

## A combination *Siddha* drug reduces anemia among adolescent girls in Virudhunagar District of Tamil Nadu, India

Mockkaya Logamanian<sup>a,#</sup>, Subramanian Mutheeswaran<sup>a,#</sup>, Murugan Shanmugam Meena<sup>a,#</sup>, Perumal Pandikumar<sup>b</sup>, Savarimuthu Ignacimuthu<sup>b,\*</sup>, Logamanian Janani Saravana<sup>c</sup>, Amaladason Mary Alphonsal Amala Hazel<sup>a</sup> & Ramasamy Meenakumari<sup>a</sup>

<sup>a</sup>National Institute of Siddha, Tambaram Sanatorium, Chennai, Tamil Nadu 600 047, India

<sup>b</sup>Xavier Research Foundation, St Xavier's College, Palayamkottai, Tamil Nadu 627002, India

<sup>c</sup>Velumailu Siddha Medical College & Hospital, Sriperumbudur, Kancheepuram, Tamil Nadu 602 105, India

\*E-mail: xrfsc@gmail.com

Received 12 August 2021; revised 28 April 2023; accepted 05 June 2024

The prevalence of anemia in India is worrisome; the Government is aiming to reduce the prevalence of anemia among women at adolescent and child bearing age. A Public Health Initiative was undertaken to mainstream the use of *Siddha* drugs to combat anemia among the adolescent girls of Virudhunagar district, Tamil Nadu, India. With the assistance from the *Siddha* physicians in Primary Health Centers and Government hospitals, adolescent girls with anemia were identified. After obtaining informed consent, the girls with anemia received a *Siddha* treatment regimen (*Annapēti centūram*, *Bāvāna kaṭukkāy*, *Mātuḷai maṇappāku* and *Nellikkāy lēkiyam*; ABMN) for 45 days. Deworming was done with *Cunṭaivarral cūraṇam* before the start of the treatment. The clinical and biochemical features were studied before and after ABMN treatment. Through this program, 14,179 adolescent girls were screened for anemia and 3,783 girls were found anemic; out of them 2,300 (86.85%) girls completed the 45 days program. Marked reduction of various clinical features of anemia was found with ABMN treatment. ABMN treatment improved the hemoglobin content by 24.30% ( $N=155$ ), 15.96% ( $N=1440$ ) and 4.29% ( $p=0.0005$ ;  $N=705$ ) in severe, moderate and mild anemic girls, respectively. Long term, multicentric investigations are needed to conclude the efficacy and safety of ABMN for treating iron deficiency anemia.

**Keywords:** *Pandu*, *Phyllanthus emblica*, *Punica granatum*, Traditional medicine, *Veluppunoi*

**IPC Code:** Int Cl.<sup>24</sup>: A61K 36/00

The burden of anemia is still high globally; the findings of global burden of disease study 2021 indicated that 24.3% of the global population was affected by anemia and South Asian countries were having a high prevalence<sup>1</sup>. It is known that even mild anemia can affect the health and decrease productivity. Anemia is associated with various diseases like chronic kidney diseases, heart diseases, etc., but anemia due to iron deficiency is the major form<sup>2</sup>. Children up to 5 years, adolescent girls and pregnant women are at higher risk of anemia than other groups. Approximately half of the pregnant women and children in non-industrialized countries were at the risk of iron deficiency anemia<sup>3</sup>. The prevalence of anemia in India is worrisome; it is estimated at 28.4% among adolescents; deficiency of iron, folate and vitamin B<sub>12</sub> are the major causes of anemia among Indian adolescents<sup>4</sup>. Various schemes

such as Intensified National Iron Plus Initiative are running and they are aimed to reduce the prevalence of anemia among women at adolescent and child bearing age by three percentage points, every year<sup>5</sup>. Many medicinal plants used in Indian traditional systems of medicine were shown to have hematinic activity<sup>6</sup>.

*Siddha* is one of the traditional healthcare systems of contemporary India and shares commonalities with *Ayurveda*; the earliest elements of this medicine were found both in *caṅkam* and post-*caṅkam* literatures. It has been practiced majorly in Tamil Nadu<sup>7</sup> and in places where *Tamils* live. *Cittarkaḷ* are known as the founders of this system; *Akattiyar* is considered as the Father of this system. The literature in *Siddha* was majorly in Tamil and in poetry form which made the system inaccessible to others. It has been institutionalized recently when compared to *Ayurveda* and is being taught in many Government and Private medical institutions in Tamil Nadu. The Traditional Knowledge Digital Library documented about 12,000

\*Corresponding author

#Contributed equally

traditional *Siddha* formulations for treating an array of health conditions.

In *Siddha*, anemia is perceived as *Veluppunōy* or *Pāṇṭu* and the literal meaning of these words is pallor; clinically it is represented by the pallor of conjunctiva, tongue and nail buds. According to *Siddha* doctrine, anemia has been classified into six types; one type *Maṇṇuṇ pāṇṭu* ( $\approx$  anemia which causes to eat soil) of *Siddha* has been correlated with iron deficiency anemia<sup>8</sup>. Lifestyle and diet changes along with various herbal, mineral and herbo-mineral formulations are recommended in *Siddha* literature for the treatment of anemia. Previous experiments assessed the efficacies of 33 *Siddha* formulations using preclinical models and it has been reviewed recently<sup>9</sup>. *Anṇapēti centūram*, a *Siddha* herbo-mineral formulation showed about 30% raise in the hemoglobin levels in a clinical study with 90 anemic participants<sup>10</sup>; in another open clinical trial with 50 anemic patients, the treatment with *Anṇapēti centūram* significantly ameliorated the clinical features of anemia in 80% of the patients<sup>11</sup>.

