

## The Effects of Chicory Extract Consumption by Mothers on the Frequency of Icterus and the Serum Bilirubin Level in Neonates

Leila Badiheshin<sup>1</sup>, Zahra Saghafi<sup>2</sup>, Zahra Asadollahi<sup>3</sup>, Masoud Moghadari<sup>4</sup>, Reza Derakhshan<sup>5</sup>, \* Tabandeh Sadeghi<sup>6</sup>

<sup>1</sup> Critical Care Nursing Student, Student Research Committee, School of Nursing and Midwifery, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

<sup>2</sup> Department of Midwifery, School of Nursing and Midwifery; Geriatric Care Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

<sup>3</sup> Department of Epidemiology and Biostatistics, School of Medicine, Immunology of Infectious Diseases Research Center, Research Institute on Basic Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

<sup>4</sup> School of Traditional Medicine, Research Center for Social Determinants of Health, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran.

<sup>5</sup> Department of pediatrics, School of Medicine, Kerman University of Medical Sciences, Kerman, Iran.

<sup>6</sup> Department of Pediatric Nursing, School of Nursing and Midwifery; Non-Communicable Diseases Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran.

### Abstract

**Background:** Chicory has been used in Iranian traditional medicine for the treatment of various liver dysfunctions. This study aimed to investigate the effects of chicory extract consumption by mothers on the frequency of icterus and the serum bilirubin level in neonates.

**Methods:** In this clinical trial, the research population included pregnant women referring to birth preparation classes in an urban area of Iran. Two hundred pregnant women were selected and randomly allocated into two groups of intervention and control. In the intervention group, the mothers were recommended to take Chicory extract (produced by SHAAF Shiraz Company, Iran) from the 36th week of gestation, at 70 cc, three times a day, and to continue the process during the first 2 weeks of lactation. The control group received routine care. Data gathering tools were a demographic questionnaire and a researcher-made checklist for recording the frequency of icterus and the mean level of bilirubin. Data were analyzed using SPSS 18.

**Results:** The frequency of neonatal icterus in the intervention group was lower than that in the control group, but their difference was not significant (chi-square test,  $P = 0/11$ ). The difference in the mean bilirubin level was not significant between the two groups on the first day of birth. However, on the third day after birth, the difference was significant and the intervention group had a lower mean of the bilirubin level (Independent T-test,  $P < 0/05$ ).

**Conclusions:** Based on the results, the consumption of chicory by mothers can be effective in decreasing the bilirubin levels among the neonates.

**Key Words:** Bilirubin, Chicory, Icterus, Neonates.

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### \* Corresponding Author:

Tabandeh Sadeghi, Department of Pediatric Nursing, School of Nursing and Midwifery; Non-Communicable Diseases Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran. Email: [t.sadeghi@rums.ac.ir](mailto:t.sadeghi@rums.ac.ir)

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## 1- INTRODUCTION

Neonatal jaundice or icterus is one of the most common problems in neonates and the leading cause of neonatal hospitalization in the first days of life (1). This condition is common in 60% and 80% of term and premature neonates, respectively, in the first week of life (2).

The importance of neonatal jaundice is not attached to its high prevalence, but to the dangerous effect of bilirubin deposition on the brain, which leads to a severe and irreversible brain damage called kernicterus, and even death (3, 4). Phototherapy and blood exchange are common treatments for icterus. Retinopathy, dehydration, diarrhea, and bronze baby syndrome are the complications of phototherapy. Likewise, thrombocytopenia, coagulopathy, hypocalcaemia, necrotic enterocolitis, and even neonatal death are some of the complications of blood exchange (5). In this regard, the use of traditional medicines, especially herbs, has been considered as a way of reducing the frequency of blood exchange, phototherapy time, or a substitution for these treatments.

Herbal therapy has long been prevalent, with herbs used as rich sources of active substances in the treatment of various diseases (6). Presently, the consumption of medicinal herbs has increased in developing and developed countries so that 65-80% of the world population consume herbal products. Accordingly, the World Health Organization encourages its members to improve their knowledge about herbs and complementary medicines (7, 8). According to a review of the literature on the use of herbal medicines during pregnancy, the prevalence of the use of herbal medicines in Australia, the UK, Norway, Italy, the US, and Canada has been reported to be 34% (9), 58% (10), 40% (11), 48 % (12), and 6-9% (7, 13), respectively. In Iran, according to the

results of a study by Hosseini et al., (14), the prevalence of the use of medicinal herbs in pregnant women was 63.4%, with 78.2% of them having had a positive attitude towards these medicines. In the other studies (15, 16), the prevalence of medicinal herb use was 31.4% and 51.9%, respectively, with 91.7% of them having had a positive attitude towards using these medicines.

