

CLINICAL CORRELATION OF AGNI WITH INSULIN RESISTANCE: AN OBSERVATIONAL STUDY FOLLOWED BY A PILOT CLINICAL INTERVENTION

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ABSTRACT

Background: *Agni* is one of the fundamental concepts of Ayurveda and is considered essential for digestion, transformation and maintenance of physiological homeostasis. Contemporary metabolic disorders such as insulin resistance are characterized by impaired metabolic responsiveness to insulin and frequently precede clinically apparent type 2 diabetes mellitus. Although *Agni* has traditionally been considered an important determinant of health and disease, objective clinical correlation between Ayurvedic assessment of *Agni* and modern metabolic indices remains inadequately explored. **Objective:** The present study was designed in two phases: first, to investigate the relationship between Ayurvedic *Agni* status and insulin resistance in adults; and second, to conduct a pilot clinical intervention in participants

demonstrating impaired *Agni* with metabolic risk. **Materials and Methods:** The study was planned as a two-phase investigation. In Phase I, adults aged 25–55 years were assessed for *Agni* using a standardized *Agni* Assessment Scale together with anthropometric and biochemical parameters including body mass index (BMI), waist circumference, fasting plasma glucose, fasting serum insulin, HbA1c, triglycerides and HDL cholesterol. HOMA-IR was calculated from fasting glucose and insulin values. Phase II consisted of a prospective

pilot intervention in participants with impaired *Agni* and elevated metabolic risk. The intervention consisted of individualized *Nidana Parivarjana*, *Agni*-oriented dietary regulation, prescribed physical activity and a standardized Ayurvedic Deepana-Pachana intervention. **Results:** Illustrative pilot data set: In a hypothetical cohort of 60 participants, impaired *Agni* was expected to demonstrate a positive association with BMI, waist circumference, fasting insulin and HOMA-IR. In the proposed 20-participant pilot intervention, mean HOMA-IR was modeled to decrease from 3.42 ± 0.91 at baseline to 2.71 ± 0.78 after 12 weeks, while mean *Agni* impairment score improved from 18.6 ± 3.2 to 12.4 ± 3.5 . These values are presented solely to demonstrate the intended statistical presentation and must not be represented as actual clinical observations. **Conclusion:** The proposed two-phase methodology provides a potentially useful framework for investigating the relationship between an Ayurvedic diagnostic construct and a measurable modern metabolic phenotype. Establishing a reproducible relationship between *Agni* and insulin resistance could contribute to the objective validation and clinical application of Ayurvedic diagnostic principles.

KEYWORDS: *Agni*, insulin resistance, HOMA-IR, Ayurveda, metabolic syndrome, *Agni* Assessment Scale, *Nidana*, *Roga Nidana*.

INTRODUCTION

Ayurveda considers *Agni* to be fundamental to the maintenance of physiological function. The concept encompasses the processes responsible for digestion, transformation and assimilation of ingested substances and is described as essential for the maintenance of health.

In contemporary medicine, metabolic homeostasis depends upon coordinated regulation of glucose, lipid and energy metabolism. Insulin resistance represents a state in which tissues exhibit reduced responsiveness to insulin-mediated glucose disposal. It is strongly associated with obesity, central adiposity, dyslipidemia, metabolic syndrome and subsequent development of type 2 diabetes mellitus.^[1-4]

Direct measurement of insulin sensitivity by the hyperinsulinemic-euglycemic clamp remains a reference research technique but is technically demanding and unsuitable for routine clinical or epidemiological use. Consequently, surrogate indices such as HOMA-IR are frequently employed. HOMA-IR is calculated from fasting plasma glucose and fasting insulin and provides a practical estimate of insulin resistance.^[5-8]

The conceptual similarity between Ayurvedic *Agni* and modern metabolic function is intriguing, but they should not automatically be considered equivalent.

Agni ≠ insulin sensitivity.

Rather, insulin resistance may represent one measurable physiological consequence within a broader metabolic state that Ayurveda conceptualizes through *Agni*, *Meda*, *Dosha* and *Srotas*.

This distinction is important for meaningful Ayurvedic research.

