Original Research Article

A case-control study for exploring the association of Prakriti with Rheumatoid Arthritis

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ABSTRACT

Background: Deha-Prakriti (DP) is a unique contribution of Ayurveda, which distinguishes the population into three main groups viz., Vata, Pitta, and Kapha predominant individuals. Its assessment helps physicians to prescribe a suitable diet, daily regimen, and lifestyle that prevents non-communicable diseases. Amavata (Rheumatoid Arthritis) is a disease that needs personalized management approach.
Aim: To evaluate the association of DP with Amavata (~Rheumatoid Arthritis).
Objective: To evaluate DP-based susceptibility in the manifestation of Amavata vis-à-vis Rheumatoid Arthritis.
Methodology: A case−control study was conducted from 18.04.2018 to 09.01.2020, involving 150 cases (patients of Amavata), and 150 controls (healthy volunteers), matching in age (between 18 to 50 years), and sex, selected from Jamnagar. CCRAS-PAS for both the groups, Health Assessment proforma of TRI-SUTRA project CSIR-AYURGENOMICS, were used. Logistic regression analyses were conducted to determine the relationship between DP and Amavata.
Results: The proportion of people with Vata dosha in the case group (53.79%) was substantially higher (P < 0.0001) than in the control group (24.91%). Pitta (39.35%) and Kapha (36.27%) doshas were found to be more prevalent in the control group (P < 0.0001). There was a six-percent rise in the likelihood of developing Amavata with every unit increase in Vata percentage, according to logistic regression analysis.
Conclusion: Vata predominant DP has a significant association with Amavata. Vata predominant DP individuals are more susceptible to Amavata than Pitta and Kapha predominant DP individuals.
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1. Introduction

Ayurveda, a traditional medical system of India, substantiates the psychosomatic constitution of an individual with the concept of Deha-Prakriti (DP), [1]. "Prakriti" is an individual's innate psychosomatic framework determined at the earliest stages of fertilisation by the relative predominance of Sperm and Ovum [2]. Human constitution is unaltered from conception to death until fatal signs appear [3]. Phenotypic heterogeneity is the main complication encountered in contemporary medicine in the context of complex disease genetics.

DP separates people into Vata, Pitta, and Kapha phenotypes. Ayurveda literature speculated that some individuals may have balanced Vata, Pitta, and Kapha, while some show either Vata or Pitta or Kapha dominance. First-category, people with Sama Prakriti, those have balance of Tridoshas and are healthy while others may develop diseases [4]. Vata, Pitta, and Kapha dominants are weak, medium, and strong respectively [5]. Sama Prakriti people are resistant to diseases. People with only one vitiated dosha are generally unhealthy, but they can stay healthy by eating and exercising according to their constitution [4]. DP determines disease susceptibility, severity, diet, and regimen in Ayurveda [1, Vimana 6/15]. The confirmation of Deha- Prakriti is essential to examine a healthy person or patient's physical, physiological, and psychological traits and recommend a diet and lifestyle for good health, preventative medicine, and therapy. Ayurvedic seers ranked Prakriti

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evaluation highest among ten key measures to be studied by a physician [1, Vimana 8/84]. DP examination helps determine *Samprapti* (pathogenesis), *Chikitsa* (treatment), and *Sadhya-Asadhyata* (prognosis) of a disease. Subdividing healthy people and patients based on DP can reduce clinical heterogeneity in complex diseases as it diagnoses health differently [1, Sutra 7/41, Cakrapanidutta commentary].

Modern medicine links *Amavata* to Rheumatoid Arthritis (RA). Heavy, incompatible, unwholesome, and irregular food consumption slows *Agni* (the digestion process), causes indigestion, and produces *Ama* (undigested material). *Ama* trapped in joints by vitiated *Vata* dosha causes pain, oedema, fever, stiffness, lack of appetite, indigestion, and general soreness [6]. The sickness may exacerbate pain, stiffness, and other symptoms, producing anomalies and impairment. Auto-immune, chronic, progressive, degenerative RA has an unknown cause. 0.5%−1% of people worldwide have this non-communicable condition, and it particularly affects middle-aged women [7,8]. Untreated or unmanaged RA can lead to joint degeneration, disability, comorbidities, and early death [9]. Comorbidities include CVD (Cardio-vascular diseases), cancer (particularly lymphoma, lung, and melanoma), anaemia, infections, depression, and gut disorders [10,11]. Early detection of *Amavata* (RA) is important because it allows doctors to restore patients' health by prescribing the best drugs, diet, and treatment plan for everyone based on their unique DP. Modern doctors believe in predictive, preventive, personalised, and participatory medicine (P4). Despite contemporary studies, Ayurveda's personalised treatment method inspired scientists to study disease presentation and drug response diversity. Joint problems are more common in *Vata*-predominant DP [1, Chikitsa 28/37], but the statement lacks vigorous evidence. Theory of causation states that exposure causes consequence which can be understood by inference [12]. Evidence-based retrospective research can be done by assessing a current expected outcome's risk factors. Observational research evaluates the aetiology, occurrence, and susceptibility of a disease. Chronological synchronisation of exposure and outcome establishes causal association. This allows to produce Prakriti-Based Medicine (PBM), or customised medication, defined as "the appropriate medicine to a specific individual at a certain moment, with the exact dose and the perfect quality." Thus, a retrospective epidemiological analytical case−control approach is opted to assess DP's role in *Amavata's* causation and its level of connection with the following aim and objectives.

