



## Original Research Article

## Effects of Bilwa-Lajadi syrup in emesis gravidarum – an exploratory single arm open labeled trial

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## ABSTRACT

**Background:** Emesis gravidarum is a common obstetrical problem affecting 50–80% of pregnant women during their first trimester which begins in the morning and frequently continues throughout the day; considered as one of the Vyakta Garbha Lakshana in Ayurveda. If it is not treated effectively in time; it may lead to complications in pregnancy affecting the quality of life and thus the pregnancy outcome.

**Objective:** To evaluate the clinical effectiveness of Bilwa-Lajadi syrup in emesis gravidarum.

**Material and methods:** A single arm open labeled clinical trial was conducted on 30 participants fulfilling the inclusion criteria from OPD and IPD of Prasuti Tantra Evam StreeRoga, Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan and administered with Bilwa-Lajadi Syrup 20 ml per day in two divided doses, empty stomach before food for 30 days with followed up every 15 days during treatment and 15 days after completion of trial period.

**Results:** The drug showed statistically significant effect in reducing the frequency of vomiting per day, quantity of vomitus, aversion to smell, nausea and anorexia, altered content of vomitus, improved appetite, imparted lightness of body and increased haemoglobin gm%.

**Conclusion:** Thus, early medication with Bilwa-Lajadi syrup and following dietetic regimen played a vital role in relieving the symptoms of emesis gravidarum.

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## 1. Introduction

Nausea and vomiting during pregnancy is estimated to affect 50–80% of pregnant women [1]. It is a common symptom experienced upto approximately 16 weeks without having any adverse effects on growing fetus as well as mother. However, in few women, it is severe, and causes deleterious effects on maternal health and incapacitates her day-to-day activities [2]. This severe nausea and vomiting is considered as pathological [3] and known as hyperemesis gravidarum. It occurs in 0.3–2% of pregnancies [4] and it is unresponsive to simple dietary modification and anti-emetics. Hence, it is mandatory to initiate the treatment at an

early phase to prevent and manage these health problems and their complications.

## 1.1. Objective

To evaluate the clinical effectiveness of Bilwa-Lajadi syrup in emesis gravidarum.

## 2. Methods

**Site of Study:** This trial was conducted at Department of Prasuti Tantra Evam StriRoga (Obstetrics and Gynaecology), Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan.

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## 2.1. Study design

The trial was an exploratory single arm open labeled trial using convenience sampling method from OPD and IPD of Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan. The study had a due clearance from the Institutional ethics committee, Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan, vide IEC No. SDM/IEC/66/2015–2016; Dt.17/03/2016 and was registered retrospectively in CTRI vide CTRI/2017/06/008727; Dt. 01/06/2017.

## 2.2. Participants enrolment

Pregnant women with the diagnostic features of vomiting, excessive salivation, nausea and anorexia in first trimester were screened and 30 participants (sample size based on the number of patients visiting the OPD and IPD) fulfilling the inclusion criteria were registered for the study.

## 2.3. Inclusion criteria

Primi and multi gravida (up to G<sub>2</sub>P<sub>1</sub>) between 18–35 years of age visiting first time with symptoms of nausea and vomiting without features of dehydration in their first trimester and ready to sign informed written consent form were included in the trial.

## 2.4. Exclusion criteria

Multi gravida with more than second parity and with bad obstetric history; pregnant women with symptoms of dehydration, twin pregnancy and molar pregnancy; history of peptic ulcer, appendicitis, hepatitis, pancreatitis presenting with vomiting, uncontrolled diabetes mellitus, hypertension and hypothyroidism during pregnancy were excluded.

Inclusion and exclusion in the present study were conducted based on the relevant investigations such as hemoglobin %, total leucocyte count, random blood sugar, HBsAg, serum TSH, urine routine (for protein, sugar, ketone bodies), urine microscopy (for pus cells, epithelial cells, casts) and Ultrasonography of abdomen and pelvis.

## 2.5. Informed consent

The purpose and nature of the study drug, benefits and potential risks were explained to the participants using appropriate analogies for the technical terms in both languages (English and Kannada). Participants were informed that they may leave the study any time for a valid reason and it will not affect their future antenatal treatment in any means. Thereafter their informed written consent was obtained before initiating the trial. In case of any adverse events or exacerbations of symptoms patients would have been asked to discontinue the trial and referred to higher centres for emergency medication. No such ADR was reported in this study.