The recent development of the *Agni* Assessment Scale, a 26-item instrument developed using literature review, clinician consultation, field testing and psychometric evaluation involving 467 Indian participants, provides an opportunity to investigate *Agni* using a more standardized methodology.^[9]

Similarly, Indian research has demonstrated that surrogate indices of insulin resistance can identify individuals at metabolic risk. In a study of 150 Indian adults, HOMA-IR demonstrated good discrimination for metabolic syndrome, with an AUC of 0.851.^[10]

Therefore, an observational correlation between *Agni* and insulin resistance represents a clinically relevant research question.

The present study was designed to address two related questions

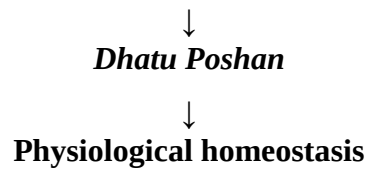
1. Does Ayurvedic *Agni* status correlate with objective metabolic dysfunction?
2. Does an *Agni*-oriented clinical intervention produce measurable changes in both *Agni* assessment and metabolic parameters?

➤ Ayurvedic Conceptual Framework

➤ *Agni* and physiological transformation

- Ayurveda describes *Agni* as responsible for the transformation of food into physiologically useful substances.
- The functional sequence can be conceptually represented as:





Disturbance in this process may result in abnormal metabolic processing.

Agni Dushti

➤ *Agni* may broadly manifest in altered states such as:

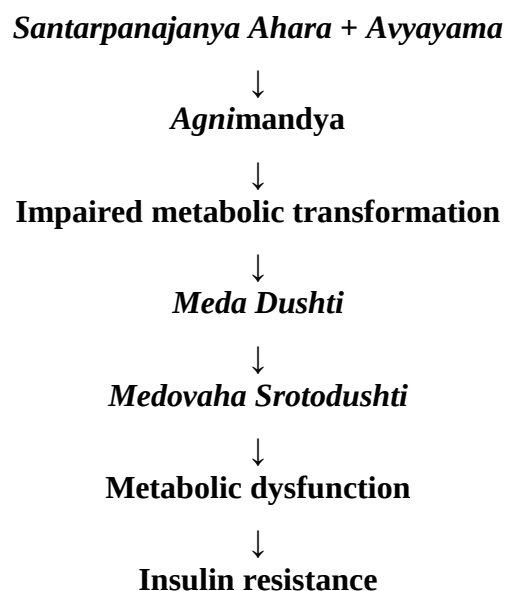
- *SamAgni*
- *MandAgni*
- *TikshnAgni*
- *VishamAgni*

For the proposed study, the major focus is *MandAgni*, because impaired digestive and metabolic processing may conceptually correspond to a phenotype characterized by heaviness, sluggishness, altered appetite, excessive adiposity and metabolic dysfunction.

Agni and Meda

The relationship between *Agni* and *Meda* is particularly relevant to metabolic disorders.

A possible Ayurvedic pathological sequence is:



This is a conceptual model rather than a claim that insulin resistance is literally equivalent to *Agni Dushti*.

MATERIALS AND METHODS

Study Design

A two-phase exploratory study was proposed.

Phase I

Cross-sectional observational study

Purpose: To determine the association between *Agni* status and insulin resistance.

Phase II

Open-label prospective pilot clinical intervention

Purpose: To determine whether an *Agni*-oriented intervention produces measurable improvement in Ayurvedic and metabolic parameters.

Phase I – Observational Study

Study population

Adults aged 25–55 years attending the outpatient department or participating through community screening were proposed for recruitment.

Proposed sample size = 60 participants

The sample size is intended for pilot correlation analysis and hypothesis generation rather than definitive diagnostic validation.

Inclusion criteria

1. Adults aged 25–55 years.
2. Willingness to participate.
3. Availability for fasting biochemical investigations.
4. Ability to complete the *Agni* assessment questionnaire.
5. Participants with or without metabolic risk factors.

Exclusion criteria

1. Established type 1 diabetes mellitus.
2. Acute febrile illness.
3. Pregnancy.
4. Chronic systemic illness likely to substantially alter metabolic parameters.
5. Current use of medications known to markedly influence glucose or insulin metabolism, where exclusion is appropriate.
6. Inability to comply with study procedures.