1.1. Aim

To study the association of *Deha-Prakriti* (Physico-Physiological Constitution) with *Amavata* (~Rheumatoid Arthritis)

1.2. Objective

* To evaluate the *Deha-Prakriti*-based susceptibility in the manifestation of *Amavata* vis-à-vis Rheumatoid Arthritis

2. Methodology

2.1. Study setting, sample size, and sampling

A case−control study establishes the link between a disease and its etiological causes and indicates their relative predominance. This approach in epidemiology allows the researcher to accomplish his destiny when the findings are generalised or applied to the community, possible only by comparing diseased and healthy risk factors. Case-control studies assist determine susceptibility,

prevention, and treatment. It seeks to uncover the inciting factor in sick people and the protective factor in healthy people [13]. In the present study, The cases and controls were taken as a 1:1 ratio matching with age (± two years) and sex in both the groups. Considering it as a pilot study, a total of 150 cases (*Amavata* Patients) and 150 controls (healthy volunteers) were selected through the random sampling method, interviewed, and the history related to the present study was collected through the direct interview method.

2.1.1. Inclusion criteria for cases

Patients aged above 18 years and under 50 years of either sex diagnosed with *Amavata* (those who were having the symptoms of *Amavata* [14] and fulfilling the ACR (American College of Rheumatology), 1987 Criteria [15] with positive RA factor-quantitative and C-Reactive Protein (CRP)-quantitative) for less than or equal to 5 years were considered as the case group. From 18th April 2018 to 9th January 2020, both incidence and prevalent cases attending IPGT& RA Hospital, Jamnagar's OPD and IPD, and those prepared to give written informed consent were recruited in the research.

2.1.2. Inclusion criteria for controls

Controls are healthy individuals, who were matched priorly (± two years) in age and sex with cases, and drawn from the same source of population (living in the Jamnagar municipal corporation region only). Every control was screened initially through a health assessment questionnaire designed by CSIR-Ayurgenomics unit-TRISUTRA, CSIR-IGIB, New Delhi (Annexure-I) to confirm them as healthy individuals followed by the investigations mentioned above, those who came under the normal range of RA factor, CRP, and who were prepared to give written informed consent were recruited for the present work.

2.1.3. Exclusion criteria for cases

Amavata patients with other comorbidities such as Diabetes, Hypothyroidism, or any other endocrinal and metabolic disorders, and those who refused to participate in the study are excluded.

2.1.4. Exclusion criteria for controls

Unhealthy individuals, less than 18 and more than 50 years of age, and those who were not willing to participate in the study are excluded.

2.1.4.1. Ethical clearance. The Institutional Ethics Committee of the Gujarat Ayurved University's Institute for Post Graduate Teaching and Research in Ayurveda, Jamnagar, gave their approval; vide **Ref. PGT/7-A/Ethics/2017−18/3042 dated 19/02/2018.**

2.2. Assessment of DP

DP of both the groups is assessed by CCRAS-Prakriti Assessment Scale (PAS) (http://ccras.res.in/ccras_pas/), administered in their convenient language to assess different traits, employing direct observation, tactile examination, and interrogation by a single person by implementing the SOP's (Standard Operative Procedures) mentioned in CCRAS-*Prakriti* Assessment Manual [16]. Based on the characters found in every individual, the relative percentage of each *dosha* is calculated, and the dominating percentage of *dosha* (output) determines the DP of that individual. Based on the output, the assessment method is as follows.

1. **Ekadoshaja Prakriti:** more than 66% of one *Prakriti* characteristics

2. **Dwandwaja Prakriti**: close to or equal percentage of two *Prakriti* characteristics & differences between two *Doshas* is 25−30%

3. **Sama Doshaja:** close to or equal percentage of three Prakriti i.e. 30-34%

2.3. Method of data collection

The present study was initiated after IEC approval and CTRI registration. The goal of the study, what is anticipated of them, and the predicted participant benefit of observing and analysing were all stated to all the participants prior to the study. After getting the informed consent, the data were collected by filling CRF (Case Record Form) and CCRAS-PAS scale. The method of one-on-one (face-to-face) interviewing was used to collect the data. The Prakriti assessment includes physical (anatomical), physiological, psychological, and sociological (behavioural) traits, which were evaluated through the SOPs/questionnaire mentioned in the CCRAS-PAS scale. Physical traits were evaluated through *Darshana* (inspection) and *Sparshana* (tactile) examination, which were found at the time of the interview. Remaining physiological, psychological, and behavioral traits were evaluated through the questionnaire, and the status was considered during disease-free status. The output of the *Prakriti* assessment was obtained in terms of the percentage of *doshas*.

2.4. Scrutiny of the medical records

The onset of the sickness, its duration, the details of medical examinations, drugs, previous illnesses, a detailed history of the condition, and anthropometric parameters were recorded. The details were filled in the CRF. Reports of the radiographs, hematological, and biochemical parameters were also screened thoroughly.

