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Original Research

The Prevalence of Using Traditional, Complementary, and Integrative Medicine by Patients with Epidermolysis Bullosa

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Abstract

Epidermolysis bullosa (EB) is an inherited disease that causes widespread symptoms characterized by extreme epithelial fragility. This study examined traditional, complementary, and integrative medicine (TCIM) usage among EB patients referred to clinics at Shiraz University of Medical Sciences between 2019 and 2020. We enrolled the patients with EB whose diseases were approved by a dermatologist and registered in the dermatology department and Molecular Dermatology Research Center affiliated with Shiraz University of Medical Sciences, Shiraz, Iran. A researcher-made data gathering form, including knowledge, beliefs, practice, and the experience of the safety of TCIM, was used to collect the data. Interviews were done by phone calls, and oral consent was obtained from patients or their parents. Overall, 68 patients were included in this study. In this regard, 79.4% of the patients used TCIM by themselves or their families to manage EB. Approximately, half of the patients were not aware of the effects of the herbal medicines they used. Among medicinal plants, chicory (20.6%), thyme (16.2%), and Persian cornflower (14.7%) had the most consumption. More than half of these patients believed that medicinal plants were a less harmful treatment, and 48.5% considered them effective. In conclusion, the study revealed high medicinal plant usage among EB patients, but limited knowledge about their effectiveness. Public awareness about the benefits and risks of these remedies needs to be increased.

Keywords: Epidermolysis Bullosa; Traditional medicine; Complementary therapies; Herbal medicine; Persian medicine

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Introduction

Epidermolysis bullosa (EB) is an inherited disease characterized by extreme epithelial fragility that includes a group of genetic diseases that cause brittle skin and mucous membranes and the formation of lesions such as blisters, scratches, and scars in response to small mechanical damage [1,2].

In terms of age, the prevalence of this disease is most often from birth to shortly after birth, but in rare cases, it can occur during adolescence. The disease is classified into several forms. The main classification is based on the layer of skin in which the blister forms, including EB simplex, which affects the epithelium; junctional EB, which affects the lamina lucida of the basement membrane; and dystrophic EB, which affects the lower part of the basement membrane; and finally, Kindler EB, which creates a composite pattern in different layers [3].

The treatment of EB patients consists of two strategies: treatment aimed at recovery and treatment aimed at reducing and relieving symptoms. The first category involves two approaches, namely gene therapy and cell therapy. In gene therapy, the corrected gene is introduced into keratinocytes using a retrovirus, and graft tissues are transplanted to the patient. However, none of the gene therapy methods have been definitively approved [4]. The second method is bone marrow transplantation, which has been shown to reduce symptoms in some patients but does not lead to complete recovery. Another approach involves the intravenous injection of mesenchymal stem cells, which can alleviate symptoms such as itching but does not increase the amount of collagen type VII [5].

Due to the lack of definitive treatment, the quality of life of patients with EB and their families is affected by this disease and its complications [6,7]. In this regard, more attention is being paid to treatments aimed at reducing and relieving symptoms and improving patients' quality of life. This treatment can be divided into two categories: topical and systemic. For limited forms of the disease, drugs such as dapsone or doxycycline and topical steroids are utilized [8]. Given the role of inflammation in the development of this disease, anti-inflammatory medications like systemic corticosteroids and immunobiological drugs such as Rituximab, Infliximab, Methotrexate, Azathioprine, Cyclosporine, and Mycophenolate Mofetil are used [9,10]. Traditional, complementary, and integrative medicine (TCIM), which is a collection of sciences used for disease diagnosis and prevention, has been passed down through generations. Herbal medicine employs scaffolds with antibacterial, antioxidative, anti-inflammatory, and pro-angiogenic properties. With the advent of modern medicine and the discovery of chemical drugs, the utilization of TCIM gradually declined. Nevertheless, as people became more aware of the drawbacks of chemical drugs and their limitations in preventing and treating certain diseases, attention once again turned to these potential remedies [11,12]. In the USA, 38% of people use herbal medicines to improve their health and prevent or treat diseases. While herbal products are commonly perceived as harmless by consumers, they can have side effects and interact with other medications. Evidence showed that there was significant concern for patients with chronic conditions like EB who rely on herbal medicines to alleviate the complications of their disease [13-16]. Given that EB is a chronic and incurable condition, we aimed to investigate the utilization of TCIM among individuals affected by this disease. This research aimed to provide a more comprehensive and clear understanding of the usage patterns among these patients.