Virudhunagar district located in the southern Tamil Nadu was formed in 1985 by bifurcation of Ramanathapuram district of Tamil Nadu. It consists of two revenue divisions and four *taluks*. This district holds 1.94 million people with a female to male ratio of 1.007:1 and a population density of 458/km<sup>2</sup>. The rural population is recorded as 49.53% compared to the total population of the district. Modern medicine facilities are given through 11 hospitals, 58 Primary Health Centers and 245 health sub-centers. Among these, 5 hospitals and 11 Primary Health Centers are providing *Siddha* treatment. A previous ethnobotanical survey in Virudhunagar district indicated a high consensus for use of *Siddha* formulations for treating anemia<sup>12</sup>. This communication summarizes the work of a Public Health Initiative taken up by the National Institute of Siddha, Chennai on mainstreaming a *Siddha* combination therapy for treating iron deficiency anemia.

## Materials and Methods

### Selection of patients

This program was conducted between September 2015 to August 2019 among the adolescent girls in Virudhunagar district (Fig. 1). Screening camps were conducted in 105 places like schools, colleges, orphanages, private industries and tribal settlements. With the assistance from the *Siddha* physicians in

Primary Health Centers and Government Hospitals the girls were primarily screened for the presence of clinical features of anemia. Haemoglobin levels of all clinically suspected girls were evaluated by taking venous blood, after obtaining informed consent from their parents/guardians.

### Inclusion & exclusion criteria

In this program, a) girls between 10 and 19 years, b) having hemoglobin levels  $\geq 6.5$  and  $\leq 11.9$  g/dL and c) willing to participate in the 45 days program were included after getting consent from their parents/guardians. The girls who were not willing to participate in the program or having hemoglobin levels  $< 6.5$  were referred for further medical investigation through their parents/guardians and excluded from the program. Similarly the patients who were a) non-compliant, b) not willing to continue and c) develop any health condition which required immediate clinical care were withdrawn from the program.

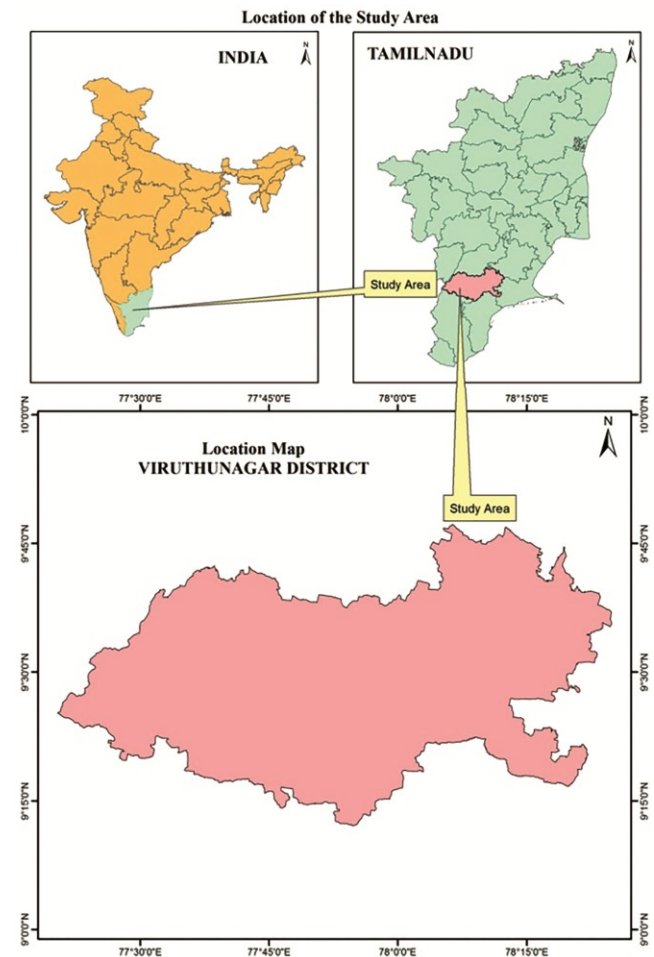


Fig. 1 — Map of the study area drawn using origin software

### Counseling & explanation of the program

A brief presentation was given about anemia and its impact to all the girls, before screening. After identifying the anemic girls, individual counseling on personal hygiene, general health management and importance of healthy, traditional diet for preventing anemia was given. The protocol of the program was explained to the girls and to their parents/guardians before the start of the program in lay terms and written consent was obtained.

### Ethics statement

The study protocol was approved by Institutional Ethics Committee at National Institute of Siddha, Chennai 600 047 (Sanction No.: NIS/1-IEC/2015-1-01/26-08-2015).