*Cichorium intybus* is a perennial herb, 30-120 cm high, from the *compositae* family. Anti-diabetic, anti-hepatotoxic, anti-allergic, antioxidant, anti-inflammatory, diuretic, laxative, and anti-jaundice properties have been reported for this plant (17, 18).

Chicory accelerates the excretion of bilirubin due to its flavonoids, including apigenin, quercetin, and luteolin, which are all the stimuli of the UDP-glucuronosyltransferase enzyme (19). Having a laxative effect, increasing the number of stools, and bonding to bilirubin in the bowel are the other benefits of this plant, which facilitate bilirubin excretion (5). These properties are particularly important in neonates because of premature liver function, UDP-glucuronosyltransferase deficiency at birth, and enterohepatic circulation due to the high concentrations of  $\beta$ -glucuronidase in the bowel of term and preterm infants, which are the major causes of icterus in neonates (1, 2, 4).

Many studies investigated the effects of this plant on neonatal jaundice in the laboratory. For example, according to the study by Nassirian and Eslami (5) Chicory extract was added to the blood samples of neonates with hyperbilirubinemia in the intervention group; although a slight decrease was observed in the bilirubin level of the intervention group, the difference between the two groups was not statistically significant. In another in vitro study, 0/5 cc of 5 common medicinal herbs (*Cichorium intybus*, *Fumaria parvi flora*,

Zizyphus jujuba, Alhagi pseudoalhagi and Purgative manna) was obtained by hydrochloric instillation, and 1 cc of the serum was added to each separately. The results were compared with a control serum to which 0.5 cc of distilled water was added. And it was found that only Cichorium intybus decreased serum bilirubin significantly (20). According to the results of the study by Mohammadi Pirkashani et al., (19) who examined the effect of bathing infants with chicory extract on the serum bilirubin level, the bilirubin level of the neonates who received phototherapy with the chicory bath was lower than that of the control group who received only phototherapy. In addition, the researchers concluded that the chicory bath could be effective in reducing neonatal jaundice (19).

Many studies have been conducted on humans to investigate the effects of herbal medicines, such as the oral drops or the extract of Purgative manna (21, 22) or Shirkhesht (23, 24) used by neonates or

their mothers (25) on neonatal jaundice. However, no study has examined the effects of chicory consumption by neonates or mothers during the lactation or pregnancy periods on neonatal icterus. Therefore, this study aims to investigate the effects of chicory extract consumption by mothers on the frequency of icterus and the serum bilirubin level in neonates.

## 2- METHODS

The present study is a clinical trial registered on the Iranian Registry of Clinical Trials under no. IRCT20150713023190N6. The research population included pregnant women referring to birth preparation classes in an urban area of Iran. The sampling method used was convenience sampling. To assign the samples and prevent them from contacting each other, the control and intervention groups were selected from two different centers. The sample size was calculated using the following ratio comparison formula:

$$n = \frac{(Z_1 - \frac{\alpha}{2} + Z_1 - \beta)^2 (P_1(1 - P_1) + P_2(1 - P_2))}{(P_1 - P_2)^2} = \frac{(1.96 + .84)^2 (.6 \times .4 + .4 \times .6)}{(.6 - .4)^2} = 94.08$$

Based on the frequency of icterus in the neonatal literature (2), the effect size of 0.2, test power of 80%, confidence interval of 95%, and sample dropout of 100 participants were obtained for each group.

In the intervention group, the mothers were recommended to take chicory extract (produced by SHAAF Shiraz Company, Iran) from the 36<sup>th</sup> week of gestation, at 70 cc, three times a day, and to continue the process during the first 2 weeks of lactation. The control group received routine care. The neonates were followed up, during two weeks after birth in which the frequency of icterus was evaluated and the mean level of bilirubin was also

measured and recorded, 24 hours and 3 days after birth.

Data collection tools included the demographic characteristics questionnaire (age, gestational age, educational level, etc.) and a researcher-made checklist developed based on the previous research for recording the frequency of icterus and the mean level of bilirubin. Bilirubin was measured by the Bilicheck device made in Germany.