2.4.1. Avoiding bias

To counteract recall bias, patients with persistent memory impairment were excluded from the present study. Recall bias was addressed by assuring research participants that both case and control groups had the same chances and motivations to recall earlier occurrences. All the participants were counseled about the importance of DP assessment, to implement a suitable diet and regimen to prevent upcoming diseases and minimize complications.

2.5. Statistical analysis

The Chi-square analysis was performed to determine the relationship between various socio-demographic variables and DP with *Amavata*. If the Cell values are less than 5 or 0 then chi-square with Yates correction was applied. The Mann−Whitney U test is applied to find the mean difference of each *dosha's* percentage in DP between the two groups as the data were not normally distributed. Both tests were analyzed using the Statistical Package for Social Sciences (SPSS, USA) version 20.0 software [17]. $P \leq 0.05$ was statistically significant. The main objective of the present study was to evaluate the DP based susceptibility in the manifestation of *Amavata* vis-à-vis Rheumatoid Arthritis (RA). Thus, the incidence of RA was regressed upon the DP through logistic regression, coding the incidence of RA as 1 and 0 otherwise. As DP is expressed in terms of percentages which add up to 100 for everyone, a mixture model was considered [18,19]. A logistic regression model was fitted taking the percentages of *Vata*, *Pitta*, and *Kapha* and their two-way and three-way interactions. The forward stepwise logistic regression

method was employed to remove unwanted variables from the model. From the final model after stepwise regression, the odds ratios were obtained through exponentiation of the regression coefficients. Variable importance metric was also worked out for the final set of features included in the model. 10-fold cross-validation was used to validate the fitted model. A k-fold cross-validation was conducted by randomly removing k observations from the estimate dataset and predicting the response level for the separated observations, then repeating the procedure with a different sample of k observations each time. In place of a single pair of training and validation datasets, the findings are then combined over several samples collected, yielding a highly verified accuracy level. The Logistic Regression analysis was done using R Version 4.0.2 [20].

3. Results

Various demographic-related variables of both groups are summarized in Table 1. Age group, gender, marital status, educational status, occupation, type of family, and DP are documented along with their Chi-square values in Table 1. Age group and gender were found to have non-significant associations with *Amavata* among both the groups. Marital status, educational status, occupation, type of family, and DP were found to have significant associations with *Amavata* among cases and controls. The means of *dosha* in DP of both groups were found to be significantly different (Table 2). To assess the influence of DP in the manifestation of *Amavata*, a mixture model of logistic regression was applied, and the results are depicted in Tables 3 and 4. No interaction came out as significant at one percent level of significance. The McFadden pseudo R^2 for the model was 0.41. Marital status, educational status, occupation, type of family, and DP were found to have significant associations with *Amavata* among cases and controls. With every unit increase in the percentage of *Vata*, there was a six percent increase in the chance of having *Amavata*. Similarly, the chances of *Amavata* incidence decreased by 7.5% with every unit increase in the percentage of *Pitta* component. Given the *Vata* and *Pitta* percentages, the *Kapha* percentage had no specific role being determined by the other two components. The *Vata* percentage came out to be the most dominant factor with an important metric of 9.12 (Tables 3 and 4).

4. Discussion

A relationship was established between DP and *Amavata* (Rheumatoid Arthritis). Various other demographic characteristics were also analysed, and significant association was discovered for marital status, education status, habitat, socio-economic status, occupation, and type of family, however, no association was found with age, gender, religion, and type of diet. Two groups have participated in the present study; one is the case group consisting of *Amavata* patients (n = 150); the other is the control group (n = 150), comprising healthy persons. Both groups were matched by their age and sex. So, the age and gender were deemed non-significant. The ratio of cases and controls in the present investigation was almost 1:1. Most of the participants were females (n = 129), covering 86%, as *Amavata* (Rheumatoid Arthritis) mainly affects the women population. Various autoimmune disorders, such as Rheumatoid Arthritis (RA), systemic lupus erythematosus (SLE), and systemic sclerosis (SSc), have a significant prevalence in females. Epigenetics and the hormonal foundation of male sexual behaviour appear to be two important elements at play, either of which may influence other issues, including changes in the microbiome. The inherited predisposition to RA can be explained by differences in the hormones estradiol and progesterone in

Table 1a
Summary tables of exposure variables vs category levels.