### Drug procurement & regimen

The drugs for the program were procured from The Indian Medical Practitioners Co-operative Pharmacy and Stores Ltd. (IMPCOPS), Chennai 600 014 and Tamil Nadu Medicinal Plant Farms and Herbal Medicine Corporation Limited (TAMPCOL), Chennai 600 106. The contents of the drugs are given in **Table 1**. The ABMN drug regimen consisted of *Annapēti centūram* (100 mg, b.d., after food), *Bāvaṇa kaṭukkāy* (500 mg, b.d., after food), *Mātuḷai maṇappāku* (5 mL., b.d., after food), and *Nellikkāy lēkiyam* (5 g, b.d., after food) (Uthamaroyan & Mudaliar, 1998). *Annapēti centūram* was given with *Mātuḷai maṇappāku*; *Bāvaṇa kaṭukkāy* and *Nellikkāy*

*lēkiyam* were given with warm water. Deworming was done with *Cuṇṭaivarral cūraṇam* (2 g) of one dose with warm water, at bed time for three days. After three days, the girls were put on ABMN regimen for 45 days.

### Physical & biochemical assessments

The presence of clinical features like breathlessness, fatigue, giddiness, headache, anorexia, pallor, etc., was evaluated by the investigators before and after completion of the program. The hemoglobin levels of the girls were also evaluated using venous blood, before and after completion of the program. Blood was drawn from antecubital vein and aspectically transferred into ethylenediaminetetraacetic acid (EDTA) coated vacutainers. Biochemical estimations were done at Medall Healthcare, Virudhunagar, Tamil Nadu. The cut-off point for hemoglobin levels for anemia was set as 11.9 g/dL. The severity of anemia was categorized as severe (hemoglobin < 8.0 g/dL), moderate (hemoglobin 8.0-10.9 mg/dL) and mild (hemoglobin 11.0-11.9 mg/dL) in accordance with WHO guidelines<sup>13</sup>. In a randomly selected subset with 283 girls, laboratory investigations such as hemoglobin, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red blood corpuscles (RBC), platelets, total WBC, neutrophils, lymphocytes and eosinophils were done.

Table 1 — Ingredients of the drugs in AMBN

S. No	Name	Ingredients
1	<i>Annapēti centūram</i>	Traditionally processed Ferrous sulphate
2	<i>Bāvaṇa kaṭukkāy</i>	Pulp of <i>Terminalia chebula</i> Retz., rhizomes of <i>Zingiber officinale</i> Roscoe, seeds of <i>Trachyspermum ammi</i> (L.) Sprague, roots of <i>Piper retrofractum</i> Vahl, roots of <i>Plumbago zeylanica</i> L., fruits of <i>Piper longum</i> L., sodium bicarbonate, sea salt and rock salt; processed in the juices of <i>Citrus limon</i> (L.) Osbeck, <i>Zingiber officinale</i> , rice water and butter milk
3	<i>Mātuḷai maṇappāku</i>	Fruit juice of <i>Punica granatum</i> L., sugar, honey and distillate of <i>Rosa × damascene</i> Herrm. flowers
4	<i>Nellikkāy lēkiyam</i>	Fruits of <i>Phyllanthus emblica</i> L., roots of <i>Aegle marmelos</i> (L.) Correa; roots of <i>Premna serratifolia</i> L., roots of <i>Albizia lebbek</i> (L.) Benth., root of <i>Gmelina arborea</i> Roxb., roots of <i>Stereospermum chelonoides</i> (L.f.) DC., roots of <i>Desmodium gangeticum</i> (L.) DC., roots of <i>Pseudarthria viscida</i> (L.) Wight & Arn., roots of <i>Solanum virginianum</i> L., roots of <i>Solanum anguivi</i> Lam, fruits of <i>Tribulus terrestris</i> , roots of <i>Pavonia zeylanica</i> (L.) Cav., fruits of <i>Piper longum</i> L., Leaf galls of <i>Pistacia integerrima</i> J.L. Stewart ex Brandis, aerial parts of <i>Phyllanthus amarus</i> Schumach. & Thonn., fruits of <i>Vitis vinifera</i> L., roots of <i>Leptadenia reticulata</i> (Retz.) Wight & Arn., roots of <i>Saussurea costus</i> (Falc.) Lipsch., wood of <i>Pinus roxburghii</i> Sarg., stems of <i>Tinospora cordifolia</i> (Thunb.) Miers, Pulp of <i>Terminalia chebula</i> Retz., <i>Rutti</i> , <i>Jivakam</i> , <i>Riṣapakam</i> , <i>Mētā</i> , <i>Kāṭṭuḷuntu</i> , <i>Kāṭṭuppararu</i> , rhizomes of <i>Curcuma zedoaria</i> (Christm.) Roscoe, rhizomes of <i>Cyperus rotundus</i> L., roots of <i>Boerhavia diffusa</i> L., fruits of <i>Elettaria cardamomum</i> (L.) Matton, wood of <i>Santalum album</i> L., rhizomes of <i>Nymphaea nouchali</i> Burm. f., roots of <i>Ipomoea mauritiana</i> Jacq., roots of <i>Justicia adhatoda</i> L., rhizomes of <i>Roscoea purpurea</i> Sm.
5	<i>Cuṇṭaivarral cūraṇam</i>	Fruits of <i>Solanum torvum</i> Swartz., leaves of <i>Murraya koenigii</i> (L.) Spreng., cotyledons of <i>Mangifera indica</i> L., fruits of <i>Trachyspermum ammi</i> (L.) Sprague, pulp of <i>Phyllanthus emblica</i> L., rind of <i>Punica granatum</i> L., seeds of <i>Trigonella foenum-graecum</i> L.