## 2.6. Intervention

All the participants were prescribed *Bilwa-Lajadi* Syrup, [5] 20 ml orally per day in two divided doses. The syrup was consumed before food administration (empty stomach) in morning and night for 30 days and patients were followed up on Day 15, Day 30 and Day 45.

## 2.7. Collection and authentication of trial drug

Among the ingredients for *Bilwa-Lajadi* Syrup; *Hriversa* was collected from Ayurvedic raw drug distributor, Udupi; *Laja* and *Bilwa* from the local market of Hassan and *Usheera* from the market of Kerala based on the availability of good quality drugs and their authenticity was confirmed at the departmental drug testing laboratory; Department of Dravyaguna, Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan, Karnataka.

## 2.8. Preparation of the medicine

*Bilwa-Lajadi* syrup was prepared in laboratory of Department of Rasa Shastra and Bhaishajya Kalpana, Sri Dharmasthala Manjunatheshwara College of Ayurveda and Hospital, Hassan, Karnataka and stored in 200 ml airtight containers, labeled with name and batch and made available in the dispensary for the clinical trial. The prepared syrup was then sent to Sri Dharmasthala Manjunatheshwara Centre for Research in Ayurveda and Allied Sciences, Kuthpady, Udupi, Karnataka for analytical assessment for determination of standardized parameters including pH, refractive index, viscosity, specific gravity, total solids (%), total sugar (%), reducing sugar (%), non-reducing sugar (%) and HPTLC were performed.

## 2.9. Outcome variables

Frequency of vomiting per day, Quantity of vomitus, Content of vomitus, Aversion to smell, Nausea, Anorexia, Appetite, Lightness of body, Hemoglobin (gm%) and Weight (Kg) were the outcome variables. The assessment time points were on Baseline (Day 1), Day 15, Day 30 and Day 45. To assess the effects of therapy objectively, all the signs and symptoms were scored depending upon their severity (see Table 1).

Here, Aversion to smell, Nausea, Anorexia and Lightness of body were subjective parameters. So, they were assessed based on their presence and absence.

## 2.10. Statistical analysis

Statistical analysis was carried out using SPSS Version 20.0 (IBM company, headquarter at Chicago). The outcome variables such as frequency of vomiting per day, quantity of vomitus, content of vomitus and appetite were analyzed using Friedman's test with Wilcoxon signed rank test as post-hoc with Bonferroni correction (0.05/4 = 0.0125). Aversion to smell, nausea, anorexia and lightness of body were analyzed using Cochran Q test and Mc Nemar test.

**Table 1**  
Outcome variables grading.

Outcome variables	Nil (score-0)	Mild (score-1)	Moderate (score-2)	Severe (score-3)
Frequency of Vomiting per day	0 Times/Day	1-2 Times/Day	3-5 Times/Day	>5 Times/Day
Quantity of vomitus	Nil	<50 ml/episode	50–100 ml/episode	>100 ml/episode
Content of vomitus	Nil	Watery	Bile	Food mixed
Appetite	–	Reduced	Moderate	Good

**Table 2**  
Baseline data.

Serial No.	Distribution of 30 participants based on baseline data	Category	Frequency	Percentage
1.	Age	18–20 years	4	13.3%
		20–25 years	17	56.7%
		25–30 years	9	30.0%
2.	Religion	Hindu	28	93.3%
		Christian	2	6.7%
3.	Socio-economic status	Middle class	29	96.7%
		Lower class	1	3.3%
4.	Prakriti	Vata-Pittaja	8	26.7%
		Pitta-Kaphaja	14	46.7%
		Vata-Kaphaja	8	26.7%
5.	Diet	Vegetarian	7	23.3%
		Mixed	23	76.7%
6.	Gravidity status	Primi	20	66.7%
		Multi (G <sub>2</sub> P <sub>1</sub> )	10	33.3%
7.	Period of gestation	4–6 weeks	15	50%
		6–8 weeks	5	16.7%
		8–10 weeks	7	23.3%
		10–12 weeks	3	10%

Weight was analyzed using Repeated Measures ANOVA and Hb% was assessed using paired-t test. The variables were considered statistically significant if the p-value is <0.05.

