

**CORRELATION OF CERTAIN BIOCHEMICAL CHANGES WITH
DOSHA-DUSHYA INVOLVEMENT IN SOME VISHAMAJWARAS
(P.VIVAX MALARIA) AND ITS THERAPEUTIC UTILITY**

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ABSTRACT: In this paper 180 cases of Anyedyushka and Thriteeyaka Vishamajwaras (P.vivax malaria) were studied for various biochemical changes before and after treatment and these changes were correlated with dosha-dushya involvement in these conditions. Their diagnostic, prognostic and therapeutic utility has also been discussed here.

The jwara or fever as a disease has been clinically divided and sub-divided under many groups in Ayurveda. Since the criterion for each classification varies, it is but natural that there will be always overlapping of certain aspects among the various jawaras described. The classification is mainly on the basis of its origin, severity of temperature, manifestation, seasonal onset, prognosis, dhatus (tissues) involved, doshic aetiology and strength or otherwise of doshas and kala.¹

There is a description of jwara as sama jawra in Kashyapa Samhita.² Jwara with less aetiological factors, mild symptoms without any complication is defined as sama-jwara. The vishama Jwara which is just opposite to sama-jwara has a great range and includes many types of jwara like Santata, satata, Anyedyushka, Thriteeyaka and Chathurthaka. Vishamajwara is a technical term indicative of a group fevers which have vishama arambha (irregular onset) and vishama visarga (irregular remission) of temperature³. They are mainly classified on the basis of bala-bala (strength or otherwise) of dosha and kala. Strictly speaking only satata Anyedyushka, Thriteeyaka and Chaturtaka are vishama jwaras. In satata jwara the temperature rises and falls twice in a day; in anyedyushka once in a day, in thriteeyaka at the interval of two days.

The vishama jwaras like satata, anyedyushka, thriteeyaka and Chaturthaka are all akin to different types of malarial fever described in modern medicine. Ayurveda makes the classification on the basis of dosha-dushya involvement whereas modern medicine makes it on the basis of different parasites associated with the pathology on this disease.

A careful perusal of different passages together with commentaries dealing with nidana chikitsa of vishama jwaras in the extent Samhita granthas clearly brings out the following facts. Bhoja, Bhaluki, Pushkalavata etc. belonging to Dhanwantari school of surgeons and Agnivesa, Harita etc. belonging to Atreya school of Physicians had slightly different approaches in describing Vishamajwaras. Salya tantra's

approaches was from the point of view of various kaphasthanas whereas kayachikitsa's approach was from the point of view of various dhatus (tissues) involved true to its spirit of describing any pathological condition in the light of metabolic changes. Susruta, though belonged to salya tantra, mentioned both views⁵.

There is a slight difference in the views of Agnivesa of Atreya school as mentioned by Susruta in his samhita redacted by Nagarjuna and the views of Agnivesa recorded in his work redacted by Charaka and Drudhabala.

According to Agnivesa's view, as quoted in Susruta Samhita, satata Jwara is caused by the involvement of Rasa and Rakta, Anyedyushka by the involvement of mamsa dhatu, Thiriteeyaka by the involvement of medodhatu and chaturthaka by the involvement of asthi and majja. But as per Agnivesa's view as found in charaka samhita, satata Anyedyushka, Thiriteeyaka and Chaturtaka are caused by the involvement of Rakta medo vaha sira, asthi and majja respectively.

Vagbhata, who attempts to reconcile the views of both the schools of thought as far as possible and tried to retain the best in his view, adopts Agnivesa's classification on the basis of dhatu-involvement but as quoted by susruta and not as found in Charaka.