## Statistics

The results for the presence of clinical features were given as percentage girls having a clinical feature before and after program. The results for the biochemical analyses were presented as mean  $\pm$  SD. Homogeneity of variance was assessed by Levene's test; if the data were homogeneous, two tailed Student's *t*-test (St) was used to analyze the significance level. For non-homogeneous data, Mann Whitney test (MW) was used and plevel was set at 0.05 as significant. All the analyses were done using GraphPad Prism software (version 11.0).

## Results

### Demography of the patients

In preliminary screening, 14,179 adolescent girls were assessed for the clinical signs of anemia and 6,286 cases were identified for further investigation. On the basis of hemoglobin content, 3,783 girls were found anemic; out of which 2,648 girls who were willing to participate in the program were included and 2,300 (86.85%) girls completed the 45 days program. The number of girls with age between 15 and 19 (70.65%) were higher than with age between 10 and 14 and 63.00% of the anemic girls were from rural areas. Majority of girls belonged to low (72%) and middle (21%) income groups. Nearly three-quarters were living either in kutchha or tiled houses; their parents were illiterate or had only high school education. Nearly half of the girls used either common toilets (36%) or open places (15%) for defecation. Agriculture (56%) was the major source of revenue of the parents followed by cracker factories (21%) and match factories (17%). A major portion of the girls (75%) used sanitary napkins supplied by the Government; 14% bought from the stores and 1% used clothes (Table 2).

### ABMN on clinical features of anemia

During the baseline, the major symptoms recorded among the patients were: fatigue (91.95%) and hair loss (87.43%) followed by headache (87.08%), lack of interest (86.43%) and weakness (86.17%). Marked reduction of these qualitative parameters by ABMN treatment was noticed. After completing the treatment, 89.07% girls were relieved from fatigue, 94.77% girls from hair loss, 85.02% from headache, 95.32 from lack of interest and 90.71% from weakness from the baseline. The menstrual irregularities were also greatly reduced by ABMN treatment (Table 3).

### ABMN on the blood biochemistry of severely anemic adolescent girls

In severely anemic girls, ABMN treatment highly significantly improved the hemoglobin content by 24.30% ( $p=0.0005$ ;  $N=155$ ) after 45 days of treatment (Fig. 2a). The treatment also significantly improved PCV and MCV by 19.81 ( $p=0.012$ ;  $N=19$ ) and 11.24% ( $p=0.020$ ;  $N=19$ ), respectively. Though ABMN treatment slightly improved RBC level in

Table 2 — Demographic profile of the anemic girls who completed the ABMN treatment

Attributes	No. of girls	%
<i>Age</i>		
9-14	675	29.34
15-19	1625	70.65
<i>Place</i>		
Rural	1449	63.00
Urban	851	37.00
<i>Religion</i>		
Hindu	2044	88.87
Christian	159	06.91
Muslim	97	04.22
<i>Income of the parents</i>		
Low	1467	63.78
Middle	681	29.61
High	152	06.61
<i>House type</i>		
Kutchha	1258	54.69
Tiled	452	19.65
Pucca	590	25.65
<i>Work</i>		
Father	1443	62.74
Mother	228	09.91
Both	629	27.35
<i>Education of the parents</i>		
Illiterate	1126	48.96
High school	617	26.83
Higher Secondary school	306	13.30
Degree	251	10.91
<i>Water source</i>		
Panchayat	1174	51.04
Municipality	798	34.69
Public well	125	05.43
Own bore well	203	08.83
<i>Diet</i>		
Non-vegetarian	1907	82.91
Vegetarian	393	17.09
<i>Toilet</i>		
Own	1080	46.96
Common	883	38.39
Open	337	14.65
<i>Napkin usage</i>		
Government	1724	74.96
Own	319	13.86
Cloths	36	01.56
Young girls	221	09.61

Table 3 — Effect of ABMN treatment on the prevalence of signs and symptoms of adolescent girls with iron deficiency anemia after 45 days treatment ( $N=2300$ )

S. No	Symptoms & Sign	Before treatment (No. of girls)	After treatment (No. of girls)	Percentage of improvement
1.	Fatigue	2115	231	89.07
2.	Weakness	1982	184	90.71
3.	Breathlessness	984	99	89.93
4.	Palpitations	1760	263	85.05
5.	Pedal edema	77	1	98.70
6.	Loss of appetite	1768	320	81.90
7.	Headache	2003	300	85.02
8.	Lack of interest	1988	93	95.32
9.	Nausea	1765	112	93.65
10.	Hair loss	2011	105	94.77
11.	Angular stomatitis	136	--	100
12.	Giddiness	875	131	85.02
13.	Pallor	1896	28	98.52
14.	Stomach pain	341	88	74.19
15.	Smooth tongue	85	--	100
16.	Amenorrhoea	46	7	84.78
17.	Menorrhagia	115	14	87.82
18.	Dysmenorrhoea	92	16	82.60
19.	Leucorrhoea	69	8	88.40

severely anemic girls, this increment was insignificant (Table 4).