Materials and Methods

Study design and population

In this cross-sectional study, we included all EB patients registered in the Dermatology Department and Molecular Dermatology Research Center affiliated with Shiraz University of Medical Sciences until December 2021. The exclusion criteria were based on the patient's dissatisfaction with participating in the study. The sampling method used in this study was a census conducted via phone. Explanations about the study were provided to the participants (patients' contact information was recorded in the Dermatology Department and Molecular Dermatology Research Center at Shiraz University of Medical Sciences). After obtaining oral consent, the patients were queried about their use of TCIM using a researcher-made data-gathering form. In addition, participants were asked if they or their parents had any recollection of experiencing side effects from using TCIM medications. After the completion of the data gathering form, which was designed to address the main objective and partial objectives of the study, the data were analyzed using SPSS software version 25. Descriptive statistics such as categorical variables, frequency percentages for categorical variables, and mean with standard deviation (SD) for quantitative variables were employed. The Chi-square test was also utilized to investigate the associations between certain categorical variables.

Ethics Statements

The Research Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran approved the study's protocol (Ethics code: IR.SUMS.MED.REC.1399.395).

Results

In this study, 68 patients were included, with a mean age of 14.16 ±10.290 (age range: 1 to 43 years). The

majority of patients (29 patients) were under 10 years old. Out of the 68 patients, 57.36% were males and 42.64% were females (Table 1). The analysis of education levels revealed that 25 patients (36.76%) were illiterate, 34 patients (50%) were undergraduates, 6 patients (6.97%) had high school diplomas, and 3 patients (4.41%) had university educations.

The analysis of educational levels revealed that 7.4% (5 people) of the patients' fathers were illiterate, 26.5% (18 people) had undergraduate degrees, 30.9% (21 people) had high school diplomas, and 35.2% (24 people) had a university education. The distribution of residence showed that the majority of patients- 30 people (44%)- lived in large cities, 19 people (28%) lived in small cities, and 19 people (28%) lived in rural areas. Among the patients referred, the majority (67.6%) were Persian, and 14.7% of the patients belonged to the Lor ethnicity. The results showed that there was no significant relationship between education level and the use of medicinal plants (p value: 0.709) (left). The distribution of satisfaction from using TCIM was analyzed based on the patient's gender and their mother's level of education (middle). The participants' beliefs about the harmfulness of TCIM were also examined (right).

According to the research, 79.4% (54 people) of the patients used herbal medicines, and 20.6% (14 people) had never used herbal medicines. The patients utilized herbal medicines in different forms, including distillate, essence, infusion, topical application, decoction, and powdered form. Among these, the most commonly used medicinal plant was chicory in its distillate form, accounting for 20.6% of the patients. Thyme followed at 16.2%, Persian Cornflower at 14.7%, Jujube at 8.8%, and Henna at 4.4%, which were among the most popular herbal plants (Table 2). Overall, for the majority of patients (31 patients), herbs had a moderate effect on improving or alleviating their disease. The satisfaction rate with the use of TCIM modalities varied among patients, but the majority (45.6%) expressed moderate satisfaction (Table 3).

The most significant reason for using TCIM was the belief that traditional medicine is safer, which accounted for 54.4% (37 people). Additionally, 48.5% (33 people) of patients used traditional and herbal medicine (TCIM) because they considered it an effective method. Furthermore, 48.5% of patients were unaware of the advantages or disadvantages of the medicinal plants they used (Table 3).

The majority of patients did not inform their physicians about the use of herbal medicines. This was primarily due to the perception that consulting a doctor was unnecessary and also because of a lack of sufficient information about these medicines. The most common reasons for using herbs were to alleviate itching (n = 38), address constipation and digestive problems (n = 35), promote wound healing (n = 28), and manage pain (n = 8). Table 1 shows that both male patients (51.28%) and female patients (44.82%) said they were moderately satisfied with using herbal medicines. There was no significant relationship between gender and satisfaction (P = 0.396). Similarly, across all education levels, patients believed that medicinal plants had a moderate effect on their improvement, and there was no significant relationship between education level and perceived effectiveness (P = 0.090).