A critical perusal of the relevant passages as found in charaka reveals that there is an omission of mamsa dhatu in the causation of Anyedyushka, Charaka's reference to the views of his contemporary people only indicates an attempt of partial correction. According to that Anyedyushka is caused by the involvement of Rakta, Thiriteeyaka by the involvement of mamsa and chaturthaka by the involvement of medas. It is silent about the causation of satata jwara. Therefore Vagbhata should have felt that if mamsa is included according to its order, Charaka's text should read almost akin to susruta's quoting the views of agnivesa school. Ayurveda prescribes medicated ghrita and milk freely in the treatment of jeerna jwaras. Curd is specially recommended in the treatment of vishama jwaras. There are vata haras and kapha medas karas. This also suggests the dosha-dushya pattern envisaged in vishama jwaras.

The following points will emerge out of critical review of the relevant literature on vishama jwaras.

- a) Satata, Anyedyushka, Thiriteeyaka and Chaturthaka are vishama jwaras.
- b) Though they are Sannipathaja Vatadhikya is envisaged in doshas.
- c) Kaphakshaya is implied as the majority of dhatus involved in the causation are seats of kapha
- d) Anyedyushka and Thiriteeyaka generally come across are Sannipathajas with Vata dominance,, decreased kapha with the involvement of mamsa and medas respectively.
- e) Ahara of Vishamajwara patients should include milk, ghee and curd all vataharas and kapha medas karas.

Presently malaria has once again staged a come-back in India and p.vivax and p.falciparum infections are encountered in endemic areas. P.vivax, which is common throughout India, is known to affect mostly reticulocytes and younger red blood cells. It is well known that liver is involved in both the pre and exoerythrocytic cycles of the parasite. Development of the sporozoites takes place in the hepatocytes before it infects red cells. Liver is commonly enlarged and congested with parasitized red cells in

sinusoids and centrilobular veins and swollen parenchymatous and Kupffer cells.⁶ There are recent reports of *P. vivax* malaria patients who develop jaundice. ⁷ Serum cholesterol is said to rise during the chill but decrease slightly during the afebrile period.⁸

Another study reports the cholesterol level rises during the chill and falls to subnormal level in the apyrexial periods.⁶ *P. vivax* is of milder type than *p.falci parum* infection and only 2% erythrocytes are attacked. Alteration in the erythrocyte count and haemoglobin concentration is known to occur in proportion to the degree of erythrocyte destruction.⁹ Varying degrees of parasitaemia are commonly seen in *P.vivax* malaria and it is likely that different levels of parasitaemia may induce corresponding changes in biochemical response. In the present study liver function tests in different age groups in *P. vivax* malaria ¹⁰ and their significance, diagnostic and prognostic utility of serum lipids¹¹ and correlation between different levels of parasitaemia and biochemical changes with special reference to serum lipids¹², have been investigated and reported for the first time, for correlating dosha-dushya involvement in the pathology of Anyedhyashka and Tritheeyaka vishamajwaras. The other advantage of using indigenous antimalarial drug and diet in the treatment of malaria is also stressed.

Methods and Materials

Fresh cases of *Plasmodium vivax* malaria admitted as in-patients at the VHS Medical centre, Adyar, Madras under the care of this unit were taken up for this study. Malaria was confirmed clinically and by microscopic examination of blood smear for malarial parasites. Malarial patients with other complications like anaemia, jaundice, and pulmonary tuberculosis were not included in the study. Patients were treated either with Ayush-64, an ayurvedic antimalarial drug at the dose level of 3 g/day for 6 days or chloroquine-primaquine as suggested by local health authorities. Blood was collected in the morning on the admission day and the following investigations were carried out.

- 1) Blood smear for malarial parasites.
- 2) Total count, Differential count and Haemoglobin (colorimetric method).
- 3) Parasites were counted for 100 leucocytes and the number of malarial parasites for cmm. Of blood calculated.
- 4) SGOT, SGPT Alkaline phosphatase, Thymol turbidity, total proteins, A/G ratio were done using standard laboratory procedures. Serum cholesterol¹³ total lipids,¹⁴

Serum triglycerides ¹⁵, and Serum phospholipids¹⁶ were also done. These investigations were repeated after the completion of treatment period and in a few cases serum cholesterol and serum total lipids were repeated after 6 weeks of treatment. Totally 34 in-patient cases of malaria were included in the study. Fasting blood was also collected from normal healthy volunteers to serve as control for estimation of serum lipids.