#### ABMN on the blood biochemistry of moderately anemic adolescent girls

In moderately anemic girls, the treatment with ABMN altered the hemoglobin content by 15.96% in a highly significant manner ( $p=0.0005$ ;  $N=1440$ ) from the baseline levels (Fig. 2b). The parameters such as PCV (11.20%), MCV (10.36%) and MCH (9.25%) were also increased in highly significant manner ( $p=0.0005$ ;  $N=137$ ) (Table 5).

#### ABMN on the blood biochemistry of mildly anemic adolescent girls

ABMN treatment increased the hemoglobin content by 4.29% in a very significant manner ( $p=0.0005$ ;  $N=705$ ) after 45 days of treatment (Fig. 2c). The parameters such as PCV (7.50%;  $p=0.0005$ ;  $N=127$ ), MCV (10.82%;  $p=0.0005$ ;  $N=127$ ) and MCH (2.61%;  $p=0.025$ ;  $N=127$ ) were also significantly increased by ABMN treatment. The treatment did not affect RBC levels; further it showed mild

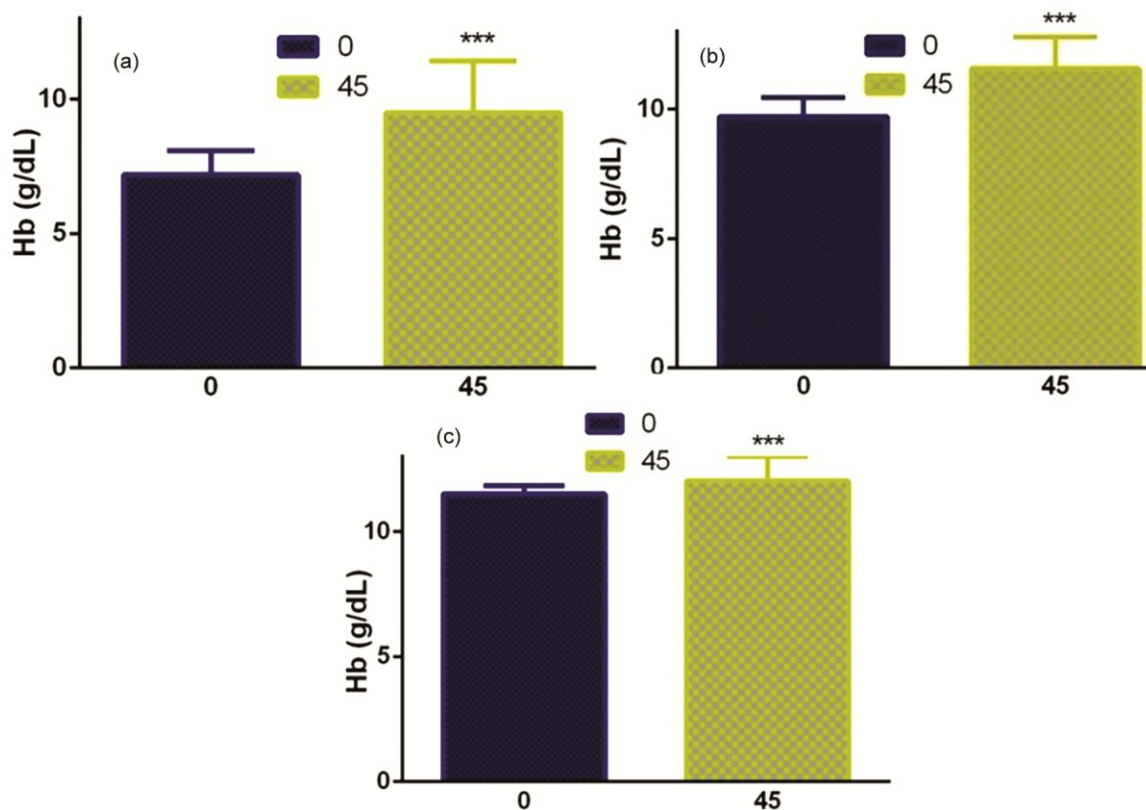


Fig. 2 — Effect of ABMN treatment on hemoglobin level of adolescent girls with iron deficiency anemia before and after 45 days treatment. Values indicate mean  $\pm$  SD of Hb levels (g/dL) from (a) severe ( $N=155$ ), (b) moderate ( $N=1440$ ) and (c) mild anemic ( $N=705$ ) girls; \*\* - deviate highly significantly from the baseline values ( $p=0.0005$ ; Mann Whitney test)

but significant neutropenia, monocytopenia and lymphocytosis (Table 6).