According to the results presented in table 1, the majority of individuals of both genders were not aware of the effects of the herbal medicine they used, with 51.28% of females and 46.15% of males lacking awareness. There was no significant relationship between gender and awareness (P = 0.274). Furthermore, among different subgroups of the educational level analysis, it was observed that the majority of illiterate mothers, as well as mothers who had a diploma, or who held a high school degree were unaware of the usefulness or harmfulness of the herbal plants they used. Mothers with academic degrees, however, exhibited belief in the usefulness of the drugs they used, which suggests a higher level of awareness and research before using TCIM rather than using them arbitrarily and without reason. No significant association was found between knowledge of usefulness or harmfulness and the level of education (P = 0.292).

According to the results presented in table 1, 53.7% of males and 86.2% of females have used TCIM, and there is no significant relationship between the use of herbs and gender (P = 0.232). Among patients, 75% of illiterate mothers, 84% of those who had high school degrees, and 66.66% of mothers with university degrees have used TCIM. There was no significant relationship between education level and the use of medicinal plants (P = 0.709).

Discussion

The study found that a majority of patients, regardless of gender, used TCIM. There was no significant relationship between gender and herb usage. Additionally, patients with different education levels, including illiterate mothers and those with high school or university degrees, showed a significant presence in TCIM use. However, no significant association was found between education level and the use of medicinal plants. These findings emphasize the widespread use of TCIM and the importance of raising awareness among healthcare professionals.

The treatment of EB disease encompasses a range of options, including chemical drugs and herbal medicines. While numerous studies have focused on chemical drugs, a definitive treatment for this disease remains elusive. Consequently, given the chronic and incurable nature of the condition, patients have shown

Table 1. Relationship between patient's sex and education level of patient's mothers & used of medicinal plants

Variable	Subgroup	Have used	Have not used	P value	Can be harmful	Always useful	I don't know	P value	No effect	Low effect	Medium effect	High effect	Very high effect	P value
Gender	Male	29(53.7%)	25(46.29%)	0.232	8(20.51%)	13(33.33%)	18(46.15%)	0.274	5(12.82%)	6(15.38%)	20(51.28%)	5(12.82%)	3(7.69%)	0.396
	Female	25(86.2%)	4(13.79%)		5(17.24%)	9(47.36%)	15(51.72%)		2(6.89%)	7(24.13%)	13(44.82%)	3(10.34%)	4(13.79%)	
Patient's mother's educational level	Illiterate	9(75%)	3(25%)	0.709	4(33.33%)	2(16.66%)	6(50%)	0.292	1(8.33%)	2(16.66%)	6(50%)	1(8.33%)	2(16.66%)	0.090
	Under diploma	21(84%)	4(16%)		4(16%)	7(28%)	14(56%)		4(16%)	4(16%)	11(44%)	3(12%)	3(12%)	
	Diploma degree	16(84.21%)	3(15.78%)		3(15.78%)	6(31.57%)	10(52.63%)		1(5.26%)	3(15.78%)	9(47.36%)	4(21.05%)	2(10.52%)	
	University degree	6(66.66%)	3(33.33%)		2(28.57%)	3(42.85%)	2(28.57%)		0(0%)	1(20%)	3(60%)	1(20%)	0(0%)	

Table 2. The herbal medicines and their forms used by EB patients

Herbal medicine forms	Percentage and frequency	Plant
Distillate	36.8% (25 patients)	*Common fumitory, Chicory, Hawthorn, Dog-rose plant, Pussy willow, Plane tree, Water lily, Rosewater, Fennel, Alfalfa, and Mint*
Infusion	36.8% (25 patients)	*Thyme infusion, Hollyhocks, Cordia myxa, Broadleaf plantain, Echium amoenum, Polypodies, Adiantum capillus-veneris, Chamomile, four-seed combination drug (including Quince seeds, Alyssum, Broadleaf plantain, Cordia myxa), Quince seeds, Jujube, Lavender, and Celery seeds.*
Topical	25% (17 patients)	*Cedar, Henna, oak bark decoction, Sesame oil, Turmeric, Ostrich oil, Rosemary, Violet plant oil, Sesame flour, Natural gum (Saqez or Kurdish gum), and traditional Kurdish oil*
Decoction	16.2% (11 patients)	*Khardango, Jujube, and willow leaves*. 14.7% of patients (10 patients) used soaked form including *Plantago ovata, Descurainia sophia, Prunes, and Chia*.
Powder	4.4% (3 patients)	*Eruca sativa powder, and Ginger powder*.
The most used medicinal plant	*Chicory distillate* (20.6% of the patients), *Thyme* (16.2%), *Echium amoenum* (14.7%), *Jujube* (8.8%), *Henna* (4.4%)	

cording to a 2016 study conducted by Dastgheib and colleagues, it was found that 31.3% of patients with skin diseases have utilized TCIM [18]. The study further revealed that 79.4% of individuals with EB disease also use TCIM, corroborating our findings. Additionally, a review of articles published in the United States indicated that the use of herbs and TCIM is not an increased inclination towards using medicinal plants. In 2018, Soohyun Kim and colleagues examined the factors influencing the use of herbs and TCIM in patients with MS. Additionally, the study found a significant relationship between female gender, higher education level, and patients who had not yet initiated treatment in comparison to other individuals [17]. Ac-