Results and Discussion

The liver function tests in various age groups and sex are given in table I. The correlation between biochemical change and age and sex is given in the table II. Of these 73 cases were Anyedyushka and 107 Thriteeyaka. With regard to the liver function tests, there was constant increase of thymol turbidity

in most of the cases. Hypo-proteinemia was present in about 40% of cases and 12% of patients showed reversal of A/G ratio and 28% of cases showed increase in SGOT, SGOT was slightly higher in males than in females. Both males and females above 30 years of age showed a tendency of increased SGOT. However SSGPT was uniform in both males and females but decrease with the increasing age was significant among females ($P < 0.03$) Thymol turbidity was higher in males and females who are above 50 years than the patients in the other groups. Albumin decreased as the age advanced. The females showing marked reduction in higher age group. Simultaneously globulin increased with the advancement of age in malarial cases. A/G ratio showed significant decrease with increasing age in both males and females ($P < 0.05$) and ($P < 0.001$) respectively Table II.

Tables III, IV and V indicate the derangement of lipid metabolism in *P. vivax* malarial cases. Serum cholesterol, total lipids and phospholipids show a statistically significant decrease while serum triglycerides significantly increased in *P. vivax* malarial cases (Table III). There was increase in serum cholesterol and total lipids and a decrease in the levels of triglycerides after treatment in these patients (Table IV). It was also observed that serum cholesterol and total lipids approached normal values at the end of six weeks after treatment (Table V). In cases where the drug treatment did not eliminate malarial parasites from the blood smears, it was found that serum cholesterol and total lipids did not show any change as compared to their initial levels on the day of admission. Table VI & VII show the effect of different levels of parasitaemia on biochemical changes and correlation between biochemical changes and different levels of parasitaemia respectively. A perusal of these tables clearly indicates that haemoglobin concentration showed a steady decreasing trend with increasing parasitaemia. The correlation also showed that there was almost significant negative correlation with increasing parasitaemia. SGOT values showed significant increase when parasitaemia

TABLE – I Liver Function Tests in P. Vivax Malaria (Values are mean- S.E)

	SGOT I.U/L	SGPT I.U/L	Alkaline Phosphatase KA Units%	Thymol Turbidity S.H. Units	Total Proteins	Albumin G%	Globulin G%	A/G Ratio
±	3-17	3-17	2-13	0-4	6.3-7.9	1.8-3.6	1.8-3.66	2.5-1.2
Normal values								
Males								
Below 30 years (22)	15.75± 2.66	10.4±1.84	8.445 ±0.609	11.11±1.10	6.098±0.122	3.69±0.125	2.48±0.195	1.59±0.148
31-49 years (7)	14.3±2.29	7.54±1.15	9.84±1.79	8.88±1.23	5.62±0.411	3.71±0.84	2.65±0.16	1.43±0.35
50 years and above (8)	16.07±3.05	7.62±0.88	8.175±1.07	16.29±1.59	6.08±0.461	3.43±0.34	2.76±0.192	1.23±0.01
Females								
Below 30 years (13)	11.81±1.59	10.4±3.8	7.56±0.76	11.4±0.93	6.26±0.179	3.765±0.198	2.45±0.185	1.611±0.16
31-49 years (13)	13.53±2.68	7.07±1.68	9.6±2.11	13.72±1.49	6.54±0.156	3.48±0.292	3.11±0.20	1.19±0.126
50 years and above (9)	15.84±4.01	6.71±1.56	9.11±1.95	13.66±1.79	6.46±0.32	3.07±0.29	3.39±0.45	1.08±0.21

Note: Figures in the parentheses indicate the number of cases in each group.