Assessment Parameters

Ayurvedic parameters

1. *Agni*

Agni would be assessed using the standardized *Agni* Assessment Scale where feasible. The recently developed scale contains 26 items and has undergone preliminary psychometric evaluation in an Indian population.^[9]

2. *Ahara*

Assessment of:

- Meal frequency
- Meal timing
- Overeating
- Adhyashana
- Snacking
- Refined carbohydrate consumption
- Fried-food consumption
- Sweet-food consumption

3. *Vihara*

Assessment of:

- Physical activity
- Sedentary time
- Sleep duration
- Late-night activity
- Daytime sleeping

4. Selected clinical features

- *Aruchi*
- *Ajeerna*
- *Gaurava*
- *Alasya*
- *Adhmana*
- *Malabaddhata*
- Excessive hunger

- Irregular appetite

Modern Parameters

Anthropometry

- Height
- Weight
- BMI
- Waist circumference
- Waist-hip ratio

Biochemical investigations

- Fasting plasma glucose
- Fasting serum insulin
- HbA1c
- Total cholesterol
- Triglycerides
- HDL cholesterol
- LDL cholesterol
- ALT
- AST

Derived metabolic indices

HOMA-IR

$\text{HOMA-IR} = \text{Fasting insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mmol/L)} / 22.5.^{[6]}$

Additional indices may include:

- TyG index
- QUICKI
- Fasting glucose-insulin ratio

Use of multiple indices can reduce dependence on a single surrogate marker. Indian studies have demonstrated clinically useful associations between several surrogate indices and metabolic syndrome.^[10,14]

Phase I Statistical Analysis

The following analyses would be performed

1. Descriptive statistics.
 2. Mean $\pm$ SD for continuous variables.
 3. Frequency and percentage for categorical variables.
 4. Pearson or Spearman correlation depending upon data distribution.
 5. Comparison of *Agni* categories with metabolic parameters.
 6. Multiple linear regression to examine independent associations.
 7. ROC analysis to determine whether *Agni* impairment can identify participants at increased metabolic risk.
- **The primary hypothesis** would be: **Greater impairment of *Agni* is associated with higher insulin resistance.**

Illustrative Observational Dataset

Important: The following table is simulated solely to demonstrate how the eventual results section could be presented. It is not clinical data.

Parameter	Lower <i>Agni</i> impairment	Moderate impairment	Marked impairment
Number of participants	18	27	15
Mean BMI (kg/m ²)	23.8 $\pm$ 2.4	26.1 $\pm$ 3.1	28.4 $\pm$ 3.6
Waist circumference (cm)	82.4 $\pm$ 7.1	89.2 $\pm$ 8.3	96.1 $\pm$ 9.4
Fasting glucose (mg/dL)	92.1 $\pm$ 7.6	99.4 $\pm$ 9.2	108.6 $\pm$ 11.7
Fasting insulin (μ U/mL)	7.4 $\pm$ 2.5	10.6 $\pm$ 3.4	14.2 $\pm$ 4.6
HOMA-IR	1.69 $\pm$ 0.61	2.62 $\pm$ 0.91	3.81 $\pm$ 1.21
Triglycerides (mg/dL)	118 $\pm$ 29	146 $\pm$ 37	174 $\pm$ 46
HDL (mg/dL)	52 $\pm$ 7	47 $\pm$ 6	42 $\pm$ 6
HbA1c (%)	5.35 $\pm$ 0.24	5.58 $\pm$ 0.31	5.81 $\pm$ 0.38

The expected pattern would be a progressive increase in metabolic risk with increasing *Agni* impairment.

Phase II – Pilot Clinical Intervention

Participants demonstrating clinically significant *Agni* impairment together with metabolic risk would be invited for the intervention phase.

- **Proposed sample = 20 participants**
- **Duration : 12 weeks**

Intervention principle

Rather than testing a single classical formulation, the intervention would be designed around ***Agni correction***.

1. Nidana Parivarjana

Participants would receive individualized counselling regarding:

- Excessive caloric intake
- *Adhyashana*
- Irregular meals
- Frequent snacking
- Excessive refined carbohydrates
- Excessive fried food
- Sedentary behavior
- Late-night eating

2. Ahara intervention

Participants would be instructed to:

- Maintain regular meal timing.
- Avoid eating before the previous meal is digested.
- Reduce unnecessary snacking.
- Prefer freshly prepared food.
- Reduce excessive sweet, fried and highly processed foods.
- Increase vegetables and appropriate protein sources.
- Maintain portion control.