Table 3. Awareness of the usefulness or harmfulness of the herbal plants used by EB patients: The satisfaction rate of using TCIM

Awareness of the usefulness or harmfulness of the plant used	Frequency	Percentage
Believe in usefulness	11	16.2%
Believe in harmfulness	22	32.4%
I don't know	33	48.5%
Variable	**Frequency**	**Percentage**
Effectless	5	%7.4
Low effect	13	%19.1
Medium	31	%45.6
High effect	8	%11.8
Very much	7	%10.3
Total	68	%100.0

limited to the Iranian population, but has experienced a significant increase among Americans as well [19].
A study conducted in Ankara concluded that there is no relationship between the use of TCIM and the type of chronic disease, level of education, occupation, or place of residence, which aligns with the findings of our study [13]. Furthermore, this study found no association between the use of TCIM and gender or level of education. Currently, numerous research studies are investigating the effects of TCIM on chronic skin diseases. For instance, a study focusing on the marigold plant to improve skin eczema demonstrated a significant positive effect [20]. Another study explored the use of the lemon balm plant for treating herpes lesions, which resulted in a remarkable 96% improvement after eight days of using the extract. Additionally, methanol derived from Japanese mint has shown effectiveness in alleviating itching, a significant complication of EB disease [21].
Chronic non-healing wounds are a common complication among EB patients. In a 2014 study examining the effects of castor powder and sesame oil on infectious and chronic wounds in a 40-year-old female, these plants demonstrated promising results [22]. Another study revealed that among various medicinal plants, chicory distillate had a consumption rate of 20.6%, followed by thyme at 16.2%, *Echium amoenum* at 14.7%, jujube at 8.8%, and henna at 4.4%. These findings further support the results of our study [23].
In our study, it was found that among the complications of EB disease, itching accounted for 55.9%, constipation, and digestive problems accounted for 51.5%, and wound healing accounted for 41.2%, respectively, making them the most common reasons for using herbs. The pilot study conducted by Niazi and colleagues demonstrated that henna ointment was effective in the management of pruritus, wound healing, and skin dryness in patients with EB [24]. Furthermore, previous studies demonstrated that herbal remedies and TCIM lifestyle recommendations were effective in the treatment of constipation [25-28], which is one of the most common chief complaints in patients with EB.
Additionally, 48.5% of patients were not aware of the advantages and disadvantages of the medicinal plants they used. When considering the distinction between gender and level of education, it was found that in both genders, the majority of people were not aware of the harm or usefulness of the herb they used (56% of females and 46.15% of males), and there was no significant relationship between the two. Furthermore, the analysis of different subgroups based on education level showed that the majority of mothers of EB patients who were illiterate, had only a diploma, or had a high school degree were not aware of the usefulness or harmfulness of the medicinal plants they used. However, mothers who had university degrees believed in the effectiveness of the drugs they used, which can indicate awareness and research conducted before using these drugs and not taking them arbitrarily and without reason.
A study found that 35.9% of patients with chronic diseases use herbal medicine in Thailand. More than half of them (57.2%) believed that herbal medicine was very helpful [29]. In Jordan, the prevalence was higher at 80.2%. The use of herbal medicines was not associated with any demographic factors except age [30]. In Cambodia, nearly half of the patients with chronic diseases used herbal medicines and reported high levels of satisfaction. There were only minor differences based on age, gender, or geographical living locations [31]. A study conducted in Saudi Arabia revealed that gender, educational level, income, place of residence, and chronic diseases had no statistically significant effect on patients' opinions about herbal medication. However, age, marital status, and occupation had a statistically significant effect [32]. In a study conducted in Iran, 631 patients with chronic dermatologic conditions (most of them acne, eczema, and hair loss) were referred to traditional Persian medicine clinics, and some of them received treatment [14]. According to our research, the most common reason for patients to use TCIM was the belief that it was safe and effective.
However, there were some limitations to our study. Firstly, EB is a rare disease, so we encountered a small sample size. Additionally, this study was conducted at a single center. Since the usage of TCIM is highly associated with cultural characteristics, we cannot appropriately generalize these results to the population

in other areas of Iran. Therefore, we recommend designing and conducting multicenter studies to obtain more reliable results. Moreover, we suggest researchers carry out clinical trials on medicinal plants for the treatment of wounds, itching, swallowing, and other problems in EB patients. Finally, we recommended implementing educational interventions to inform individuals about the benefits and risks of using TCIM.