TABLE II Correlation Coefficient (Age Vs Biochemical Parameters) in T. Vivax Malaria

Parameters	Males	Females
SGOT	0.11	-0.01
SGPT	-0.06	-0.32**
Alkaline Phosphatase	0.03	0.15
Thymol turbidity	0.08	0.11
Total proteins	0.15	0.19
A/G ratio	-0.32*	-0.61***

Note P value *<0.05

**<0.03

***<0.001

_ve indicate negative correlation

+ ve indicate positive correlation

TABLE III Serum Lipids in P. Vivax Malaria (Values are mean \pm S.R.E)

	Normals	p. vivax malaria	t	P value
Serum Cholesterol mg%	170.4 \pm 4.3 (39)	109.0 \pm 3.54 (30)	10.87	<0.001
Serum total Lipids mg%	596.2 \pm 15.24 (33)	436.4 \pm 9.98 (24)	8.77	<0.001
Serum triglycerides mg%	113.92 \pm 15.43 (13)	204.30 \pm 21.5 (26)	3.415	<0.001
Serum Phospholipids mg%	227.0 \pm 11.39 (10)	145.4 \pm 10.6 (11)	5.26	<0.001

TABLE IV Serum Lipids in P. Vivax Malaria Report and after treatment.

(Values are Mean \pm S.E.)

	Initial treatment)	(before 6 th day treatment)	(after Mean Difference
Serum Cholestrerol Mg% (22)	112.3 \pm 3.7	176.1 \pm B 4.14	13.8 \pm B 3.52
Serum total Lipids mg% (19)	435.9 \pm 12.2	508.0 \pm C 14.7	72.1 \pm C 15.59
Serum triglycerides mg% (10)	270.7 \pm 37.9	165.9 \pm A 27.47	104.8 \pm A 43.01

PA < 0.05

B<0.02

C<0.001

Figures in the parentheses indicate number of cases.

TABLE V Serum Cholesterol and Total Lipids in P. Vivax Malaria before and 6 weeks after treatment.

(Value are Mean \pm S.E)

	Initial	After 6 weeks	Mean Difference
Serum cholesterol Mg% (10)	114.6 \pm 5.6	159.9 \pm 6.49	45.3 \pm 5.88
Serum total Lipids mg% (10)	442.6 \pm 11.26	601.6 \pm 31.11	159.0 \pm 35.35

P value < 0.001

TABLE – VI Biochemical Changes in Different levels of Parasitaemia in P Vivax Malaria.

Parasitaemia Per mm blood	Hb g%	SGOT I.U3/L	SGPT I.U/L	Alkaline Phosphatase KA units%	Thymol turbidity SH units	Total proteins	Albumin g%	Globulins g%	Cholestrol mg%	Total lipid mg%
0-100 (8)	9.775± 0.54	6.3± 1.14	6.55± 1.18	7.74± 0.91	9.3± 1.49	6.35± 0.335	3.63± 0.203	2.71± 0.35	102.8± 6.31	486.25± 33.39
101-1000 (18)	9.01± 0.49	8.8± 1.09	6.02± 0.76	8.58± 0.69	14.6±B 1.02	6.196± 0.168	3.448± 0.125	2.738± 0.217	108.8± 3.9	535.8± 26.47
1001-2000 (11)	8.96± 0.51	12.2±A 2.1	7.6± 1.22	9.92± 0.77	15.56±A 2.26	5.67± 0.17	3.32± 0.18	2.346± 0.156	99.184± 5.3	518.6± 36.07
2001-4000 (10)	8.73± 0.48	10.33±A 1.6	8.86± 1.39	9.06± 0.82	14.31±A 1.45	6.04± 0.22	3.548± 0.236	2.497± 0.236	89.4± 7.6	430.5± 12.56

(Groups having parasitaemia more than 101 compared with I group having parasitaemia 0-100 level)

A= P< 0.05

B= P< 0.01

Data are mean ± S.E.

TABLE VII correlation between parasitaemia per mm³ Blood and Biochemical parameters.