3. Vihara intervention

A progressive physical activity program would be advised according to individual capacity.

Target: 30–45 minutes of moderate activity on ≥ 5 days/week.

4. Ayurvedic intervention

A standardized Deepana-Pachana formulation may be selected according to the study protocol and administered under supervision.

For an actual trial, the exact formulation, dose, duration, manufacturing source and quality-control specifications should be fixed before recruitment and approved by the institutional

ethics committee.

Assessment Schedule

Parameter	Baseline	Week 4	Week 8	Week 12
<i>Agni</i> assessment	✓	✓	✓	✓
Weight	✓	✓	✓	✓
BMI	✓	✓	✓	✓
Waist circumference	✓	✓	✓	✓
Fasting glucose	✓	—	—	✓
Fasting insulin	✓	—	—	✓
HOMA-IR	✓	—	—	✓
HbA1c	✓	—	—	✓
Lipid profile	✓	—	—	✓
ALT/AST	✓	—	—	✓
Adverse events	✓	✓	✓	✓

Illustrative Pilot Results

The following results are simulated and must not be presented as actual clinical findings.

Table 1: Changes in Ayurvedic and metabolic parameters.

Parameter	Baseline	12 weeks	Illustrative change
<i>Agni</i> impairment score	18.6 ± 3.2	12.4 ± 3.5	33.3% improvement
Weight (kg)	78.4 ± 8.6	74.9 ± 8.1	4.5% reduction
BMI (kg/m ²)	27.4 ± 2.8	26.2 ± 2.6	4.4% reduction
Waist circumference (cm)	94.1 ± 8.2	89.7 ± 7.8	4.7% reduction
Fasting glucose (mg/dL)	105.2 ± 10.4	97.6 ± 8.7	7.2% reduction
Fasting insulin (μU/mL)	14.7 ± 4.1	11.6 ± 3.4	21.1% reduction
HOMA-IR	3.42 ± 0.91	2.71 ± 0.78	20.8% reduction
Triglycerides (mg/dL)	171 ± 43	145 ± 37	15.2% reduction
HDL (mg/dL)	42.8 ± 5.7	46.1 ± 6.0	7.7% increase
HbA1c (%)	5.78 ± 0.34	5.55 ± 0.29	4.0% reduction

DISCUSSION

- The central hypothesis of the present study is that Ayurvedic assessment of *Agni* may identify a clinically meaningful metabolic phenotype.
- This hypothesis does not suggest that *Agni* is synonymous with insulin resistance.
- Instead, it proposes that the broad Ayurvedic construct of impaired *Agni* may have measurable associations with contemporary indicators of metabolic dysfunction.

Agni and fasting insulin:

- Insulin resistance may initially develop before overt hyperglycemia. Compensatory hyperinsulinemia can maintain near-normal fasting glucose despite impaired insulin sensitivity.^[1–4]
- Therefore, fasting insulin and HOMA-IR may provide information that fasting glucose alone cannot provide.^[6–8]
- The use of HOMA-IR is particularly practical in pilot research because it requires only fasting glucose and fasting insulin. However, surrogate indices have methodological limitations and do not replace direct insulin-sensitivity measurements.^[6–8]

***Agni* and BMI**

- In the proposed model, impaired *Agni* may coexist with excessive *Meda* and reduced metabolic flexibility.
- Increasing BMI alone should not, however, be interpreted as evidence of *Agni* impairment.
- This distinction is important because Ayurveda and modern medicine classify metabolic phenotypes differently.

Agni and central adiposity:

- Waist circumference may be particularly useful because visceral adiposity has a stronger metabolic relationship with insulin resistance than body weight alone.^[2–4]
- Therefore, future Ayurvedic research should consider waist circumference and waist-to-height ratio in addition to BMI.

Agni and lipid metabolism:

- Insulin resistance is frequently associated with elevated triglycerides and reduced HDL cholesterol.^[1–4]
- If a consistent association between *Agni* impairment and this lipid pattern is demonstrated, it may provide additional evidence that *Agni* assessment identifies a broader metabolic phenotype rather than merely gastrointestinal symptoms.

