvedic concepts is necessary for furthering integrative prospects.[64,78] **Objective:** To systematically review the existing studies available on pathophysiological, diagnostic, and therapeutic correlations between hypothyroidism and Ayurvedic principles with emphasis on *Agnimandya* and *Kapha-Siddhanta*. **Methods:** We performed a comprehensive literature search according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guideline.[11,53] An electronic search of databases (PubMed, Scopus, Web of Science, AYUSH Research Portal, DHARA, and IndMED) was carried out from inception

until October 2023. The authors used search terms such as "hypothyroidism," "thyroid vitamins," "Ayurveda," and also Indian names for the conditions, namely "*Agnimandya*, *Kapha* vitiation", *Bhasmaka*, *Sthaulay* (Obesity), *Galaganda*. Theoretical correlations, including clinical and Ayurvedic interventions, along with biomarker studies were considered in the systematic review. Data were reviewed and synthesized thematically. Risk of bias in clinical trials was evaluated with Cochrane RoB 2 and NIH tools.[54,55] **Results:** From the 2,587 records identified, 187 studies were included. The synthesis there was a good second degree of concordance in terms of conceptuality between hypothyroidism and the Ayurvedic state *Agnimandya* (especially with respect to the impairment of *Jatharagni* and *Dhatvagni* as a result, Ama formation and *Srotodusti*).[12-15,56] *Kapha* and *Vata* dosha imbalance, in particular *Avalambaka Kapha* and *Prana Vata* disturbance, have been frequently highlighted.[18-21,51] Clinical manifestations of hypothyroidism resemble very much with those of *Kapha Vata Pitta* symptoms, fatigue (*Daurbalya*, *Alasya*), weight gain (*Sthaulya*) cold intolerance (*Sheetaasahatva*), dry skin (*Rookshata*), and depression (*Avasad*).[4,26-28,49] Analysis and Diagnosis Both of them have the same parallels in analysis and diagnosis, with *Nadi Pariksha* (pulse reading) indicating a *Kapha-Vata* dominant pulse.[29,30,70] Treatment modalities of Ayurveda are based on *Dipana* (boosting digestive fire), *Pachana* (digestion of Ama), *Kapha-Vata* balancing, and *Rasayana* (rejuvenation) utilizing herbs like *Kanchanara* (*Bauhinia variegata*), *Guggulu* (*Commiphora wightii*), *Ashwagandha* (*Withania somnifera*), and *Shilajit.*[32,33,34,35,36,37,62,66,67,76] **Conclusion:** The current review provides strong theoretical as well as clinical correlation of aetiopathogenesis between hypothyroidism and Ayurvedic syndromes, *Agnimandya* and *Kapha-Vata* Imbalance. Although biomedicine is accepted as the gold standard of diagnosis[5,46], Ayurved may be used for a holistic functional appraisal.[69,85] The most effective bridging therapies Integrated approaches are considered monotherapies in disguise[40,65], but prospective RCTs Integrative approaches look promising with regard to validation of its efficacy, optimization of the protocols and determination of the safety profile of the combined treatment regimens.[44,87,90] Work is needed (translational research) on determining the effects of Ayurvedic interventions on single molecular therapeutic biomarkers and QoL indices.[42,82-84,96]

KEYWORDS: Hypothyroidism; Ayurveda; *Agnimandya*; *Kapha* Dosha; *Ama*; Integrative Medicine; Thyroid Hormones; Systematic Review.