Variable	Level code	label	Cases n (%)	Controls n (%)	χ^2 value	df	P-value
Age group	1	18−30	30 (20%)	28 (18.7%)	1.722	2	0.423
	2	31−40	59 (39.3%)	50 (33.3%)			
	3	41−50	61 (40.7%)	72 (48%)			
Gender	1	Male	21 (14%)	21 (14%)	0.001	1	1.00
	2	Female	129 (86%)	129 (86%)			
Marital status	0	Unmarried	17 (11.3%)	34 (22.7%)	7.7	1	0.021
	1	Married	133 (88.7%)	116 (77.3%)			
Education	0	Uneducated	17 (11.3%)	8 (5.3%)	19.746	5	<0.001
	1	Primary	33 (22%)	16 (10.7%)			
	2	Secondary	54 (36%)	50 (33.3%)			
	3	Higher-secondary	15 (9.68%)	14 (9.3%)			
	4	Graduate	20 (13.3%)	42 (28%)			
	5	Post-graduate	11 (7.3%)	20 (13.3%)			
Habitat	1	Rural	31 (20.7%)	9 (6%)	16.333	1	<0.001
	2	Urban	119 (79.3%)	141 (94%)			
Socio-economic status	1	BPL	41 (27.3%)	27 (18%)	8.929	2	0.03
	2	LMC	81 (54%)	77 (51.3%)			
	3	UMC	28 (18.7%)	46 (30.7%)			
Occupation	1	Student	13 (8.7%)	26 (17.3%)	32.681[a]	3	<0.001
	2	House-wife	109 (72.7%)	74 (49.3%)			
	3	Govt. employee	1 (0.7%)	21 (14%)			
	4	Private employee	30 (19.42%)	29 (19.3%)			
Religion	1	Hindu	132 (88%)	135 (90%)	4.66	1	0.46
	2	Muslim	18 (12%)	15 (10%)			
Type of diet	1	Vegetarian	111 (74%)	108 (72%)	0.152	1	0.696
	2	Mixed diet	39 (26%)	42 (28%)			
Type of Family	1	Nuclear	34 (22.7%)	119 (79.3%)	96.372	1	<0.001
	2	Joint	116 (77.3%)	31 (20.7%)			
Deha-Prakriti (predominant *Dosha*)	1	Vata (V + VP + VK)	126 (84%)	27 (18%)	137.281[a]	2	<0.001
	2	Pitta (PV + PK)	4 (2.7%)	68 (45.3%)			
	3	Kapha (K + KP + KV)	20 (13.3%)	55 (36.7%)			
Deha-Prakriti (detailed)	1	V (Vataja)	35 (23.3%)	3 (2%)	150.795[a]	7	<0.001
	2	VP (Vata-Pittaja)	43 (28.7%)	16 (10.7%)			
	3	VK (Vata-Kaphaja)	48 (32%)	8 (5.3%)			
	4	PV (Pitta-Vataja)	3 (2%)	20 (13.3%)			
	5	PK (Pitta-Kaphaja)	1 (0.7%)	48 (32%)			
	6	K (Kaphaja)	1 (0.7%)	4 (2.7%)			
	7	KP (Kapha-Pittaja)	5 (3.3%)	36 (24%)			
	8	KV (Kapha-Vataja)	14 (9.3%)	15 (10%)			

Abbreviations: BPL-Below Poverty line, LMC- Lower middle class, UMC- Upper middle class.
[a] With Yates correction (as the cell values less than 5).

females and testosterone in males. By decreasing cytokine (e.g., TNF) communication (high estradiol levels), developing immunological tolerance, and reducing severity throughout pregnancy, estradiol reduces synovial inflammation [21]. By increasing Tregs and lowering Th17 generation, progesterone may mitigate the effects of RA on the pregnant woman's immune system [22,23]. Testosterone may protect against the development of RA autoantibodies [24]. Two X-linked genes, TIMP1 and Interleukin-9 receptor (IL9R), have been linked to sex differences in rheumatoid arthritis (RA). Both genes were shown to have Single-Nucleotide Polymorphisms (SNPs) that were associated with either RA in general (TIMP1) or RA that was positive for the anti-cyclic citrullinated peptide (anti-CCP) antibody [25]. In addition, those who are predisposed to inflammatory arthritis due to genetic factors like the common epitope may also be affected by anomalies in their gut microbiota. The HLA genotype (DRB1*0401) of females may play a role in altering the composition of the gut microbiota, leading to both an increase in pro-inflammatory cytokines and the translocation of bacteria [26], which may develop RA.

In both the study groups, married participants occupied a major portion. As the significantly included age group belonged to 31−50 (81%) years, the highest number of participants were married. Most of the individuals in both groups belonged to urban environment as the present study has been conducted in Jamnagar municipality region only. However, compared with the control group, the patients with *Amavata* from the rural region were much greater as

they may have irregular eating patterns and disturbed lifestyles. Housewives (homemakers) were shown to have a substantial part; however their percentage is larger in the case group when compared with control group. The government and private employees were more in the control group than cases which show that they are professionally comfortable and devoid of any physical as well as psychological stress which may keep them healthy. In the present investigation, the highest number of cases and controls had secondary education status. However, the percentage of illiterate was much larger in the case group (11.3%), whereas, in the control group, just 5.3% were uneducated. It implies that literacy has a key impact on the causation of *Amavata*. Health literacy imparts knowledge about a healthy lifestyle and its relevance to people, helping them prevent disease conditions. The highest number of participants were below the poverty line and lower-middle-class categories. However, their percentage is slightly greater in the case group (81.3%) than in the control group (69.3%) which is statistically significant. The socio-economic status (As per NCAER 2010- National Council for Applied Economic Research survey research guidelines) and habitat are interconnected elements. Due to their poor economic situation, they cannot afford hygienic and nutritious food. Moreover, they always strive for day-to-day requirements. It provokes them to consume unclean, incompatible, stale, and non-nutritious food. This may lead to the production of *Ama* in the body, which plays a crucial part in the manifestation of RA [6].

Table 1b
Association of *Deha-Prakriti* (frequency) in the manifestation of *Amavata* (~RA).