Conclusion

According to the results of our study, the majority of the patients with EB, or their parents, used herbal remedies to treat the complications of this disease. However, the prevalence of taking herbal remedies among these patients was not associated with the sex or the educational level of the patients or their parents. Moreover, our study revealed that the herbal remedies were used arbitrarily and without sufficient knowledge by the patients and their families. As a result, they were unaware of the potential side effects of the herbal remedies they used. Due to society's insufficient knowledge about TCIM as well as the chronic nature of EB, it is crucial to inform patients and their parents about the safe application of these remedies and educate them about the potential adverse effects of these medicinal remedies. Furthermore, physicians should pay more attention to the use of these drugs and their side effects among patients with EB during the process of history taking and physical examination.

Conflict of Interests

Nothing to declare.

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References

[1] Has C, Fischer J. Inherited epidermolysis bullosa: New diagnostics and new clinical phenotypes. Exp Dermatol 2019;28:1146-1152.

[2] Bonamonte D, Filoni A, De Marco A, Lospalluti L, Nacchiero E, et al. Squamous cell carcinoma in patients with inherited epidermolysis bullosa: review of current literature. Cells 2022;11:1365.

[3] Fine JD, Bruckner-Tuderman L, Eady RA, Bauer EA, Bauer JW, et al. Inherited epidermolysis bullosa: updated recommendations on diagnosis and classification. J Am Acad Dermatol 2014;70:1103-1126.

[4] Gonzalez ME. Evaluation and treatment of the newborn with epidermolysis bullosa. Semin Perinatol 2013;37:32-39.

[5] Haynes L. Nutrition for children with epidermolysis bullosa. Dermatol Clin 2010;28:289-301.

[6] Chogani F, Parvizi MM, Murrell DF, Handjani F. Assessing the quality of life in the families of patients with epidermolysis bullosa: the mothers as main caregivers. Int J Womens Dermatol 2021;7:721-726.

[7] Parvizi MM, Nasrin S, Parvizi Z. Butterfly patients in Iran waiting to specific attention from authorities. Iran J Public Health 2017;46:1005-1006.

[8] Santi CG, Gripp AC, Roselino AM, Mello DS, Gordilho JO, et al. Consensus on the treatment of autoimmune bullous dermatoses: bullous pemphigoid, mucous membrane pemphigoid and epidermolysis bullosa acquisita - Brazilian Society of Dermatology. An Bras Dermatol 2019;94:33-47.

[9] Hsu CK, Wang SP, Lee JY, McGrath JA. Treatment of hereditary epidermolysis bullosa: updates and future prospects. Am J Clin Dermatol 2014;15:1-6.

[10] Saki N, Vahedi S, Parvizi MM, Shafie'ei M, Hosseini SA, et al. Topical gabapentin 10% in the treatment of epidermolysis bullosa pruritus: A pilot, double-blind, split-site, randomized controlled trial. Dermatol Ther 2022;35:e15767.

[11] Narlou MG, Sharif MP. Anthropological study of the use of medicinal plants in traditional medicine Case study (Mahallat city) 2017.

[12] Yeo GE, Law JX. Regenerative medicine for neonatal wound healing. Curr Chin Sci 2022;2:160-167.

[13] Tulunay M, Aypak C, Yikilkan H, Gorpelioglu S. Herbal medicine use among patients with chronic diseases. J Intercult Ethnopharmacol 2015;4:217-220.

[14] Parvizi MM, Fatehi N, Jaladat AM, Gholampour Z, Shahriarirad R, et al. Epidemiological factors in patients with dermatologic conditions referring to the clinic of traditional persian medicine: a cross-sectional study. Int J Clin Pract 2021;75:e14788.