## Discussion

Though it is largely preventable and treatable, anemia is still a major healthcare issue in many countries including India despite the strategies of the

Government through various initiatives like National Nutritional Anemia Control Programme. National Health Policy 2017 of the Government of India has identified anemia as one of the major deterrents<sup>5</sup>. Further, the National Health Policy strongly recommended the integration of AYUSH with modern healthcare system. With this view, a Public

Table 4 — Effect of ABMN treatment on various biochemical parameters of adolescent girls with severe iron deficiency anemia after 45 days treatment (N=19)

Parameters	Before treatment	After treatment	Statistics	P
Hemoglobin (g/dL)	6.92±0.72	8.63±2.89*	MW	0.017
PCV (%)	26.51±3.34	33.06±6.76*	St	0.012
RBC (Million cells/mm <sup>3</sup> )	4.49±0.49	4.56±0.53	St	0.693
MCV (fL)	63.47±4.83	71.51±10.79*	MW	0.020
MCH (pg)	16.78±2.39	18.81±4.36	St	0.084
Platelets (Lakhs/mm <sup>3</sup> )	3.47±1.01	3.63±1.03	MW	0.680
Total WBC (cells/mm <sup>3</sup> )	7889.15±2910.86	7498.42±2488.29	St	0.659
Neutrophils (%)	56.15±6.80	55.26±6.95	St	0.694
Lymphocytes (%)	36.53±6.16	37.00±6.27	St	0.896
Eosinophils (%)	2.78±1.69	3.61±2.63	St	0.261
Monocytes (%)	4.15±1.11	3.67±2.31	St	0.421

Values indicate mean ± SD; \* - deviate significantly from the baseline values; \*\* - deviate highly significantly from the baseline values; St – Student's *t* - test; MW - Mann Whitney test

Table 5 — Effect of ABMN treatment on various biochemical parameters of adolescent girls with moderate iron deficiency anemia after 45 days treatment (N=137)

Parameters	Before treatment	After treatment	Statistics	P
Hemoglobin (g/dL)	9.91±0.73	10.91±1.13**	MW	0.000
PCV (%)	33.44±2.71	37.66±3.46**	MW	0.000
RBC (Million cells/mm <sup>3</sup> )	4.28±0.43	4.32±0.39	St	0.484
MCV (fL)	78.39±51.84	87.45±9.36*	St	0.045
MCH (pg)	23.03±3.06	25.38±3.46**	St	0.000
Platelets (Lakhs/mm <sup>3</sup> )	3.43±7.57	3.36±7.13	St	0.434
Total WBC (cells/mm <sup>3</sup> )	8558.10±2173.56	8457.63±2254.03	St	0.708
Neutrophils (%)	56.36±8.01	53.72±7.11**	St	0.004
Lymphocytes (%)	34.75±7.45	37.94±7.04**	St	0.000
Eosinophils (%)	4.19±3.29	4.62±4.13	MW	0.149
Monocytes (%)	4.88±2.11	3.12±1.81**	St	0.000

Values indicate mean ± SD; \* - deviate significantly from the baseline values; \*\* - deviate highly significantly from the baseline values; St – Student's *t* - test; MW - Mann Whitney test

Table 6 — Effect of ABMN treatment on various biochemical parameters of adolescent girls with mild iron deficiency anemia after 45 days treatment (N=127)

Parameters	Before treatment	After treatment	Statistics	P
Hemoglobin (g/dL)	11.55±0.31	11.98±0.92**	MW	0.000
PCV (%)	38.68±2.23	41.82±3.32**	MW	0.000
RBC (Million cells/mm <sup>3</sup> )	4.32±0.38	4.37±0.33	St	0.349
MCV (fL)	85.56±10.70	95.95±7.44**	MW	0.000
MCH (pg)	26.85±2.63	27.57±2.37*	St	0.025
Platelets (Lakhs/mm <sup>3</sup> )	3.22±0.61	3.83±6.38	St	0.287
Total WBC (cells/mm <sup>3</sup> )	10048.71±9220.83	8532.91±1776.90	MW	0.323
Neutrophils (%)	55.54±8.06	55.43±9.40	St	0.917
Lymphocytes (%)	35.63±7.88	36.84±9.33	St	0.263
Eosinophils (%)	3.95±1.95	4.13±3.04	MW	0.474
Monocytes (%)	4.78±2.09	2.97±1.55**	MW	0.000

Values indicate mean ± SD; \* - deviate significantly from the baseline values; \*\* - deviate highly significantly from the baseline values; St - Student's *t* - test; MW - Mann Whitney test

Health Initiative was taken up to reduce anemia through *Siddha* interventions among the adolescent girls of Virudhunagar district of Tamil Nadu, India.

In this study, ABMN regimen was used; it is a combination of five classical *Siddha* drugs. The *Annapēti centūram* was given as an iron supplement; it is made by processing green vitriol (ferrous sulphate); iron oxide ( $\text{Fe}_2\text{O}_3$ ) was reported as the major constituent (93.58%) of *Annapēti centūram* and the size of these particles were found less than 100 nm<sup>14</sup>. This iron supplement was given with *Mātuḷai maṇappāku* to increase the absorption of iron. *Bāvaṇa kaṭukkāy* and *Nellikāy lēkiyam* were used to increase appetite and to decrease fatigue, respectively. *Cuṇṭaivaṛral cūraṇam* was given for deworming; giving these drugs simultaneously might improve the clinical features of anemia in a synergistic manner.