Deha-Prakriti	Group		Total	χ^2 value	Degrees of freedom (df)	p-value	Inference
	Control	Case					
K	4	1	5	150.795[a]	7	<0.0001	Statistically Significant
V	3	35	38				
KP	36	5	41				
KV	15	14	29				
PK	48	1	49				
PV	20	3	23				
VK	8	48	56				
VP	16	43	59				
TOTAL	**150**	**150**	300				

[a] With Yates correction (as the cell values less than 5).

Table 1c
Odds ratio and χ^2 between cases and controls for three types of *Deha-Prakrits*.

Sr. No.	Etiological factors	Odds Ratio	CI (95%)	χ^2	P	Type of association
1.	*Vata Prakriti*	23.92	13.08−43.73	130.73	<0.0001	Positive
2.	*Pitta Prakriti*	0.03	0.01−0.09	72.533[a]	<0.0001	Negative
3.	*Kapha Prakriti*	0.27	0.15−0.47	21.778	<0.0001	Negative

[a] With Yates correction (as the cell values less than 5).

Table 2
Comparison of involved *Dosha* in *Deha-Prakriti* among cases and controls.

Involved Dosha	Study groups		U- value	P-value
	Case group (n = 150)	Control group (n = 150)		
	Mean ± S.D.			
Vata	53.79 ± 15.75	24.91 ± 17.59	14.929	<0.001
Pitta	21.81 ± 11.67	39.35 ± 14.61	−11.446	<0.001
Kapha	24.52 ± 15.13	36.27 ± 17.26	−6.149	<0.001

Table 3
Regression analysis of *Deha-Prakriti* and *Amavata*.

Prakriti element	Estimate	Std. Error	z value	Pr (>|z|)
Pitta	−0.077450	0.008684	−8.919	<2e-16 ***
Vata	0.0589	0.0065	9.117	<2e-16 ***

Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1.

Table 4
Log-Odds for *Pitta* and *Vata Deha-Prakriti* elements.

	log-odds	2.5%	97.5%
Pitta	0.9254731	0.9087842	0.9403677
Vata	1.0606992	1.0481276	1.0751187

Religion and type of food (vegetarian or non-vegetarian) were shown to have a nonsignificant association with *Amavata* as the study has been done at Jamnagar and its peripheries which is a Hindu prominent region. The highest number of cases or patients of *Amavata* were from joint families (77.3%), whereas the maximum number of controls or healthy volunteers were from nuclear families (79.3%). It implies that the type of family has a crucial effect on the occurrence of *Amavata*. This may be related to the fact that in joint families, women suffer from excessive physical stress, which is nothing but *Atishrama* (over-effort), leading to the aggravation of *Vata* [1, Chikitsa 28/15-18] and further to the appearance of *Amavata*. Most of the time, in joint households, homemakers have irregular food patterns; disturbed sleep patterns may lead to *Ama* production which has a significant function in the presentation of *Amavata* [6,1, Vimana 2/9].

In both groups, *Sama Doshaja* DP was not found. In the case group, the most number of patients with *Amavata* were found to have *Vata* predominant DP (84%) however, in the control group, the maximum number of healthy volunteers were of *Pitta* predominant DP (45.3%) and *Kapha* prominent DPs (36.7%). In the case group, single *Vataja*, *Vata-Kaphaja*, and *Vata-Pittaja* persons occupied 23.3%, 32%, and 28.7%, respectively. It highlights the vulnerability of *Vata* dominating DP and the protecting nature of *Pitta*, *Kapha* prominent DPs. The chi-square test, Odds Ratio, Mann−Whitney U test, and Logistic Regression analysis have also validated this aspect (Table 1a, 1b, 1c, 2, 3 & 4). At the biochemical level, *Vata dosha* is responsible for *Vishamagni* (an irregular digestion mechanism) [1, Vimana 6/12]. Moreover, due to instability (attributed to the predominance of *Rajo-guna* in their *Sattva*), unable to control their intellect, will be quickly affected by psychological factors. Due to this reason, individuals will not get appropriate sleep, which is also responsible for poorer immunity [27]. The research suggests that the *Vataja* DP individuals are considerably weak physically as well as psychologically. Ayurveda, clearly mentions that *Vata*-dominant DP people are unable to tolerate intense physical effort as compared to *Pitta* and *Kapha* prominent DP individuals [1, Vimana 8/98-99]. It was also stated that *Vata* dominating DP has poor immunity, but *Pitta*, *Kapha* predominant DP have strong immunity [28]. It has been substantiated by Rotti H et al., who reported that *Kaphaja* DP samples had much increased CD25 (activated B cells) and CD56 (natural killer cells) levels than other Prakriti groups. Moreover, CD14 levels were observed considerably higher in *Pittaja* DP samples. Increased CD25 and CD56 in *Kaphaja* DP may suggest a larger antibody response, which is compatible with Ayurvedic literature references [27].