1. INTRODUCTION

1.1. Biomedical Perspective on Hypothyroidism

Hypothyroidism is one of the most common endocrine diseases and its estimated prevalence varies from 1 to 2% in iodine replete populations, but it is much lower than this in iodine deficient areas, while high-prevalence areas could be found among elderly and females, especially if sex-specific considerations are considered reaching even up to 10-15% for women over the age of 60.[1,45,46] It is characterized by a defect in the synthesis and secretion of thyroid hormones thyroxine (T4) and triiodothyronine (I3) from the thyroid gland, causing a slowing down of all metabolic processes in general.[2,47] The myriads of causes ranges from autoimmune diseases of the thyroid (Hashimoto's thyroiditis being the most prevalent cause in iodine-replete areas), iatrogenic disorders [post-surgical or post-(R) radioiodine ablation], iodine deficiency, central (pituitary or hypothalamic) pathology, to congenital lesions.[3,48]

The clinical picture is frequently insidious and pleomorphic, with this being a reflection of the systemic action of thyroid hormones. Cardinal features are easy fatigability, weight gain, cold intolerance, dry skin (xerosis), hair coarseness, constipation, bradycardia, muscle weakness, cognitive slowing ("brain fog"), and depression.[4], [49], [60] Biochemically, it's characterized by elevated serum Thyroid-Stimulating Hormone (TSH) with low free T4 (overt hypothyroidism) or elevated TSH with normal free T4 (subclinical hypothyroidism).[5,48] The treatment of choice is lifelong levothyroxine (LT4) replacement therapy, which normalizes serum TSH and relieves symptoms in the majority. However, a considerable proportion of patients (about 10-15%) complain of persistent symptoms mainly fatigue, cognitive complaints and reduced quality of life in the absence of abnormal blood tests despite biochemical restoration of euthyroidism, suggesting that a purely biomarker-based therapeutic strategy is inadequate and calling into questions also for extrathyroidal determinants such as cell thyroid hormone metabolism and systemic metabolic inertia.[6,7, 61]

1.2. The Ayurvedic Paradigm of Health and Disease

Ayurveda, the "science of life" (*Ayuh*: life, *Veda*: knowledge), is a holistic medical system originating in the Indian subcontinent over 5,000 years ago.[64,78] Its foundational premise is that health (*Swasthya*) is a state of dynamic equilibrium between the body's three fundamental bio-energetic principles or *Doshas Vata* (kinetic principle of movement), *Pitta* (transformative principle of metabolism), and *Kapha* (cohesive principle of structure and lubrication) as well as a state of balanced digestion (*Sama Agni*), properly formed tissues

(*Sama Dhatu*), efficient waste elimination (*Sama Mala*), and a contented state of senses, mind, and consciousness (*Prasanna Atma, Indriya, Manah*).[8,51,69]

Disease (*Vyadhi*) is conceived as a state of imbalance (*Vaishamya*) in these factors, often originating from impaired digestive and metabolic fire (*Agnimandya* or *Agni Vaishamya*).[9,14] *Agni*, in its numerous forms (*Jatharagni* [gastric], *Dhatvagni* [tissue- specific], *Bhutagni* [elemental]), is the cornerstone of all metabolic transformations. Its diminution (*Mandagni*) is considered the root cause of most diseases, as it leads to the formation of *Ama*, a poorly digested, toxic, and sticky metabolic by-product that obstructs the body's micro- and macro-channels (*Srotas*).[9,15,57] This *Srotodusti* (channel pathology) impairs the nourishment of tissues (*Dhatus*) and disrupts homeostasis.[16,21]

1.3. Rationale for Correlation and Objectives

Given the central role of *Agni* in governing metabolism and the universal metabolic slowdown characteristic of hypothyroidism, a profound conceptual intersection exists.[10,12,80] Hypothyroidism, from an Ayurvedic lens, can be viewed as a quintessential *Agni*-deficiency disorder, primarily involving *Dhatvagni* (tissue-level metabolism) and correlating with *Kapha* and *Vata* imbalances. *Kapha*, with its qualities (*Guna*) of heavy, slow, cool, soft, and stable, mirrors the physical (weight gain, edema) and physiological (lethargy, bradycardia) features of hypothyroidism.[18,20] *Vata* imbalance, particularly of its subtypes like *Prana Vata* (governing the brain, motivation) and *Apana Vata* (governing elimination), can explain associated neurological symptoms and constipation.[10,19,50]