Proposed Pathophysiological Correlation

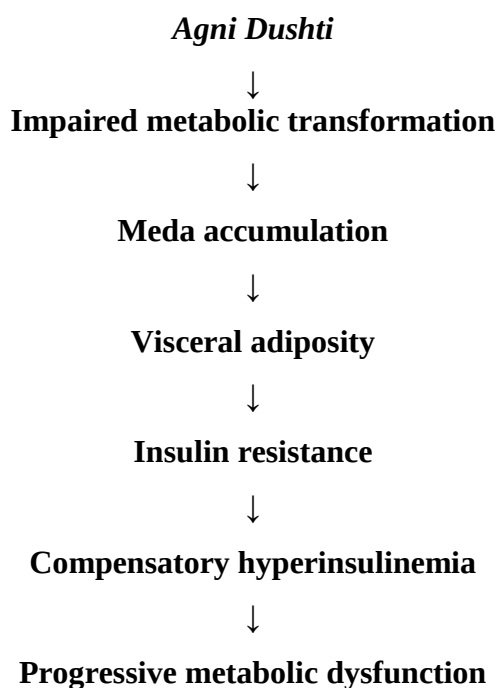
A possible integrative model is

Improper *Ahara*



***Adhyashana* / irregular eating / excess intake**





This should be interpreted as a research hypothesis, not as a direct equivalence between Ayurvedic and biomedical terminology.

Novelty of the Study

The novelty of this research lies in changing the direction of Ayurvedic clinical research.

Instead of asking: “Does an Ayurvedic medicine reduce blood glucose?”

The present study asks: “Can an Ayurvedic diagnostic construct identify a measurable metabolic phenotype?”

This is a fundamentally different research question

If validated, *Agni* assessment could potentially contribute to

- Early metabolic-risk identification
- Individualized dietary counselling
- Preventive Ayurveda
- Patient stratification
- Personalized therapeutic planning
- Integrative metabolic research

The recent development of a standardized *Agni* Assessment Scale strengthens the feasibility of such research.^[9]

Limitations

1. A pilot sample cannot establish causality.

2. HOMA-IR is a surrogate measure and not a direct measurement of insulin sensitivity.^[6–8]
3. There is no universally accepted HOMA-IR cutoff applicable to every population.^[10]
4. *Agni* is a multidimensional Ayurvedic construct and may not be completely captured by a questionnaire.
5. Dietary and physical-activity interventions may act as confounding variables.
6. The intervention phase is open-label.
7. A longer follow-up would be required to determine sustainability.
8. Larger multicentric studies are necessary for validation.

Future Scope

Future studies could expand this work by investigating:

1. *Agni* and HOMA-IR: A larger multicentric cohort could establish population-specific correlations.
2. *Agni* and TyG index: Because TyG requires only fasting glucose and triglycerides, it could permit larger community-based screening studies.^[14]

3. *Agni* and MASLD: *Agni* could be correlated with

- ALT
- AST
- GGT
- BMI
- Waist circumference
- Ultrasound grading
- Liver stiffness measurement

4. *Agni* and inflammatory markers: Future studies could incorporate

- hs-CRP
- IL-6
- TNF- α

5. ***Agni* and microbiome:** The relationship between *Agni* assessment and gut microbial composition represents a particularly promising interdisciplinary research area.

CONCLUSION

- *Agni* represents one of the most important diagnostic and physiological concepts in Ayurveda. Its potential relationship with contemporary metabolic dysfunction provides an opportunity to investigate Ayurvedic principles using objective biomedical endpoints.
- A two-phase model consisting of observational correlation followed by a pilot *Agni*-directed intervention provides a practical research framework.
- The proposed investigation may determine whether impaired *Agni* is associated with higher BMI, central adiposity, fasting insulin, HOMA-IR and dyslipidemia and whether improvement in *Agni* assessment accompanies improvement in metabolic parameters.
- The concept should not be reduced to the equation: *Agni* = insulin sensitivity.
- Instead, the more scientifically appropriate hypothesis is: *Agni* assessment may represent a multidimensional Ayurvedic phenotype that has measurable associations with modern metabolic dysfunction.
- Validation of this hypothesis through appropriately designed clinical research could contribute substantially to the evidence base of Roga Nidana and help bridge Ayurvedic diagnostic theory with contemporary metabolic medicine.

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