Contributing factors of anemia are diverse and population-specific in India; a previous study indicated that low income was an indicator of anemia. The girls at late adolescent age were more prone to anemia; this was in accordance with a previous survey in Tamil Nadu<sup>15</sup>. A survey in Karnataka also indicated that the prevalence of anemia was high among rural adolescent women than their urban counterparts<sup>16</sup>. Previous surveys showed a correlation between the indicators of income like concrete houses, clean fuel usage, etc., with anemia<sup>17</sup>; similarly the poor sanitation has also had strong correlation with anemia as reflected in our case<sup>18</sup>. High income increased the diet diversity and improved personal hygiene; however increased income alone did not reduce the anemic prevalence<sup>19</sup>. A survey in India clearly showed a strong correlation between maternal literacy with increased prevalence of childhood anemia<sup>20</sup>. In our program, lack of literacy indicated that it might be an important factor for anemia among their children.

Fatigue is universal and is one of the cardinal symptoms of iron deficiency anemia which severely affects productivity<sup>21</sup> and the treatment with AMBN markedly lowered it. In a small randomized, controlled trial with 25 anemic patients, supplementation with *Amalaki rasayana* (an *Ayurvedic* preparation which contains *Phyllanthus emblica*) significantly improved all clinical features of iron deficiency anemia including fatigue<sup>22</sup>. Supplementation of pomegranate juice did not affect iron metabolism<sup>23</sup>, but significantly lowered fatigue in athletes<sup>24</sup>. Further, AMBN treatment also markedly lowered menstrual abnormalities; the use of

pomegranate might be beneficial for this, since a clinical trial supported the use of pomegranate to control menstrual bleeding<sup>25</sup>.

ABMN treatment significantly increased the hemoglobin content in all categories of anemic girls in a highly significant manner; further it also improved PCV, MCV and MCH levels. No adverse events were reported during the program; ABMN showed a mild but significant neutropenia and monocytopenia. Some case studies reported the occurrence of neutropenia<sup>26,27</sup> and monocytopenia<sup>28,29</sup> with iron supplementation in iron deficiency anemia. The findings of this program indicated the usefulness of ABMN in ameliorating the clinical features of iron deficiency anemia and in improving the hemoglobin levels. In this study, the clinical efficacy of ABMN therapy on adolescent girls with anemia was documented. However long term, multicentric investigations are needed to conclude the efficacy and safety of ABMN for treating iron deficiency anemia and to mainstream it.

## Conclusion

A Public Health Initiative was conducted to combat anemia among adolescent girls in Virudhunagar district, Tamil Nadu, India. Through this program, 14,179 adolescent girls were screened and 3,783 were found anemic.

2,648 girls were willing to receive a *Siddha* treatment regimen; they were given *Annapēti centūram*, *Bāvaṇa kaṭukkāy*, *Mātuḷai maṇappāku* and *Nellikāy lēkiyam*(ABMN) for 45 days. Deworming was done with *Cuṇṭaivaṛral cūraṇam*, before the start of the program.

2,300 girls completed the treatment; demographic analysis of the girls who completed the treatment indicated that they were from rural background, lower economic background and had poor sanitation facilities. Illiteracy of the parents might be the crucial factor for anemia among the girls.

The treatment with ABMN markedly lowered the clinical features of anemia like fatigue, hair loss, headache, loss of interest, etc.; it also lowered menstrual irregularities.

Similarly the treatment with ABMN significantly improved haemoglobin levels as well as PCV, MCV and MCH levels in all categories of anemic girls.

Long term, multicentric investigations are needed to conclude the efficacy and safety of ABMN for treating iron deficiency anemia.

### Acknowledgments

The supports received from the Departments of School & Higher Education, Health & Family Welfare and Tamil Nadu Forest Department in Virudhunagar district are highly appreciated. The authors are grateful to the National Institute of Siddha, Chennai for their support. The authors acknowledge the comments given by the two anonymous reviewers, which helped to improve the quality of the manuscript. The authors acknowledge Dr K. Kannadasan, Department of Geology, Madurai Kamaraj University, Tamil Nadu 625 021 for drawing the map used in this study.

### Financial Support

The authors acknowledge the financial support by the Ministry of AYUSH, Government of India (Sanction No.: Z 28014/16/204).

### Conflicts of Interest

The authors declare that they do not have any conflicting interests.

### Author Contributions

Conceptualization of research & overall monitoring of the project (ML, SI); Execution of field studies and data collection (SM, MSM, AMA, RM, LJS); Analysis of the data and interpretation (PP, SI, ML, AMA); preparation of manuscript (ML, PP, SM, SI).