Parameters	Correlation coefficient	Sample size	Level of significance
Haemoglobin	-0.24	46	Approach significance
Albumin	-0.15	39	N.S
Globulin	0.02	39	N.S
A/G	-0.13	38	N.S
Thymol turbidity	0.09	40	N.S
Cholesterol	-0.36	47	<0.01
Total lipids	-0.26	47	<0.05

N.S.: Not significant

- : denotes negative correlation with increasing parasitaemia

Was more than 1001 when compare to the low levels of parasitaemia. Thymol showed a steep significant rise in groups having more than 101 parasites/mm³ blood (Table-VI). Serum albumin showed a negative correlation and the correlation coefficient of serum cholesterol and total lipids showed a significant negative correlation ($P < 0.01$) and < 0.05 respectively) with increasing parasitaemia (Table VII).

It was mentioned earlier that Vatadhikya is envisaged in vishama jwaras. Kaphakshaya also is implied as the dushtas involved are mainly the seats of kapha particularly in Anyedyushka and Thriteeyaka jwaras with the involvement of mamsa and medas. The term praya (mostly) used while describing the dhatu involvement 17 does not rule out the possibility of involvement of other dhatus.

Vata is endowed with ruksha guna¹⁸, snigdha guna is opposed to ruksha guna Medas and vasa are snigdha dravyas. Vasa is the sneha contained in the mamsa¹⁹. Involvement of these dhatus by vata will cause decrease in them. Mamsa ad medas kshaya will imply kaphashaya and vata vridhi. Liver is the seat of Rakta dhatu and Rakta is in turn a seat of pitta ²⁰ any impairment of liver will cause raktakshaya and impairment of liver function and decrease of albumin and A/G ratio will be more as the age advances. Old age is associated with vata vridhi²² Derangement of lipid metabolism in general and decrease of serum cholesterol total lipids ad phosphor lipids I particular indicates kaphakshaya as well was vatavridhi. Serum triglycerides is the breakdown product of adipose tissue. The increase of triglycerides only indicates more of adipose breakdown and kshaya of medad and kapha and increase of vata. Increase of serum cholesterol and total lipids and decrease in the levels of triglycerides after treatment indicates decrease of vata and increase of medo dhatu and return of kapha to normalcy. Absence of change in the level of serum cholesterol totrl lipids compared with initial level whenever the malarial parasites are not eliminated even after treatment indicates the continuance of dhoshic vitiation even after treatment. Such resistant cases require special therapeutic and dietetic regimens for better response to treatment.

A steady decreasing trend of haemoglobin concentration, with increase of SGOT and Thymolturbidity and decrease of Serum albumin with increasing parasitaemia onllly indicates the severity of the illness and increase of vata and decrease of medas and kapha with increasing parasitaemia. The altered metabolism of lipids especially of serum cholesterol, total lipids and serum triglycerides observed in this study and their subsequent reversal after treatment suggest the diagnostic and prognostic utility of these parameters in p. vivax malaria along with other clinical and haematological parameters.

Ayurveda prescribes medicated ghees and milk in the treatment of Jeernajwara²² (chronic fevers), curd is specially recommended in the treatment of various vishamajwaras.²⁴ these are Vataharas and kapha-medas karas An additional oral supply of ghee and curd may increase the level of serum cholesterol and total lipids and thereby aiding the response rate.

Pathya (dietetic and other regimen) is very important supplement to therapeutics. Vishamajwaranthaka loha will help in conditions with raktakshaya. Drug therapy supplemented with dietetic therapy may have better response than the drug therapy alone. It was found that the ayurvedic compound causes less side effect and the patients regain their normal digestion soon. The compound containing Swertia

chirata and Katukarohini² may act as liner stimulars and held return to normal metabolic activity. The biochemical change noted in Anyedyushka and thriteeyaka vishamajwaras (p. vivax malaria) serve as diagnostic and prognostic aid in planning of suitable drug and diet for speedy recovery. It is clear from the above that the study of certain biochemical changes in Anyedyushka and Thriteeyaka vishamajwaras (p. vivax malaria) helps correlation of dosha-dushya involvement in the pathology and seves as diagnostic and prognostic aid. It will also facilitate prescribing suitable drug and diet leading to better response even in cases otherwise not responding satisfactorily.

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