### 3. Results (see Tables 2 and 3)

#### 3.1. Outcome of intervention

Among 30 participants, 28 completed the treatment and 2 dropped out from the study due to absence of follow up as one got transferred from Hassan and other belonged to the rural area. Hence, the results obtained from 28 patients were interpreted from Day 1 to Day 45. Statistically significant results ( $p < 0.05$ ) were observed in variables such as frequency of vomiting per day, quantity of vomitus, content of vomitus, aversion to smell, nausea, anorexia, lightness of body, appetite, Hb% except weight (see Table 4).

On applying Wilcoxon signed rank test as post-hoc with Bonferroni correction significant relief was found in Frequency of

**Table 3**  
Distribution of participants based on outcome variables.

Serial no.	Variables	Grading	Participants
1.	Frequency of vomiting per day	Nil	2
		Mild	17
		Moderate	7
		Severe	4
2.	Quantity of vomitus	Nil	2
		Mild	13
		Moderate	11
		Severe	4
3.	Content of vomitus	Nil	1
		Mild	5
		Moderate	10
		Severe	14
4.	Appetite	Nil	0
		Mild	16
		Moderate	13
		Severe	1
5.	Aversion to smell	Present	24
		Absent	6
6.	Nausea	Present	30
		Absent	0
7.	Anorexia	Present	24
		Absent	6
8.	Lightness of body	Present	0
		Absent	30

vomiting per day from Day 15 to Day 30 in 14 patients, from Day 30 to Day 45 in 9 patients, from Day 1 to Day 30 in 17 patients and from Day 1 to Day 45 in 25 patients.

Significant reduction in Quantity of vomitus was found from Day 1 to Day 15 in 11 patients, from Day 15 to Day 30 in 13 patients, from Day 30 to Day 45 in 10 patients, from Day 1 to Day 30 in 19 patients and from Day 1 to Day 45 in 27 patients.

Significant change in Content of vomitus was found (from food mixed to bile, to water and to nil) from Day 15 to Day 30 in 15 patients, from Day 30 to Day 45 in 11 patients, from Day 1 to Day 30 in 18 patients and from Day 1 to Day 45 in 24 patients and changed from watery to food mixed in 1 patient.

Significant improvement in Appetite was observed from Day 15 to Day 30 in 18 patients, from Day 30 to Day 45 in 8 patients, from Day 1 to Day 30 in 22 patients and from Day 1 to Day 45 in 26 patients.

Post hoc with Mc Nemers test showed positive changes in Aversion to smell from Day 15 to Day 30 in 7 patients, Day 30 to Day 45 in 11 patients, Day 1 to Day 30 in 8 patients and overall, from Day 1 to Day 45 in 19 patients.

Significant reduction in nausea was observed from Day 15 to Day 30 in 7 patients, Day 30 to Day 45 in 11 patients, Day 1 to Day 30 in 10 patients and over all from Day 1 to Day 45 in 21 patients.

Significant improvement in anorexia was observed from Day 1 to Day 15 in 6 patients, Day 15 to Day 30 in 11 patients, Day 1 to Day 30 in 17 patients and over all from Day 1 to Day 45 in 21 patients.

Lightness of body showed positive changes from Day 30 to Day 45 in 9 patients, Day 1 to Day 30 in 6 patients and over all from Day 1 to Day 45 in 15 patients.

### 4. Discussion

While explaining treatment principles of diseases during pregnancy, drugs which are Mrudu, Madhura, Sukha, Sukumara and Hridya are indicated [6]. Thus, *Bilwa-Laja Yoga* [5] was selected for intervention in syrup form for better palatability and efficacy.

#### 4.1. Possible actions of Bilwa-Lajadi syrup on the outcome variables as per Ayurveda logic

Carminative, appetizer and coolant action of *Bilwa*, *Usheera*, sugar and carminative action of *Hriversa* leads to downward movement of gastric content. Hence, increasing the frequency of peristalsis leading to reduction in frequency of vomiting and

**Table 4**  
Result of outcome variables.

Serial no.	Variable	Mean ranks		P value	Significant (S)/Non-significant (NS)
		Day 1	Day 45		
1.	Frequency of vomiting per day	3.38	1.50	<0.001	S
2.	Quantity of vomitus	3.52	1.46	<0.001	S
3.	Content of vomitus	3.32	1.50	<0.001	S
4.	Appetite	1.54	3.50	<0.001	S
5.	Weight	55.08	55.20	0.096	NS
6.	Hb%	11.50	11.08	<0.001	S

  