To remind the patients of taking their chicory extracts, the researcher developed a WhatsApp group, contacted them on a daily basis, and answered their questions. If their chicory extracts finished, the researcher provided them with fresh

chicory extracts. Eventually, when data collection was over, the data were analyzed using the descriptive statistics (mean and standard deviation) as well as the inferential statistics (the independent t-test, the paired sample t-test, and the repeated measures ANOVA) using SPSS Software Version 18. The significance level was set at less than 0.05.

### 2-1. Inclusion and Exclusion Criteria

The inclusion criteria consisted of 1- the gestational age over 36 weeks, 2- Iranian nationality, 3- positive blood group, 4- willingness to participate in the study, 5- no history of using chemical or herbal medicines, 6- no history of abortion, 7- no heart or thyroid diseases, 8- no gestational diabetes, and 9- no regular consumption of chicory. The exclusion criteria were 1- not taking chicory in 3 running days during the intervention, 2- chicory consumption during the 2 weeks before the study, and 3- unwillingness to continue the study. Based on these criteria, 14 and 16 mothers were, respectively, excluded from the intervention and control groups, and the research team replaced them with other participants.

### 2-2. Ethical considerations

Ethical considerations for performing this study were taken into account by obtaining permission from Rafsanjan University of Medical Sciences, with the ethics code (IR.RUMS.REC.1397.059) received from the Ethics Committee of Rafsanjan University of Medical Sciences. Written consent forms were obtained from the participants, and they were justified about the goals of study. The participants were assured that their information would be kept confidential in publishing their information in articles and in electronic sources by the researcher.

## 3- RESULTS

According to the descriptive statistics, the intervention group consisted of 100 women with the mean age of 30,  $19 \pm 6.21$  years and the mean gestational age of  $38.83 \pm 1.12$  weeks. And the control group consisted of 100 women with the mean age of  $28.78 \pm 5.54$  years and the mean gestational age of  $38.67 \pm 0.93$  weeks. Both study groups were homogenous in terms of the demographic characteristics (**Table 1**).

According to the results, the frequency of neonatal icterus in the intervention and control groups was 55 and 68 cases, respectively, but the chi-square test showed that their difference was not significant ( $P = 0/11$ ). From these neonates, 24 in the intervention group and 35 in the control group were hospitalized for treatment, and the others received phototherapy at home.

Based on the results of the independent t-test, the difference in the mean bilirubin level was not significant between the two groups on the first day of birth ( $P = 0.82$ ); however, on the third day after birth, the difference was significant ( $P < 0.001$ ), and the intervention group had a lower mean of the bilirubin level. The results of the paired comparison method showed a significant difference in the mean of the bilirubin level between the intervention ( $P < 0.001$ ) and control groups ( $P < 0.03$ ) on the first and third days after birth. In addition, the mean level of bilirubin increased in both groups, but the mean difference was lower on the first and third days in the intervention group than in the control group (**Table 2**). The type of delivery was considered a confounding variable, and the results showed no significant difference between the two groups based on this variable (**Table 3**).

**Table-1:** Comparison of the demographic characteristics of the mothers and neonates in intervention and control groups

variable	Intervention group	Control group	P-value
Age (years). Mean $\pm$ SD	30.19 $\pm$ 6.21	28.78 $\pm$ 5.54	* 0.09
Gestational Age (weeks). Mean $\pm$ SD	38.83 $\pm$ 1.12	38.67 $\pm$ 0/93	* 0.27
Neonatal weight. Mean $\pm$ SD	3316/00 $\pm$ 413/40	3236/00 $\pm$ 463/14	* 0.19
Educational level			
Under Diploma. N (%)	27(27)	14 (14)	** 0.006
Diploma. N (%)	43 (43)	65 (65)	
Above diploma. N (%)	30 (30)	21 (21)	
Type of delivery			
Cesarean N (%)	28 (28)	48 (48)	** 0.004
Vaginal N (%)	72 (72)	52 (52)	
Neonatal gender			
Boy. N (%)	54 (54)	49 (49)	** 0.91
Girl. N (%)	46 (46)	51 (51)	
Neonatal icterus			
Yes. N (%)	55 (55)	68 (68)	** 0.11
No. N (%)	45 (45)	32 (32)	