### References

- Kassebaum N J, The global burden of Anemia, *Hematol Oncol Clin North Am*, 30 (2) (2016) 247-308.
- Lopez A, Cacoub P, Macdougall I C & Peyrin-Biroulet L, Iron deficiency anaemia, *Lancet*, 387 (2016) 907-916.
- Anonymous, Iron deficiency anaemia: assessment, prevention and control: A guide for programme managers, World Health Organization, Geneva, 2001.
- Sarna A, Porwal A, Ramesh S, Agrawal P K, Acharya R, *et al.*, Characterisation of the types of anaemia prevalent among children and adolescents aged 1-19 years in India: a population-based study, *Lancet Child Adolesc Health*, 4 (7) (2020) 515-25.
- Kapil U, Kapil R & Gupta A, National iron plus initiative: Current status & future strategy, *Indian J Med Res*, 150 (3) (2019) 239-47.
- Patel H, Prajapati S, Ranade A, Acharya R & Kumar N M, Evaluation of the haematinic activity of *Opuntia elatior* Mill. fruit, *Indian J Nat Prod Resour*, 9 (2018) 39-46.
- Juliet L, Karthik Raja S, Reena V L, Aarthi V, Sunil Kumar K N, *et al.*, Traditional methods of purification (detoxification process) for Schedule E poisonous drugs, *Indian J Tradit Know*, 20 (3) (2021) 740-748.
- Mudaliyar K K, *Siddha Maruthuvam* (7<sup>th</sup> edition). Department of Indian systems of Medicine and Homeopathy, Chennai (2007) 345-52.
- Kumar A R, Gunalan G, Firdouse K H H & Archana A, Pre-clinical studies of *Siddha* formulations advocated for anaemia: A systematic review and meta-analysis, *J Appl Pharm Sci*, 13 (8) (2023) 185-203. DOI: 10.7324/JAPS.2023.126389.
- Jayakaran D S, Meenakshinathan E & Gopakumar K, A clinical study on *Annabedi chenduram* in *Pandu* based on *Siddha* concept, *J Res Ayurveda Siddha*, 7 (1-2) (1986) 23-32.
- Kumar K M D & Manickavasakam K, An open clinical trial of *Annabedi chenduram* in the treatment of *Vadha paandu* (anaemia), *J Siddha*, 2 (1) (2009) 1-5.
- Mutheeswaran S, Pandikumar P, Chellappandian M, Ignacimuthu S, Durairandiyam V, *et al.*, Consensus analysis of *Sastric* formulations used by non-institutionally trained *Siddha* medical practitioners of Virudhunagar and Tirunelveli districts of Tamil Nadu, India, *J Ethnopharmacol*, 153 (2014) 290-6
- Anonymous, Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity, World Health Organization, Geneva (2011).
- Perumal R, Sudeer R G, Vadivel V, Sahayam C S & Brindha P, Analytical studies on *Annabedi Chenthuram* - A *Siddha* herbomineral formulation, *Indian J Pharm Sci*, 79 (6) (2017) 987-93.
- Chandrakumari A S, Sinha P, Singaravelu S & Jaikumar S, Prevalence of anemia among adolescent girls in a rural area of Tamil Nadu, India, *J Fam Med Prim Care*, 8 (4) (2019) 1414-7.
- Shedole D T, Vidya G S, A Suryakantha H & Vijaykumar B, A comparative study on prevalence of anaemia among urban and rural adolescent high school girls of Davangere, Karnataka, *Int J Community Med Public Heal*, 4 (12) (2017) 4638-43.
- Baranwal A, Baranwal A & Roy N, Association of household environment and prevalence of anemia among children under 5 in India, *Front Public Health*, 2 (2014) 196.
- Coffey D, Geruso M & Spears D, Sanitation, disease externalities and anaemia: Evidence from Nepal, *Econ J (London)*, 128 (2018) 1395-432.
- Alderman H & Linnemayr S, Anemia in low-income countries is unlikely to be addressed by economic development without additional programs, *Food Nutr Bull*, 30 (3) (2009) 265-9.
- Onyeneho N G, Ozumba B C & Subramanian S V, Determinants of childhood anemia in India, *Sci Rep*, 9 (2019) 1-7.
- Sobrero A, Puglisi F, Guglielmi A, Belvedere O, Aprile G, *et al.*, Fatigue: A main component of anemia symptomatology, *Semin Oncol*, 28 (2001) 15-18.
- Layeeq S & Thakar A B, Clinical efficacy of *Amalaki Rasayana* in the management of *Pandu* (Iron deficiency anemia), *Ayu*, 36 (2015) 290-7.
- Urbaniak A, Basta P, Ast K, Wołoszyn A, Kurianska-Woloszyn J, *et al.*, The impact of supplementation with pomegranate fruit (*Punica granatum* L.) juice on selected antioxidant parameters and markers of iron metabolism in rowers, *J Int Soc Sports Nutr*, 15 (2018) 35.
- Trexler E T, Smith-Ryan A E, Melvin M N, Roelofs E J & Wingfield H L, Effects of pomegranate extract on blood flow

- and running time to exhaustion, *Appl Physiol Nutr Metab*, 39 (4) (2014) 1038-42.
- 25 Goshtasebi A, Mazari Z, Gandevani S B & Naseri M, Anti-hemorrhagic activity of *Punica granatum* L. flower (Persian Golnar) against heavy menstrual bleeding of endometrial origin: a double-blind, randomized controlled trial, *Med J Islam Repub Iran*, 29 (2015) 199.
- 26 Kloub M N & Yassin M A, Oral iron therapy-induced neutropenia in patient with iron deficiency anemia, *Case Rep Oncol*, 13 (2020) 721-724.
- 27 Abdelmahuod E, Yassin M A & Ahmed M, Iron deficiency anemia-induced neutropenia in adult female, *Cureus*, 12 (2020) e8899.
- 28 Hassan S, Augustine T & Mahgoub N, Leucopenia, neutropenia, lymphopenia and monocytopenia in a 15 year old girl with iron deficiency anemia responding to iron therapy: A case report, *Am J Pediatr*, 6 (2020) 322-6.
- 29 Ganti A K, Shonka N A & Haire W D, Pancytopenia due to iron deficiency worsened by iron infusion: A case report. *J Med Case Rep*, 1 (2007) 175.