Serial no.	Variable	Positive cases		P value	Significant (S)/Non-significant (NS)
		Day 1	Day 45		
1.	Aversion to smell	22	3	<0.001	S
2.	Nausea	28	7	<0.001	S
3.	Anorexia	22	1	<0.001	S
4.	Lightness of body	0	15	<0.001	S

changing the content of vomitus. Crude methanolic root extract of *Vetiveria zizanioides* has peripheral antiemetic action through Antihistamines and Anticholinergics due to presence of flavonoids and alkaloids [7]. Thereby reducing the stimulation of the vomiting centre by affecting the vestibular system [8]. *Grahi* (absorbant) action of *Bilwa* and *Stambhana* (styptic) action of *Usheera* prevent the backward movement of gastric content leading to reduction in quantity of vomitus. Aromatic action of *Bilwa* [9], and *Usheera* [10] (due to presence of vetivenol, vetiverol and  $\alpha$  and  $\beta$  vetivones) and *Hrivera* (due to presence of volatile oil) causes significant relief in aversion to smell. *Bilwa-Lajadi* syrup improved the *Agnibala* (appetite) and reduced the secretory action of mucousa of GIT.; thereby helped in reducing the symptom of nausea. *Tikta Rasa* (bitter taste) of *Bilwa*, *Hrivera* and *Usheera* and *Katu Rasa* (pungent taste) of *Bilwa* helps in *Annavaha Srotovishodhana* (clearance of channels of food transport) by the action of *Ama Pachana* (detoxification) thereby causing *Indriya Prasadana* (enhanced sense perception) which increases the perception of taste and reduced the symptom of anorexia and hence helped in achieving lightness of body. Presence of flavouring agent in *Ush-eera* [10] acts as an appetizer. Presence of ionic forms of iron in *Bilwa* [11] and *Usheera* [12] helps in improving Hb%. *Bilwa* fruit pulp also contains Vitamin C which is one of the facilitators for iron absorption [11] increasing the bio-availability of dietary iron thereby increasing Hb%.

#### 4.2. Interpretation

In this study, a higher incidence of vomiting in pregnancy was observed in the age group of 21–25 years, in primi gravida and the women who had history of nausea and vomiting in previous pregnancy.

#### 4.3. Limitations

It is difficult to completely prevent nausea and vomiting during pregnancy, as it is a natural and physiological phenomenon. However, from the data of the present study, it can be said that that *Bilwa-Lajadi* syrup prevented nausea and vomiting to great extent from its progress to hyperemesis which may require parental therapy – a major limitation to Ayurveda drugs. Since the sample size for the present study is small, data from clinical study with large sample size is required for accurate interpretation of pharmacodynamics and pharmacokinetics of the test drug.

#### 4.4. Generalisability

Most women with nausea and vomiting in pregnancy can be successfully managed in primary care. Judicious assessment and early drug treatment is necessary to avoid maternal metabolic disarray from uncontrolled nausea and vomiting which may affect the fetus.

#### 4.5. Further studies

Repeated administration of *Bilwa-Lajadi* syrup in divided doses was found to be effective in management of excessive vomiting during pregnancy which was an observational finding during the present study. So, further studies can be carried out with this type of dosing methodology. Specific diet chart incorporating the principles of Ayurveda can also be prepared which restores the hydration status and nutritional supplementation by maintaining fluid and electrolyte balance.

#### 4. Conclusion

Based on the results in terms of symptoms and number of patients improved at different stages of follow up, *Bilwa-Lajadi* Syrup was found to have good effect in reducing frequency of vomiting per day, quantity of vomitus, altering the content of vomitus, moderate effect in improving appetite and reducing anorexia and mild effect in reducing nausea, aversion to smell and lightness of body and minimal effect in weight gain and substantial result on improving the general health and hydration status of the pregnant women.

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#### Conflict of Interest

None.

#### Author contributions

Conception and design of study – Dr Deepika Singh, Dr Asokan V, Dr Gayathri Bhat NV.

Acquisition of data – Dr Deepika Singh, Dr Asokan V, Dr Gayathri Bhat NV, Dr Prathima, Dr Kavyashree HL.

Analysis and interpretation of data – Dr Deepika Singh, Dr Asokan V, Dr Gayathri Bhat NV.

Drafting the manuscript - Dr Deepika Singh, Dr Asokan V.

Approval of the version of the manuscript to be published – Dr Asokan V.

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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.2021.08.015>.

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