Despite numerous individual studies and narrative reviews proposing this correlation[17,65,71], a systematic, PRISMA-guided synthesis of the literature is lacking. This review aims to:

1. Systematically identify and analyze literature describing the pathophysiological correlation between hypothyroidism and Ayurvedic concepts.
2. Map the clinical symptomatology of hypothyroidism onto Ayurvedic *Doshic* and *Ama*-based symptomatology.
3. Review the evidence base for Ayurvedic diagnostic tools (e.g., *Nadi Pariksha*, *Ashtavidha Pariksha*) in assessing hypothyroid states.
4. Systematically categorize and evaluate the proposed Ayurvedic therapeutic strategies, including herbal formulations, dietary (*Ahara*), and lifestyle (*Vihara*) interventions.
5. Identify gaps in the current evidence and propose a framework for future high-quality integrative research.[86,88]

2. METHODS

This systematic review was conducted and reported in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 statement.[11,53]

2.1.Eligibility Criteria

- **Population/Concept:** Studies focusing on hypothyroidism (overt or subclinical) in human subjects or its conceptual analysis within the Ayurvedic framework. In vitro and in vivo preclinical studies elucidating mechanisms of Ayurvedic herbs were also included for the pathophysiology and pharmacology sections.[73,74,94]
- **Intervention/Exposure:** Ayurvedic concepts (e.g., *Agnimandya*, *Kapha* imbalance), diagnostic methods, or therapeutic interventions (herbal, dietary, lifestyle, *Panchakarma*).[38,39]
- **Comparator:** For clinical studies, placebo, no intervention, or standard levothyroxine therapy.
- **Outcomes:** For conceptual studies: descriptions of correlation. For clinical studies: changes in serum TSH, T3, T4 levels, thyroid antibody titers, symptom scores, quality of life measures, and adverse events.
- **Study Designs:** Original research articles (clinical trials, observational studies, case series >10 patients), comprehensive review articles, classical text commentaries, and relevant preclinical studies.[92,98] Editorials, letters, and non-peer-reviewed articles were excluded.

2.2. Information Sources and Search Strategy

A systematic search was performed across electronic databases from inception to October 2023. Databases included: PubMed/MEDLINE, Scopus, Web of Science, Cochrane Library, AYUSH Research Portal, DHARA (Digital Helpline for Ayurveda Research Articles), and IndMED. A manual search of reference lists of included articles and key Ayurvedic texts (*Charaka Samhita*, *Sushruta Samhita*, *Ashtanga Hridaya*) was conducted.[8,9,22,56]

The search strategy combined MeSH terms and keywords: ("hypothyroidism" OR "myxedema" OR "Hashimoto disease" OR "thyroid insufficiency") AND ("Ayurveda" OR "Ayurvedic" OR "*Agnimandya*" OR "*Mandagni*" OR "*Kapha*" OR "*Ama*" OR "*Srotodusti*" OR "*Galaganda*" OR "*Bhasmaka*").

2.3. Study Selection and Data Collection Process

Search results were imported into Covidence software for deduplication and screening. Two

independent reviewers (SK and PM) screened titles and abstracts against eligibility criteria. Full texts of potentially relevant articles were retrieved and assessed independently. Any disagreements were resolved through discussion or consultation with a third senior reviewer (VD). Data from included studies were extracted using a standardized form: author, year, study design, sample size, Ayurvedic diagnosis, intervention details (if any), outcomes, and key findings related to correlation or efficacy.

2.4. Data Synthesis and Analysis

It was not possible to perform a pooled analysis for this factor, because of heterogeneity in the overall design of studies (conceptual analyses, clinical trials and preclinical studies). Narrative synthesis was completed, organized around the objectives of the review. Results were organized in the form of thematic sections:

(1) Pathophysiological Correlation,

(2) Diagnostic Concordance,

(3) Therapeutic Interventions

(4) Integrative Models.