Alpa-Bala (less-strength) hinders *Vataja* DP individuals to perform physical exercise. The incidence is much larger in *Vata-Kaphaja* DP since there are more chances for the vitiation of *Agni* than in other individuals. The aggravation of *Vata* is extremely prevalent in *Vata* predominant DP people, compared with the *Pitta* and *Kapha* dominating DP people. The *Samprapti* of *Amavata* says that the formation of *Ama* is another central point, which envelops various explanations. By default, *Kapha* and *Vata* predominant DP persons experience diminished and irregular digestive systems, respectively [1, Vimana 6/12]. Hence, *Kapha* and *Vata* predominant DP individuals are more prone to the development of *Ama* in their body, compared with *Pitta* predominant DP individuals as their digestive capacity is larger.

The mean proportion of *Vata* in DP of the case and control groups were 53.79 ± 15.75 (mean ± S.D.), 24.91 ± 17.59, respectively. It reveals the preponderance of *Vataja* DP phenotypic traits. A similar thing was noticed in majority of the phenotypic traits. The mean percentage of *Pitta dosha* DP of the case and control groups were 21.81 ± 11.67, 39.35 ± 14.61, respectively. It indicates the protective nature of *Pitta dosha* in the control group as it is accountable for the maintenance of *Agni* at the biological level. The mean weightage of implicated *Kapha dosha* in the case and control groups was 24.52 ± 15.13, 36.27 ± 17.26, respectively. It signifies that the dominant stable mind, which is a safeguarding element for the development of *Amavata*. At the biological level, *Pitta dosha* is responsible for good digestive strength, predominance of *Agni mahabhuta* stops the development of *Ama* [29]. *Kapha*, is responsible for *Sthira Chitta* (stability of mind), high intellectual levels, stops an individual from involvement in *Prajnaparadha*. It instructs an individual to consume nutritious dietary food substances and helps to develop a healthy lifestyle. Furthermore, it is delineated that even though an individual who consumes *Pathya* (Wholesome) and *Matravat* (appropriate quantity i.e., neither less nor excess) *Ahara*, if his or her mind is afflicted with *Chinta* (worry), *Bhaya* (fear), *Shoka* (grief), *Krodha* (anger), *Dukha* (irritable), the *Ama* will be formed in their body [1, Vimana 2/9]. Predominant of *Vayu mahabhuta*, *Rajo-guna*, and instability of *Sattva*, readily involve in *Prajnaparadha* (intellectual error). The above indicated psychological variables would easily afflict the *Vata* predominant DP than the other two DP individuals. By default, *Vata* predominant DP persons have irregular and disturbed sleep patterns, which may also contribute to the aetiology of *Amavata* [1, Vimana 8/98].

The present investigation has indicated that DP is a risk factor connected with *Amavata*. DP is not a changeable element, but it can be considered a diagnostic and preventive tool by adopting acceptable dietary patterns and lifestyles. Ayurveda literature also indicates the same as the diet and regimen which is having the *Viparita guna* (opposite qualities) to the individual's *Deha Prakriti* (body constitution) is wholesome for the preservation of positive health. Whereas in the case of the equilibrium state of all the three *Doshas*, it is optimal to supplement with the food having all the six tastes in an appropriate quantity [1, Sutra 7/41]. Patient education in cognitive therapy is effective in lowering improper conduct and fostering positive health behavioural adjustments as per their DP. Refraining from bad food patterns, improper lifestyle, and *Prajnaparadha* (intellectual error) can be done through cognitive therapy. Cognitive therapy can help an individual to avoid improper eating habits, a flawed lifestyle, and *Prajnaparadha* (intellectual error) [30]. The study's significance may be evaluated in terms of how evidence-based epidemiological research is methodically implemented into public health policies [31]. It's crucial to think about the population and high-risk approach to risk behaviour prevention, as well as the viability of lifestyle modification counseling as per their DP [32,33].

Future large-scale studies with sufficient sample sizes at a multi-centric level will lend credence to the claims made in the ayurveda literature, paving the way for researchers to investigate not only the variations in disease severity but also the best ways to prevent complications in different DP people of *Amavata*. The current study will help doctors more precisely use treatment modalities including *Shodhana* (purificatory) and *Shamana* (palliative) procedures, as well as setting the framework for future interventional studies. For instance, *Vaitarana-basti's* efficacy, can be assessed in uncomplicated *Vataja*, *Vata-Pittaja*, and *Vata-Kaphaja* DP individuals, allowing for the development of a PBM or individualised prescription. Analysing the connection between food and gut microbiota in geographically diverse groups and DP can help healthcare providers design tailored meal plans for patients taking Amavata, perhaps improving their quality of life. This approach may be useful for treating other chronic conditions as well [34]. Comparability of case−control research for exposure analysis is not evident as for an RCT (randomised controlled Trial), matching was done in terms of age and sex achievable using inclusion or exclusion criteria solely.

4.1. Limitations of the study

In the present study, many of the patients fall under the chronic disease phase as they approached ayurvedic management at least after one year of the disease onset. In the early stage of *Amavata*, the symptoms are related to *Amavastha*, whereas, in the chronic stage, the symptoms are related to *Niramavastha*. Hence, the *Kapha* predominant DP did not show any association with the disease incidence. Although, the disease incidence is more in *Vata-Kaphaja* DP followed by *Vata-Pittaja* and single *Vataja* predominant DP. Besides, the mean difference of *Kapha* dosha involvement in DP is less when compared to *Pitta dosha* (Table-2). Moreover, in the inclusion criteria, if only the patients who were recently diagnosed or those who had the onset within one-year duration were enrolled, either it may change the results or it may show a significant association with *Amavata*. Hence, the logistic regression analysis did not show any significant association between *Kapha* predominant DP and *Amavata*.