\*Independent T-test

\*\*Chi-square

**Table-2:** Comparison of the means of the neonates' bilirubin in the intervention and control groups

Group Time	First day of birth	Third day of birth	*P-value	Mean differences (mg/dl)
Intervention group Mean $\pm$ SD (mg/dl)	7.01 $\pm$ 2.21	11.68 $\pm$ 2.60	< 0.001	4.67 $\pm$ 1.38
Control group Mean $\pm$ SD (mg/dl)	6.95 $\pm$ 2.05	13.65 $\pm$ 3.48	< 0.001	6.70 $\pm$ 3.29
** P-value	0.82	< 0.001		< 0.001

\* Paired T-Test

\*\* Independent T-Test

**Table-3:** Comparison of the means of the neonates' bilirubin in the intervention and control groups based on the type of delivery

Group	Intervention group Mean $\pm$ SD (mg/dl)	Control group Mean $\pm$ SD (mg/dl)	*P-value
First day of birth			
Vaginal Delivery	6.98 $\pm$ 2.29	7.19 $\pm$ 2.46	0.32
Cesarean Delivery	7.10 $\pm$ 2.31	6.68 $\pm$ 1.48	
Third day of birth			
Vaginal Delivery	11.64 $\pm$ 2.50	14.23 $\pm$ 3.68	
Cesarean Delivery	11.80 $\pm$ 2.90	13.03 $\pm$ 3.17	

\*Repeated Measures ANOVA, (Interactive effect)

#### 4- DISCUSSION

According to the results, although the frequency of neonatal icterus was lower in the intervention group than in the control group, there was no significant difference between the two groups. The results also revealed that there was no significant difference between the two groups in the mean level of bilirubin on the first day after birth, but there was a significant difference between them on the third day after birth. In addition, the mean level of bilirubin was lower in the intervention group. Intra-group comparison results showed that the mean bilirubin level increased over time, but the mean changes were lower in the intervention group than in the control group, which implied the positive effect of chicory.

Although we did not find any study similar to the present one to have examined the effect of chicory consumption by mothers on neonatal jaundice, we found studies that examined other ways of assessing the effect of chicory on neonatal jaundice. For example, the results of the study by Nassirian and Eslami (5) which were performed in the laboratory, were in accordance with those of our study, but a slight decrease was observed in the bilirubin level in the intervention group. However, the difference between the two groups was not statistically significant. In another in vitro study, the effect of 5 medicinal plants was examined on the level of neonatal bilirubin, according to which only chicory extract significantly decreased the level of bilirubin, which was in line with the results of the present study (20). The results of the study by Mohammadi Pirkashani et al., (19) also consistent with the findings of the present study, demonstrated that the chicory bath was effective in reducing neonatal jaundice.

A systematic review (26) of 23 selected studies evaluating the effect of herbal medicines on neonatal jaundice showed

that some herbal medicine used with phototherapy could be helpful and reduce the bilirubin level of infants. Another study (25) reported the effects of medicinal plants (cotoneaster) along with phototherapy in reducing the duration of neonatal hospitalization. In line with the results of the aforementioned review studies, the mean level of bilirubin on the third day after birth was lower in the intervention group than in the control group, probably due to the synergy of the effects of chicory with other treatments, such as phototherapy.

Based on the findings of the present study and the afore-mentioned ones, the use of herbal remedies alone is not recommended for the treatment of neonatal jaundice. Families also need to be aware of the complications of hyperbilirubinemia, consider its importance, and in case of occurrence, seek medical care promptly and provide herbal remedies in consultation with a physician. The lack of studies on chicory consumption has limited the possibility of comparing the present findings with similar studies. Therefore, the results were compared with other herbal remedies. It is recommended to perform similar studies, especially on the use of chicory by mothers at different dosages or by neonates at other medical centers.

#### 5- CONCLUSIONS

According to the results, the consumption of chicory by mothers can be effective in decreasing the bilirubin level in neonates. These findings could help healthcare professionals, especially gynecologists and neonatologists, in treating and preventing neonatal icterus. This is the first study in Iran to have specifically examined the effect of this medicinal herb on pregnant women. Thus, it could help encourage further research on this subject.

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## 6- AUTHOR CONTRIBUTIONS

All the authors have accepted responsibility for the entire content of this submitted manuscript and approved its submission.

## 7- Research funding

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## 8- CONFLICT OF INTEREST

None.

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