The risk of bias of clinical trials was evaluated through the Cochrane Risk of Bias tool v 2 (RoB 2) in RCTs, and the National Institutes of Health Quality Assessment Tool for Before-After (Pre-Post) Studies.[54,55]

3. RESULTS

3.1. Study Selection

The PRISMA flow diagram (Figure 1) illustrates the study selection process. The initial search yielded 2,587 records. After deduplication, 1,845 titles and abstracts were screened. 278 full-text articles were assessed for eligibility, resulting in 187 studies included in the final synthesis.

3.2. Pathophysiological Correlation

3.2.1. *Agnimandya* as the Fundamental Lesion: Most of the conceptual analyses (n = 89) suggested impaired Agni to be the pivotal pathological event preceding hypothyroidism.[12-15,80] Imbalanced *Jatharagni* provokes the formation of Ama. This Ama, flowing through *Rasavaha Srotas*, influences *Dhatvagni* at the Dhatu level. The derangement of *Medo Dhatvagni* (Lipid metabolism) and *Majja Dhatvagni* in particular is a commonly referred cause for alteration in lipid profile, elevation in body weight, and neuroavisual symptoms.[16,60] It then involves deeper Dhatu where Ama gets lodged in the *Galaganda* Khana (thyroid region), which results in blockage of *Srotas* leading to defective functioning

of the glands.[17,71]

3.2.2. *Doshic* Imbalance (*Kapha-Vata* Predominance): One of the common features found in 121 articles was its correlation with augmented *Kapha* and *Vata*.[18-21,85] The *Guru* (heavy) and Sthira (stable) gunas of *Kapha* translate to weight gain and lethargy; its *Sheeta* (cold) *Guna* relates to cold intolerance. The *Rooksha Guna* of *Vata* is seen as dryness, and the *Chala* instability disturbed can cause anxiety, shaking the Kshaya /decrease in *Vata* can cause constipation or bradycardia. The principle of '*Avalambaka Kapha*' localized in the chest and the thyroid area is directly applicable as far as structural physiological support to the gland.[22],[51] *Vata Prana* aggravation in the head field also leads to cognitive dysfunctions.[19,49]

3.2.3. *Ama* and Autoimmunity: Several articles (n=34) compared *Ama* to the concept of autoimmunity in Hashimoto's thyroiditis.[23–24,99] This would indicate that Ama is antigenic, immunogenic (*Ojakshaya* or essence depletion as an analogue of immunodeficiency), etc. Production of anti-TPO antibodies is considered a consequence of Ama modifying the thyroid tissue, causing it to be "non-self".[25,97]

3.3. Diagnostic Concordance

3.3.1. Symptom Mapping: Clinical studies comparing symptom profiles (n=17) confirmed high overlap. Fatigue mapped to *Daurbalya* and *Alasya* (100%), weight gain to *Sthaulya* (95%), cold intolerance to *Sheetaasahatva* (98%), dry skin to *Twak Rookshata* (92%), constipation to *Malabaddhata* (88%), and depression to *Avasada* (85%).[26-28,49]

3.3.2. *Nadi Pariksha* (Pulse Diagnosis): In observational studies (n = 9), it was observed by experienced *Vaidyas* [Ayurvedic physicians] that features of *Kapha-Vata* pulse were present in patients with biochemical hypothyroidism, connoting a magnitude down regulation phenomenon which is characterized by deep slow broad pulse under *Kapha* and thin weak irregular pulse under *Vata* among subjects.[29,30,70] Nevertheless, verification for scientific use is limited by inter-rater reliability.[52]

3.3.3. *Ashtavidha Pariksha* (Eightfold Examination): Features like *Jihva* (coated tongue - *Ama*), *Mala* (constipated stools - *Vata*), *Mutra* (pale urine - *Kapha*), and *Shabda* (hoarse, slow speech - *Kapha-Vata*) were commonly reported in case series.[31,59]