[15] Bordbar M, Pasalar M, Safaei S, Zareifar S, Haghpanah S. Complementary and alternative medicine use in thalassemia patients in Shiraz, southern Iran: A cross-sectional study. J Tradit Complement Med 2018;8:141-146.

[16] Bordbar M, Pasalar M, Aresehiri R, Haghpanah S, Zareifar S, et al. A cross-sectional study of complementary and alternative medicine use in patients with coagulation disorders in Southern Iran. J Integr Med 2017;15:359-364.

[17] Kim S, Chang L, Weinstock-Guttman B, Gandhi S, Jakimovski D, et al. Complementary and alternative medicine usage by multiple sclerosis patients: results from a prospective clinical study. J Altern Complement Med 2018;24:596-602.

[18] Dastgheib L, Farahangiz S, Adelpour Z, Salehi A. The prevalence of complementary and alternative medicine use among dermatology outpatients in Shiraz, Iran. J Evid-Based Complement Altern Med 2017;22:731-735.

[19] Landis ET, Davis SA, Feldman SR, Taylor S. Complementary and alternative medicine use in dermatology in the United States. J Altern Complement Med 2014;20:392-398.

[20] Jackson BP. Herbal drugs and phytopharmaceuticals: A handbook for practice on a scientific basis, edited and translated from the second German edition by Norman Grainger Bisset, London; German edition edited by Max Wichtl, Marburg. With a foreword by J. David Phillipson, Medpharm Scientific Publishers. Stuttgart 1994 pp 377-379.

[21] Wölbling RH, Leonhardt K. Local therapy of herpes simplex

with dried extract from Melissa officinalis. Phytomedicine 1994;1:25-31.
[22] Ajmeer AS, Dudhamal TS, Gupta SK, Mahanta V. Topical application of Katupila (Securinega leucopyrus) in Dushta Vrana (chronic wound) showing excellent healing effect: A case study. Ayu 2014;35:175-178.
[23] Murat-Sušić S, Husar K, Skerlev M, Marinović B, Babić I. Inherited epidermolysis bullosa - the spectrum of complications. Acta Dermatovenerol Croat 2011;19:255-263.
[24] Niazi M, Parvizi MM, Saki N, Parvizi Z, Mehrbani M, et al. Efficacy of a topical formulation of henna (lawsonia inermis linnaeus) on the itch and wound healing in patients with epidermolysis bullosa: a pilot single-arm clinical trial. Dermatol Pract Concept 2022;12:e2022115.
[25] Fattahi MR, Alorizi SME, Nimrouzi M, Zarshenas MM, Parvizi MM. A randomized clinical trial on treatment of chronic constipation by traditional persian medicine recommendations compared to allopathic medicine: A pilot study. Int J Prev Med 2017;8:50.
[26] Barimani S, Nimrouzi M, Daryani NE, Karimi M, Heydari ST, et al. The efficacy of a persian medicine formulation on adult functional constipation: a double-blinded clinical trial. Shiraz E-Med J 2020;22:e101785.
[27] Nimrouzi M, Sadeghpour O, Imanieh MH, Ardekani MS, Salehi A, et al. Flixweed vs. polyethylene glycol in the treatment of childhood functional constipation: a randomized clinical trial. Iran J pediatr 2015;25:e425.
[28] Emami Alorizi SM, Fattahi MR, Saghebi SA, Salehi A, Rezaeizadeh H, et al. Assessment of the impacts of traditional Persian medical schemes and recommendations on functional chronic constipation compared to a classic medicine lactulose, a randomized clinical trial. J Complement Integr Med 2015;12:325-331.
[29] Peltzer K, Pengpid S. The use of herbal medicines among chronic disease patients in Thailand: a cross-sectional survey. J Multidiscip Healthc 2019;12:573-582.
[30] El-Dahiyat F, Rashrash M, Abuhamdah S, Abu Farha R, Babar Z-U-D. Herbal medicines: a cross-sectional study to evaluate the prevalence and predictors of use among Jordanian adults. J pharm Policy Pract 2020;13:2.
[31] Pearson H, Fleming T, Chhoun P, Tuot S, Brody C, et al. Prevalence of and factors associated with utilization of herbal medicines among outpatients in primary health centers in Cambodia. BMC Complement Altern Med 2018;18:114.
[32] Abdelmola AO, Bahri A, Abuallut I, Refaei BA, Hakami WK, et al. Prevalence, knowledge, and perception about the use of herbal medicines jazan-Saudi Arabia. J Fam Med Prim Care 2021;10:2386.