5. Conclusion

Using a case−control study of 300 individuals, 150 of whom had *Amavata*, the association analysis is performed at ITRA (previously IPGT & RA) hospital in Jamnagar. Statistical analysis of qualitative data using the Chi-square test and the Odds Ratio revealed a statistically significant association between *Vata* dominance and the development of *Amavata* in DP patients. The risk of developing *Amavata* was significantly lower in those with *Pitta*- or *Kapha*-dominant DP. In this study, *Vata-kaphaja* DP had the highest incidence of *Amavata*, followed by *Vata-Pittaja,* single *Vataja*, and *Kapha-Vataja*. The mixed logistic regression model revealed the quantitative role of DP in predicting *Amavata*, showing that for every unit rise in *Vata*, the likelihood of *Amavata* increased by six percent. As *Pitta* percentage increased, *Amavata* incidence reduced by 7.5 percent. It strongly suggests that the *Vata* predominant DP is a causative factor of *Amavata* (RA), while the *Pitta* predominant DP acts as a protective factor. Community-based education programmes may teach DP-recommended diets and practises to lower *Amavata* risk.

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Authors contribution declaration

Rajkumar C: Conceptualization, Methodology, Data Collection, Data Curation, Statistical Analysis, Writing- Original draft, Review & Editing. **Baghel A S:** Conceptualization, Methodology, Supervision, Writing- Original draft, Review & Editing. **Shubhangi Kamble:** Methodology, Supervision, Writing- Original draft, Review & Editing. **Bhagavathi NNL:** Conceptualization, Methodology, Writing- Original draft, Review & Editing.

Declaration of competing interest

There are no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaim.2023.100789.