3.4. Therapeutic Interventions

3.4.1. Herbal Pharmacotherapy (*Dravyaguna*): A total of 63 clinical trials and numerous preclinical studies were analysed.[91,95]

- *Kanchanara* (*Bauhinia variegata*): Commonly referred to as an herb for *Galaganda* (goiter). Research indicates that it can decrease thyroid volume and be anti-inflammatory.[32,72] Its *Kashaya* (astringent) and Laghu (light) properties are antagonistic to *Kapha*.[50]
- *Guggulu* (*Commiphora wightii*) A classic *Medohara* and *Ama-Pachana* drug. Several of the studies, including RCTs, indicated there were marked reductions in TSH, cholesterol, and body weight when taken as formulations containing *Kanchanara Guggulu*.[33,34;66,70] It's the Tikshna (penetrating) and Ushna (hot) that are important.
- *Ashwagandha* (*Withania somnifera*): An adaptogenic *Rasayana*[67,77]). RCTs showed their effect on correcting serum T3 and T4 levels and decreasing stress in subclinical hypothyroidism, possibly via regulation of positive feedback between the hypothalamic-pituitary-adrenal-thyroid axis and accomplishment of thyrotropic action.[35,36,62,68] The *Vata-Kapha* balancing and *Brumhana* (nourishing) effects of the same are made use of.
- *Shilajit* (Mineral Pitch): Employed as *Rasayana* and *Yogavahi* (bioenhancer). It has also been reported to enhance mitochondrial function and cellular energy metabolism, which is an essential aspect of the primary *Dhatvagni* deficiency and degeneration.[37,75]

3.4.2. Dietary (*Ahara*) and Lifestyle (*Vihara*) Modifications: Universal recommendations include favouring warm, light, easily digestible foods (*Laghu* and *Ushna*), cooked with spices like ginger, black pepper, and cinnamon (*Dipana* agents). Cold, heavy, damp foods (dairy, processed items) that aggravate *Kapha* and produce *Ama* are to be minimized.[61] Regular, moderate exercise (*Vyayama*) to kindle *Agni* and practices like *Pranayama* (breathing exercises) to balance *Prana Vata* are emphasized.[38,58]

3.4.3. *Panchakarma* (Bio-purification Procedures): Case series (n=12) reported benefits with procedures like *Vamana* (therapeutic emesis) for *Kapha* reduction and *Virechana* (therapeutic purgation) for *Pitta* and *Ama* clearance, followed by *Basti* (medicated enema) to pacify *Vata*.[39,72] These are considered *Shodhana* (purification) therapies that address the root *Doshic* imbalance.

3.5. Integrative Clinical Studies

Several RCTs (n=14) investigated Ayurvedic add-on therapy to levothyroxine. A meta-analysis

of 8 comparable RCTs (total n=620) suggested that combined therapy (*Kanchanara Guggulu* + *Ashwagandha* + LT4) resulted in a greater reduction in TSH (Mean Difference: -1.45 mIU/L, 95% CI: -2.12 to -0.78) and symptom scores compared to LT4 alone, with no significant increase in adverse events.[40,65] However, the risk of bias was often high due to inadequate blinding and randomization procedures.[54,87]

4. DISCUSSION

4.1. Summary of Evidence

From the available literature, it is obvious that there exists ample evidence for a fundamental relationship between hypothyroidism and *Agnimandya* with *Kapha-Vata* vitiation and Ama accumulation in Ayurveda.[12,18,23] And the relationship here is not incidental but causal, and it goes beyond aetiology to the etiopathogenesis, where low *Agni* provides a functional nexus for what is going slowly with or through life.[10,13] The correspondence between *Doshic* attributes and clinical findings shows a high concordance throughout the literature.[26,28] Therapies based on this model are complex, concentrating themselves the digestive, tissues, and mental levels with good preliminary outcomes from clinical trials.[33],[35],[40]

4.2. Interpretation and Implications

The observations indicate that Ayurveda does not diagnose ‘hypothyroidism’ (per se) but rather regards the Prakriti-based (unique constitution) dysfunctional state presenting as a hypothyroid syndrome.[41,82, 84] This offers a personalized framework. For example, a *Vata*-predominant hypothyroidic patient will be relatively more anxious with lack of sleep and constipation, but the *Kapha*-predominant one is likely to manifest as deep lethargy with edema, excessive weight gain.[19,41] This suggests personalized treatment even in the same biomedical diagnosis.[59,91]

The potential role of integrative therapy is the treatment of the continued symptomatology by LT4 supplementation.[6,7] Ayurvedic approaches to restore *Agni* and remove *Ama* have the potential to improve disturbances of cellular metabolism, inflammation, and oxidation caused by hypothyroidism that are not directly addressed with hormone replacement.[42,75,97] Specifically with respect to the more chronic hyperthyroidism we observed in this study, *Ashwagandha’s* effects on the stress axis are potentially of importance because cortisol has known effects both directly and indirectly on the thyroid.[35,43,68]

4.3. Limitations of the Evidence Base

Although the theory is convincing, the clinical evidence is methodologically constrained.[86,87] The quality of most of the studies is single-center, open-label, and is overall at high risk for bias. Standardization of Ayurvedic therapies is a huge challenge a formulation from one manufacturer can differ in its content and strength from those of another.[90,94] Ayurvedic diagnosis (*Nadi Pariksha*) is also subjectively based and not well defined for reliable research purposes.[29,52] In addition, long-term safety studies are lacking, especially with herbs such as *Guggulu* that may be hepatotoxic in predisposed patients and herb-drug interaction (e.g., on absorption) with LT4.[44,100]

4.4. Future Research Directions

To progress the field, we recommend[88,89]:

- Large, multicentre RCTs with standardized Ayurvedic interventions as an adjunct to usual care that were double-blinded and placebo-controlled, preregistered protocols, rigorous methodology IY = Oversized placenta).[54-55] Types of studies: RCT of standard quality (None) High-Quality Controlled Trials (as applicable): High-quality Montgomery.[54]
- Biomarker Exploration: Research to understand mechanisms by which AyVPs may affect novel biomarkers, including reverse T3, selenium status, inflammatory cytokines (IL-6/TNF-α), and oxidative stress markers (MDA/SOD).[42,76,96]
- Phenotyping Studies: Investigation to link Prakriti types with subtypes of hypothyroidism, genetic markers (such as DIO2 polymorphisms), and response to treatment, in addition to personalized integrative medicine.[41,82-84]
- Pharmacological standardization: Development of standardized, chemically characterized botanical drug substances for privileged herbs such as *Kanchanara Guggulu*[90,93,94] prescribing habits. It also includes a guiding principle to modulate lifestyle and diet which in turn helps to lead a disease-free life.
- Safety Pharmacovigilance: Creation of databases to investigate long-term safety and the potential for herb-drug interaction in mixed-medication users.[44,100]

5. CONCLUSION

This systematic review forms a consistent and multidimensional association of hypothyroidism as a biomedical entity with the Ayurvedic syndrome complex via *Agnimandya*, *Kapha-Vata* imbalance and *Ama*.[12,17,65] While replacement with levothyroxine continues to be the

cornerstone biomedical intervention, providing lifesaving treatment[4,5], the Ayurvedic model offers a complementary, comprehensive, and individualized framework for interpreting underlying functional metabolic abnormalities and their attendant symptomatology.[69,85]

Such integrated therapies, utilizing the precision of biomarker-normalized hormone therapy alongside the systemic, *Agni*-kindling, and *Dosha*-balancing methods promoted by Ayurveda, have great potential to improve treatment efficacy in patients with residual symptoms.[40,42] Realizing this potential into evidence-based practice will require mature, collaborative research collaborations that span the epistemological and methodological gulf between two of the world's oldest medical systems.[78,86,89]

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