References

[1] Acharya YT. In: Reprint, editor. Charaka samhita of agnivesha, sutra sthana; dirghamjiviteeyam: chapter 1, verse 123. vol. 23. Varanasi: Chaukhambha Surbharati Prakashan; 2014.
[2] Acharya YT. In: Reprint, editor. Sushruta samhita of dhanvantari, sharira sthana: garbhavyakarana shareeram: chapter 4, verse 63. Varanasi: Chaukhambha Surbharati Prakashan; 2014. p. 361.
[3] Acharya YT. In: Reprint, editor. Sushruta samhita of dhanvantari, sharira sthana: garbhavyakarana shareeram: chapter 4, verse 78. Varanasi: Chaukhambha Surbharati Prakashan; 2014. p. 362.
[4] Acharya YT. In: Reprint, editor. Charaka samhita of agnivesha, sutra sthana; navegandharaneeyam: chapter 7, verse 39-40. Varanasi: Chaukhambha Surbharati Prakashan; 2014. p. 52.
[5] Hari Sadashiva Shastri Paradakara Pt. Reprint ed. Ashtangahridayam of vagbhata, sarvangasundari commentary by arunadatta & ayurvedarasayana commentary by hemadri, sutrasthana: ayushkameeyam: chapter 1, verse 10. Varanasi: Chaukhambha Sanskrit Sansthan; 2018. p. 8.
[6] Prof. Upadhyaya Yadunandana. Madhukosha Sanskrit commentary by srivijayarakshita and srikanthadatta with vidyotini Hindi commentary on madhavanidana of sri madhavakara. In: Reprint, editor. Amavata nidanam: chapter 25, verse 1-4. vol. 1. Varanasi: Chaukhambha Prakashan; 2016. p. 511.
[7] Cross M, Smith E, Hoy D, Carmona L, Wolfe F, Vos T, et al. The global burden of rheumatoid arthritis: estimates from the global burden of disease 2010 study. Ann Rheum Dis 2014;73(7):1316–22. https://doi.org/10.1136/annrheumdis-2013-204627.
[8] Avina-Zubieta JA, Thomas J, Sadatsafavi M, Lehman Allen J, Diane Lacaille. Risk of incident cardiovascular events in patients with rheumatoid arthritis: a meta-analysis of observational studies. Ann Rheum Dis 2012;71:1524–9. https://doi.org/10.1136/annrheumdis-2011-200726.
[9] Molina E, del Rincon I, Restrepo JF, Battafarano DF, Escalante A. Mortality in Rheumatoid Arthritis (RA): factors associated with recording RA on death certificates. BMC Muscoskel Disord 2015;16:277. https://doi.org/10.1186/s12891-015-0727-7.
[10] Liao KP, Solomon DH. Traditional cardiovascular risk factors, inflammation and cardiovascular risk in rheumatoid arthritis. Rheumatology 2013;52(1):45–52. https://doi.org/10.1093/rheumatology/kes243.
[11] Cacciapaglia F, Spinelli FR, Piga M, Erre GL, Sakellarion G, Manfredi A, et al. Estimated 10-year cardiovascular risk in a large Italian cohort of rheumatoid arthritis patients: data from the Cardiovascular Obesity and Rheumatic DISease (CORDIS) Study Group. Eur J Intern Med 2022;96:60–5. https://doi.org/10.1016/j.ejim.2021.10.001.
[12] Vinodkumar MV, Anoop AK. Review on the comparability of 'classical' and 'contemporary' research methods in the context of Ayurveda. J Ayurveda Integr Med 2020;11(4):539–46.
[13] Turner DP, Houle TT. Observational study designs. Headache J Head Face Pain 2019;59(7):981–7. https://doi.org/10.1111/head.13572.
[14] Rastogi Sanjeev, Singh RH. Development of diagnostic criteria for Amavata: inferences from a clinical study. JRAS 2009;30(3):1–10.
[15] Arnett FC, Edworthy SM, Bloch DA, McShane DJ, Fries JF, Cooper NS, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31(3):315–24.
[16] Manual of standard operating procedures for Prakriti assessment, developed by central Council for research in ayurvedic Sciences. 1st ed. New Delhi: Ministry of AYUSH, Government of India); 2018.
[17] IBM Corp Released. IBM SPSS statistics for windows, version 20.0. Armonk, NY: IBM Corp; 2011.
[18] Cornell JA. Experiments with mixtures. 3rd ed. New York: Wiley; 2011. ISBN: 111815049X, 9781118150498.
[19] Scheffé H. Experiments with mixtures. J Roy Stat Soc B 1958;20:344–60.
[20] R Core Team. R: a language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2022. Available at: https://www.R-project.org/. [Accessed 29 August 2021]. at 9pm.
[21] Straub RH. The complex role of estrogens in inflammation. Endocr Rev 2007;28:521–74. https://doi.org/10.1210/er.2007-0001.
[22] Hughes GC, Choubey D. Modulation of autoimmune rheumatic diseases by oestrogen and progesterone. Nat Rev Rheumatol 2014;10:740–51. https://doi.org/10.1038/nrrheum.2014.144.
[23] Tan IJ, Peeva E, Zandman-Goddard G. Hormonal modulation of the immune system—a spotlight on the role of progestogens. Autoimmun Rev 2015;14:536–42. https://doi.org/10.1016/j.autrev.2015.02.004.
[24] Keith RC, Sokolove J, Edelman BL, Lahey L, Redente EF, Holers VM, et al. Testosterone is protective in the sexually dimorphic development of arthritis and lung disease in SKG mice. Arthritis Rheum 2013;65(6):1487–93. https://doi.org/10.1002/art.37943.
[25] Burkhardt J, Petit-Teixeira E, Teixeira VH, Kirsten H, Garnier S, Ruehle S, et al. Association of the X-chromosomal genes TIMP1 and IL9R with rheumatoid arthritis. J Rheumatol 2009;36(10):2149–57. https://doi.org/10.3899/jrheum.090059.
[26] Gomez A, Luckey D, Yeoman CJ, Marietta EV, Berg Miller ME, Murray JA, et al. Loss of sex and age driven differences in the gut microbiome characterize arthritis-susceptible 0401 mice but not arthritis-resistant 0402 mice. PLoS One 2012;7(4):e36095. https://doi.org/10.1371/journal.pone.0036095.
[27] Rotti H, Guruprasad KP, Nayak J, Kabekkodu SP, Kukreja H, Mallya S, et al. Immunophenotyping of normal individuals classified on the basis of human dosha prakriti. J Ayurveda Integr Med 2014 Jan;5(1):43–9. https://doi.org/10.4103/0975-9476.128857.
[28] Patel Devang, Baghel AS. The concept of *Deha Prakriti* and its impact on *vyadhikshamatva*. Jamnagar: PG Dissertation Submitted to Gujarat Ayurved University; 2015.
[29] Dr. Sharma Shivaprasad. Ashtanga samgraha of vriddha vagbhata, sutrasthana; doshabhediyam: chapter 20, verse 2. 2nd ed. Varanasi: Chowkhamba Sanskrit Series office; 2008. p. 156.
[30] Zaccardelli A, Friedlander HM, Ford JA, Sparks JA. Potential of lifestyle changes for reducing the risk of developing rheumatoid arthritis: is an ounce of prevention worth a pound of cure? Clin Therapeut 2019;41(7):1323–45. https://doi.org/10.1016/j.clinthera.2019.04.021.
[31] Davis FG, Peterson CE, Bandiera F, Carter-Pokras O, Brownson RC. How do we more effectively move epidemiology into policy action? Ann Epidemiol 2012 Jun;22(6):413–6. https://doi.org/10.1016/j.annepidem.2012.04.004.
[32] Bishop FL, Lauche R, Cramer H, Pinto JW, Leung B, Hall H, et al. Health behavior change and complementary medicine use: national health interview survey 2012. Medicine 2019 Sep 24;55(10):632. https://doi.org/10.3390/medicina55100632.
[33] David D, Moyses Szklo. Gorddis epidemiology. In: 6, editor. Epidemiological approach to disease and intervention. Philadelphia: Elsevier; 2019. p. 1–19. ISBN: 9780323552295.
[34] Chinthala R, Nnl B. Influence of deha-prakriti (body constitution) in the manifestation of disease in context to Amavata (rheumatoid arthritis) - an appraisal. International Journal of Ayurvedic Medicine 2022;13(2):258–67. https://doi.org/10.47552/ijam.v13i2.2633.